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Constraint Induced Movement Therapy

influence of restraint and type of training
on performance and on brain plasticity

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To my family

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ABSTRACT

Partial paralysis of the hand is one of the main impairments after stroke. Constraint Induced Movement Therapy (CIT) is a new treatment technique that appears to improve upper extremity function after stroke. CIT consists of 6 hours of training/day for the affected arm (mainly with shaping exercises) and of restraint (mitt) of the non affected arm for two weeks. There are concerns about the practicality and resource issues in carrying out CIT according to the original model. In this thesis the benefit of modifications of CIT, of an assessment tool and of two common types of hand training have been evaluated.

CIT (n=16) administered *in groups* for two weeks (paper I) seems to be a feasible alternative to improve upper limb motor function after chronic stroke. The arm/hand motor performance improved significantly on Motor Assessment Scale (MAS; $p=0.003$) and on Sollerman hand function test ($p=0.037$). The median self reported motor ability (MAL) also improved ($p < 0.001$). No additional effect was seen from wearing a mitt for an extended period of three months.

The reliability of the Sollerman hand function test (paper II) was studied in patients with chronic stroke. Three examiners observed 24 patients at three experimental sessions. There was agreement ($\kappa \geq 0.4$) between the examiners for 15/20 subtests. Using total sum scores, the agreement *within* the examiners was higher than 0.96 (for Spearman's ρ s and ICCs) and agreement *between* the examiners was higher than 0.96 (Spearman's ρ s) and 0.92 (ICCs), respectively.

In a cohort of 24 patients with subacute stroke (paper III) forced use therapy (FUT; mitt use and 3 hours of training/day for 2 weeks) improved arm/hand function, but not more than regular arm therapy given to the control group. Significant improvements in arm/hand motor performance were found in the FUT group (n=12) as well as in the control group (n=12) on the Sollerman hand function test ($p=0.001$), on MAS ($p < 0.05$) and on MAL ($p < 0.05$). No significant differences were seen between the groups pre- or post training or at three months follow up, demonstrating that the mitt had limited importance.

In a separate study on 30 healthy subjects (paper IV), employing transcranial magnetic brain stimulation (TMS), we found that shaping exercises but not general activity training increased dexterity ($p < 0.001$; Purdue peg board test) of the trained non dominant hand. After shaping exercises the cortical motor map shifted forwardly into the premotor area but did not expand. After general activity training the cortical motor map expanded significantly ($p=0.03$) in the posterior (sensory) direction. Shift of location of active TMS positions rather than their numbers might therefore be a critical factor for the interpretation of cortical plasticity.

In conclusion, the studies in this thesis have shown that less resource consuming modifications of CIT may be feasible to improve upper limb motor function after stroke. The type and amount of training for the more affected arm seems to be an important factor rather than the mitt use in itself. Shaping exercises, at least in healthy people, are effective in improving dexterity and the Sollerman hand function test reliable to evaluate arm/hand function after stroke.

Key words: Constraint induced movement therapy, hand, stroke, group practise, reliability, mode of training, dexterity, brain plasticity

ABBREVIATIONS

APB	Abductor Pollicis Brevis muscle
ANOVA	Analysis of variance
CI	Confidence interval
CIT	Constraint induced movement therapy
EMG	Electromyography
GABA	γ -amino-butyric acid
ICC	Intraclass correlation coefficient
LTP	Long-term potentiation
MAL	Motor Activity Log
MAS	Motor Assessment Scale
MCA	Middle Cerebral Artery
MEP	Motor Evoked Potential
2-PD	Two-point discrimination test
SD	Standard deviation
SPSS	Statistical Package for the Social Sciences
TMS	Transcranial magnetic stimulation

ORIGINAL PAPERS

This thesis is based on the following papers, which will be referred to by their Roman numbers:

I. Brogårdh C, Sjölund BH. Constraint Induced Movement Therapy in patients with stroke: A pilot study on effects of small group training and of extended mitt use. *Clin Rehabil* 2006; 20: 218-227.

II. Brogårdh C, Persson AL, Sjölund BH. Intra- and inter-rater reliability of the Sollerman hand function test in patients with chronic stroke. Accepted for publication in *Disability & Rehabilitation* 2006.

III. Brogårdh C, Vestling M, Sjölund BH. Forced use therapy in patients with subacute stroke: The mitt can be thrown! A randomised controlled study with blinded observers. Submitted.

IV. Brogårdh C, Johansson FW, Nygren F, Sjölund BH. Mode of hand training determines cortical reorganisation. A randomized controlled study in healthy adults. Submitted.

PREFACE

In my daily work as a physiotherapist with a focus on rehabilitation in patients with stroke, I often see patients that regain their walking ability but are unable to reuse their hand in different activities. The tradition of research in rehabilitation is rather young, and it has often been discussed which of the physiotherapeutic approaches in a rehabilitation program that is most beneficial. So-called constraint induced movement therapy (CIT) became very popular in Sweden at the end of the nineties without much scientific proof of benefit. Since there is a need to find effective treatment techniques for upper extremity functioning in stroke rehabilitation, the interest of evaluating CIT arose to me and became the subject for my thesis.

INTRODUCTION

Stroke epidemiology

Stroke is a major global health problem. In Sweden approximately 25 000-30 000 people are diagnosed with stroke every year. It is the third most common cause of death in Sweden and risk factors for stroke onset are high blood pressure, smoking, diabetes, heart failure, carotid artery stenosis and hyperlipidemia (SBU 1992; Gresham et al. 1995). Approximately 85% of all stroke cases are ischemic, and most ischemic strokes affect one of the cerebral hemispheres by occlusion of the middle cerebral artery (MCA). In the acute stage, mechanisms such as oxygen depletion, necrosis, brain edema, excitotoxicity and inflammatory processes are at play. After the acute stage there is a phase of regeneration with neuronal plasticity and (partial) functional recovery (Dahlquist 2003).

Impairments and functional recovery after stroke

Many stroke survivors experience impairments such as hemiparesis, spasticity, sensory/perceptual disorders, hemianopsia, dysphasia or cognitive impairments (Gresham et al. 1995). Most patients regain their walking ability (Jorgensen et al. 1995; Dobkin 2005), but between 30 and 60% (Wade et al. 1983; Heller et al. 1987; Dobkin 2005) are no longer able to use their more affected hand after 3-6 months. Only 11% (Kwakkel et al. 2003) to 18% (Nakayama et al. 1994) of those sustaining a severe post stroke upper extremity paresis achieve full upper extremity function. The inability to reach, to grasp and to manipulate objects limits activities and causes particular difficulties to perform daily personal care. Perceived loss of arm function has been reported as a major problem in approximately 65% of patients with stroke (Broeks et al. 1999). Thus, there is a strong need to develop effective arm-hand treatment methods in stroke rehabilitation.

