Enriched, task-specific therapy in the chronic phase after stroke

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Gothenburg 2021

Cover photography: Anna Sjöholm and Pablo Cárdenas Rìos

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ISBN 978-91-8009-262-3 (PRINT)
ISBN 978-91-8009-263-0 (PDF)
http://hdl.handle.net/2077/67639

Printed in Borås, Sweden 2021
Stema Specialtryck AB

“Always more questions than answers, there are”
Yoda

Till Linus, Ossian och Elis

Abstract

A stroke often radically changes the life situation for the affected individual, both physically, as well as psychologically and socially. Recent findings in neuroscience suggest that the adult brain structure can change in response to learning but also environmental demands. New research give reason to believe that different kinds of sensory stimulating activities and exercises can enhance the neuroplasticity and reorganizational processes and improve mobility and cognition. In animal studies, an *Enriched Environment (EE)* - including socialization, exercise, sensory and cognitive stimulation and *task-specific exercise* has proved to be an effective intervention for boosting the brain's ability to reorganize and recover after a stroke. Until recently, an EE has remained mainly a laboratory phenomenon with few examples of translation to the clinical setting. There are now several studies showing that functional improvements are possible many years after stroke. Most rehabilitation therapies are primarily offered during the acute and subacute stages while it is unusual for stroke-affected individuals to be offered comprehensive rehabilitation during later stages of stroke.

This thesis includes four papers.

Study I is a longitudinal uncontrolled observational study, with a within-subject, repeated-measures design. The study assessed whether enriched task-specific therapy (ETT) contributed to any motor and health-related changes, in individuals with chronic stroke. The intervention was a 3-week long, high intensity, task-specific training program in an enriched environment in Spain. The ETT program also

included social and sensory stimulation and speech and language therapy (SLT) to support those with speech, language and communication needs. The 39 participants who completed the ETT program did improve functional motor ability, balance, gait speed and endurance, and were shown to achieve gains in multiple dimensions of health. The improvements were sustained at the 6-month follow-up.

Study II is a qualitative study using interviews as a tool to create an understanding of how individuals in a chronic stage of stroke experience ETT. Focus group interviews were conducted with twenty participants after their completion of the ETT program. Analysis was performed using qualitative content analysis. Three main categories were identified describing the informants' experiences of the ETT program. These categories were; 1. *The program—different and hard* – describing the participants' experience of the ETT as strenuous and different compared to earlier rehabilitation; 2. *My body and mind learn to know better* – describing the experience of improvements of the participants' body function and functional ability, as well as behavioural changes experienced throughout the ETT; and 3. *The need and trust from others* – highlighting trust in rehabilitation clinicians and the support of family and other participants. From these categories, a main theme could be extracted: It's hard but possible—but not alone!

Study III is a longitudinal observational study using advanced three-dimensional gait analyses to assess gait and movement-patterns. The aim of the study was to investigate whether the ETT program did produce any significant changes in spatiotemporal gait parameters or kinematic features of gait. The study had a single-subject-experimental design (SSED) and four participants from study I (all were men) in chronic phase after stroke participated. The study showed that two of

the four participants had significant improvements in gait kinematics, symmetry, and spatiotemporal variables after the intervention.

Study IV is a cross-sectional observational controlled study in which we studied the relationship between comfortable and maximum gait speed in individuals with mild to moderately severe disability after stroke. Furthermore, we studied if this relationship in individuals with chronic stroke differed from that of a control group of community-dwelling elderly. We found that the maximum gait speed in the individuals with stroke can be predicted by the comfortable gait speed, with a coefficient at 1.41. This relationship differed significantly from that of the control group, for which the corresponding coefficient was 1.20. In the control group, higher age and being a woman had a negative relationship with maximum gait speed and the corrected relationship was 1.07. In the stroke group, age, gender and time since stroke did not affect this relationship, while the degree of disability was negatively correlated with maximum gait speed - but not when included in the multiple analysis.

In conclusion, this thesis shows that ETT applied to individuals in a chronic phase after stroke produce beneficial gains in functional motor ability, gait speed, balance and multiple dimensions of health. ETT also seem to have profound emotional impact and might improve kinematic gait pattern. In order to understand the underlying mechanisms of recovery and improvement, further research is needed.

Keywords

stroke; rehabilitation; function; activity; participation; health; enriched environment; intense training; qualitative research; gait analysis; gait speed.

Sammanfattning på svenska

En stroke kan ofta förändra livet radikalt för den som drabbas, såväl på ett fysiskt, psykologiskt som på ett socialt plan. Ny forskning ger anledning att tro att olika typer av sensorisk stimulering, aktivering och träning kan påskynda hjärnans återhämtning och läkning av både motorisk och kognitiv funktion. Djurstudier har visat att en *berikad miljö* – som innefattar såväl sociala interaktioner, fysisk aktivitet, sensorisk som kognitiv stimulering - och även *uppgiftsspecifik träning* visat sig vara ett sätt att nyttja och förstärka hjärnans plasticitet och omorganisation och bidra till återhämtning efter en stroke. Fram tills nu har begreppet berikad miljö varit främst ett forskningsbegrepp med få försök till överföring i klinisk rehabilitering. Det finns dock ett flertal studier som visar att återhämtning och förbättring är möjlig även flera år efter en stroke. Trots detta är många rehabiliteringsinsatser fokuserade till det tidiga skedet efter insjuknandet i stroke, och det är ovanligt att individer med stroke erbjuds sammanhängande intensiva rehabiliteringsinsatser i senare skeden efter sin stroke.

Denna avhandling innehåller fyra delarbeten.

Delarbete I är en okontrollerad longitudinell observationsstudie med upprepade mätningar där varje individ utgör sin egen kontroll. I studien undersökte vi om ett uppgiftsspecifikt intensivt träningsprogram i en berikad miljö (ETT) för individer i ett kroniskt skede efter stroke resulterade i förändringar avseende motorik och olika aspekter av hälsa. Interventionen var ett tre veckor långt, högintensivt, uppgiftsspecifikt program i en berikad miljö i Spanien. ETT-programmet innefattade även social och sensorisk stimulering samt tal- och språkträning för deltagare med behov av sådana insatser. De 39 deltagarna som genomförde programmet uppvisade förbättring avseende funktionell motorisk förmåga, balans, gånghastighet och uthållighet i gång. Programmet resulterade även i upplevd förbättring av olika hälsorelaterade domäner. Förbättringarna kvarstod 6 månader senare.

Delarbete II är en kvalitativ studie med intervjuer som verktyg för att skapa en förståelse om hur individer i ett kroniskt skede av stroke upplever ETT. Fokusgruppsintervjuer utfördes med 20 individer efter att de deltagit i ETT-programmet. Intervjuerna resulterade i att tre huvudkategorier kunde identifieras, vilka beskrev upplevelsen av programmet.1. *Programmet – annorlunda och tufft* – beskrev deltagarnas upplevelse av programmet som ansträngande, krävande och olikt annan rehabilitering de upplevt. 2. *Kroppslig och mental inlärning* – beskrev positiva förändringar på kroppsfunktioner och aktiviteter, men också insikter och beteendeförändringar som en följd av ETT-programmet. 3. *Behovet av tillit till och motivation från andra* – tryckte på vikten av tillit till rehabiliteringspersonalen och stödet från anhöriga och andra deltagare. Från dessa tre kategorier kunde ett övergripande tema utrönas – *Det är svårt men möjligt - men inte ensam!*

Delarbete III är en longitudinell observationsstudie som undersöker gångmönstret i ett tredimensionellt rörelselaboratorium. Syftet med delstudien var att undersöka om ETT-interventionen resulterade i signifikanta förändringar avseende spatiotemporala gångparametrar (parametrar i tid och rum), symmetri eller kinematik (ledvinklar) vid gång. Studien hade en single-subject-experimental design (SSED) och fyra deltagare från studie I (samtliga var män) i kronisk fas efter stroke deltog. Av dessa fyra individer, sågs signifikanta och kliniskt relevanta förändringar för två av deltagarna, gällande gångens kinematik, symmetri och spatiotemporala gångparametrar efter ETT-programmet.

Delarbete IV är en observationsstudie där sambandet mellan maximal och självvald gånghastighet hos individer i ett kroniskt skede efter stroke och med mild till måttligt svår funktionsnedsättning, undersöktes. Vidare undersöktes hur detta samband skilde sig mellan strokegruppen och friska äldre individer. Strokegruppen bestod av deltagare från delstudie I samt individer från en annan studie-kohort, sammanlagt 104 individer. Dessa jämfördes mot kontrollgruppen, 154 äldre friska hemmaboende försökspersoner. Analysen visade att kontrollgruppen gick signifikant snabbare än strokegruppen. Ett linjärt samband sågs mellan maximal och självvald hastighet i båda grupperna. Regressionskoefficienten mellan självvald och maximal hastighet hos strokegruppen var 1.41 dvs maxhastigheten kunde förklaras genom 1.41 gånger den självvalda hastigheten. I kontrollgruppen var motsvarande ojusterade siffra 1.20. I kontrollgruppen var dock lägre ålder och att vara man korrelerat till högre maxhastighet och den justerade koefficienten var 1.07. I strokegruppen sågs grad av funktionsbortfall vara negativt korrelerat till maximal gånghastighet, men föll inte ut signifikant då denna parameter inkluderades i multivariabel-analysen.

Sammanfattningsvis visar denna avhandling att ETT resulterade i förbättringar av funktionell motorisk förmåga, gånghastighet, balans, hälsorelaterad livskvalitet och flera andra aspekter av hälsa hos individer i ett kroniskt skede efter stroke. ETT verkar också ha inneburit starka emotionella upplevelser och kan ha haft en påverkan på gångmönstret hos deltagarna. Mer forskning krävs för att förstå de underliggande mekanismerna för återhämtning och förbättring.

List of papers

This thesis is based on the following studies, referred to in the text by their roman numerals.

I. Vive S, Af Geijerstam JL, Kuhn HG, Bunketorp-Käll L. Enriched, Task-Specific Therapy in the Chronic Phase After Stroke: An Exploratory Study. J Neurol Phys Ther. 2020 Apr;44(2):145-155. doi: 10.1097/NPT.0000000000000309. PMID: 32118616; PMCID: PMC7077970

II. Vive S, Bunketorp-Käll L, Carlsson G. Experience of enriched rehabilitation in the chronic phase of stroke. Disabil Rehabil. 2020 Jun 1:1-8. doi: 10.1080/09638288.2020.1768598. Epub ahead of print. PMID: 32478573.

III. Vive S, Zügner R, Tranberg R, Bunketorp-Käll L. Gait Kinematics and Spatiotemporal Variables after Enriched, Task-Specific Therapy in the Chronic Phase after Stroke. A Single-Subject Experimental Design Study. Archives of Clinical and Medical Case Reports 5 (2021): 325-338.

IV. Vive S, Elam C, Bunketorp-Käll L. Comfortable and maximum gait speed in individuals with chronic stroke and community-dwelling controls. 2021 Submitted.

Content

Abbreviation

10MWT	10-meter walk test
30MWT	30-meter walk test
6MWT	6-minute walk test
BBS	Berg Balance Scale
BBT	The Box ´n Blocks Test
CIMT	Constraint-Induced Movement Therapy
DLS	Double-limb support
EE	Enriched Environment
EQ5D	European Quality of Life five-dimension questionnaire
ETT	Enriched Task-Specific Therapy
FES	Falls Efficacy Scale
FIS	Fatigue Impact Scale
HRQOL	Health Related Quality of Life
ICF	The International Classification of Functioning, Disability and Health
ITT	Intention To Treat
LISAT	Life Satisfaction Checklist
LOCF	Last Observation Carried Forward
MADRS	Montgomery Åsberg Depression Rating Scale
MCID	Minimal Clinically Important Difference
MDC	Minimal Detectable Change
M-MAS UAS	Modified Motor Assessment Scale according to Uppsala Akademiska Sjukhuset
MoCA	Montreal Cognitive Assessment
MRS	Modified Rankin Scale
QOL	Quality of Life
SLP	Speech-Language pathologist
SLT	Speech-Language Therapy
TSDB	Two Standard Deviation Band Method
UC	Usual Care

Definitions

Activity	The execution of a task or action by an individual (WHO, 2001)
Body Functions	The physiological functions of body systems (WHO, 2001)
Body structures	Anatomical parts of the body such as organs, limbs and their components (WHO, 2001)
Impairment	Problems in body function or structure as a significant deviation or loss (WHO, 2001)
Functioning	Umbrella term of Body Functions and Structures and Activities and Participation, positive aspects (WHO, 2001)

Participation	Involvement in a life situation (WHO, 2001)
Capacity	Ability to execute a task or an action in a standardised envi-ronmental (WHO, 2001)
Performance	What a person does in his or her current environment (WHO, 2001)

1. Introduction

1.1 Stroke

1.1.1 Stroke definition and epidemiology

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 lasting >24 hours unless interrupted by surgery or death."[1] The prevalence of stroke in Sweden is 300 cases per 100 000 inhabitants, where 200 are individuals who have their first time stroke. Every year in Sweden, 25 000 - 30 000 individuals suffer from acute stroke, and about 25 % of those unfortunately die from the stroke within a month. About 74% are over 70 years when the stroke occurs, and about 4% are under 50 years of age. [2] Although the stroke mortality rate over the past two decades has declined, the amount of people affected by, or with long-lasting disabilities from stroke has increased around the world, in both men and women of all ages. [1] Stroke is the second most common cause of death and a leading cause of adult disability worldwide. [3] Stroke often lead to lasting consequences, which usually are multifaceted and can result in problems across multiple domains of functioning, activities and participation. [4]

1.1.2. Plasticity after stroke

Most of those who survive the acute phase improve spontaneously the first months after stroke onset. [4] The mechanisms causing these functional improvements are not completely known. [5] One possible explanation is that the stroke-affected individuals develop compensatory strategies in an attempt to regain lost functions. One other possible explanation is the reorganization that takes place in the cerebral tissues around the lesion within the damaged hemisphere, as well as in the undamaged hemisphere. [6] The brain´s ability to reorganize and modify itself after an injury is known as neuroplasticity, which is considered to be the main reason why individuals with brain damage can improve function after a stroke. [7] Neuroplasticity is seen during the developmental stages of the brain and during learning. Research over the last 50 years has led to an increased knowledge about the brain's ability to change. Previously, the regrowth of connections after damage in the adult human brain was viewed upon as impossible. This knowledge contributes to a paradigm shift with positive implications for the rehabilitation of individuals with stroke. [8] The latest research findings on stroke have shown that the brain has a significant and life-long potential of plasticity. [9-12]

1.1.3. Consequences of stroke

Regardless of the etiology of a cerebrovascular disease, the symptoms of stroke vary depending on the area of the brain exposed to oxygen deficiency and the extent of the damage. The signs and symptoms of a stroke as well as the degree of difficulty therefore vary from person to person. One of the most frequently observed symptoms is a mild (hemiparesis) to severe weakness (hemiplegia) of one side of the body opposite the side of the brain affected by the stroke. In addition to the motor difficulties that often follow a stroke, other common symptoms are lack of sensory functions, language and speaking problems, perceptive problems, visual loss, attention deficits, other cognitive problems and motor planning disorders. [4] Initially, 80% of the survivors suffer a hemiparesis of the body, with consequences regarding the individual´s activities of daily living (ADL), such as eating, drinking, talking, walking and grasping, which in turn affect the individuals' ability to participate in social, family and personal activities. [1,3,4,13] Previous research describe that most recovery from stroke occurs within the first six months, and most commonly, the individual then reaches a plateau. [14,15] Approximately 1/3 of the survivors suffer from substantial impairments still present 6–12 months after stroke onset. [16] As much as 40 to 60% of stroke-affected individuals reach an acceptable degree of functional independence, however, at a highly variable speed during the period 3 months to 10 years after the stroke onset. [17,18]

1.1.4 Stroke in the ICF context

The consequences of a stroke can be described and defined using a specific classification system, The International Classification of Functioning, Disability and Health (ICF, figure 1). [19,20] In ICF, status of health, illness or injury can be placed in a dynamic system together with dimensions such as body functions and structures, activity and participation. The system may be affected by contextual factors, e.g. environmental and personal ones (Figure 1). In the case of the activity and participation list of domains, two important qualifiers are described: capacity and performance. The performance qualifier describes what an individual does in his or her current environment. The capacity qualifier describes an individual's ability to execute a task. [19] The evaluation in the present studies aims at describing several levels of functional ability and impairment in relation to health according to the ICF. ICF is commonly used in rehabilitation and research worldwide. However, several issues has been raised concerning the system, for example the need to include subjective dimensions in the framework, such as quality of life (QOL). [19,21] The definition of QOL and Health-related Quality of Life (HRQoL) are often overlapping, but in this thesis, the definition of HRQoL used is set to *self-perceived health-status* [22]

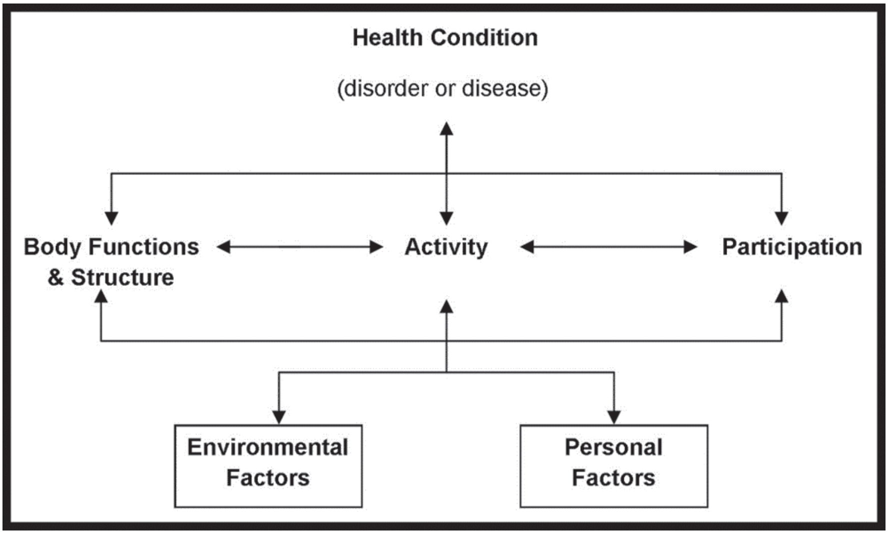

Figure 1. The model of International Classification of Functioning, Disability and Health (ICF).