Theories of motor control

Various neurofacilitation approaches have been applied in stroke rehabilitation during the last decades, for example Bobath's neurodevelopment technique (Bobath 1970), Brunnström's movement therapy (Brunnström 1970) and proprioceptive neuromuscular facilitation (PNF) developed by Knott and Voss (Knott and Voss 1968). These treatment techniques have been developed in response to reflex/hierarchic models of motor control (Shumway-Cook and Woollacott 2001; Wolf et al. 2002) as well as on clinical observations. They are based on theories that sensory input is a prerequisite for motor control in normal

movement, resulting from cerebral and cerebellar control over spinal-level reflexes. Each approach focuses on retraining motor control through techniques designed to facilitate and/or inhibit various movement patterns to achieve normal movements. Compensatory movement strategies are often used in addition to traditional rehabilitation, even if components of training are used for the more affected limb. Thus, the traditional approaches still dominate the way clinicians manage patients with neurological deficits even if the effectiveness has been shown to be minor to moderate (Butefisch et al. 1995; Duncan 1997). In addition, due to present reductions in rehabilitation length of stay, therapists are often forced to use compensatory strategies and to focus on independence training rather than on restitution of motor function to achieve independence of daily activities (Ostendorf and Wolf 1981).

A more recent theory on motor control refers to system's theory, in which a dynamic interplay between perception, cognition, and action systems results in organized and normal movements. In this approach impairments are treated most effectively through repetitive, task-oriented and goal-directed activities (Shumway-Cook and Woollacott 2001; Wolf et al. 2002).

Modern knowledge about motor control of the hand

Key elements in normal reach, grasp and manipulation skills require (i) the ability to locate the target (coordination of eye-head movements), (ii) the ability to transport the arm and the hand in space as well as postural support, (iii) the ability to grasp (including grip formation and release), and (iv) hand manipulation skills (Shumway-Cook and Woollacott 2001).

Motor execution (movements) is planned using sensory frames of reference. Different motor commands must result in predictable and effective sensory states to be able to achieve a task or goal (Johansson and Cole 1994; Johansson 1996b; Johansson 1998). The vision and eye movements have been shown to play an important role in goal directed movements (Land et al. 1999; Johansson et al. 2001; Battaglia-Mayer et al. 2003), and help us to locate, to identify and to reach objects in space. Once the hand comes into contact with the object, critical tactile and pressure sensors of the skin give us information to identify the texture and the density of the object for developing proper grip and load forces when moving the object (Johansson et al. 1992; Carr and Shepherd 2000). Earlier experience (internal sensorimotor memory) influences the prediction of an adequate grip and load force (Flanagan et al. 2001; Flanagan et al. 2003), and the posterior parietal cortex seems to be particularly important in this process of prediction (Ehrsson et al. 2003; Crawford et al. 2004). Manipulation of objects require the execution of motor programs in a feed forward manner on the basis of sensory feedback from cutaneous, proprioceptive and visual afferents, as well as from activation of spinal reflexes

(Ohki et al. 2002), to be able to update and correct the accuracy of hand movements (Shumway-Cook and Woollacott 2001; Whitney et al. 2004).

Constraint Induced Movement Therapy

Constraint Induced Movement Therapy (CIT) is a fairly new treatment technique that claims to improve the arm motor ability and the functional use of a paretic arm - hand. The CIT concept has been derived from basic research with monkeys (see below) and consists of a family of techniques, i.e., constraining movements of the less affected arm and intensively training of the more affected arm (Taub et al. 1993; Taub et al. 1999; Morris and Taub 2001). In the original concept, the less affected arm-hand was immobilized in a sling (Ostendorf and Wolf 1981; Wolf et al. 1989; Taub et al. 1993), but soon an emphasis on intensive, repetitive training (massed practise) of the more affected arm- hand evolved. In the current application of the method, the patients wear a mitt on the less affected arm 90% of their waking hours and perform repetitive exercises with the more affected arm six to seven hours per day during two to three weeks (Taub and Wolf 1997; Taub et al. 2002).

The learned non-use phenomenon

Decades ago, it was observed that patients with hemiparesis did not use their affected extremity even when capable of doing so (Lashley 1924; Taub 1980; Levin and Page 2004). Taub and colleagues have investigated this phenomenon using basic research on monkeys (Lashley 1924; Lassek 1953; Knapp et al. 1958; Knapp et al. 1963; Taub et al. 1965). When one of the two forelimbs was deafferented (i.e. the somatic sensation was surgically abolished) the animal stopped using the affected extremity and never spontaneously regained use of it in a free life situation. Taub et al concluded that the pattern with three-limb use, initially necessary after the spinal chock, was positively reinforced, whereas attempts to use the deafferented forelimb resulted in incoordination and failures. It was postulated that the monkeys did not use the limb due to “learned non-use”, or learned behaviour suppression (**fig 1**). By immobilizing the intact arm for a period of consecutive days (1-2 weeks), the monkey started to reuse the deafferented forelimb again and “the learned non-use” was overcome (Taub 1980) (**fig 2**).

Learned non-use

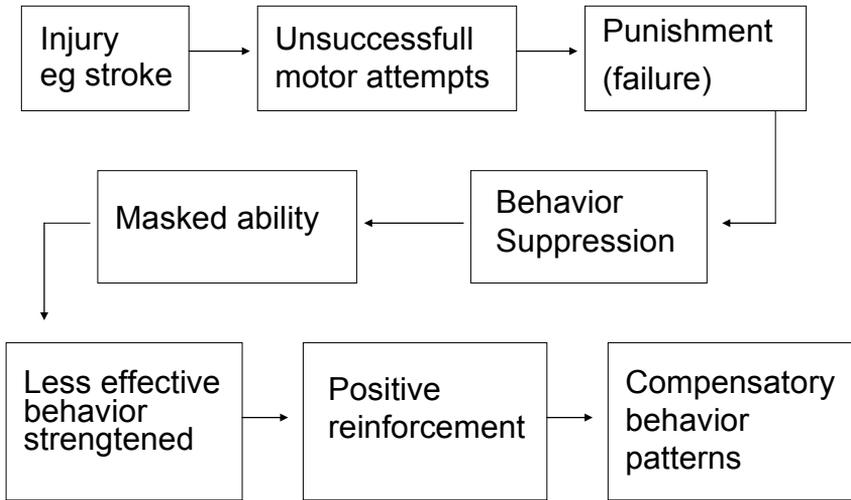


Fig 1. Schematic model for the development of learned non-use (modified from Taub).

Overcoming learned non-use

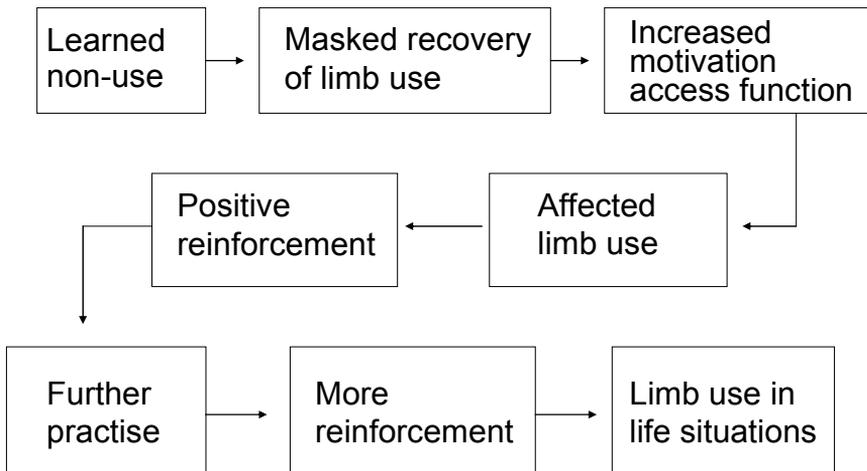


Fig 2. Schematic model for overcoming learned non-use (modified from Taub).