Improvements in the ICF components body structures, body functions, activity and participation after a stroke might be due to plasticity processes, restorative processes and compensatory mechanisms. [23,24] True recovery defines the restoring of the ability to perform a movement in the same kinematic manner as it was performed before the injury, and compensation is described as performing an old movement in a new manner, using alternative movement pattern, resulting in a change in muscle activation, different timing and kinematic patterns. [23-25] Decisions about whether behavioural improvement reflects true recovery or use of compensatory strategies is difficult to make [22,128] and clinical rehabilitation studies are often unsuccessful in distinguishing if their results reflect true recovery or compensation. [23-25]

1.1.5 Normal gait

The biomechanics of normal gait are rather reproducible. [26] The prerequisites of gait according to Perry are: stability in stance, foot clearance during swing, appropriate prepositioning during swing, adequate step length and energy conservation. [27] A gait cycle consists of steps and strides, each foot has a stance phase and swing phase, where the stance phase takes about 60% of the cycle and the swing phase about 40%. These two phases can further be described in 8 temporal phases: Initial contact, loading response, midstance, terminal stance, pre swing, initial swing, mid swing and terminal/late swing. [28] The normal gait and its common described temporal phases described in figure 2.

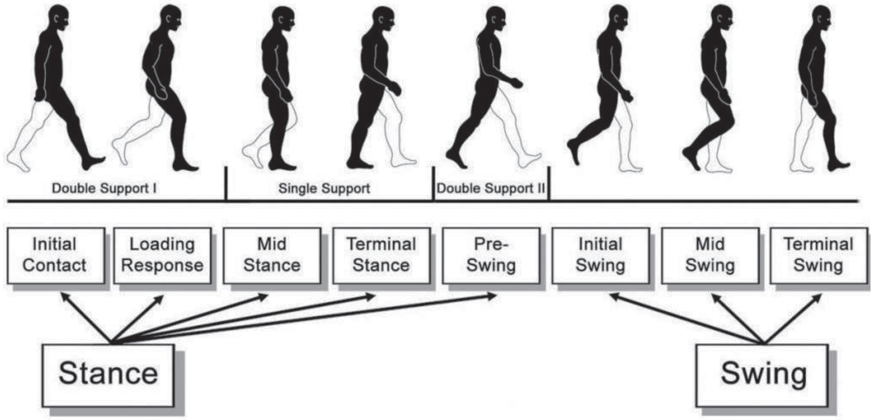

Figure 2. Normal gait and its phases and events. The picture is cropped and reprinted with permission. [29]

1.1.6 Gait after stroke

Hemiparesis after stroke is one of the most commonly observed symptoms after stroke. As a consequence of hemiparesis, walking dysfunction is the most frequently described limitation of activities after stroke and may affect independence, quality of life (QoL), and participation. [30] Hemiparesis and walking dysfunction are shown to hamper postural control, predispose individuals to sedentary behaviours [31], and also increase the risk of falling. [11] The literature describes that improvements in gait are seen over the first 3 to 6 months after the stroke and then plateaus. [32] During the first week after a stroke, only one third are able to walk without support. [33] Three weeks after the stroke, 50–80% can walk unaided. [34] Even if 85% of individuals with stroke regain independent walking ability and are able to walk independently without assistance from another person [35], there are only about 7% who are able to walk the speeds and distances required to walk independent in the community. [36,37] Not being able to walk independent is shown to be a predictor for discharge to nursing homes in stroke individuals. [38] Gait speed is shown to be an important predictor for the levels of physical activity and sedentary behaviour [31] and many individuals with stroke are not able to reach the recommended amount of physical activity after stroke specified as: cardiovascular activity 20-60 minutes 3-5 times a week.[39] The measure of gait speed in comfortable or maximum paces are commonly used in rehabilitation evaluations [40] but the relationship between maximum and comfortable gait speed for individuals with long-term residual disability in the chronic phase is not fully known.

1.2 Stroke Rehabilitation

WHO has defined rehabilitation as "a set of measures that assist individuals, who experience or are likely to experience disability, to achieve and maintain optimum functioning in interaction with their environments", and is “instrumental in enabling people with limitations in functioning to remain in or return to their home or community, live independently, and participate in education, the labour market and civic life”. [41]

Physiotherapy is defined as “health profession with the expertise in movement and exercise prescription throughout the lifespan across the health spectrum.”[42] Physiotherapy has the aim of promote health, minimise suffering and keep or regain optimal movement ability and movement performance. [43] ”Physiotherapy involves specific interventions to individuals and populations where movement and function are, or may be, threatened by illness, ageing, injury, pain, disability, disease, disorder or environmental factors. Such interventions are designed and prescribed to develop, restore and maintain optimal health.” [42]

The phases after a stroke are often defined and divided into acute (from stroke onset to 7 days after the stroke), subacute (7 days to 6 months) and chronic phase (later that 6 months after stroke). [24] The care after an acute stroke is recommended to be offered in a stroke unit. [44] The Swedish National Board of Health and Welfare describes that rehabilitation interventions should start early and be offered as long as the individual have a need of it. [44] Unfortunately, the stroke care and rehabilitation offered to individuals with stroke are unequal around the country. [44]

1.2.1 Stroke rehabilitation interventions

A considerably large amount of research has been done on different rehabilitation approaches designed to reduce functional impairments after stroke. The current perspective on motor learning is focused on task-specific and goal-directed training, such as training of activities and functions that are meaningful for the individual and where the goal is set to improve these activities. [45] The present paradigm within motor relearning utilizes feedback, repetition, intensity and specificity with the aim to provide long-term recovery. [4,30,46]

Motor training and relearning is an important part of stroke rehabilitation. [47] Several promising approaches are based on theories of motor learning such as training of a non-compensatory nature, so-called constraint-induced movement therapy (CIMT), focusing on avoiding compensation of the non-affected side of the body and enforcing the use of the affected side. [48] Weight-supported treadmill training [49], robotic training [50], cardiovascular training [51], bilateral arm training [52], and goal-directed physical exercise [53] are other examples of interventions with possibilities to improve recovery during subacute or chronic stages after stroke. Task-oriented, goal-directed training that includes feedback, repetition, intensity and specificity has proven to be promising rehabilitation interventions in improving movement function, ability and performance. [54,55] For individuals with chronic stroke, some interventions have proven beneficial in terms of walking velocity, distance walked, and level of independence [45,56,57], but improvements are not always sustained in the long term. [56,58] Additionally, new studies give reason to believe that different kinds of sensory stimulating activities and exercises can speed up the healing process and functional recovery in the brain concerning both mobility and cognition. [59]

As much as 40 to 60% of stroke-affected individuals reach a level of independence regarding transfers and activities in daily living at a highly variable speed during a period from 3 months until 10 years after the stroke onset. [17] Hard work is required to keep an achieved level of independence, and individuals often lose relearned functions again over time. [60] Most rehabilitation measures are mainly applied during the acute and subacute stages while it is unusual for stroke affected individuals to be offered comprehensive rehabilitation during later stages after stroke [30], even though there are several studies showing that functional improvements are possible in later phases after stroke. [4,61] Even though there are National guidelines for stroke care in Sweden [44], individuals with stroke experience unfulfilled needs in rehabilitation services received. [62]

Issues related to rehabilitation have been investigated in not just quantitative but also qualitative studies. A previous study on experience of physiotherapy after stroke showed that the individuals appreciated physiotherapy since it was viewed on as leading to functional improvement. [63] They also found that therapists were considered as a source of advice and information and a source of faith and hope. [63]

However, individuals living with stroke are in growing numbers left with long-lasting impairments [4], and many lack stimulation, exercise and socialization. [11] The stroke rehabilitation field needs to focus both on implementing new strategies to improve long-term outcome [64], and tailoring treatment interventions to the needs of the individual. [65] Stroke survivors are often inactive and alone, even in a comprehensive acute stroke unit [66], although recent results show that it is possible for individuals with stroke to spend more time active and out of bed and to engage in higher motor activities. [67] There is a need to increase opportunities for training and socializing and promote activity in and outside of therapy time. Creating an enriched environment may be a way to approach these needs. [68]

1.3 Enriched Environment

1.3.1 Development of the Enriched Environment paradigm

Enriched environment (EE) was first described by Donald O Hebb. He found, as early as 1947, that rats that were able to roam freely performed better in problem solving, than rats kept in cages. [69] Several studies have shown that stroke-lesioned rats being exposed to a so-called EE show signs of tissue regeneration/plasticity, e.g. thickened cortex, stronger synapses, increased neural sprouting, and increased neurogenesis in the hippocampus. [70-72] In rat studies, an EE condition often consists of housing animals in groups of up to 10 animals per cage. The cages are large, equipped with toys like boards, chains, swings, wooden blocks and objects of different sizes and materials. The objects in the cages are moved around and exchanged for new ones several times a week to accomplish a variation in the environment. Research has shown that rats exposed to this EE, with possibilities for physical activity and social interactions, are recovering significantly faster than rats in standard cages, despite the fact that the total tissue loss between the rats did not differ. [73-76] Figure 3 presents a typical EE condition and a standard housing condition.

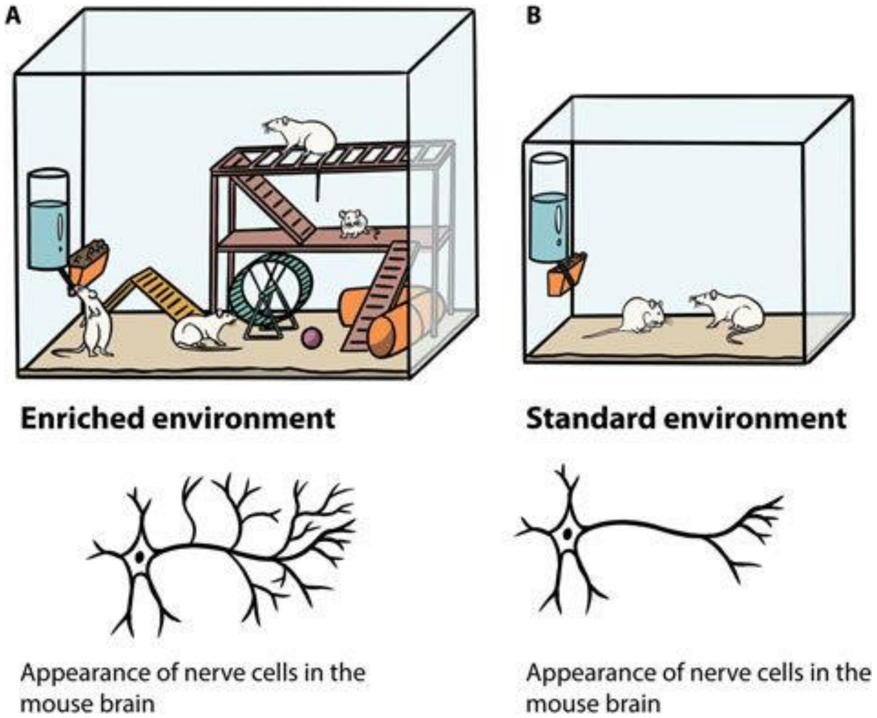

Figure 3. (A). Appearance of nerve cells in the mouse brain after being in an enriched environment, including increased space and equipped with a variety of objects that encourage exercise, balancing or climbing, and challenge cognitive functions. The animals are introduced to the stimulating environment in groups to facilitate social interaction. (B). A standard housing condition that generally entails a cage with bedding and access to water and food.

1.3.2 Enriched Environment in stroke rehabilitation

In rodents, an EE - including socialization, exercise, sensory and cognitive stimulation is proved to have a powerful and positive impact on the brains plasticity and to enhance recovery after a stroke. [11,74,77] However, very few studies have tried to translate the EE paradigm to a clinical human stroke setting. (Figure 4.) Reasons for the lack of clinical EE studies include difficulties in defining and standardizing EE across different clinical sites, lack of knowledge concerning what aspect of enrichment that represents the most important element for enhancing brain plasticity, and the lack of knowledge about the actual required “dose” of enrichment.

Figure 4. Translation of basic research to clinical research.

Nevertheless, a few studies on EE have been performed in clinical stroke settings. [78-81] In these studies, the environmental enrichment has been applied in communal or individual areas. The opportunities for enrichment has been suggested to include the provision of music, reading or listening to books, performing puzzles, playing games and/or other hobby supplies, and also offering tablets and computers. Other possibilities could be the availability of recreational activities, and offering communal areas for meals, social and other group activities.

Janssen et al. [82], first presented a study protocol and design of a study on individuals with stroke participating in rehabilitation in a mixed rehabilitation unit. [82] In that study, the EE was defined as a stimulating environment, with communal areas for eating and socializing and daily group activities. A few years later, they published findings from a post-acute mixed stroke rehabilitation unit showing that individuals in an EE ward were more likely to engage in cognitive, physical and social activities and were less likely to be inactive, alone or asleep compared to subjects who received usual care. [79] A qualitative study on the care staff of these individuals showed that the staff experienced that the use of EE in their rehabilitation unit promoted activity and participation in the individuals with stroke. The results highlighted the significance of social support to participate in the ward environment and the positive consequences for the individuals' mood levels. [83] The same group, with White as first author, published another qualitative study describing stroke survivors´ experience of participation in an EE. The results reported various benefits including increased motor, cognitive and sensory stimulation and social interaction, less degree of boredom and increased feelings of personal control. The participants also identified several obstacles that effected the implementation of the EE. [84] Rosbergen et al. (from the same research group as Jansen et al.) changed the protocol from Jansen´s study [79], and investigated whether an EE embedded in an acute stroke unit could increase activity levels and reduce adverse events in individuals with acute stroke. [80] The individuals in the EE group spent more time of the day engaged in 'any' activity in comparison to the usual care group. They were more active in physical, social and cognitive domains and these behavioural changes were lasting six months after the intervention. Subjects in the EE group had a significantly shorter length of stay. [80] The same author, Rosbergen et al. did also investigate the effect of EE applied in an acute stroke unit on how and when subjects undertake activities and the number of staff assistance needed, in comparison with a control environment with no enrichment. [81] Higher activity levels in the EE group occurred during periods of scheduled communal activity, when compared to the control group, but no differences were observed outside of scheduled activities. The enriched group spent more time on upper limb activities, communal socializing, and listening and tablet activities. The amount of total staff assistance during activities showed no difference between groups. [81] The same group also investigated qualitative the caregivers perceptions and showed that teamwork and careful change of management was important factors for implementing the EE in the unit. [85] In a study by Khan et al. [78], individuals with stroke and individuals with other neurological disorders enrolled in an RCT were studied as they received an EE intervention at a rehabilitation hospital. The EE interventions consisted of an “Activity Arcade” and included an additional 2-h activity session provided on weekdays along with their daily ward activities, based on participant clinical need. Various enrichment activities were available for the participants to choose between. Compared with controls, the EE group showed significant improvement at discharge in "depression", and "stress"; MoCA and the motor (total) subscale as well as the self-care and mobility subscales of Functional Independence Measure (FIM). At the 3-month follow-up, significant gains in the majority of the secondary outcomes were maintained for the EE participants. Cognitive function and activities improved most frequently in participants with stroke, as compared to the group with other neurological diagnoses. [78] Khan et al. did also publish an article showing that the EE program was feasible and effective in improving upper limb function and increasing the activity of individuals during their inpatient subacute care. [86]

Table 1 presents specifications of the EE interventions included in the previous translational studied (dose of therapy, enriching components included [social, physical, cognitive and sensory], study design and the phase post-stroke).

Table 1. Specification of the EE interventions included in the previous translational studies (Y=yes; N=No).

Author	Dose	Social	Physical	Cognitive	Sensory	Type	Phase
Janssen et al. **White at al.** **(same research group)**	13 days, 4 mapping days	Y	N	Y	Y	Controlled before-after, Mapping, Feasibility, Qualitative participants, qualitative caregivers	Post-acute stroke unit
Rosbergen et al.	10-12 days, 3 mapping days	Y	Y/N	Y	Y	Uncontrolled before/after, Behavioural mapping, Qualitative caregivers	Acute stroke unit
Khan et al.	2h/day during weekdays mean 14 days	Y	Y/N	Y	Y	Feasibility RCT	Subacute /chronic stroke + other neurologic diagnoses

1.3.3 Studies using terminologies including elements of an EE

A few studies using terminologies synonymous with EE have been published. These studies describe the intervention as providing some kind of enrichment. In these articles, the authors discuss the results in the context of the concept of EE, but their interventions were not described as an EE per se.

One study investigated the effectiveness of an exercise rehabilitation music program. [87] The findings implied that the music-based exercise program had effects on the mood in the individuals with stroke. Moreover, the individuals had a higher recovery rate when the exercise rehabilitation program also included an enriched sound environment with experiential music. [87]

A previous RCT investigated the effectiveness on multimodal interventions, more specifically horse-riding and rhythm and music-based therapy. [59] The findings, including individuals with chronic stroke, showed that both therapies led to gains in self-rated recovery, balance, gait, grip strength, and working memory. [59] A qualitative study on the participants in the aforementioned study who received the music- and rhythm-based therapy showed that the individuals' described positive experiences in terms of motor, cognitive, and emotional benefits after partaking in the multimodal rehabilitation program. Important factors were the music, the social interaction, the challenging exercises, and the skilled instructor. [88] A qualitative study on the participants who received the horse-riding intervention showed that the participants reported having learned new skills, increased their self-efficacy and self-esteem and had improvements in balance and gait. The horse played a crucial role and also the other group members, the instructors, and the challenging tasks. [89]

Another RCT did investigate whether music listening could improve recovery of cognitive functions after stroke. [90] Results from this RCT showed that the music group increased their verbal memory, their attention improved significantly, and they experienced less depression, than the control group. [90] Another recent RCT on individuals with aphasia after stroke showed that daily traditional experiential music listening increased the recovery rate compared to standard care.[91]

A pilot study on a virtual reality rehabilitation system applied to help improving reaching movements of people with hemiparesis after stroke was performed by Duff et al. [92] The feedback was provided by vision and music as a stimulating EE, promoting multimodal sensory-motor integration. Improvements was seen including the speed and smoothness in reaches, better coordination and reduced compensatory activation in the torso and shoulder. [93]

The effect of different walking environments in dual-task walking after stroke has been studied by Timmermans et al. [94] They concluded that the walking environment was influencing the cognitive-motor interference and prioritization of tasks during dual-task walking in the individuals. [94] Other authors have described how the environment affects motor outcomes. Wang et al. showed that a motion-based virtual reality training intervention is a feasible supplementary intervention in rehabilitation that might facilitate the improvement of motor skills in individuals with subacute stroke. [95]

1.3.4 Summarization of EE in clinical stroke setting

The main findings regarding clinical applications of EE in a clinical stroke rehabilitation indicate that an EE is feasible to embed in an acute stroke settings [82], and that the individuals with stroke in an acute and subacute EE ward are more engaged in activities as compared to controls [79-81], and have shorter length of stay in the acute hospital ward. [80] Further, EE applied to in-patient stroke settings can lead to significant improvement in cognitive function and motor activities. [78] The main qualitative findings regarding EE in a clinical stroke setting suggest that the rehabilitation caregivers perceive that EE enhanced patient activity, the authors emphasise the importance of social support and participation in the ward environment in order to affect the mood of the individuals. [83] Further, stroke survivors who participated in an EE report of increased stimulation on many levels. [84]

However, the translation of the EE concept to a clinical setting differs a lot between studies. The studies on individuals with acute and subacute stroke did investigate EE as an “add on” to usual care. [79,81] For example, an “EE-area” was offered with games, puzzles, music and possibilities of socialisation and the dosage of EE was not fully described. The level of evidence in most of the published studies on EE is weak, only one RCT was found. [78] Three more RCTs did evaluate interventions based on enriching components (horse-riding, rhythm/music-therapy [59] and music-listening [90,91]). The studies on enriching components could have aspects of EE, enrichments through technical devices such as virtual reality [95,96], animal enrichments for example with horse-riding therapy [59], music-listening [90], music exercise programs [87] or rhythm-and music-based therapy. [59]

The dose and the content of an EE applied in stroke rehabilitation as well as its effectiveness compared to usual care are aspects that are yet unknown. Further, it remains to be clarified which component of EE - including a number of behavioural components – or enriched rehabilitation, in combination with components of exercise, that best promote recovery after stroke. [77]

2. Aims

Overall aim

The overall aim of this thesis was to study whether ETT contributed to any changes with respect to function, activity, participation and different aspects of health in individuals with chronic stroke.

Specific aims

I. The aim of study I was to assess whether the ETT contributed to any changes in functional motor performance as well as balance, gait, hand strength, and dexterity in individuals with residual hemiparesis in the chronic phase after stroke. Further, to assess whether ETT led to any changes of confidence in task performance, fatigue, depression, life satisfaction and HRQoL.

II. The aim of study II was to explore the experiences of individuals who participated in an ETT program in the chronic phase after stroke.

III. The aim with study III was to assess whether any changes in spatiotemporal gait parameters, gait kinematics or symmetry could be shown in individuals who participated in an ETT program in the chronic phase after stroke.

IV. The aim of study IV was to study the relationship between comfortable and maximum gait speed in individuals with chronic stroke with mild to moderately severe disability. Further, to examine if the relationship between comfortable and maximum gait speed in individuals with chronic stroke differ from that of a community dwelling elderly control group, and also to study which parameters that did affect this relationship in respective group.

3. Materials and Methods

3.1 Material

3.1.1 Study setting and design

This thesis contains four papers that altogether include three study cohorts. Table 2 presents the study design and the number of participants in each study.

Study I is a longitudinal uncontrolled observational study, in which the participants received a 3-week long intervention (ETT), preceded by a 3-week long baseline phase. Follow-up assessments were performed at 3 and 6 months.
Study II is a qualitative study where focus group interviews was performed directly after the intervention (ETT).
Study III is a longitudinal observational study using a single-subject ABA experimental design [97], with follow-up at 6 months. The initial phase (A1) was a baseline period before the intervention, lasting for 3 weeks. During A1, three to five analyses were done at least one day apart. [98] The B-phase was the 3-week intervention period (ETT). Immediately after the intervention, the A-phase was repeated (A2 phase). A single follow-up was done 6 months after the intervention.
Study IV is a cross-sectional observational controlled study, where baseline data from three study cohorts (Study I, [59] and [99]) was merged.

Table 2. Number of individuals who were part of the different study cohorts, description of study designs, and at which timepoints the outcome measure data were collected.

Study nr	Nr included (also in study I)	Study design	Measurement timepoints
Study I	41	Longitudinal uncontrolled observational study	Before/after control phase, after ETT, 3 and 6 months after ETT
Study II	23 (13)	Qualitative focus group interview study	Directly after ETT
Study III	4 (3)	Longitudinal observational study with a SSED-ABA-design	3-5 assessments during A1, and 3-5 assessments during A2, one assessment at 6 months
Study IV	258 (17)	Cross-sectional observational controlled study	One assessment before any intervention.

3.1.2 Subject recruitment

Subjects in study I, II and III were recruited from the waiting list from Neuro Optima Forsk Rehab AB´s rehabilitation programs. The company requested permission for the project leader to contact individuals who had applied to the rehabilitation program. The project leader provided the individuals with information of the study along with a screening of potential study participants, after which oral and written consent were collected. In addition to participants who underwent the ETT program, additional subjects in study IV were retrieved from two other research projects [59,99] in Gothenburg.

3.1.3 Subjects

The study subjects are described in table 3. In study IV, including 258 individuals, 17 subjects were part of the cohort in study I (those over 60 years), 87 from another intervention study on chronic stroke [59], and 154 community-dwelling older controls from another study on individuals over 65 years. [99]

Table 3. Demographic variables and baseline characteristics in the four studies. Mean (SD)/median [min;max] is given for continuous variables and n (%) for categorical variables.

Characteristics	Study I	Study II	Study III	Study IV stroke	Study IV controls
Participants	41	20	4	104	154
Women n(%)	8 (20)	8 (40)	0 (0)	39 (37.5)	81 (52.6)
Men n(%)	33 (80)	12 (60)	4 (100)	65 (62.5)	73 (47.4)
Mean age, years (SD) median [min;max]	59.6 (13.9) 64 [22;84]	61 (13.1) 64 [25;84]	61.8 62.5 [57;65]	66.5 (4.2) 66[60;80]	72.1 (4.7) 72 [65;81]
Months since stroke onset, mean (SD) median [min;max]	35.5 (29.5) 26 [6;130]	30.4 (34.1) 17.0 [6;156]	36.3 (30.9) 30.0 [11;88]	35.2 (20.0) 30.4 [6;122]	-
Modified Rankin Scale[a]					
Mean grade, mean (SD) median [min;max]	3.4 (0.7) 3.0 [2;4]	3.4 (0.7) 3.5 [2;4]	2.8 (0.4) 3.0 [2;3]	2.6 (0.6) 3.0 [2;4]	-
Grade 2 n(%)	5 (12)	3 (15)	1 (25)	48 (46)	-
Grade 3 n%)	16 (39)	7 (35)	3 (75)	50 (48)	-
Grade 4 n(%)	20 (49)	10 (50)	0 (0)	6 (6)	-

[a]An ordinal disability rating scale scored 0–6. 2 - Slight disability; Able to look after own affairs without assistance, but unable to carry out all previous activities. 3 -Moderate disability; Requires some help, but able to walk unassisted. 4 - Moderately severe disability; Unable to attend to own bodily needs without assistance and unable to walk unassisted.

3.1.4 Eligibility

The eligibility criteria in **study I, II and III** were: At least 6 months and a maximum 10 years since the onset of stroke; Disability grade 2–4 on the modified Rankin Scale[100]; Baseline motor deficit defined as less than a full score on the primary outcome measure (M-MAS UAS) [101]; No other injury, illness, or addiction, making the individual unsuitable for participation, including exercise-induced epilepsy, assessed by the referring or prescribing physician; Cognitive and speech ability that enables instruction, intervention, and evaluation; Ability and willingness to travel to the place of evaluation; Able to perform sit-to-stand and stand-to-sit transfers independently or with assistance, without assistive technology such as mechanical lifts; Not having participated in a similar high-dose rehabilitation program (other than post-stroke acute and subacute rehabilitation) within the previous 6 months; Not scheduled for other treatment focused on intensive, high-dose training during the study period.

In study II, additionally criteria was: Cognitive and speech ability that enabled being included in a group interview.

In study III, the additionally criteria were: Affected/asymmetric gait pattern; Ability to walk independently 10 m indoors without assistive devices; and Live near Gothenburg, to enable repeated assessments in the gait laboratory.

In study IV, the eligibility criteria for the cohorts with chronic stroke were the same as in study I with the addition that the subjects had to be ≥60 years. For the community-dwelling control group, the criteria were: No severe musculoskeletal injuries or problems affecting physical performance; No detectable neurological, cardiopulmonary or cognitive problems; or arthroplastic surgery in the lower extremity, and ≥65 years.

3.2 Intervention

3.2.1 ETT

ETT refers to Enriched, task-specific therapy, where "enriched" refers to environmental enrichment—an intervention to increase motor, sensory, cognitive, and social activity by providing a stimulating environment. "Task-specific" refers to repetitive functional training in everyday tasks, meaningful for the individual. The ETT program was conceptualized by the medical board of former *Neuro Optima Forsk Rehab AB*.

Directly after the baseline phase, the 3-week long ETT program took place at two rehabilitation facilities in Spain, near Marbella and Malaga. The ETT was performed in groups of four to nine, but the content was individually tailored, and supervised by physiotherapists (PTs) (and speech-language pathologists [SLPs] when needed). Depending on the group size, and the participants' disability level, as many as three PTs were sometimes required to supervise and assist the training. The ETT was characterized by large dosage of therapy. Rehabilitation activities was scheduled 5.5 hours on weekdays, 3.5 hours on Saturdays, and Sundays off, for three weeks. The therapy was divided into three sessions of 1.5–2 hours each weekday, mixed with social activities, such as scheduled coffee breaks and lunch. Participants with speech impairments received individualized treatment with a SLP for a maximum of 2 hours per day, included in the 5.5 (weekdays) or 3.5 hours (Saturdays). The content of the program is described in Table 4. The various components acting in the clinical translation of the EE model in this study are presented in Figure 5 and examples of the physical environment in the ETT in figure 6.

Table 4. The content of the enriched task-specific therapy (ETT) program.

Therapy domain	Description/Content
Functional training for transfers and upper/ lower limb **(1–3 daily sessions depending on the individual need)**	Training of functional tasks included practicing lying, sitting, and standing transfers. An example of the noncompensatory strategies applied in this area is sit-to-stand training with the non-affected foot on a balance plate or small ball, with the aim of transferring the balance focus and body weight to the affected side. The ETT program also focused on mobility, balance, and gait exercises on treadmills and while walking indoors and outdoors in various environments. The program contained various exercises to improve arm and hand function, focusing primarily on functional-task training such as lifting and carrying and on fine motor skills such as holding, picking, carrying, lifting, writing, or grasping with the affected upper limb (for participants with some preservation of motor abilities in arm and hand).
Impairment based training for both upper and lower limb **(1–3 daily sessions depending on the individual need)**	The program also contained elements of impairment-based training. As an example, for a participant with impaired dorsiflexion of the foot, the program included not just functional training such as walking, stepping over hindrances indoors or outdoors with a focus on lifting the foot, but also sitting or lying dorsiflexion routines, and/or stretching and other mobility exercises. Impairment based upper limb training include strength and mobility training for shoulder, arm and hand.
Environmental training **(Self-directed training)**	Beyond scheduled activities, participants were encouraged to physically engage themselves in a challenging outdoor environment, consisting of curbs, stairs, slopes, and different surfaces.
Cardiovascular training **(30 minutes/day)**	Each day, participants did 30 minutes of submaximal cardiovascular training on a stationary or sitting bicycle (arms and/or legs), treadmill, or cross-trainer.
Aquatic exercise **(2–3 sessions per week)**	Participants had aquatic exercise for 2–3 sessions per week, focusing on individual goals and consisting of aquatic walking exercises, arm/shoulder training, balance, core stability, and relaxation exercises.
Enriching excursions and social stimulation **(A couple of half-day excursions and one full-day excursion)**	The ETT included enriching beach or village excursions with rehabilitation personnel, enabling goal-directed training in various environments. The participants also interacted with each other and with accompanying family members at training sessions, meals, and social events after the scheduled activities.
Lectures **(About 1 lecture per week)**	The program also consisted of lectures designed to widen the knowledge about the brain, stroke, rehabilitation, exercise and recovery.

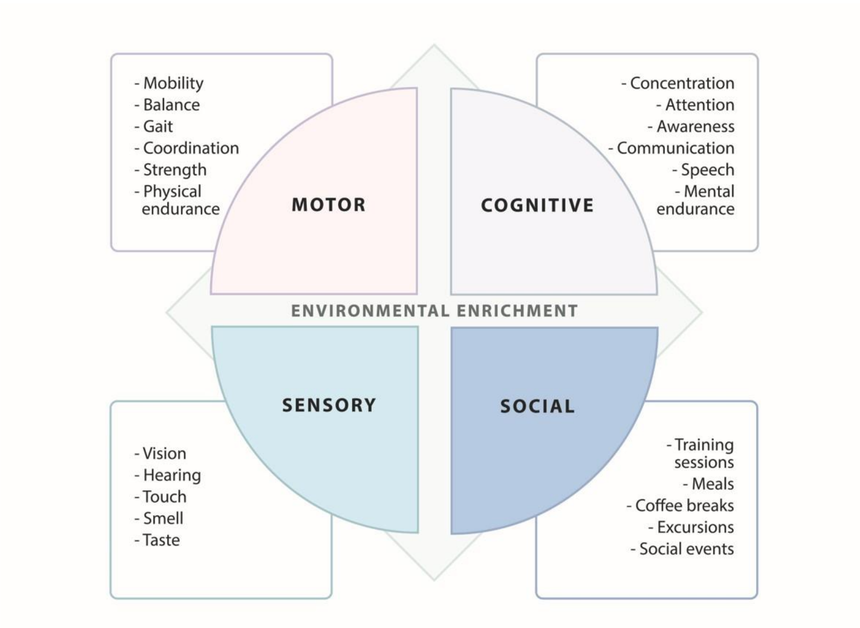

Figure 5. The different components of the ETT program

3.2.2 Baseline phase

The intervention was preceded by a baseline phase of usual care (UC) for 3 weeks, which served as a control in study I, and as phase A1 in study III. During the 3-week baseline phase, the participants were allowed to continue their regular treatment for a maximum of 3 hours per week (e.g. outpatient physiotherapy, occupational therapy, or SLT). They were advised not to start any new rehabilitation or therapy during this phase and were also asked to record all rehabilitative activities performed during the baseline phase.

Figure 6. Examples of the physical environment in the ETT-program.

3.3 Measures

In study I, the participants were assessed at five time points by a physiotherapist: 3 weeks before the intervention, immediately before and immediately after the intervention, and 3 and 6 months after the intervention. The physiotherapist was independent and had no prior relation with the rehabilitation centre or the participants. The first assessment in study I, and all test in the gait laboratory in study III took place in Sweden. The assessments before and after the intervention were done by the same physiotherapist at the rehabilitation facility in Spain. The 3-month follow-up included established patient-reported outcome measures, assessed with questionnaires that were sent by postal mail to participants, and we also tried to maximize the responses by telephone and postal reminders. The 6-month follow-up took place at the two Swedish assessment sites (Danderyd Hospital and Clinical Trial Center (CTC-centrum för klinisk prövning/Sahlgrenska University Hospital) and included the whole assessment battery. A schematic overview of the flow of the four included studies is described in figure 7.