The mechanism of learned non-use was also thought to apply to humans who suffer from hemiparesis after brain injury (Taub 1980; Wolf et al. 1989; Taub and Wolf 1997). Although motor function may gradually return as the result of a combination of spontaneous recovery and rehabilitation, the actual use of the more affected arm often seems to be less than its potential use (Andrews and Stewart 1979; Taub 1980; Sterr et al. 2002b) .

Patients eligible for CIT

Constraint Induced Movement Therapy has been applied in humans after different diagnoses, for example after stroke (Taub et al. 1993; Kunkel et al. 1999; Miltner et al. 1999; van der Lee et al. 1999; Dromerick et al. 2000; Page et al. 2002b; Sterr et al. 2002a; Atteya 2004; Page et al. 2004; Dettmers et al. 2005; Page et al. 2005; Taub et al. 2005; Brogårdh and Sjölund 2006; Taub et al. 2006), after traumatic brain injury (Wolf et al. 1989; Sterr et al. 2002a; Page and Levine 2003) and in children with hemiparesis (Glover et al. 2002) and cerebral palsy (Taub et al. 2004; Eliasson et al. 2005).

Inclusion criteria for patients with stroke to participate in CIT interventions are usually some limitation of hand function, high motivation, minimal cognitive dysfunctions, adequate balance and walking ability when wearing the restraint (Taub et al. 1993; Miltner et al. 1999; van der Lee et al. 1999; Brogårdh and Sjölund 2006). According to Taub, the patient's hand function can be divided into quartiles: (1) the first quartile includes ability to extend the wrist at least 20°, ability to extend the fingers at least 10° and to abduct the thumb at least 10°; (2) the second quartile includes ability to extend the wrist at least 10°, ability to extend two fingers at least 10° and to abduct the thumb at least 10°; (3) the third quartile includes ability to grasp and release a tennis ball or washrag; and (4) the fourth quartile implies little or no finger function (Taub et al. 1999).

CIT or modifications of CIT have been applied mainly in chronic stroke patients, when the patients are supposed to have reached a plateau in recovery (Wolf et al. 1989; Taub et al. 1993; Morris et al. 1997; Kunkel et al. 1999; Miltner et al. 1999; Sterr et al. 2002a; Page et al. 2004; Dettmers et al. 2005; Taub et al. 2005; Brogårdh and Sjölund 2006; Taub et al. 2006). The technique has also been applied after subacute (Blanton and Wolf 1999; Page et al. 2002b; Atteya 2004) and after acute stroke (Dromerick et al. 2000; Grotta et al. 2004; Ploughman and Corbett 2004; Page et al. 2005).

Doubts regarding intensive training early in the acute phase after a cerebrovascular incident have been reported from studies on animals. Thus, "forced overuse" of the affected limb, including restraint of the non affected limb, within the first seven days after a sensory motor cortex lesion, has been

shown to impede motor recovery and to enlarge the lesion volume (Humm et al. 1998; Bland et al. 2000). This assumption has so far not been confirmed in humans in the acute phase after stroke (Grotta et al. 2004).

Modes of hand training in CIT

Different approaches of hand training, such as general task practise (i.e., eating a meal, making coffee, dialling phone numbers and so on) as well as focussed “shaping” exercises are used in CIT (Taub et al. 2006). It has been suggested that shaping exercises is of outmost importance for improving upper limb motor function and to transfer arm-hand use to real life situations (Taub et al. 1994; Taub et al. 2002). The shaping technique is defined as a behavioural technique in which movements are approached in small steps of progressively increasing difficulties including verbal feedback. The shaping exercises are similar to ordinary training techniques used by physiotherapists and occupational therapists, but a shaping task is broken down to subtasks, is quantifiable and is repeated many times so small improvements in performance can be measured and systematically made apparent to the patient (Morris et al. 1997; Taub and Wolf 1997; Wolf et al. 2002; Taub et al. 2006). The benefit of the shaping exercises for improving upper motor function after stroke has been confirmed by independent authors (Sterr and Freivogel 2003; Yen et al. 2005). On the other hand, it has also been reported that forced use therapy (FUT) without shaping exercises may improve upper extremity function after stroke (Liepert et al. 2001; Ploughman and Corbett 2004).

Limitations of traditional CIT

Traditional CIT with one patient per therapist requires a lot of resources and the six hours training protocol may be strenuous for the patients. According to Page et al (Page et al. 2002a), CIT is not widely viewed by clinicians as a useful therapeutic intervention and considered unfeasible due to patients’ concerns about the intensive schedule of treatment. In addition, therapists are concerned about patients’ compliance, about safety issues and about clinical resources.

Modifications of CIT

To make CIT clinically adaptable with limited resources as regards therapists, various modifications of the original concept have been attempted, for example shortened CIT (Sterr et al. 2002a) (i.e 3 hours of training/day for two weeks); forced use therapy (FUT; restraint of the less affected arm but without specific shaping exercises for the affected arm) (van der Lee et al. 1999; Ploughman and Corbett 2004), modified CIT (Page et al. 2001; Levin and Page 2004) (consisting of 3 hours of training per week for 10 weeks with the intact arm in

restraint 5 hours/day for 5 days/week), automated delivery of constraint induced therapy (AutoCITE) i.e., a computerized form of CIT (Taub et al. 2005), distributed CIT (3 hours of training per day distributed for 20 days) (Dettmers et al. 2005), and group CIT (with 2-3 patients per therapist) (Brogårdh and Sjölund 2006).

Effects of CIT

Gains in upper extremity function after constraint induced therapy have been reported in all stages after the onset of stroke (Wolf et al. 2002; Hakkennes and Keating 2005). Two possible mechanisms for the observed effects are believed to be (1) overcoming the learned non-use of the more affected arm (i.e., increased use of the more affected arm) and (2) use dependent cortical reorganisation (Taub et al. 1999; Liepert et al. 2000; Morris and Taub 2001; Taub et al. 2002; Wolf et al. 2002).

Brain Plasticity

Decades ago it was widely believed by neuroscientists that the human brain was a rather static organ and that no new neural connections could be formed in the adult brain (Kandel et al. 2000). It was assumed that once neural connections had been established in the early foetal stage of life, they would hardly change later in life. This assumption has radically been changed since research in animals and humans has established that the nervous system can modify its organization and function continuously throughout the individual's lifespan, depending on internal and environmental factors, a phenomenon called brain plasticity (Carr and Shepherd 2000; Kandel et al. 2000; Chen et al. 2002).