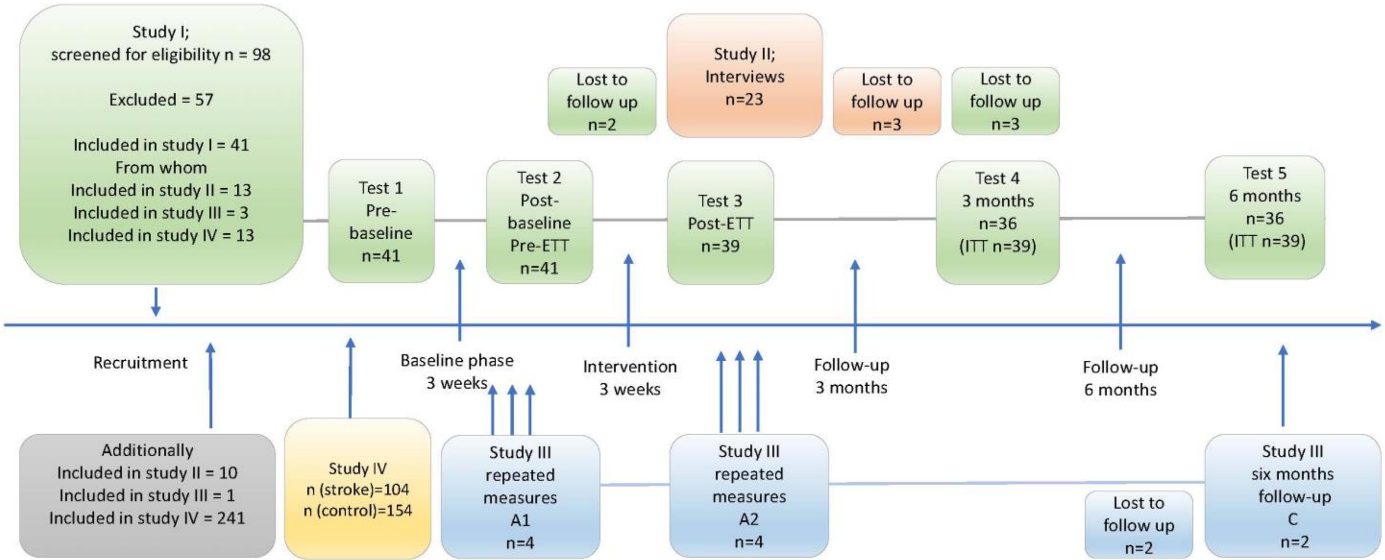

Figure 7. Flowchart of the studies included in the thesis. Study I in green. Study II in red, study III in blue and study IV in yellow.

3.2.1 Demographic data

The characteristics of study participants were age, gender, time since stroke, stroke type and affected hemisphere. These measures are classified as *personal factors*, according to the ICF.

3.2.2 Observer assessed measures

The measures used as screening measures included The Modified Rankin Scale (MRS), used to describe the degree of disability [100] in study I, II, III and IV. MRS measures *activity* and *participation* according to the ICF. Further, as a screening measure, the Montreal Cognitive Assessment (MoCA) [102], was used to measure cognitive performance in study I. MoCA measures aspects of *body function, activity* and *participation* according to the ICF.

Functional motor ability was measured with the Modified Motor Assessment Scale according to Uppsala University Hospital -99 (M-MAS UAS). [101,103] The M-MAS UAS is a Swedish ordinal scaled instrument developed on the bases of Carr and Shephard's Motor Assessment Scale (MAS)[104] [105,106] and the Modified Motor Assessment Scale. [107] [108] The MAS part of muscle tone is removed in the M-MAS and assessment of the intact side is added for upper extremity function. This new scale was first tested for validity and reliability and since 1991, the instrument has been modified and developed twice. In 1995 [101], some modifications in the scale and instructions were made, and in 1999[103]), the general guidelines for the instrument regarding sitting, walking and hand movements were clarified. M-MAS UAS version-95 is tested with respect to both validity and reliability

[101] [109], whereas M-MAS UAS version -99 is only tested with respect to reliability. [103] In Sweden, M-MAS UAS -99 is the most commonly used version both in clinical work and research. [110-112] The M-MAS UAS -99 is designed to assess eight motor components in individuals with stroke: supine to side lying, supine to sitting over side of bed, sitting, sitting to standing, walking, upper arm function, hand movements, and fine motor activities; the latter three components are assessed on both sides. Each item is scored from 1 to 5; the maximum score of 55 indicates optimal movement function. In study I, we combined the first five components into the domain bed mobility and lower limb functional tasks (BM-LL) and the last three components into the domain upper limb function (UL). The M-MAS UAS total score as well as the domains BM-LL and UL were used for statistical analyses. The M-MAS UAS measures *activity* according to the ICF.

Balance was measured with Berg Balance Scale (BBS). [113] Balance ability was assessed using Berg's balance scale (BBS). [113] The test contains 14 elements, where the ability to maintain a position with or without volitional movement, and the ability to change position is assessed. Each element is scored using a five-point scale (0-4), adding up to a total score (maximum 56). To perform the test a manual with assessment questionnaires is required, a standard chair with armrests and one without, or a bed (the same design for all measurements), a stopwatch or a clock with second hands, a ruler, a shoe or slipper, and a step or a footstool with the same step height. Subjects, who achieve a score below 45, may be at increased risk of falling and may therefore need assistance. The test has high validity, reliability and inter-and intra-rater reliability. [114] The Swedish version was prepared in accordance with and approved by the author of the original test. [115] The Berg balance scale measures *body function* and *activity* according to the ICF.

Measures of gait was assessed with the 10-meter walk test (10MWT maximum speed and comfortable speed. [40,116,117] In study IV the 30-meter walk test (30MWT maximum and comfortable speed) was used for the community-dwelling controls. [118]
The tests are performed on a 10- or 30-meter distance marked by tape on the floor of a spacious gym. The subject is asked to walk either in their comfortable speed or as quickly as possible, starting behind one tape and finishing after the other. A walking aid (cane, 4-point cane or Nordic walking stick) and/or orthoses (Ankle-foot-Orthosis, AFO) were allowed if needed. If the subject used a walking aid or orthosis, all tests was performed with the same circumstances at all test occasions. The tests are considered to have high reliability and low variability in interrater-reliability and test-retest. [117-119]10MWT and 30MWT measures *activity* according to the ICF.

Distance walked during 6-minutes was measured using the 6-m walk test (6MWT) [120]. The test measures the maximum distance a person can walk for six minutes and is a modification of the 12-minute walk / run test, originally developed by Cooper [121]. According to ICF, the test measures the *level of activity*.

Gross manual dexterity was assessed with the Box and Blocks Test [122], The test is made up of a box with a partition directly in the centre creating two equal sides. A number of small wooden blocks are placed in one side of the box. The subject being tested is required to use the dominant hand to grasp one block at a time and transport it over the partition and release it on the opposite side. The subject is given 60 seconds in which to complete the test, and the number of blocks transported to the other side is counted. The test is then repeated with the non-dominant hand. The Box and Blocks test measures gross motor speed and has good reliability and validity. [123] [122] The test measures *activity* according to the ICF.

Maximum isometric grip strength was assessed with a JAMAR dynamometer. [124] JAMAR has good reliability [124] and validity [125]. The subject is asked to sit down in an ordinary chair but with the underarm resting on a table and the dynamometer in the hand with the wrist in a neutral position between pronation and supination. The start position is with the arm adducted to the torso and the elbow angle at 90°. The subject is then asked to press as forcefully as possible with a cylindrical grip for 3-5 seconds. The force in Newton (N) is registered and two trials are recorded with three minutes rest in between [126] . The test measures *body function* according to the ICF.

3.2.3 Patient Reported Outcome Measures

Confidence in task performance was assessed with the Swedish modification of the Falls Efficacy Scale (FES). Perceived confidence in task performance was measured using the FES measures an individual's perceived confidence in performing 13 common daily activities without falling. The scale is divided into two sub-scales, one of which consists of the personal activities of daily living (personal ADL) (Activity 1-6) and the second covers the activities of daily living, (instrumental ADL) (Activity 8-13). Activity 7 (walking up and down the stairs) is considered an intermediate activity but is included in the total FES score. Self- efficacy in performing each task without falling is estimated on a visual analogue scale from 0 (not confident at all) to 10 (completely sure), giving a possible maximum score of 130. FES has been tested in terms of reliability [127] and validity [128]. The test measures *activity* and *participation* according to the ICF.

Life satisfaction was assessed with Life Satisfaction Checklist (LISAT-9), which is used for measuring general quality of life. [129,130] The nine questions address general life satisfaction and satisfaction in eight areas of life, including vocational and employment situation, economy, leisure time, social life, sex life, the basic ability to care for oneself, family and partner relationships. There are norm values available from a Swedish population aged 18-64 years. [131] The test is placed in the *activity* and *participation* level according to ICF. Further, aspects of *environmental* and *personal factors* are assessed.

Effect of fatigue in ADL was measured with the Fatigue Impact Scale (FIS). [132] FIS contains 40 statements divided into three dimensions: a physical, a cognitive and a psychosocial dimension. The physical and the cognitive parts contain 10 statements each, and the psychosocial part consists of 20 statements. Each item is estimated from 0 (no problem) to 4 (very severe problems). Questions about physical fatigue measures how physical activity is experienced. The cognitive component focuses on memory and attention and the psychosocial dimension deals with work and social activities (including family-related activities). FIS has demonstrated good reliability and validity [132]. The test measures *body function* (physical and cognitive subscale) and *participation* (psychosocial subscale), according to ICF.

Depression was measured with the Montgomery Åsberg Depression Rating Scale (MADRS). [133] MADRS contains a series of statements about how one may feel in various respects and highlights the symptoms typical of depression. The nine items express varying degrees of discomfort, from the absence of discomfort to the maximum stated discomfort. Each item can yield a maximum of 6 points, totaling a maximum of 54 points. MADRS has shown good validity and reliability. [133] The test measures *body function* according to the ICF.

Health-related quality of life (HRQoL) was assessed with the EuroQol five-dimensions questionnaire (EQ5D 3L). [134] The EQ5D is a standardized self-assessment questionnaire about health-related quality of life. The EQ5D is based on five dimensions: 1) mobility, 2) self-care, 3) usual activities, 4) pain/discomfort and 5) anxiety/depression. For each dimension the degree of difficulty is estimated on three levels. For each condition there is a weight that indicates the corresponding level of quality of life. Self-assessment of perceived health is also expressed on a 20 cm long vertical visual analogue scale where the endpoints are labeled 'Best imaginable health state' and 'Worst imaginable health state'. A body of literature presents data on reliability and validity of the EuroQol in population-based studies and studies of various diseases, including stroke. [135] The test measures *activity* and *participation* according to the ICF.

3.2.4 Kinematics and spatiotemporal gait parameters

Advanced analysis of gait patterns and components of gait was performed at the Orthopaedic Research Unit at Sahlgrenska University Hospital, Gothenburg, Sweden. The gait analysis was performed using an instrumental gait analysis system (Qualisys AB, Göteborg, Sweden). The subject, wearing shorts or underwear, was instructed to walk independently without shoes, orthoses or assistive walking devices until 3–10 trials were registered. In order to detect the participant's movements, 35 reflective markers were placed on well-defined anatomical landmarks on the skin with double-sided adhesive tape (Figure 8). The participant was asked to walk in a comfortable speed approximately 10 meters straight across the calibrated volume in the gait laboratory. A total of 12 cameras (Oqus 4) simultaneously recorded the refection of the markers on the body during the assessment. This enabled analysis of spatiotemporal gait parameters and lower limb kinematics. [136-141] Calculations of symmetry between affected and unaffected limb was also performed. In order to calculate spatiotemporal variables and kinematics Visual 3D™ (C-Motion, Inc., Germatown, USA) software was used (Figure 8). [136-141] The analysis of gait kinematics measures *body functions/structures* and *activity* according to the ICF.

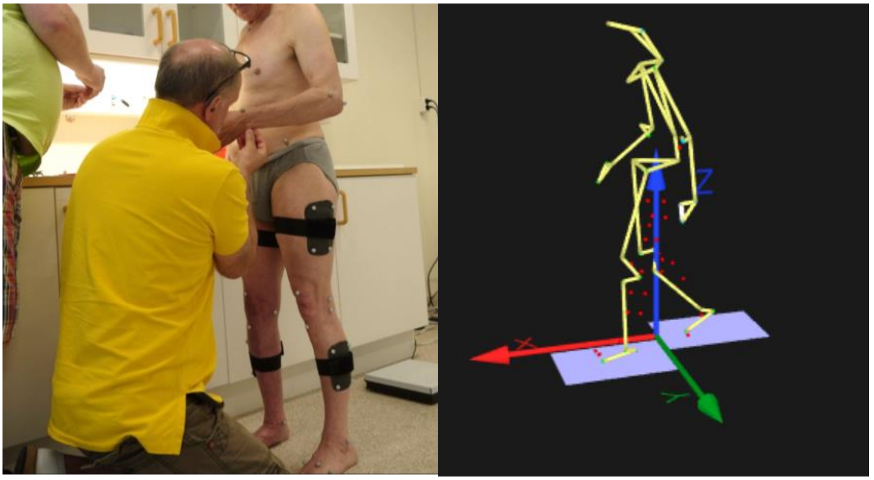

Figure 8. The photograph to the left shows the physiotherapist applying reflect markers on anatomical landmarks on one study participant. The figure to the right depicts the 3-D-model in the Virtual 3D-software.

3.2.5 Qualitative methods

In study II, the focus group interviews were analysed using content analysis. When research theory on a subject or phenomenon is limited, as in study II, the inductive approach is preferable. [142] The inductive analysis approach refers to a systematic procedure that primarily use detailed readings of raw data to derive codes, concepts (categories), themes, or a model through interpretations made from the raw data. [142,143] Baxter and Krippendorff argue that content analysis is suitable for analyzing communication about individuals' experiences. Further, they describe that content analysis may capture the complexity of interventions. [39, 40] The focus group interviews were semi-structured and conducted in groups of 3-5 individuals. The focus groups were carried according to the description of Kreuger and Casey. [144] A semi-structured interview guide was used, described in Figure 9. The questions in the guide were used as starting points for the discussion, and as the discussion went further, additional questions were raised. The interviewer tried not to push the conversation in any direction if the subjects themselves raised a topic. Data were not analyzed until all interviews were performed. The interviews were recorded and transcribed and the content was analyzed using the steps described by Graneheim and Lundman. [41] First, one of the authors listened to each interview several times to get a general idea of the data content and then scrutinized the transcript to identify meaning units—one or more sentence or paragraphs of a narrative. The meaning units were then condensed, interpreted, and coded. Next, the co-authors read the initial analysis, discussed the condensations and codes, and modified them if needed. The codes were then analyzed and grouped into subcategories. After reading the analysis as a whole, the authors discussed and compared the findings until agreement was reached. Next, categories were expressed from the subcategories, and an overall theme was extracted. [41] The interviews in their original form served as a reference point throughout the analysis, and the results were reported according to the Consolidated Criteria for Reporting Qualitative Research (COREQ). [145] The data from the interviews describes *activity* and *participation*, but also envi*ronmental* and *personal factors*, according to the ICF.

Questions included in the semi-structured interview guide:

- Describe with your own words how you experienced participating in the ETT program.
- Has the ETT program affected your physical/psychological/social abilities? If so, in what way?
- Has the ETT program meant anything to you in your relationships with other people? If so, in what way?
- Has the ETT program affected your choice of activities in life? If so, in what way?
- Has the ETT program affected your life situation in any way? If so, in what way?
- Has the participation in the ETT program affected your mood, quality of life, or confidence in the future? If so, in what way?

Figure 9. Interview guide used in the semi-structured focus group interviews.

3.2.6 Statistics

Study I. Demographics and baseline characteristics were summarized with descriptive statistics. The data were not normally distributed, and therefore the Wilcoxon signed-rank test and sign test were used. The intention-to-treat (ITT) principle was used and missing data from the 3 and 6 months follow up were replaced with the last observation carried forward (LOCF) approach. Effect sizes were calculated using the Standardized Response Mean (SRM) (mean post-ETT – mean pre-ETT) / SD (post-ETT – pre-ETT).[146] To assess whether baseline characteristics (gender, age, time since stroke, stroke type, stroke localization, MRS, MoCA, balance [BBS] and motor ability [M-MAS UAS] -at baseline) and dose-related aspects of rehabilitation activities (the number of therapist-led and self-managed rehabilitation hours during the baseline phase and the number of physiotherapy hours during the ETT program) could predict functional gains from the ETT program, an univariate correlation and a multiple stepwise regression analyses were performed. Mann-Whitney U-test was used to assess the relation between dichotomous and continuous variables. Spearman's test was used to assess correlation between two continuous variables, and the Jonckheere-Terpstra test was used to calculate correlations between ordered categorical data (MRS), with the change of M-MAS UAS during ETT as the dependent variable. The variables significant at 0.10 level were included in a multiple stepwise linear regression analysis, which was corrected for heteroscedasticity.

Study III. For the kinematic data, maximum and minimum joint angles was extracted for each gait cycle. The mean of all maximum and minimum values was then calculated for each assessment timepoint. Excel was used for summarizing data and for calculation of maximum and minimum value for each measure, and SPSS was used for statistical analyses. A semi-statistical approach was applied using visual inspection of graphs and consideration of statistical significance – the two standard deviation band (TSDB) method. As suggested by Ottenbacher [147], treatment effects were considered obvious from visual inspection of the data. The method uses the standard deviation of baseline data (phase A1), by drawing bands on the graphs as horizontal lines of 2 SD from the mean level at baseline (phase A1). A significant change has occurred if at least two successive observations in one phase points fall outside the 2 SD range from the previous phase. [148] Since the TSDB-method is not applicable for single assessments, the results of the 6 months assessment for each subject was presented in the text and plotted.