Mechanisms of plasticity

Mechanisms of brain plasticity include the capacity for neurochemical, neuroreceptor and neuronal structural changes. Normally, many connections between the periphery and the cortex as well as intracortical connections are probably physiologically silent because of inhibitory influences (Wall 1977). There seems to be a wide overlap in cortical neuronal networks targeting different body parts (Carr and Shepherd 2000). Both strengthening and weakening of synaptic connexions have been proposed as learning mechanisms (Schweighofer et al. 2001; Jörntell and Ekeröth 2003). The mechanism of plasticity probably differs depending on the time course (Chen et al. 2002). Rapid changes (within minutes) in motor representation are likely due to unmasking of silent synapses involving mediation by gamma-aminobutyric acid (GABA) (Jones 1993). GABA seems to be the most important inhibitory neurotransmitter in the brain and evidence is strong that a reduction of

GABAergic inhibition is crucial in mediating short-term plasticity changes (Chen et al. 2002). The major mechanism mediating long-term plasticity changes, by which learning and memory consolidation takes place in the brain, is probably LTP (long-term potentiation) (Kandel et al. 2000). Other mechanisms regarding changes over longer time are axonal regeneration and sprouting (Carr and Shepherd 2000; Chen et al. 2002).

Since repetitive stimulation or activation results in increased excitability and facilitation of the transmission in relevant synapses, repeated practise of a task may lead to improved performance and learning. Thus, the synaptic transmission and the effectiveness of synaptic connections are continuously remodelled in response to functional demands. In the brain, reorganisation of cortical areas was first studied in monkeys, demonstrating that increased use/tactile stimulation of the hand (Jenkins et al. 1990; Recanzone et al. 1992; Nudo et al. 1996) could enlarge the representational cortical areas of a trained body part. In humans, long-lasting immobilisation (Liepert et al. 1995) or deprivation of sensory feedback with anaesthesia of a body part (Rossini et al. 1996; Rossi et al. 1998) has been shown to decrease the representational cortical areas, whereas exercises or use of a body part have been reported to enlarged and/or to shift such areas (Elbert et al. 1995; Pascual-Leone et al. 1995; Liepert et al. 1998; Liepert et al. 2000). It has been reported that neural plasticity can occur quickly, and cortical representational changes have been observed after only 5-30 minutes of simple repeated thumb movements (Classen et al. 1998).

Enriched environment, probably by stimulating activity, has been found to have a positive influence on brain plasticity and on functional outcome after experimental stroke in hypertensive rats (Johansson 1996a; Risedal et al. 2002). In humans, it has been reported that, following rehabilitation of the upper extremity after stroke (Cicinelli et al. 1997; Traversa et al. 1997; Koski et al. 2004) and especially after CIT, the motor output area of the contralateral (injured) hemisphere expanded (Liepert et al. 1998; Liepert et al. 2001; Wittenberg et al. 2003) in parallel to an improvement in motor function/ability. Interestingly, a new activation in the contralateral premotor and motor areas in parallel to an improved hand function has also been observed after CIT (Kim et al. 2004).

How to measure brain plasticity

To enhance the understanding of the underlying mechanisms of functional recovery and cortical reorganisation different neuroimaging techniques such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) as well as transcranial magnetic stimulation (TMS) have been used in neurorehabilitation research (Wolf et al. 2002). The TMS technique has been used in studies with constraint induced movement therapy to

evaluate the cortical organisation (Liepert et al. 1998; Liepert et al. 2000; Liepert et al. 2001; Wolf et al. 2002, Wittenberg et al. 2003), and has been reported to be a safe, relatively painless and a reliable technique (Mortifee et al. 1994). TMS is based on the principle of electromagnetic induction. A strong electrical current pulse is directed through a hand-held coil. When held over the scalp, a rapidly changing magnetic field is able to induce a small electrical current in the underlying brain tissue. By stimulating the motor cortex the muscle responses can be recorded as motor evoked potentials (MEP), and monitored by electro-myography (EMG) (Ellaway et al. 1999; Wolf et al. 2002).

Methodological considerations

There are two ways of approaching hand function assessment, either by (a) instruments for observation by independent observers or by (b) instruments for self assessment.

Commonly used observation tests for assessing the upper extremity function in the literature are the Fugl-Meyer Assessment of Physical Performance (Fugl-Meyer et al. 1975), the Action Research Arm Test (ARA test) (Lyle RC 1981), the Wolf Motor Function Test (Wolf et al. 1989) and the Arm Motor Ability Test (Kopp et al. 1997). Some of these tests are used to assess the patient's ability to perform a specific activity of daily living (ADL), but lack either in the assessment of quality of movement (Wolf et al. 1989) or in the assessment of performance time (Fugl-Meyer et al. 1975; Lyle RC 1981). Only one of these tests has been translated into Swedish and has been tested for validity and reliability (Fugl-Meyer et al. 1975). The Sollerman hand function test (Sollerman and Ejeskar 1995) is often used in clinical rehabilitation settings in Scandinavia. The test is standardised and includes 20 subtests reflecting daily activities of the hand (see methods). It has been developed to evaluate the patient's hand function before and after hand surgery (Sollerman and Ejeskar 1995). Despite being utilized in patients' after injury to the central nervous system, it has not been evaluated for reliability in patients with stroke.

A commonly used self-assessment tool in CIT is the Motor Activity Log test (MAL) (Taub et al. 1993). The MAL is a self reported questionnaire that asks how often (amount of use [AOU]) and how well (quality of movement [QOM]) the affected hand is used for the daily activities (see methods). The improvements in arm motor ability after CIT have, however, often been reported to be much larger in the self reported MAL than in more objective observation tests.

AIMS

The overall aims of this thesis were to elucidate the effectiveness of modified forms of Constraint Induced Movement Therapy for arm-hand function and to evaluate the effectiveness of wearing restraint as well as the benefit of two different types of hand training.

The specific aims were:

- (i) to evaluate the effectiveness of constraint induced *group* therapy for chronic stroke patients (paper I).
- (ii) to explore if extended mitt use may enhance the treatment effect (paper I).
- (iii) to evaluate whether the Sollerman hand function test is reliable for patients with chronic stroke (paper II).
- (iv) to investigate the effectiveness of a three hour forced use protocol for two weeks in patients with subacute stroke (paper III).
- (v) to explore if the mitt use may enhance the treatment effect (paper III).
- (vi) to examine how shaping versus activity training influences the dexterity of the non dominant hand and the plasticity of the contralateral motor cortex hand area in normal adults (paper IV).

METHODS

In all the randomised, controlled studies (papers I, III, IV) independent observers performed the assessments.

Patients and subjects

In all, 64 patients with stroke and 30 volunteers participated in the present studies.

In paper I, 16 stroke patients (nine men and seven women; mean age 56.7 years; in average 28.9 months post stroke, five of which were 6-9 months post stroke) with moderate motor impairments in their contralateral upper limb participated. In paper II, 24 patients with chronic stroke (mean age; 59.7 yrs, mean time since stroke onset 29.6 months) and with mild to moderate impairment of hand function were enrolled. In paper III, 24 patients with subacute stroke (18 men and six women; mean age 57.6 ± 8.5 years; in average seven weeks post stroke) with moderate motor impairments in their affected upper limb participated. In paper IV 33 healthy volunteers (25 women, 5 men; mean age: 24.2 years) were enrolled and 30 subjects fulfilled the study.

Inclusion criteria

The patients in papers I, II and III had at least moderate hand function (ability to extend the wrist on the more affected hand at least 10° and to extend two fingers at least 10° and to abduct the thumb at least 10°), only minimal balance problems and no gross language deficits (De Renzi and Vignolo 1962) or severe cognitive impairments (Folstein et al. 1975). In papers I and II the patients were in a chronic stage (≥ 6 months post stroke) and in paper III in a subacute stage (0.5-3 months post stroke). In paper IV the subjects were included if they were healthy and between 18-40 years.

Interventions

Paper I: Constraint-induced *group* therapy (mitt on the less affected hand [**fig 3**] 90% of waking hours for 12 days) with 2-3 patients per therapist and six hours of training per day for two weeks. After the training period, the patients were randomized either to using the mitt at home every other day during two week periods for another three months (in total 21 days) or to no further treatment. Assessments were performed before and after the constraint-induced group therapy and after three months.

Paper III: Three hours of arm - hand training per day for two weeks. The participants were randomized to either forced use therapy (FUT, i.e a mitt [fig 3] on the less affected hand 90% of waking hours for 12 days) or to regular therapy (control group). The training program was individual for each patient according to the patient's sensorimotor capacity and goals. Assessments were performed pre-and post treatment and at three months follow up.

Paper IV: The subjects were randomly assigned to (A) shaping exercises or (B) general activity training of the non dominant hand for 25 minutes. The shaping exercises consisted of three standardised exercises with progressively increasing difficulties. The general activity training consisted of three tasks of daily arm-hand activities. Simultaneously, the subjects wore a mitt (fig 3) on the dominant hand to avoid compensatory movements.



Fig 3.The mitt used in papers I, III and IV.

Test Procedure paper II:

Three examiners (occupational therapists) simultaneously assessed the patient hand function by the Sollerman hand function test (fig 4) on three occasions; on two adjacent days in week 1 (short term test-retest) and on one day in week 4 (long term test-retest). The time interval between the assessments was the same as in the other two studies of constraint induced therapy (papers I and III). At each session the patients' performed 20 subtests (score 0-4 points) with the affected hand, with one of the examiners being a test leader. The role of test leader rotated between the examiners in a fixed order. If one examiner not could be present during the live assessment, the session was videotaped and the patient's hand function assessed later point in time.



Fig 4. Illustration of the test equipment in the Sollerman hand function test.

Outcome measures

The instruments used for assessments in papers I and III were the modified version of the Motor Assessment Scale (MAS) (Carr et al. 1985; Arnell et al. 1996; Barkelius et al. 1997), the Sollerman Hand Function Test (Sollerman and Ejeskar 1995), the 2-Point Discrimination Test (2-PD) (Moberg 1958) and the Motor Activity Log (MAL) (Taub et al. 1993).

The modified Motor Assessment Scale for upper extremity has been tested for validity and reliability (Arnell et al. 1996; Barkelius et al. 1997) and consists of 15 tasks from gross arm to fine finger movements in a 0-5 point scale, where the observer assesses the quality of movement and the speed of performance of each task. The Sollerman Hand Function test has been tested for validity and reliability in some diagnosis (Sollerman and Ejeskar 1995) and consists of 20-subtests reflecting daily hand activities. The type of grasp, the quality of movement and the speed of performance for the more affected arm is assessed in a 0-4 point scale. The 2-PD test measures the tactile somatosensation in a 0-10 point scale. The MAL (tested for validity and reliability) (van der Lee et al. 2004; Uswatte et al. 2005) is a 30-item self reported questionnaire and asks how often (amount of use [AOU]) and how well (quality of movement [QOM]) the affected hand is used in daily activities in a 0-5 point scale.

In paper II the Sollerman test was used only to assess the reproducibility of the test. In paper IV the subjects went through dexterity testing and cortical mapping before and after 25 minutes of hand training. The dexterity was evaluated by the Purdue Peg Board test (Tiffin and Ascher 1948) which includes four tasks: place as many pins as possibly with the right hand, with the left hand, and with both hand in 30 seconds as well as an assembly task (within 60 seconds).

Transcranial Magnetic Stimulation

The cortical motor maps of the abductor pollicis brevis (APB) muscle were obtained employing transcranial magnetic stimulation (TMS) of the non-dominant hemisphere and surface electromyographic (EMG) recording of motor evoked potentials (MEPs) (**fig 5**).



Fig 5. (A) the transcranial magnetic stimulator and (B) the coil for stimulating the cortical motor area of the abductor pollicis brevis muscle.

Statistics

In papers I, II and III the data was tested for normality using the Graph Pad InStat Software (InStat guide to choosing and interpreting statistical tests. GraphPad Software Inc 1998. San Diego, CA, USA). The data were analysed using the Statistical Package for the Social Sciences (SPSS) version 12.0 Software for Windows (SPSS, Chicago, IL, USA). For the parametric data the paired sample *t*-test was used to detect significant mean differences *within* groups pre- and post treatment for the MAS test (paper I); the Sollerman hand function test (paper I and III); the 2-PD test (paper I and III); the Purdue Peg Board test (paper IV) and for the MEP data from the abductor pollicis brevis muscle (paper IV). To detect significant median differences within groups for the non-parametric data the Wilcoxon Signed Rank Test was used for the MAS and MAL in paper III, and the Friedman test (nonparametric repeated measures) was used for the MAL in paper I.

To detect significant mean differences for the parametric data *between* the groups the ANOVA method for repeated measures was used followed by the post hoc Tukey-Kramer Multiple Comparison Test in paper I, whereas the independent sample *t*-test was used in paper III and IV. To detect significant median differences between the groups for the non parametric data, the Kruskal Wallis Test was used for the MAS and MAL in paper III.

To analyse the reliability of the Sollerman hand function test (agreement *within* and *between* examiners; paper II), both the ordinal data and total sum scores was used in the analysis. A graphical display of median raw scores for each subtest, examiner and experimental session and the method of generalised kappa (Fleiss 1971) for more than two observers was utilized. The Spearman's rank correlation test (Spearman's rho) (Altman 1991) of the total sum scores, examining the agreement within and between examiners was carried out. The Friedman test (nonparametric repeated measures) was used for analysing systematic differences within and between the examiners. Since the present data turned out to be normally distributed, the intraclass correlation coefficient (ICC_{2, 1}) (Shrout and Fleiss 1979) of the total sum scores were also calculated, examining the agreement within and between examiners.

Differences between means (rejection of the null hypothesis) were considered significant if the probability of chance occurrence was < 0.05 using two-tailed tests (papers I-IV). When applicable, 95% confidence intervals (CI) were calculated.

Ethics

The research protocols in paper I, II and III were approved by the Medical Ethics Committee of Lund University and the research protocol in paper IV was approved by the Medical Ethics Committee of Umeå University.