Study IV. To investigate whether maximum gait speed was dependent on comfortable gait speed and characteristics in the two groups, Spearman's test was used to assess univariate correlation between two continuous variables (gait speed, age, time since stroke). The strength of the relationships was classified as poor ($r<0.30$), fair ($0.30 \leq r<0.60$), moderate ($0.60 \leq r<0.80$), very strong ≥ 0.80 or perfect =1. [19] The statistical difference between groups with respect to the correlations was evaluated using Fisher's r to z transformation. The Mann-Whitney U-test was used to assess the relation between dichotomous (gender) and continuous variables (gait speed), and the Jonckheere-Terpstra test was used to assess the relationship between ordered categorical data (MRS), and maximum gait speed. Independent samples t-test was used for comparison of gait speeds between groups. The variables significant at 0.10 level were included in a stepwise linear regression analysis.

All analyses in study I, III and IV were done with SPSS v. 22.0 (IBM, Armonk, NY, USA) and SAS software version 9.4 (SAS Institute, Cary, NC, USA) and the Cocor package: A Comprehensive Solution for the Statistical Comparison of Correlations. [149] in study IV. All tests of significance were two-sided; $P < 0.05$ was considered statistically significant. Values are reported as mean ± SD.

4. Ethical Considerations

Ethics approval was granted by the Regional Ethical Review Board in Gothenburg, Sweden (Ref number: 549-12), and the study was conducted in accordance with relevant ethical guidelines. Written informed consent was obtained from each participant before inclusion in the studies and all participants were told they could withdraw from the study at any time. The results from the interviews were presented at a group level to ensure confidentiality. The studies are registered at ClinicalTrials.com. All included studies complies with the Declaration of Helsinki.

5. Results

This thesis contains four papers from three study cohorts. This section summarizes the main results of the thesis (Study I-IV). Detailed results are provided within each publication and manuscript.

5.1 Demographics

Recruitment of participants in the main study (I) took place between September 1, 2012, and November 30, 2016. Some of the 41 participants who were included in study I were also part of the study cohorts in study II and III. In study IV, cohorts from 3 different studies were merged, including 17 participants from study I (those over 60 years) (Fig. 4). The recruitment for the study participants in study IV that were merged to the main study cohort took place between the years 2008 and 2012. Demographics and baseline characteristics of the participants included in this thesis work are described in the previous Table 3.

5.1.1 Activities during baseline phase

In study I, all 41 participants participated in the 3-week baseline phase. During this phase, 26 of 41 (63%) reported that they had performed a mean of 5.6 ± 3.8 hours of therapist-led rehabilitation activities. Furthermore, 24 reported that they had been engaged in self-managed rehabilitation activities (for example gait training, home exercise programs and stationary bike training) with a mean of 7.7 ± 4.2 hours. All 41 participants were assessed at test 2, the second baseline assessment, and begun the 3-week ETT program.

5.1.2 Adverse events and missing data

In study I, 3 participants had adverse events and discontinued the assessments after the post-ETT assessment; one had an infection that started during ETT, one fell and suffered an arm fracture during the ETT, and one participant had a myocardial infarction at home before the 3 months follow up. Two participants had a protocol deviation; one did receive extended SLT (additionally 1.5 hours per day) and one became ill during the intervention period, but after he got better he did resume the ETT. In study II, 23 participants in seven focus groups were included in the study and interviewed, but only six groups and 20 participants were included due to technical recording and sound problems in the fifth interview. In study III, two of the four subjects did not participate in the 6-month follow-up, owing to a lack of time and the long journey it would have entailed.

5.2 Motor findings

No motor change was seen during the baseline phase.

The motor findings of the analyses after the end of the ETT program are described in Table 5. Immediately after the intervention, significant gains in functional motor ability were shown (2.3-point improvement in the M-MAS UAS, $p<0.001$) [Figure 10]. Further, gains in balance and gait, was shown by a 5.0-point improvement on the BBS ($p<0.001$) (Figure 11) and an average increase in comfortable gait speed in 10MWT from 0.64 m/s to 0.78 m/s ($p<0.001$) as well as maximum gait speed in 10MWT from 0.87 m/s to 1.11 m/s ($p=0.001$) and finally, an increased distance walked over 6 minutes of 26.3 m in ($p<0.001$). The intervention improved manual dexterity somewhat but not grip strength. (Table 5).

The 6-month follow-up demonstrated sustained improvement in functional motor ability measured by M-MAS UAS (figure 10) and continued improvement in balance relative to participants' baseline ability on BBS (5.7 points) (Figure 11). The significant improvements in comfortable and maximum gait speed were sustained, as were improvements in the distance walked over 6 minutes. The small change in manual dexterity seen after ETT was lost at the 6-months follow up.

The correlational analyses, investigating whether baseline characteristics and amount of training during both the baseline phase and during ETT showed a significant negative correlation between baseline balance and the outcome of M-MAS UAS (r=-0.42, p=0.0071). Baseline motor ability according to M-MAS UAS and baseline disability according to MRS was shown to be significantly correlated to the outcome of M-MAS UAS (r=-0.35, p=0.029 and r=0.37, p=0.022, respectively). Furthermore, a univariate correlation between hours of therapist-led activities during baseline phase and the M-MAS UAS outcome was also detected (r=0.46, p=0.0084). When including these four variables in to a multiple stepwise regression analysis, no significant and independent correlation could be detected. No other baseline characteristics (stroke type, gender, age, time since stroke, cognition, hours of self-managed training during baseline phase and amount of physiotherapy during ETT) influenced the outcome of M-MAS UAS.

Table 5. Outcome Measures at ETT-Pretest (Test 2) and ETT-Posttest (Test 3) and 6-Month Follow-up (Test 5) Abbreviations: BBS: Berg Balance Scale; BBT: The Box and Block Test; BM: bed mobility; LL: lower limb functional tasks; M-MAS UAS: Modified Motor Assessment Scale (Uppsala University Hospital); 6MWT: 6-minute walk test; SRM:, Standardized Response Measure; 10MWT: 10-meter walk test, UL: upper limb function.

		ETT-pretest (test 2)		ETT-posttest (test 3)				6 Months (test 5)			
Outcome measures	n	Mean (SD)	Median (min-max)	Mean (SD)	Median (min-max)	*p*	*Effect size (SRM)*	Mean	Median (min-max)	*p*	*Effect size (SRM)*
M-MAS UAS (0-55)	39	38.4 (8.9)	38 (22-55)	40.7 (8.2)	40 (25-55)	<0.001	1.28	40.8 (7.6)	41 (24-55)	<0.001	0.92
M-MAS UAS UL (0-30)	39	18.5 (4.6)	17 (13-30)	19.5 (5.0)	17 (14-30)	<0.001	0.80	19.5 (4.6)	18 (15-30)	<0.001	0.76
M-MAS UAS BM+LL (0-25)	39	19.9 (5.4)	22 (8-25)	21.2 (4.6)	23 (11-25)	<0.001	0.81	21.4 (4.13)	23 (9-25)	<0.001	0.66
6MWT, meters	36	212.2 (164)	160 (0-555)	238.5 (165.8)	195 (27-555)	<0.001	0.94	234.3 (163.8)	173 (32.585)	<0.001	0.64
10MWT, m/s											
Comfortable speed	35	0.56 (0.38)	0.48 (0.06-1.33)	0.69 (0.42)	0.68 (0.06-1.47)	<0.001	1.01	0.68 (0.43)	0.53 (0.09-1.49)	<0.001	0.80
Fast speed	32	0.78 (0.52)	0.73 (0.07-1.61)	1.01 (0.67)	0.91 (0.11-2.50)	<0.001	0.70	0.93 (0.63)	0.78 (0.12-2.44)	0.001	0.58
BBS (0-56)	39	37.3 (18.3)	43 (3-56)	42.3 (16.1)	49 (4-56)	<0.001	1.25	43.1 (15.2)	49 (4-56)	<0.001	1.01
BBT n/min	17	11.8 (14.3)	7 (0-46)	13.1 (13.7)	0 (0-44)	0.028	0.61	11.5 (14.9)	0 (0-45)	0.82	-0.08
Jamar maximum grip, N											
Affected hand	39	10.9 (13.6)	7 (0-59)	12.1 (14.7)	9 (0-63)	0.11	0.20	8.6 (10.5)	5 (0-52)	0.33	-0.23
Nonaffected hand	39	37.2 (13.5)	36 (3-67)	36.4 (11.8)	36 (9-67)	0.565	0.11	36.8 (11.7)	36 (12-64)	0.07	0.00

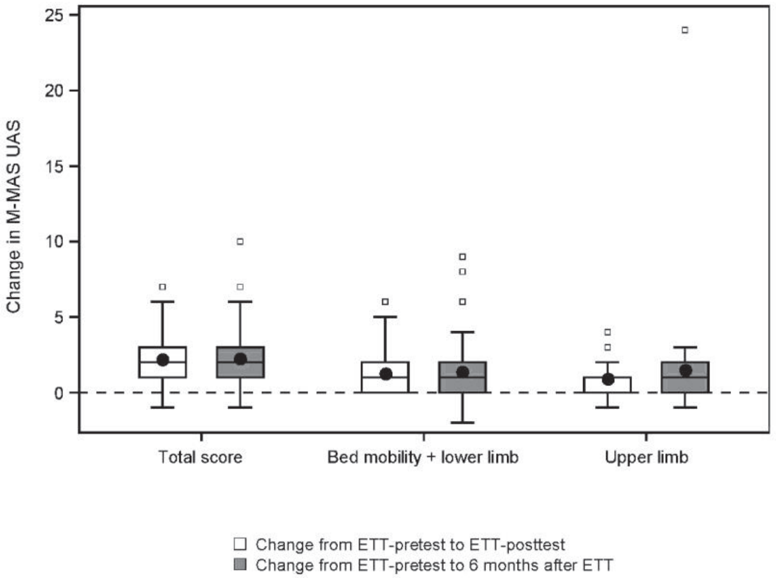

Figure 10. Change in M-MAS UAS in total score to the left, bed mobility + Lower limb functional tasks in the middle, and upper limb to the right. Change from ETT-pretest to ETT-posttest in white and 6 months after ETT in grey.

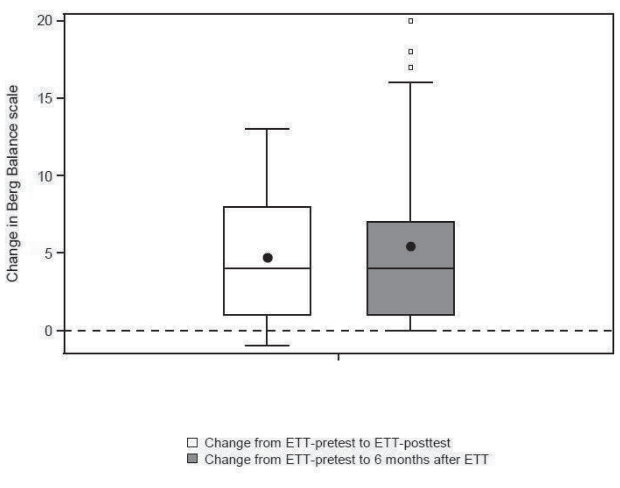

Figure 11. Change in the Berg Balance Scale from from ETT-pretest to ETT-posttest in white and to 6 months after ETT in grey.

The results of the in-depth study of four ETT participants' kinematics, symmetry and spatiotemporal parameters measured in an advanced three-dimensional gait laboratory are presented in study III. The results varies among the participants.

Subject 1 had increased dorsiflexion during stance (from -1.9° in phase A1 to 9.4° in phase A2, and to 17.1° at C- the 6-month follow-up). He also had an increased knee flexion during swing in both the affected knee (from 48.7° to 52.3° and 53.1° at 6 months) and the non-affected knee (from 42.4° to 45.6°, and 46.2° at 6 months). Subject 1 also showed a significant increase in gait speed (from 0.77 to 1.0 m/s) and a decreased in DLS time (0.25 to 0.22 s), after ETT. The increase in gait speed was sustained at 6 months (1.0 m/s), but not the reduction in DLS. Further, an increase in stride length (0.77 m in phase A1 to 0.94 m in phase A2), which was sustained at the 6-month follow-up (0.93 m), and increased cadence in both the affected leg (from 120 to 125 steps/min) and the unaffected leg (from 123 to 130 steps/min). At 6 months (phase C), these gains were sustained (130 steps/min in both legs). Symmetry index calculations showed significant improvement of step length for subject 1.

Subject 2 had no significant improvement in kinematic or spatiotemporal gait variables after ETT. However, swing time for subject 2 was slightly, but significantly more symmetrical after the intervention (symmetry index from 1.44 to 1.37).

Subject 3 had no significant kinematic changes on the affected side but increased maximum knee-flexion during swing on the non-affected side (from 26.8° to 33.6°) after ETT. Further, subject 3 had a significant increase in gait speed (0.19 to 0.35 m/s), a slightly but significantly narrower stride width (from 0.20 to 0.19 m), and increased stride length (from 0.46 to 0.64 m).

Subject 4 had no significant kinematic changes but had a significant increase of cadence in the affected limb (108 to 118 steps/min) after ETT. This increase was not sustained at the 6-month follow-up, C (107 steps/min).

A selection of the graphical interpretation of the two standard deviation band method in two of the four subjects are described in figure 12.

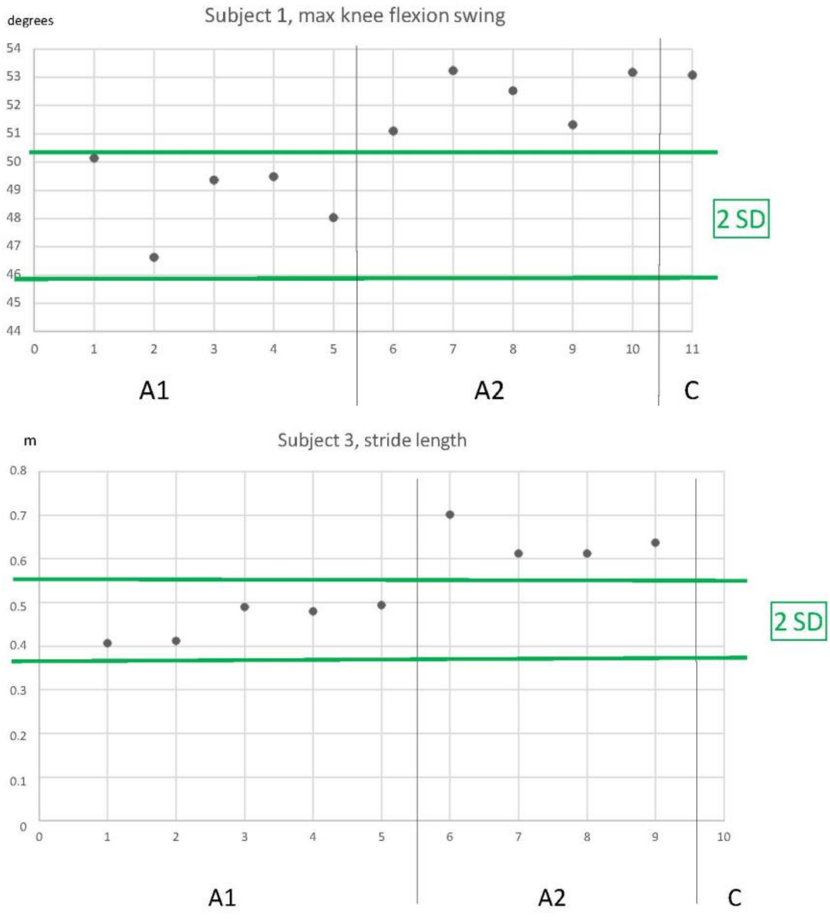

Figure 12. Selection of the graphical interpretation according to the 2 SD (standard-deviation) band method. The green lines limits the +- 2SD bands. A1, A2 and C describe the phases.

5.3 PROMs findings

5.3.1 Baseline phase findings

The measures during the baseline phase were stable. The only significant change between test 1 and 2 was a decrease in HRQoL, measured with the EQ-5D usual activity dimension (mean change 0.23 [SD 0.62] p=0.029).

5.3.2 Post-ETT

An overview of the changes in results from pre-ETT (test 2) to post-ETT (test 3) is presented in table 6 and 7. Confidence in the performance of ADL tasks measured with the FES improved, both regarding total score (p=0.002) and instrumental ADL score (p=0.011) as well as personal ADL score (0.011). The rating of life satisfaction improved (p<0.001) whereas the levels of depression (0.001) and fatigue (cognitive 0.004, social 0.007 and physical 0.011) were significantly reduced after ETT. The EQ-5D scale showed improvements in mobility (p=0.012), anxiety/depression (p=0.022) and the overall health status (p=0.034). However, the overall health improvement had a smaller effect size (SRM=0.31).

5.3.3 Three months follow up

The 3-month postal evaluation (test 4) showed sustained improvement in confidence in the performance of instrumental ADL tasks (p=0.002) and the perception of life satisfaction (p=0.032), as well as sustained reductions in cognitive fatigue (p<0.001), physical fatigue (p<0.001) and depression (p=0.003). Sustained improvement was also shown in patient-reported mobility (p=0.016), depression (p=0.039), and overall health status (p=0.038) measured by EQ-5D. The evaluation at 3 months also showed additional improvement in ADL according to the EQ-5D usual activity subscale dimension (p=0.001).