SUMMARY OF RESULTS

Effectiveness of modified forms of CIT (papers I and III)

Constraint induced therapy was beneficial even when limiting the therapist availability through training in small groups. Gains in arm- hand function were seen in chronic stroke patients after two weeks of group CIT (paper I) on the MAS ($p= 0.003$) and on the Sollerman hand function test ($p= 0.037$). The changes in self reported use of the more affected arm on Motor Activity Log scores were also significant ($p < 0.001$).

Also in patients with subacute stroke (paper III), gains in upper extremity function were found after three hours of arm therapy per day during two weeks, but the forced use therapy (FUT) was not more effective than regular training. The arm/hand motor performance improved significantly within both groups after two weeks of therapy on the Sollerman hand function test ($p= 0.001$), on MAS ($p < 0.05$) and on self reported motor ability (MAL; $p < 0.05$). After three months some additional improvements in arm motor performance and self reported motor ability were seen mainly in the FUT group. However, no significant differences between the groups were found in any measures or point in times.

Effects of mitt use (papers I and III)

In paper I no additional effects of extended mitt use for three months were seen in any of the assessments. The hand function scores measured by the Sollerman hand function test seemed to improve slightly for the participants with extended mitt use, but the mean difference was not significant. In addition, patients randomized to extended mitt use reported some difficulties in compliance. In paper III no significant differences in arm-hand function were found between the patients wearing a mitt 90% of the time during waking hours and the control group in any of the measures or point in time, despite satisfactory mitt compliance in the FUT group.

Effects on somatosensory function (papers I and III)

No significant difference in sensory discrimination with the 2-PD test was seen in any of the intervention studies on patients with stroke.

Effects on dexterity and brain plasticity after shaping and general activity training (paper IV)

In a group of young healthy adults, shaping exercises of the non-dominant hand increased the dexterity significantly ($p < 0.005$) for both hands, mostly so in the non dominant hand. After the general activity training, no significant improvement in dexterity of the non dominant hand was found. The cortical motor map (number of excitable positions) of the APB muscle upon TMS shifted forward into the premotor area after the shaping exercises but did not expand, whereas after general activity training the cortical motor map of the non dominant APB muscle expanded significantly in the posterior (sensory) direction ($p = 0.03$).

The usefulness of the Sollerman hand function test in patients with stroke (paper II)

The Sollerman test seems to be a reliable test to evaluate a patient's hand function pre-and post treatment after stroke. When analysing each subtest the median scores of each examiner generally agreed for all of the 20 subtests in all three sessions (paper II, fig 2). In the kappa analysis the agreement *between* the examiners was very strong ($\text{kappa} > 0.9$) for one subtest. For seven other subtests the kappa values were between 0.6 - 0.9, and for another seven subtests the kappa values were between 0.4 - 0.6. Only for five subtests were the kappa values lower than 0.4 in some of the sessions. When analysing the total sum scores the agreement *within* each examiner was ≥ 0.96 (Spearman's rhos and ICCs, respectively) for short- as well as long term test-retests. The agreement *between* the three examiners was also high at all three sessions (Spearman's rhos ≥ 0.96 ; ICCs ≥ 0.92). However, statistically systematic differences (Friedman's test: $p < 0.05$) were found between examiners A-B and A-C for all three sessions, indicating that the same assessor should perform pre- and post treatment evaluations.

Video assessments were found to be a good alternative to live assessments, since no systematically differences in total sum scores were found within any of the examiners regarding live versus video assessments.

GENERAL DISCUSSION

This thesis has focused on evaluating the benefit of modified forms of constraint induced movement therapy, and to elucidate which mode of hand training is most effective for improving dexterity, and also to evaluate the usefulness of a hand function test after stroke.

Is there a learned non-use phenomenon in humans after stroke?

It has been reported that constraint induced movement therapy can improve hand function through overcoming the learned non-use phenomenon in parallel to a use dependent cortical reorganisation in the brain (Liepert et al. 1998; Taub et al. 2002; Wolf et al. 2002; Sterr 2004). However, it has been questioned whether the “learned non-use” phenomenon from basic research in monkeys with secondary lesions in spinal cord after deafferentation of a single fore-limb, can be transferred into humans after stroke with lesions in the brain (Siegert et al. 2004; Sunderland and Tuke 2005). Our data strongly indicate that the restraint is an unimportant factor in regaining hand function (papers I and III), speaking against the relevance of a learned non-use phenomenon in patients with stroke. However, we cannot exclude that the results are at least partly due to that all patients included had accepted the possibility of being restrained from the general information given at study entry. It can be hypothesised that the patients in the control group had developed a “cognitive mitt”, i.e. were aware of the importance of preferably using the affected arm in daily activities. The notion of a “cognitive mitt” that might influence the results in human studies, but does not occur in animals has not previously been described.

Furthermore, it has been argued that the large improvements in self-reported motor ability (as measured by MAL) that have frequently been reported after only one week of CIT (and also was observed in our study of group CIT; paper I), as well as the cortical changes measured by TMS, reflect normal adaptive learning rather than restoration of representation lost due to brain injury or non-use of the limb (Sunderland and Tuke 2005). According to Taub, the main effect of CIT is an increased arm-hand use in real life situations (Morris and Taub 2001), i.e. improved activity. However, there are reports of decreases in impairment such as improved grip strength, reduced spasticity (Dettmers et al. 2005), improved force control in dexterous function (Alberts et al. 2004) as well as increased finger coordination after shaping exercises (Sterr et al. 2002c).

Which component in the CIT concept seems to be most beneficial?

CIT consists of a family of techniques (Taub et al. 1999), but it is not clear which component in the CIT concept that influence the outcomes (Siegert et al. 2004): (1) the restraint, (2) the combination of training and restraint, (3) the amount of training (volume) or (4) the mode of hand training e.g. shaping or general activity exercises.

A restraint is used in almost all studies concerning CIT, but the importance of it to improve upper extremity function is contradictory. In the first studies of CIT that were carried out (Ostendorf and Wolf 1981; Wolf et al. 1989) only restraints were used without specific exercises for the affected arm, and with promising results. In paper I, we studied the benefit of an extended mitt use in itself, but no enhanced improvements in arm-hand function were observed. In paper III, mitt use was the main difference in training protocol between the experimental group and the control group, but no differences in gains were found. On the other hand, in one of the hitherto largest study of FUT (van der Lee et al. 1999) a small difference between groups in favour for the FUT group (using restraint) was observed. Gains in upper extremity function after modified constraint induced therapy (mCIT), where the amount of restraint per week is much larger than the amount of training per week, (Page et al. 2001; Page et al. 2002b; Page et al. 2004) have also been reported.

The combination of training and restraint is very common in CIT studies, reporting gains in upper extremity function or self reported motor ability (Taub et al. 1993; Miltner et al. 1999; Sterr et al. 2002a; Pierce et al. 2003; Bonifer et al. 2005b). In our study with 6 hours of group CIT/day for two weeks (paper I) we also found positive outcomes. However, without using representative control groups it is difficult to evaluate which component is the most effective.

The amount of training (volume) might be critical to improve upper extremity function. In a review of randomised controlled studies of different exercise therapies for upper extremity function (van der Lee et al. 2001) it was found that more amount of training produced more gains in effectiveness. Gains in upper extremity function have been reported in many studies (Taub et al. 1993; Miltner et al. 1999; van der Lee et al. 1999; Sterr et al. 2002c; Dettmers et al. 2005; Yen et al. 2005) after the (original) 60 hour CIT protocol (six hours of arm-hand training per day for 10 days), but also after a 30 hour training protocol (Page et al. 2001; Sterr et al. 2002a).

In our studies, the improvements in upper extremity function were much larger for the patients in the subacute phase after the 30 hour training protocol (paper

III), than for the patients in the chronic stage after the 60 hour training protocol (paper I). Thus, the point in time when training is received and not only the amount of training might be a critical factor. However, the large improvements we found in arm- hand function in patients with subacute stroke after three hours of training/day (paper III), might partly be because they were in early phase after stroke onset, where most of the spontaneous recovery occurs (Nakayama et al. 1994). Furthermore, it is unclear whether the volume of training should be condensed in time or can be distributed over time. Recent studies have reported gains when the 60 hour training protocol was distributed over four weeks (Dettmers et al. 2005), and when the 30 hour training protocol of mCIT was distributed over 10 weeks (Page et al. 2001; Page et al. 2005).

In more recent studies the importance of the mode of hand training has been emphasized. Benefits of task-specific training in stroke rehabilitation has been reported (Butefisch et al. 1995; Carr and Shepherd 2000; Sterr 2004; van Peppen et al. 2004), and is suggested to be more important than the intensity of training (Page 2003). Taub emphasizes the importance of shaping exercises in the CIT (Taub and Wolf 1997; Taub et al. 2006), which has also been observed in independent studies (Sterr et al. 2002c; Sterr and Freivogel 2003; Yen et al. 2005). It has been suggested that the use of shaping to train arm function is more important for treating lower functioning patients than higher functioning patients (Morris and Taub 2001). Nevertheless, gains in upper extremity function without using shaping exercises have also been observed (Ploughman and Corbett 2004). In paper IV, assessing healthy subjects in a controlled paradigm, we found that shaping exercises rather than general activity training improved dexterity for the non-dominant hand.

Context dependent cortical plasticity

It is known that the effectiveness of synaptic connections is continuously remodelled in response to functional demands and that a cortical reorganisation can occur quickly (Classen et al. 1998). In paper IV, we investigated the effect on dexterity and cortical motor changes of the APB muscle after shaping exercises and general activity training, respectively. We chose to investigate healthy subjects since it would be very difficult to enrol a large homogenous group of patients with stroke with the same location, size and type of brain injury. The function of the non-dominant hand was used as a model for hand training and for cortical plasticity, since it is known that implicit knowledge (new learning) rather than explicit knowledge (deliberate recollection of information) will have an impact on the rapid plasticity of the cortical output maps to the muscles involved in a task (Pascual-Leone et al. 1994). Unexpectedly, the improved dexterity observed after shaping exercises was not reflected in an expanded motor output area of the trained muscle, but rather in

shifts of its location. An enlargement of the motor output area in parallel to improvements is the more commonly reported change after CIT (Liepert et al. 1998; Liepert et al. 2000; Liepert et al. 2001; Wittenberg et al. 2003) but some studies have reported minor shifts in location after repetitive movements (Liepert et al. 2000; Pearce et al. 2000; Kim et al. 2004). Hence, a shift of location rather than the size of a motor area may be a critical factor in evaluating cortical plasticity in humans after common behavioural tasks. Furthermore, in our subjects the improved dexterity was paralleled by a shift into the premotor area, known to be active in motor planning. General activity training, on the other hand, expanded and extended the area in the posterior (and inferior) direction. It is tempting to assume that this may be related to spatial coordination necessary for global activities.

The clinical relevance of CIT

To be able to evaluate a possible treatment effect it is important to use reliable test instruments. We therefore examined the Sollerman hand functions test (paper II) that was found to be a useful and reliable test for stroke patients with mild to moderate impairments of hand function. It would be interesting to know what “cut off level” in the total Sollerman scores that indicates a patient’s independence to perform hand –related activities in daily life, but such data are so far anecdotal. Statistically significant changes in outcome measures cannot automatically be interpreted as clinically relevant. However, in our clinical studies (papers I and III) we consistently found that the improvements in observation tests were in accordance with the patients’ opinion, expressed by spontaneous comments of improved motor ability as well as reports in MAL.

Only one study has evaluated the impact on the patients’ quality of life after CIT (measured by the Stroke Impact Scale), and improvements in domains such as physical function, social participation and communication were reported either post treatment or at six months follow-up (Dettmers et al. 2005). The MAL test has most frequently been used to measure the patients’ opinion of changes in arm use and quality of arm movement after CIT. The questionnaire has been found to have sufficient internal consistency and reliability, but the construct validity has been questioned (van der Lee et al. 2004). In one study, the quality of movement scale (QOM) but not the amount of use scale (AOU) was found to be reliable (Uswatte et al. 2005).

Most studies regarding CIT have been carried out in patients with a considerable residual functional capacity of the hand (referred as to the first quartile) (Taub et al. 1993; Kunkel et al. 1999; Miltner et al. 1999; Taub et al. 1999; van der Lee et al. 1999; Sterr et al. 2002a; Page et al. 2004; Dettmers et al. 2005), in which also the gains seem to be the largest (Taub et al. 2002),

probably due to a strong potential for improved hand use (Sunderland and Tuke 2005). In papers I and III we chose to include patients with mild to moderate impairment of hand function (representing the first and second quartiles), partly because of difficulties in recruiting patients. Other recent studies have included patients with lower hand function (referred to as second quartile) (Taub et al. 1998; Bonifer et al. 2005b), as well as minimal hand function (representing the third quartile) (Bonifer et al. 2005a) with promising treatment effects. Also patients using wheelchairs for transportation have been reported to be able to participate in CIT (Tarkka et al. 2005) and it is conceivable that CIT can be applied in a larger part of the stroke population than was originally thought (Morris and Taub 2001).

CIT has, in a recent review article (van Peppen et al. 2004), been reported to be beneficial to improve upper extremity function as compared to traditional neurological treatment approaches, biofeedback, neuromuscular electrical stimulation etc. Few studies have, however investigated the long-term clinical benefits of CIT (Wolf et al. 1989; Taub et al. 1993; van der Lee et al. 1999) and more research is warranted (Sterr 2004). To gain acceptance in clinical settings, modifications of the original CIT concept is probably needed. In accordance with the reports of others (Page et al. 2001; Sterr et al. 2002a; Dettmers et al. 2005), our modifications of CIT (paper I and III) were found to be feasible and beneficial.

Our findings of large improvements for the control group in the subacute study (paper III) contrast to other CIT studies (Page et al. 2002b, Page, 2001 #16; Atteya 2004). However, differences in established practises of stroke rehabilitation programs between countries, both regarding the amount of training per day and regarding the length of stay for inpatient stroke rehabilitation could be one explanation for this observation (Dobkin 2005).