5.3.4 Six months follow up

An overview of the changes in outcome measures from pre-ETT (test 2) to 6 months post ETT (test 5) are presented in table 6 and 7. The significant improvement of participants' confidence in task performance was sustained at the 6 months-follow (FES total score p=0.003, instrumental ADL p=0.012 and personal ADL p=0.016 [effect sizes according to SRM= 0.44-0.55]). Further, the increase in life satisfaction as measured by LISAT was sustained (p=0.016). The 6-month follow-up also showed sustained improvement of all three aspects of fatigue (cognitive p=0.005, social p=0.022 and physical 0.001), and depression (p<0.001). The demonstrated gains in patient-reported overall health status (0.032) measured by EQ-5D were also sustained, with the exception of the mobility subscale of EQ5D (p=0.29). The analyses at 6 months showed a significant change from the ETT to the 6-month follow-up in the usual activities domain measured by the EQ-5D (p=0.007) (table 7).

Table 6. Changes in Outcome Measures Between ETT-Pretest (Test 2) and ETT-Posttest (Test 3) and Between ETT-Pretest (Test 2) and 6-Month Follow-up (Test 5) Abbreviations: LISAT: Life Satisfaction Checklist, MADRS: Montgomery Åsberg Depression Rating Scale, EQ5D VAS: European Quality of Life five-dimension questionnaire; VAS, visual analogue scale of perceived overall health. The changes from ETT-pretest to ETT-posttest/6 months post-ETT were analyzed with the Wilcoxon signed-rank test.

		Change ETT-pretest (test 2) to ETT-posttest (test 3)				Change ETT-pretest (test 2) to 6 Months follow up (test 5)			
Outcome measures	n	Mean	Median (min;max)	*p*	*Effect size (SRM)*	Mean	Median (min;max)	*p*	*Effect size (SRM)*
Falls Efficacy Scale, points									
Total	39	11.5 (19.9)	8 (-20;61)	0.002	0.58	10.7 (19.3)	11 (-29;51)	0.003	0.55
Instrumental ADL	39	4.9 (10.0)	2 (-13;26)	0.011	0.49	4.4 (10.1)	2 (-21;20	0.012	0.44
Personal ADL	39	4.7 (10.5)	2 (-14;32)	0.011	0.46	4.8 (10.5)	3 (-12;31)	0.016	0.46
LISAT, total points	36	2.9 (4.1)	2 (-5;15)	<0.001	0.71	2.4 (5.2)	1.5 (-8;15)	0.016	0.46
Fatigue Impact Scale, points									
Cognitive	36	-2.4 (4.24)	-2 (-13;5)	0.004	-0.56	-3.7 (6.9)	-2 (-29;7)	0.005	-0.53
Social	32	-4.7 (8.2)	-2 (-27;9)	0.007	-0.57	-6.0 (13.2)	-3 (-44;16)	0.022	-0.45
Physical	36	-2.1 (5.0)	-2 (-13;10)	0.011	-0.42	-4.7 (8.0)	-2 (-27;9)	0.001	-0.59
MADRS, points	39	-2.9 (4.6)	-4 (-12;10)	0.001	-0.63	-3.4 (5.1)	-2 (-19;5)	<0.001	-0.67
EQ5D VAS	38	4.4 (14.1)	6 (-40;30)	0.034	0.31	5.1 (14.7)	4.5 (-30;30)	0.032	0.35

Table 7. Changes in EQ5D subscales between ETT-Pretest (Test 2) and ETT-Posttest (Test 3) and Between ETT-Pretest (Test 2) and 6-Month Follow-up (Test 5) Abbreviations: EQ5D: European Quality of Life five-dimension questionnaire; The changes from ETT-pretest to ETT-posttest/6 months post-ETT were analyzed with the sign test.

EQ5D	*n*	*n (%) change ETT-pretest–ETT posttest*		*p*	*SRM*	*(%) change ETT-pretest–6 months*		*p*	*SRM*
Mobility (0–2)	39	Improved	10 (25.6%)	0.012	-0.48	Improved	6 (15.4%)	0.29	-0.23
		Deteriorated	1 (2.5%)			Deteriorated	2 (5.1%)		
		Ties	28(71.8%)			Ties	31 (79.5%)		
Self care (0–2)	39	Improved	2 (5.1%)	1.0	0.07	Improved	4 (10.3%)	0.75	0.10
		Deteriorated	3 (7.7%)			Deteriorated	6 (15.4%)		
		Ties	34 (87.2%)			Ties	29 (74.4%)		
Usual activities (0–2)	39	Improved	11 (28.2%)	0.210	-0.28	Improved	13 (33.3%)	0.007	-0.50
		Deteriorated	5 (12.8%)			Deteriorated	2 (5.1%)		
		Ties	23 (58.9%)			Ties	24 (61.5%)		
Pain/discomfort (0–2)	39	Improved	7 (17.9%)	0.34	-0.20	Improved	7 (17.9%)	0.77	-0.09
		Deteriorated	3 (7.8%)			Deteriorated	5 (12.8%)		
		Ties	29 (74.3%)			Ties	27 (69.2%)		
Anxiety/depression (0–2)	39	Improved	11 (28.2%)	0.022	-0.43	Improved	8 (20.5%)	0.39	-0.19
		Deteriorated	2 (5.1%)			Deteriorated	4 (10.3%)		
		Ties	26 (66.7%)			Ties	27 (69.2%)		

5.3 Qualitative findings

5.3.1 Main categories

The informants´ diverse experiences of partaking in the ETT program could be identified in three main categories; ***The program – different and hard, My body and mind learn to know better,*** and ***The need and trust of others.***

5.3.2 Subcategories

Two to three subcategories within each category could be identified. The subcategory ***Hard, innovative therapy*** (subcategory of *The program – different and hard*) describes how strenuous the training was. In this category, the informants described how the rehabilitation team increased the level of difficulty when the participants were able to perform a task. One subject put it like this:

"The philosophy is that the things that are easy, that you know how to do, those things you don´t have to practice. But the things that are hard, are the most important to manage."

The subcategory ***Unlike rehabilitation at home*** (subcategory of *The program – different and hard*) describes that the content of the intervention was perceived more fitted and individualized as compared to previous rehabilitative involvements at home. One subject stated:

"The big difference is, I think, that it´s very customized here. Adapted for each and every one. What you got at home was a standard program. One should

kick a little bit there and pull a little here and then it´s supposed to be fine. Here it´s totally different for everyone, or everyone that´s been here."

The respondents' experience of training in a totally different environment than the regular care they had experienced at home formed the subcategory: ***The significance of the environment*** (subcategory of *The program – different and hard*). The experience of being in a warm climate in a nice environment close to the ocean was described:

"This clearly means a lot. Positive surroundings. I only see the colours, the ocean… Most of us have been ill for a long time, and have perhaps not experienced many other things during this time. Maybe you´ve had to give up travelling or other things that you used to do."

The subcategory ***Perceived functional improvement*** (subcategory of *My body and mind learn to know better*) described the experience of increased movement functions and/or abilities:

"There have been a lot of things that one haven´t been able to do upon the arrival… that has gone very well the last week. Maybe not exercises but rather in practice."

In the subcategory ***Experiences of insights and challenges throughout the program*** (subcategory of *My body and mind learn to know better*)**,** the responders described the importance of perceiving the knowledge and understanding of *how* and *why* the rehabilitation was organized and performed the way it was**.** This was described as elemental among participants in order to motivate themselves to continue the high-intensity training**.**

"It has meant a whole lot to gain knowledge also about how the brain works to keep the motivation and stimulation going and…it is the effort that counts. It has carried me a lot. Hmm, especially when it doesn't work."

The subcategory ***The trust in competence of physiotherapists and rehab personnel*** (subcategory of *The need and trust of others*) described the trust of the rehabilitation staff, that was developed, and that was necessary in order to accept to undertake the intense ETT program. One subject put it like this:

"And that doesn´t mean that the exercises was rather demanding and you thought that... but I knew that she was there (the doctor) and that felt safe in a way."

Along the ETT program, a strong connection grew between the group members. The subcategory ***The group as a source for motivation and feel-good*** (subcategory of *The need and trust of others*) described the inspiration and comfort that meeting with other individuals in the same situation was perceived as.

"And you are sweating and you are crying and you are laughing together, goddammit"

Another factor that was exposed was ***The support from family and relatives*** (subcategory of *The need and trust of others*). Many of the subjects had an accompanying relative and their attendance was described as significant, both to verify the achievements and also to assist in translating some of the functional gains into the home environment.

"It feels good that someone have seen what I have done, bridging over to home..."

5.3.3 Overall theme

From these categories, a main theme was derived; ***It´s hard but possible – but not alone!*** The categories, subcategories and the theme are presented in figure 13.

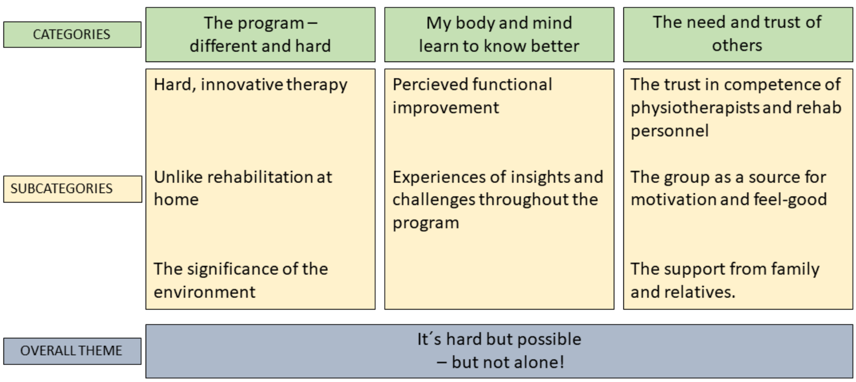

Figure 13. Categories, subcategories and an overall theme

5.4 Gait speed correlation findings

In study IV, we showed that maximum gait speed in individuals with chronic stroke with mild to moderately severe disability can be predicted by the comfortable gait speed, with the coefficient 1.41. The correlation was very strong with a Spearman’s rho=0.929, and $p<0.001$.

When comparing the linkage between comfortable and maximum speed in the stroke cohort with the linkage between these variables in the community-dwelling older population, it was shown to differ significantly ($p<0.001$, Fishers $z=-15.81$). The correlation coefficient in the control group was found to be 1.20 ($r=0.66$; $p<0.001$). The variables age, gender and time since stroke were shown to not affect this relationship in the stroke group. However, the degree of disability was negatively correlated with maximum gait speed in the stroke group, but not when included in the multiple analysis. In the community-dwelling older population, younger age was negatively correlated with both comfortable gait speed ($r=-0.36$; $p<0.001$) and maximum gait speed ($r=-0.39$; $p<0.001$) and being a woman had significant negative association ($p=0.001$) with maximum gait speed. After correcting for gender and age, the coefficient was found to be 1.07. (fig 14)

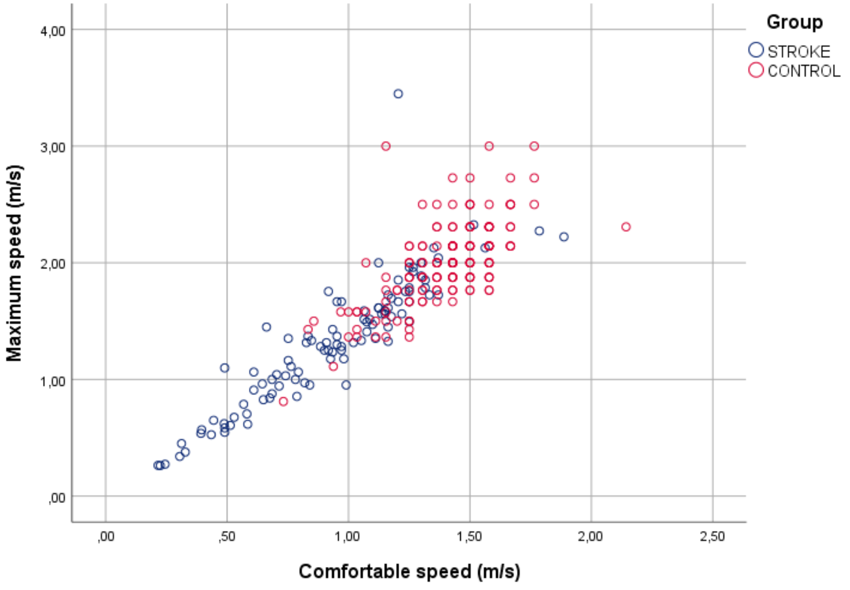

Figure 14. Scatterplot for the association between comfortable speed and maximum speed in individuals with stroke (blue) and community-dwelling older controls (red)

6. Discussion

The studies included in this thesis show that an ETT program including task-oriented therapy in an EE led to gains in motor ability, improved health status and multiple positive experiences despite participants being in a chronic phase after stroke. According to the participants, the ETT program was unique and different as compared to rehabilitation they had previously received. It was more individualized and intense, and they appreciated being in a warm climate in an environment out of the ordinary.

The participants, being in a chronic phase after stroke demonstrated lasting improvements in functional motor ability as measured by M-MAS UAS after partaking in the ETT program. The M-MAS UAS was selected as a primary measure since it measures motor ability in a wide range of stroke deficits. The minimal detectable change (MDC) and the minimal clinically important difference (MCID) of the scale, however, remain to be established. The findings in study I and III, show that ETT increased gait speed, balance and confidence in task performance. Confidence in task performance has earlier been described to be related to movement function and observer-assessed balance. [150] These findings are positive, since balance and ability of walking helps protect against secondary complications common after a stroke. [151] In previous studies of populations with chronic stroke, the MDC of balance measured with the BBS was reported to be 2.5, 4.13, and 4.66, respectively [152-154], and the smallest real difference for a single individual was 8%. [154] Study I showed a 5-point increase (13%) in the BBS immediately after the intervention and a 5.5-point increase (15%) at 6 months; results that exceeds the previous described MDC limits.

The risk of falling is twice as high in stroke survivors as in healthy controls of the same age [155], and gait speed is both a significant, sensitive, and reliable marker of deficit severity and community walking ability and a cardinal indicator of post-stroke gait ability and performance. [156] In study I, the mean increases in comfortable and maximum gait speed at intervention completion were 0.14 and 0.24 m/s, respectively. The 6-month follow up showed sustained gait speed improvements, reaching the established level for clinically meaningful change (0.14 m/s). [157] The gains in gait speed in study I are in accordance with the finding that an increase in gait speed enhances the capacity for distance walking needed for community ambulation. [158] According to previously reported figures, the cohort as a whole in study I went from having a severe gait impairment to having a moderate gait impairment [157]. At the same time, the gait speed results showed in study I as well as in study IV suggest that the included individuals in a chronic phase after stroke did not reach the gait speed needed to cross a street in a comfortable manner, but closer to their maximum gait speed.
In study II, the subcategory *perceived functional improvement* attests the participants own experience of the motor improvements. In study III, two of the four subjects showed significant changes in comfortable gait speed.
Post-stroke gait speed is shown to be an important factor for long-distance walking capability,[158] suggesting that the gait speed improvement in study I might be a determinant to the increased distance walked in 6 minutes (26.3 m).

In study IV, we found a relationship between comfortable and maximum gait speed of 1.41 in a group of individuals with chronic stroke. To the best of our knowledge, no previous study has investigated this relationship among individuals with residual disability in the chronic phase after mild to moderately severe stroke in relation to community dwelling older controls. However, our result is comparable with findings by Kollen et al. [159], who studied individuals up to 1 year after acute stroke and found a relationship of 1.32. Bohannon et al. [119] studied this relationship in 20 individuals with subacute stroke and found a linear regression coefficient of 1.40 for comfortable speed versus maximum gait speed. Beaman et al. studied a cohort of individuals with chronic hemiparesis and found that the difference in gait speed (from self-selected to fastest-comfortable) was correlated with self-selected speed. [160] The authors to the Beaman study suggest that assessment of only self-selected speed may not be sufficient to identify impairments not visible at slow speeds in hemiparetic walking, in contrast to the findings by Kollen et al. [159] (suggesting that maximum speed may not necessary to measure, since it can be predicted by comfortable speed). [160] Nevertheless, our findings support the findings from Kollen [159], that therapists can predict the maximum speed by measuring the comfortable speed – and therefore also safely perform gait training at a higher speed than the comfortable speed, regardless of stroke severity, age, gender and time since stroke.

The ICF core sets for stroke describes the domains and the levels of body functions, structures, activities, participation and environmental factors important to measure after stroke.[20] The ICF also describes what a person with a health condition can do in a standard environment (their level of capacity), as well as what they actually do in their usual environment (their level of performance).[19,20] In the literature, the understanding and difference between whether behavioural improvement reflects true recovery or use of compensatory strategies is highlighted. [23,161] Levin et al. describes a model to distinct between recovery and compensation at the body functioning and activity level according to the ICF, but does not use the classification on the participation level of the ICF. This is because on the participation level, discrepancies in the processes of recovery and compensation are harder to detect. [23]

In study I, the measurement of M-MAS UAS, BBS, the gait speed and endurance tests admittedly measures motor ability mainly on an activity level according to the ICF, but it cannot differ between compensation and recovery. Neither can the JAMAR or the NHPT distinguish between recovery or compensation, since they cannot differ between if the performance of the movements are executed in the same manner as it was performed before injury or not.[23] On the other hand, in study I, the PROMs used (EQ5D, FIS, LISAT, MADRS and FES) might measure performance, given that the participants reported their true situation in performance. This might also be confirmed by the qualitative findings in study II highlighting the experience of motor improvement in the category *Perceived functional improvement* as a result of the ETT-program.