The benefit of CIT for subgroups of patients

One of the hitherto largest studies of CIT after stroke, including 66 patients in the chronic phase, has shown that CIT was only clinically relevant for patients with sensory disorders and hemineglect (van der Lee et al. 1999). In our studies (papers I and III) we could not confirm this, perhaps due to smaller sample sizes. In another study, the influence of individual factors, such as sensory loss, spasticity, age, gender, amount of rehabilitation after stroke onset or affected hemisphere, have not, however, been shown to impact the outcome of CIT (Rijntjes et al. 2005).

Side-effects associated with CIT

Few studies have reported harms associated with CIT, such as burns, minor skin lesions and muscle soreness (stiffness and discomfort) in the affected upper extremity (Taub et al. 1993; van der Lee et al. 1999; Hakkennes and Keating 2005). Shoulder pain in the acute phase after stroke has not been shown to increase after wearing a constraint (Ploughman and Corbett 2004).

Concluding remarks

The studies in this thesis indicate that modifications of traditional constraint induced movement therapy into group therapy or with less hours of training per day, are both feasible and beneficial. Wearing a restraint, frequently considered to be an integral part of CIT, seems to be of minor importance for improving upper extremity function, both in patients with chronic and with subacute stroke. Shaping exercises rather than general activity training improved dexterity for the trained non dominant hand and was interestingly coupled to a shift rather than to an expansion of the involved motor output brain area. Additionally, the Sollerman hand function test seems to be reliable and useful in patients with stroke.

Although many studies have reported gains in upper extremity function after CIT, conclusive evidence is still limited. To clarify the benefit of CIT, randomised controlled studies with large sample sizes and with long-terms follow up are required. There is a need to elucidate the optimal CIT protocol (or the modification of it) to assess what mode of hand training is most beneficial, the impact of quality of life, the costs associated with the intervention, and also the clinical relevance for subgroups of patients.

SAMMANFATTNING PÅ SVENSKA

Kvarstående nedsättning av arm-hand funktionen är ett vanligt problem efter insjuknande i stroke. En ny träningsmetod kallad Constraint Induced Movement Therapy (CIT eller CI-terapi) tycks kunna förbättra arm-hand funktionen lång tid efter insjuknandet. CI-terapi är en intensiv och forcerad träningsmetod, som innebär restriktion att använda den normala handen (genom att bära en vante eller slynga) 90 % av vaken tid i förening med 6 timmars träning/dag för den försvagade handen. Eftersom CI-terapin är mycket resurskrävande, finns det ett behov av att modifiera träningsmetoden. Inom ramen för denna avhandling har följande utvärderats: effekten av modifieringar av CI-terapin, vilken typ av hand träning som tycks förbättra fingerfärdigheten och dess inverkan på hjärnbarkens organisation samt tillförlitligheten av ett test för bedömning av handfunktionen efter stroke, Sollerman handfunktions test.

Två veckors CI-terapi i *grupp* (n=16) (delarbete I) tycks kunna förbättra arm-hand funktionen hos strokepatienter i kroniskt skede. En signifikant förbättring av arm- hand funktionen noterades enligt utvärderingsinstrumenten Motor Assessment Scale (MAS; $p= 0.003$) och Sollerman handfunktion test ($p= 0.037$). Handens känsel var dock oförändrad (mätt med 2- punktsurskiljande). Patienternas subjektiva förmåga att använda handen med nedsatt funktion i vardagliga aktiviteter förbättrades också signifikant enligt Motor Activity Log (MAL; $p < 0.001$). En längre tids användning av vante i hemmet (under tre månader) gav dock inte någon ytterligare förbättring av arm- handfunktionen.

Forcerad arm/handträning (FUT; 3 timmars träning/dag i 2 veckor samt vante på icke paretisk hand 90% av vaken tid) i subakut skede efter stroke (delarbete III), förbättrade arm-hand funktionen signifikant, men inte mer än traditionell träning utan vante. I både FUT gruppen (n=12) och kontrollgruppen (n=12) noterades förbättringar mätt med Sollerman hand funktionens test ($p= 0.001$), MAS ($p < 0.05$) och i självskattad förmåga att använda armen med nedsatt funktion (MAL; $p < 0.05$). Inga signifikanta skillnader mellan grupperna noterades.

Sollerman handfunktionstest tycks vara ett tillförlitligt och reproducerbart bedömnings-instrument efter stroke (delarbete II). Testet består av 20 uppgifter som avspeglar dagliga hand aktiviteter (skala 0-4). Tjugofyra patienter med mer än 6 månader sedan insjuknandet deltog i studien. Patientens handfunktion bedömdes tre gånger; två gånger v 1 (test 1 och 2) samt en gång v 4 (test 3) av tre erfarna arbetsterapeuter (AT) samtidigt. En AT utsågs till testledare enligt ett rullande schema. För 15/20 uppgifter fanns det en tillfredsställande överensstämmelse ($\kappa \geq 0.4$) mellan bedömarna. Vid beräkning av total

summan var pålitligheten hög för varje bedömare vid upprepade bedömningar (Spearman's rho/ICC > 0.96) såväl mellan test 1 och 2 som mellan test 2 och 3. Även mellan bedömarna var reproducerbarheten hög: > 0.96 (Spearman's rho) och 0.92 (ICCs). Vi fann dock systematiska skillnader ($p < 0.05$) mellan bedömarna, där en AT genomgående skattade patienternas handfunktion lägre än de två andra bedömarna.

I en separat studie med 30 friska försökspersoner (delarbete IV) fann vi att sk shaping-övningar (med gradvis ökande svårighetsgrad och återkopplande kommentarer av behandlaren) förbättrade fingerfärdigheten ($p < 0.001$; Purdue peg board test) jämfört med aktivitetsbaserad handträning (hushållsgöromål, rituppgifter) av den tränade icke-dominanta handen. Efter shaping-övningar noterades en förskjutning av den kortikala motoriska kartan av den tränade muskeln (abductor pollicis brevis muskeln) mot områdena framför den motoriska hjärnbarken (mätt med transkraniell magnetstimulering; TMS). Efter aktivitets-baserad handträning expanderade däremot den kortikala motoriska arean signifikant ($p = 0.03$) bakåt. En förskjutning av antalet aktiva TMS punkter, snarare än en utökning av antalet tycks vara en viktig faktor i utvärderingen av hjärnbarkens förändringsförmåga (plasticitet).

Sammanfattningsvis har studierna i denna avhandling visat att mindre resurskrävande modifieringar av CI-terapi tycks vara möjliga med bibehållen förbättring av arm-hand funktionen hos patienter med stroke. Typen av handträningsövningar samt mängden träning för den påverkade handen verkar vara viktiga komponenter och inte användningen av själva vanten i sig. Shaping-övningar tycks förbättra fingerfärdigheten och Sollerman hand funktions test tycks vara ett tillförlitligt bedömningsinstrument för att utvärdera arm-hand funktionen hos patienter efter stroke.

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