The aim of adding a kinematic study to this thesis was to study if the motor improvements we could measure in study I was compensatory or due to true recovery. However, analysing gait in a 3-dimentional gait laboratory measures capacity in gait, not performance, since the test is performed in an environment with very few similarities to the individuals' common environment. Only two of the four studied participants in study III increased their gait speed and parts of their kinematic gait pattern pointing towards possible true recovery in gait pattern for these two individuals. However, generalizations of these results may not be done, due to the small sample size and the study design. Jonkers et al. showed that stroke individuals with low gait function could not increase their gait kinematics and kinetics to increase gait speed because they had already maxed their power output at their comfortable gait speed. [162] These results does not seem applicable on our small study cohort in study III where the two individuals who did not improve in terms of gait kinematics, both were above the limit by Jonkers definition to low functioning. [162] At the same time, one of the improved subjects could be considered an individual in the lower functioning group.

This is more in line with the findings of Jonsdottir et al, meaning that every individual is functionally different and adopts an individual strategy to increase their gait speed. [163]

The degree of movement function, balance, walking capacity, and independence in ADL is shown to be of importance for the perception of HRQoL. [164] This suggests that improved function, mobility, and confidence in task performance in our study cohort may have enhanced the health status and well-being of the participants, as indicated by the significant improvements in multiple health-related outcome measures. During the 6-month follow-up, the results showed a new improvement in the participants rating of usual activities as measured by the EQ-5D, not present at the post ETT-assessment. This might be a consequence continued use of achieved improvements after treatment completion.

Our findings contradict the earlier described view that individuals with stroke reach a recovery plateau after stroke [14,15,165] and are supported by research suggesting that multimodal interventions provide greater benefits to the injured brain [59] and that combining modalities has synergistic effects on stroke recovery. [166,167] Nonetheless, as mentioned before, our motor results cannot differ between true recovery due to plasticity processes and compensatory mechanisms. However, many individuals with stroke lack stimulation and socialization [11], why the social and physical environment might be very important components of the ETT program. The results in study II gives information about components of the program that were experienced as important: *The group as a source for motivation and cheerfulness* and *The significance of the environment.* A strong connection between participants and identification with other group members was shown to be a motivator for partaking in the therapy, also shown in other studies on multimodal enriching group interventions. [88] The use of an outdoor environment might be a way to reintegrate from inpatient to the home community environment. The ETT program was performed in a Mediterranean climate, and as described in study II, the participants experienced this climate as enriching. However, what enriched environment means in terms of climate and surroundings for other individuals, is not known.

A previous systematic review exploring the experience of physical rehabilitation in individuals with stroke showed negative experiences of boredom and frustration and absence of personal goals in the rehabilitation. [168] Increasing activity both within therapy sessions and during free time might improve the results of rehabilitation, according to Luker et al. [168] In study II, the interviews discovered statements of disappointment of previously received rehabilitation. The category *Unlike rehabilitation at home* the participants described the intervention to differ from the rehabilitative interventions they had been given at home. Possible, the ETT program met the needs of the participants that are not usually addressed by traditional rehabilitation interventions.

No clinically interesting hand-specific gains were shown in study I. Previous findings has shown that repetitive task training results in modest improvement across a range of lower limb outcome measures, but not upper limb outcome measures. [169] However, the most efficient interventions to reduce upper limb impairments after stroke, such as constraint-induced movement therapy and other task-oriented training [45,170], mainly apply to individuals with some degree of movement function in the wrist and fingers. Many of the participants in study I were severely impaired, many with total paralysis below the wrist, and this might explain why no improvements in hand function was seen. Most previous intervention studies have focused on mildly to moderately impaired stroke survivors, and less attention has been paid to the severely impaired. By including individuals with moderate to moderately severe hemiparesis late after stroke, our sample of individuals with stroke, also including a large number of individuals with significant impairments, might be more representative of the stroke cohort as a whole.

The credibility of data in study II was strengthened by including individuals with a broad range of limitations following the stroke, also including mild aphasia. Groups of 3–4 participants were interviewed and the interview leader did endeavour to get responses from all respondents during all interviews. Yet, it might have been difficult for some individuals to state their opinion in the group setting. Some of the participants had aphasia, or a cognitive decline, which might have led to an imbalance in the group dynamic, the answers, and also the discussion as a whole. Some of the discussions became somewhat incoherent and in some situations when a participant stated something, another statement by another respondent could follow in a focus area not related to the first statement. Nevertheless, we did make sure that all data answering the question of the participant's experiences of ETT was included in the analysis.

Ethical discussion

All included participants were provided with detailed study information and signed a written informed consent form and were told they could withdraw from the study at any time. A relatively large number of outcome measurements was conducted in study I at the different test occasions, which may have been time consuming for the participants. The evaluation required that participants travelled back and forth to the test site (Stockholm and Gothenborg). The test situation did however offer a unique opportunity for the participants to meet with an experienced therapist and get better insight and knowledge about their situation and current health status. The participants travelled together with their group and relatives by charter flight to the rehabilitation centre, and special flight assistance was offered to those who needed. All participants were accommodated in a handicap-friendly rehabilitation hotel, and most were accompanied by relatives or assistants. The intervention was conducted safely with trained staff.

The ETT was conceptualized by the medical board of Neuro Optima Forsk Rehab AB, based on preclinical research on enriched environment. The ETT programs have been developed and performed since 2002, and I, the author of this theses were engaged as a physiotherapist in the rehabilitative work in the beginning of this development. (But not since the start of my PhD-studies.) I have worked as a physiotherapist within the field of neuro-rehabilitation for 20 years. This naturally affects the way I approached this research. To avoid bias, an independent assessor unrelated to the ETT program was used. By being aware of the potential risk of my preunderstanding, especially during analyse of the qualitative data, the discussion with the co-authors of the content and analysis throughout the evaluation of data became important.

Regarding the interviewed participants, confidentiality was guaranteed through coding of the transcripts of the interviews and data was presentation at group level.

Additionally, more than half of the study participants in study I reported that they had received any form of therapist-led rehabilitation during the baseline phase, and about equally as many had been performing self-managed rehabilitation during this phase. This might highlight that these participants may represent a population of individuals with stroke who actively seek possibilities of rehabilitation and training, and are probably not be representative for the stroke population as a whole. Furthermore, all included participants chose to apply to the ETT program themselves, and some participants even took part in the ETT program partly at their own expenses. Others had the costs covered by the Swedish Social Insurance Agency, the county council or employers. It is therefore important to address that the results might have been affected by the participants' own anticipations.

Limitations

Several limitations of the research methods used in this thesis must be considered. Since participants who had applied to the ETT program themselves were recruited, a longitudinal uncontrolled observational study with a repeated-measures design was used in study I. Therefore, there was no comparison group to measure any effects from participating in a rehabilitation program without the environmental component, or just the environmental component and no intense training, which would have been preferable. However, the baseline phase did control for the passage of time and since no improvement was found after the baseline phase, spontaneous recovery cannot explain the outcome of ETT. Also, valid and reliable outcomes measures were used.

The interviews were performed during the last day of the ETT program. If the interviews would have been performed a few weeks later, it would have been possible to explore the participants' perceptions of the consequences of the program on their activity level and emotional impacts back in their home environment. Unfortunately, this was not possible because of the large geographical spread of the participants.

To establish trustworthiness of findings from qualitative research, the credibility, confirmability, transferability, dependability, and reflexivity must be addressed [27]. In study II, the credibility would have been increased if the codes, categories and subcategories would have been confirmed by the participants.

In study III, we used a single-subject experimental design including only 4 participants. Any conclusions drawn from this study must therefore be drawn with a large dose of cation. Additionally, although the applied TSDB method [171] has a high agreement with the C statistic method,[172] it is is very sensitive to extreme values. One outlier can influence the variance in a small set of data and produce misleading results. Also, it considers only mean changes, and not the clinical importance of results, why the results on an individual level must be looked upon as exploratory. On the other hand, the data from one timepoint in study III represents the mean of several gait trials during that assessment, which minimizes the risk of influence of extreme values.

One important limitation in study IV is that gait speed was measured using different distances in the two groups; the 30MWT test for the community-dwelling older controls, and the 10MWT test for the stroke cohort, which might have introduced some bias. However, the gait speeds among controls are in agreement with other studies, [118], and the 10MWT are preferable in the stroke group, since 30MWT would rather measure gait endurance than speed.

Furthermore, the cohorts in study IV differed significantly regarding age. To achieve the best possible match for the group of controls (>65 years), an equally large group of individuals with stroke who were aged 60 were included.

7. Conclusion

Our findings suggest that ETT produced gains in functional motor ability measured with M-MAS UAS and increased balance measured with the Berg Balance Scale in individuals with chronic stroke. Further, the participants showed an improvement of comfortable and maximum gait speed, an increased distance walked over 6 minutes, and significant improvements in multiple dimensions of health and HRQoL. Improvements were sustained at 3 and 6 months.

The only significant change after the baseline phase was a decrease in HRQoL, measured with the EQ-5D usual activity dimension, showing that the participants were not in a phase of spontaneous improvement, but in a stable chronic phase.

Further, we found that the ETT program might provide experience of perceived improvements in functional capability, increased knowledge, insights and also perceptions of rehabilitation needs. Further, the participants described their external needs of support.

Our findings also suggest that ETT might have beneficial impacts on spatiotemporal and kinematic gait variables in the chronic phase after stroke. Two of four study participants had significant improvements in the symmetry, kinematic and spatiotemporal variables of gait after ETT, possible pointing towards true motor recovery rather than compensation in aspects of the gait-pattern, for these two individuals.

Moreover, we concluded that, independent of age, gender, time since stroke and stroke severity, the maximum gait speed in individuals over 60 years with chronic stroke and mild to moderately severe disability can be predicted by the comfortable gait speed, with a coefficient at 1.41. This relationship differed significantly from that of a community-dwelling control-group population over 65 years. Age and gender affected the correlation in the control group, and after correction the coefficient was found to be 1.07.

8. Future Perspective

In this thesis, a novel translation of EE in combination with task-specific training – ETT- is evaluated and found promising. This thesis does not answer the question if the actual change of environment, the warm climate or just the intense training was the most important component of the ET program. As suggested in the literature, the combination of different ETT components most likely had augmented or even synergistic effects on improvements of stroke-related limitations. Until now, there are very few studies aiming to translate these components to the clinical stroke setting, and in those who have tried, the difficulties in how to standardize the EE conditions across different clinical sites are obvious. It is also not known what aspect of the enrichment that represents the most important ingredient for enhancing brain plasticity, and the ultimate dosage of training and therapy are also unknown. Moreover, what aspects of the environment that are perceived as enriching in human most likely differs between individuals. Follow-up studies could reveal whether intense physical or cognitive training or the physical or social environment significantly contribute to the effect on their own or whether a combination of intensive, task-oriented training with environmental enrichment is necessary to achieve the observed effects.

Future studies should include larger study cohorts, blinded assessments, randomized control groups and between-group comparisons. It also remains to be investigated whether improvements are induced by real recovery involving neuroplasticity processes or a behavioral compensation, or a combination of both.

To further explore this within the context of the ETT program, the study protocol in study I included blood-based biomarker studies and long-term individual interviews, which are not part of this thesis, but remain to be completed.

Acknowledgements

Mitt varmaste tack går till alla patienter som deltagit i studierna. Det är ju er rehabiliteringsprocess, era tankar, era citat och er tid som gett oss våra resultat. Utan er hade denna avhandling inte kunnat göras.

Jag vill tacka min huvudhandledare Lina Bunketorp Käll. Tack för att du tog dig an mig som doktorand, för att du hela tiden har trott på mig, peppat mig när det varit mer kämpigt, för att du har lyssnat på mina idéer, kommit med egna förslag och för att du har guidat mig genom forskningens alla vägar och snår. Du har givit mig ett stort stöd längs med hela vägen, och samtidigt ett stort utrymme att själv utvecklas. Din kapacitet, din kunskap och din närvaro har varit helt fantastiskt att få ta del av. Jag har inte kunnat önska mig en bättre handledare! TACK!

Tack även till min bihandledare Georg Kuhn för ditt stora kunnande och ditt stöd längs med vägen. Ett speciellt tack också för hjälp med förbättring av min skriftliga och muntliga engelska.

Tack även till bihandledare Jean-Luc af Geijerstam, som kommit med goda råd och glada tillrop genom hela processen. Ett speciellt tack även för kontakt och logistik kring testningen på Danderyds Sjukhus Hjärnskaderehab.

Tack till Gunnel Carlsson som genom sin gedigna kunskap inom kvalitativ metodik har guidat, handlett och rådgivit mig genom detta kluriga men spännande forskningsfält. Ditt stöd längs med vägen har betytt jättemycket.

Tack också till Roy Tranberg och Roland Zügner på gånglabbet, avdelning för Ortopedi, för att ni introducerat, handlett och guidat mig genom den snåriga värld som rörelseanalys innebär. Ni har fått något jag upplevt som svårt att fortsätta vara svårt - och kul!

Tack till Aldina Pivovic, Nils-Gunnar Pehrsson, Jan Kowalski och Akademistatistik för statistisk rådgivning.

Tack till Anna Sjöholm och Pablo Cárdenas Rìos för omslagsfotot! Ni förstod min målbild och genomförde det till perfektion!

Tack till Eva Deurloo, som utfört patienttesterna och de flesta fokusgruppsintervjuerna. Tack till Anna Karlsson som utfört de första två fokusgruppsintervjuerna.

Tack till alla medarbetare och det medicinska rådet på fd Neuro Optima, samt fd Centro Forestal Sueco, för flexibilitet, samarbetsvillighet och praktisk hjälp!

Tack Danderyds Sjukhus Hjärnskaderehabilitering samt CTC – Centrum för klinisk prövning, Sahlgrenska Universitetssjukhuset för testlokaler, stickhjälp och logistikhjälp.

Tack även till alla stöttande patienter på Neurocampus! Ett stort tack till bästa kollegorna på Neurocampus för stöttning, peppning, intresse, och bra diskussioner längs med vägen. Anneli, Hanne, Karin, Lotta, Maria, Monika, Sandra och Sanna – ni är bäst! Och tack till mina chefer Camilla och Tor för att ni varit så tillåtande och positiva till att jag delat min tid mellan klinik och forskning.

Tack till mina finest: Kristina, Eva, Sara, Nina och Cissi – och alla andra fantastiska stöttande vänner – ni vet vilka ni är. Ingen nämnd och ingen glömd.

Tack till älskade mamma, pappa, mina bröder, kära svägerskor och övrig släkt!

Sist men absolut inte minst - tack till Linus, Ossian och Elis. Ert stöd och kärlek betyder allt.

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Appendix

2013-08-25

Manual till Modifierad Motor Assessment Scale enligt Uppsala Akademiska Sjukhus M MAS UAS -99

0 poäng anger oförmåga att utföra steg 1.

A. Ryggliggande till sidliggande
1. Ryggliggande. Gör en ansats till att vända sig till sidliggande, men behöver mycket hjälp av en person för att vända sig åt båda håll.
2. Ryggliggande. Vänder sig åt ena sidan med lätt hjälp av en person. Vänder sig åt andra sidan med mycket hjälp (ve
3. Vänder sig med lätt hjälp av en person åt båda håll.
4. Klarar att vända sig själv åt ett håll och med lätt hjälp (verbal eller fysisk) åt andra hållet.
5. Vänder över själv på sida. Klarar detta åt båda håll.

B. Ryggliggande till sittande på sängkant.
1. Pt hjälps till sidliggande. Lyfter huvudet men kan ej medverka till att sätta sig upp.
2. Har huvudkontroll. Hjälps till sittande. Vid behov assisteras pt via sidliggande.
3. Sätter sig upp med lätt stöd av en person. Vid behov assisteras pt via sidliggande.
4. Sätter sig upp själv på mer än 10 sek.
5. Sätter sig upp själv på mindre än 10 sek.

C. Sittande
1. Sitter 2 min med stöd och med öppna ögon. Hjälps till sittande.
2. Sitter utan stöd i 10 sek utan att hålla ihop knän och fötter.
3. Sitter utan stöd i 2 min.
4. Sitter utan stöd med jämn tyngdfördelning och ett icke bakåttippat bäcken. Vrider huvud och bål. Fötterna i golvet.
5. Sitter utan stöd. Böjer sig fram och rör vid golvet och återtar sedan startpositionen. Ben och fötter i stillhet. Affekte

D. Sittande till stående
1. Kommer upp till stående med hjälp. Valfri metod.
2. Kommer upp till stående. Någon står bredvid och är beredd att hjälpa. Ojämnt fördelad tyngd eller handstöd.
3. Kommer upp till stående. Ej handstöd (att stödja händerna på låren tillåts).
4. Sittande till stående till sittande utan att någon står bredvid. Normal sträckning i höft och knä. Jämn tyngdfördelning.
5. Sitt stå sitt 3 gånger på 10 sek. Jämn tyngdfördelning

E. Gång
1. Stödjer på det affekterade benet och tar ett steg framåt med det andra. Assistans vid behov av 1-2 personer.
2. Går med assistans från en person med eller utan gånghjälpmedel.
3 Går 3 meter själv eller med gånghjälpmedel.
4. Går 10 meter utan stöd, vänder om och går tillbaka på totalt 25 sek.
5. Går upp och ner för 8 trappsteg på 20 sek, med eller utan lätt stöd av trappräcket. God höft- och knäkontroll.

F. Armfunktion
1. Ryggliggande. Armen sträckt mot taket, ca 45° böjning i armbågen tillåts. Får hjälp att inta läget. Håller armen själv eller får stöd vid överarmen.
2. Ryggliggande. Armen som i punkt 1. För handen mot pannan och sträck igen. Vid sträckt läge ska skulderbladet vara framdraget.
3. Sittande. Håller armen sträckt med 90° flex i axelleden i 2 sek. Ej uppdragen skuldra. Får vid behov hjälp att inta läget.
4. Sittande. Pt lyfter armen själv till 90° flex i axelleden. Håller i 10 sek. Sänker armen.
5. Sittande. Håller båda armarna 90° flex i axelleden. Handflatorna uppåt. Blundar. Håller kvar i 10 sek. Testa båda armarna samtidigt men bedöm var sida för sig.

G. Handrörelser
1. Sitter vid ett bord med underarmsstöd. Lyfter handen från bordet med handledsextension utan att böja i armbågen.
2. Ett glas placeras i pt:s hand. Lyfter det från underlaget med armbågsstöd utan ulnardeviation.
3. Sittande. Pt pronerar och supinerar. Armbågen ej understödd.
4. Håller i en kam. Kammar håret på handsidan av huvudet.
5. Greppar om ett glas fyllt med vatten. För det till munnen (dricker) utan att spilla. Ställer ner glaset och släpper.

H. Finmotorik
1. Tar upp en tändsticksask (ca 1,5 x 3,5 x 5,5 cm) och lägger ner den igen. Underarmen får vara understödd.
2. Tar upp en tändsticka ur en i övrigt tom tändsticksask och lägger den på bordet. Underarmen ej understödd. Asken ska stå fritt på bordet.
3. Opposition tumme och varje finger. 10 fingrar på 10 sek.
4. Plocka i 10 tändstickor i en tändsticksask på 35 sek. En tändsticka i taget. Asken ska stå fritt på bordet.
5. Plocka ur 10 tändstickor ur en i övrigt tom tändsticksask på 25 sek. En tändsticka i taget. Asken ska stå fritt på bordet.

Patientuppgifter

Motorisk bedömning

MMAS UAS

Jönköpings län

Beh sjukgymnast:

Enhet:

Testet utfört på: □ brits □ säng

Pt godkänner överrapportering □

Modifierad Motor Assessment Scale enl Uppsala Akademiska Sjukhus 1999

Modifierad efter Motor Asssessment Scale enligt Carr & Shepherd

År:

Datum	**A** Ryggligg till sidligg	**B** Ryggligg till sittande på sängkant	**C** Sittande	**D** Sittande till stående	**E** Gång	**F** Armfunktion vänster	**G** Handrörelser vänster	**H** Finmotorik vänster	**F** Armfunktion höger	**G** Handrörelser höger	**H** Finmotorik höger	
5												5
4												4
3												3
2												2
1												1
0												0

Summa: ____________________

Kommentar: ____________________

Mål: ____________________

Manual:
Alla uppgifter ska utföras självständigt av pt om inget annat anges.
Patienten ska om möjligt bedömas på sitt bästa utförande av tre försök. Eftersom instrumentet är konstruerat för att bedöma det bästa utförandet bör sjukgymnasten ge allmän uppmuntran men får ej ge specifik feedback under testningen. Instruktionerna kan om det behövs upprepas och demonstreras för patienten.
Ordningsföljden på uppgifterna kan variera efter lämplighet.
Testet bör utföras i så lugn miljö som möjligt, med standardiserat tillvägagångssätt och utrustning. Testet bör utföras då patienten är maximalt pigg.
Anteckningar bör göras om patienten är under påverkan av medicinering.
Patienten ska informeras när tidtagning sker.
Testet är uppbyggt av uppgifter som har hierarkiska skalor, d v s det förutsätts att om patienten bedöms på nivå 5 på en uppgift så klarar patienten också nivåerna 1-4. Om det skulle inträffa att en patient klarar nivå 1-3, ej 4 men även 5, bedöms nivån till 3.

Utrustning:
Säng/brits
Pall eller stol utan armstöd, ca 45 cm hög
Tidtagarur
Kam
Glas fyllt med vatten
Liten tändsticksask med 10 stickor i
Trappa

UPPLEVD-BALANS: UTFÖRA AKTIVITETER UTAN ATT FALLA
Falls-Efficacy Scale Swedish version FES(S)

Skatta på en skala från 0 till 10, där 0 är inte säker alls och 10 är helt säker, hur säker Du är på att utföra följande aktiviteter utan att falla:
Om Du inte brukar/kan utföra aktiviteten tänk Dig att Du gör/kan utföra aktiviteten och försök föreställa Dig hur säker Du skulle känna Dig.
Upprepa för varje aktivitet:
- Hur säker är du på att du kan... (fråga om nedanstående aktivitet) ... utan att falla?

	Inte säker alls					Ganska säker					Helt säker
1. Gå i och ur sängen	0	1	2	3	4	5	6	7	8	9	10
2. Gå på toaletten	0	1	2	3	4	5	6	7	8	9	10
3. Tvätta dig själv	0	1	2	3	4	5	6	7	8	9	10
4. Sätta dig och resa dig ur en stol	0	1	2	3	4	5	6	7	8	9	10
5. Klä av och på dig	0	1	2	3	4	5	6	7	8	9	10
6. Bada eller dusha	0	1	2	3	4	5	6	7	8	9	10
7. Gå upp och ned för trappor	0	1	2	3	4	5	6	7	8	9	10
8. Gå runt kvarteret	0	1	2	3	4	5	6	7	8	9	10
9. Sträcka dig in i garderober och skåp	0	1	2	3	4	5	6	7	8	9	10
10. Städa lägenheten (dvs sopa eller damma)	0	1	2	3	4	5	6	7	8	9	10

Skalan är utarbetad av M E Tinetti, MD. Yale University Scool of Medicine, New Haven, Connecticut. USA. Skalan är efter tillåtelse av Dr. Tinetti översatt och omarbetad av Karin Hellström, Uppsala Universitet, Institutionen för neurovetenskap, Sjukgymnastikutbildningen. Akademiska sjukhuset, ing 15. 751 85 Uppsala.

Senast uppdaterad 2006-05-19

	Inte säker alls					Ganska säker					Helt säker
11. Laga mat som inte innebär att bära heta eller tunga saker	0	1	2	3	4	5	6	7	8	9	10
12. Skynda dig att svara i telefon	0	1	2	3	4	5	6	7	8	9	10
13. Vardagshandla	0	1	2	3	4	5	6	7	8	9	10

Summa PADL (1-6): poäng

Summa IADL (8-13): poäng

Summa Total (1-13): poäng

Personnummer:
Namn:
Klinik. Ort:
Undersökare:
Datum:

Skalan är utarbetad av M E Tinetti, MD. Yale University Scool of Medicine, New Haven, Connecticut. USA. Skalan är efter tillåtelse av Dr. Tinetti översatt och omarbetad av Karin Hellström, Uppsala Universitet, Institutionen för neurovetenskap, Sjukgymnastutbildningen. Akademiska sjukhuset, ing 15. 751 85 Uppsala.

Skala över trötthetens inverkan

Personnummer: ______________________ Kod: ______________ Datum: ____________

Nedan är en lista med påståenden som beskriver hur trötthet kan orsaka problem i människors liv. Var god läs varje påstående noggrant. Ringa in siffran som bäst anger hur stort problem trötthet har varit för dig de senaste fyra (4) veckorna, inklusive idag. Var god ringa in en siffra för varje påstående och hoppa inte över några påståenden.

Ringa in en siffra på varje rad	Inget Problem	Litet Problem	Måttligt Problem	Stort Problem	Extremt Problem
1. *Pga min trötthet,* känner jag mig mindre pigg.	0	1	2	3	4
2. *Pga min trötthet,* känner jag att jag är mer isolerad från social kontakt.	0	1	2	3	4
3. *Pga min trötthet,* måste jag minska min arbetsbörda eller mina ansvarstaganden.	0	1	2	3	4
4. *Pga min trötthet,* har jag mer humörsvängningar.	0	1	2	3	4
5. *Pga min trötthet,* har jag svårt att vara uppmärksam under en längre tidsperiod.	0	1	2	3	4
6. *Pga min trötthet,* känner jag att jag inte kan tänka klart.	0	1	2	3	4
7. *Pga min trötthet,* arbetar jag mindre effektivt. (Detta gäller både arbete i och utanför hemmet).	0	1	2	3	4
8. *Pga min trötthet,* måste jag förlita mig mer på att andra hjälper mig eller utför saker åt mig.	0	1	2	3	4
9. *Pga min trötthet,* har jag svårt att planera aktiviteter i förväg, eftersom min trötthet kan komma i vägen för dem.	0	1	2	3	4
10. *Pga min trötthet,* är jag klumpigare och mer okoordinerad.	0	1	2	3	4
11. *Pga min trötthet,* upplever jag att jag är mer glömsk.	0	1	2	3	4
12. *Pga min trötthet,* är jag mer lättretlig och blir lättare arg.	0	1	2	3	4
13. *Pga min trötthet,* måste jag vara försiktig med hur ofta och hur länge jag kan delta i fysiska aktiviteter.	0	1	2	3	4
14. *Pga min trötthet,* är jag mindre motiverad att göra någonting som kräver fysisk ansträngning.	0	1	2	3	4
15. *Pga min trötthet,* är jag mindre motiverad att delta i sociala aktiviteter.	0	1	2	3	4
16. *Pga min trötthet,* begränsas min rörelsefrihet utanför hemmet.	0	1	2	3	4
17. *Pga min trötthet,* har jag problem att klara fysiska ansträngningar under längre tidsperioder.	0	1	2	3	4
18. *Pga min trötthet,* upplever jag att det är svårt att fatta beslut.	0	1	2	3	4

Ringa in en siffra på varje rad	Inget Problem	Litet Problem	Måttligt Problem	Stort Problem	Extremt Problem
19. *Pga min trötthet,* har jag få sociala kontakter utanför mitt eget hem.	0	1	2	3	4
20. *Pga min trötthet,* känns normala vardagliga händelser stressiga för mig.	0	1	2	3	4
21. *Pga min trötthet,* är jag mindre motiverad att göra saker som kräver tankeverksamhet.	0	1	2	3	4
22. *Pga min trötthet,* undviker jag situationer som är stressiga för mig.	0	1	2	3	4
23. *Pga min trötthet,* känns mina muskler mycket svagare än de borde göra.	0	1	2	3	4
24. *Pga min trötthet,* ökar mina fysiska obehag.	0	1	2	3	4
25. *Pga min trötthet,* har jag svårt att hantera allt som är nytt.	0	1	2	3	4
26. *Pga min trötthet,* är jag mindre kapabel att slutföra sysslor som kräver tankeverksamhet.	0	1	2	3	4
27. *Pga min trötthet,* känner jag mig oförmögen att uppfylla de krav som människor ställer på mig.	0	1	2	3	4
28. *Pga min trötthet,* känner jag mig mindre kapabel att försörja mig själv och min familj.	0	1	2	3	4
29. *Pga min trötthet,* är jag mindre sexuellt aktiv.	0	1	2	3	4
30. *Pga min trötthet,* upplever jag att det är svårt att organisera mina tankar när jag gör saker hemma eller på jobbet.	0	1	2	3	4
31. *Pga min trötthet,* är jag mindre kapabel att slutföra sysslor som kräver fysisk ansträngning.	0	1	2	3	4
32. *Pga min trötthet,* oroar jag mig över hur jag ser ut i andra människors ögon.	0	1	2	3	4
33. *Pga min trötthet,* är jag mindre kapabel att hantera känslomässiga frågor.	0	1	2	3	4
34. *Pga min trötthet,* känner jag att jag tänker långsammare.	0	1	2	3	4
35. *Pga min trötthet,* upplever jag att jag har svårt att koncentrera mig.	0	1	2	3	4
36. *Pga min trötthet,* har jag svårt för att delta i familjeaktiviteter fullt ut.	0	1	2	3	4
37. *Pga min trötthet,* måste jag begränsa mina fysiska aktiviteter.	0	1	2	3	4
38. *Pga min trötthet,* behöver jag vila oftare eller under längre stunder.	0	1	2	3	4
39. *Pga min trötthet,* är jag oförmögen att ge så mycket känslomässigt stöd åt min familj som jag borde.	0	1	2	3	4
40. *Pga min trötthet,* upplever jag små problem som stora.	0	1	2	3	4

Livstillfredsställelse

Personnummer: ______________________ Kod: ______________ Datum: ____________

Här följer ett antal påståenden gällande hur tillfredsställd Du är med olika aspekter av Ditt liv. Ringa för vart och ett av dessa påstående in en siffra mellan 1 och 6, där 1 betyder mycket otillfredsställande och 6 mycket tillfredsställande.

1= mycket otillfredsställande
2= otillfredsställande
3= ganska otillfredsställande
4= ganska tillfredsställande
5= tillfredsställande
6= mycket tillfredsställande

Livet är i allmänhet för mig		1	2	3	4	5	6
Min förmåga att klara mig själv (gäller klädsel, tvätt/bad, gångförmåga o dyl) är		1	2	3	4	5	6
Min fritidssituation är		1	2	3	4	5	6
Min arbetssituation är	☐ arbetar ej	1	2	3	4	5	6
Min ekonomiska situation är		1	2	3	4	5	6
Mitt sexliv är		1	2	3	4	5	6
Min relation till min partner är	☐ har ingen stadig partnerrelation	1	2	3	4	5	6
Mitt familjeliv är	☐ har inget familjeliv	1	2	3	4	5	6
Min kontakt med vänner och bekanta är		1	2	3	4	5	6

MADRS-S
(självskattningsskala)

Namn	Datum

Genom att besvara följande nio frågor kan du och din läkare få en detaljerad bild av hur du mår och om du har symtom, som är typiska för depression. Genom att lägga ihop den "poäng" du får på frågorna får du och din läkare en bild av graden av depression. Sätt en ring runt siffran som du tycker bäst stämmer med hur du mått de senaste tre dagarna. Använd gärna mellanliggande alternativ. Tänk inte alltför länge, utan försök arbeta snabbt.

1. Sinnestämning

Här ber vi dig beskriva din sinnesstämning, om du känner dig ledsen, tungsint eller dyster till mods. Tänk efter hur du har känt dig de senaste tre dagarna, om du har skiftat i humöret eller om det varit i stort sett detsamma hela tiden, och försök särskilt komma ihåg om du har känt dig lättare till sinnes om det har hänt något positivt.

0 Jag kan känna mig glad eller ledsen, alltefter omständigheterna.
1
2 Jag känner mig nedstämd för det mesta, men ibland kan det kännas lättare.
3
4 Jag känner mig genomgående nedstämd och dyster. Jag kan inte glädja mig åt sådant som vanligen skulle göra mig glad.
5
6 Jag är så totalt nedstämd och olycklig att jag inte kan tänka mig värre.

2. Oroskänslor

Här ber vi dig markera i vilken utsträckning du haft känslor av inre spänning, olust och ångest eller odefinierad rädsla under de senaste tre dagarna. Tänk särskilt på hur intensiva känslorna varit, och om de kommit och gått eller funnits nästan hela tiden.

0 Jag känner mig mestadels lugn.
1
2 Ibland har jag obehagliga känslor av inre oro.
3
4 Jag har ofta en känsla av inre oro som ibland kan bli mycket stark, och som jag måste anstränga mig för att bemästra.
5
6 Jag har fruktansvärda, långvariga eller outhärdliga ångestkänslor.

3. Sömn

Här ber vi dig beskriva hur bra du sover. Tänk efter hur länge du sovit och hur god sömnen varit under de senaste tre nätterna. Bedömningen skall avse hur du faktiskt sovit, oavsett om du tagit sömnmedel eller ej. Om du sover mer än vanligt, sätt din markering vid 0.

0 Jag sover lugnt och bra och tillräckligt länge för mina behov. Jag har inga särskilda svårigheter att somna.
1
2 Jag har vissa sömnsvårigheter. Ibland har jag svårt att somna eller sover ytligare eller oroligare än vanligt.
3
4 Jag sover minst två timmar mindre per natt än normalt. Jag vaknar ofta under natten, även om jag inte blir störd.
5
6 Jag sover mycket dåligt, inte mer än 2-3 timmar per natt.

4. Matlust

Här ber vi dig ta ställning till hur din aptit är, och tänka efter om den på något sätt skiljt sig från vad som är normalt för dig. Om du skulle ha bättre aptit än normalt, sätt din markering vid 0.

0 Min aptit är som den brukar vara.
1
2 Min aptit är sämre än vanligt.
3
4 Min aptit har nästan helt försvunnit. Maten smakar inte och jag måste tvinga mig att äta.
5
6 Jag vill inte ha någon mat. Om jag skulle få någonting i mig, måste jag övertalas att äta.

5. Koncentrationsförmåga

Här ber vi dig ta ställning till din förmåga att hålla tankarna samlade och koncentrera dig på olika aktiviteter. Tänk igenom hur du fungerar vid olika sysslor som kräver olika grad av koncentrationsförmåga, t ex läsning av komplicerad text, lätt tidningstext och TV-tittande.

0 Jag har inga koncentrationssvårigheter
1
2 Jag har tillfälligt svårt att hålla tankarna samlade på sådant som normalt skulle fånga min uppmärksamhet (t ex läsning eller TV-tittande).
3
4 Jag har påtagligt svårt att koncentrera mig på sådant som normalt inte kräver någon ansträngning från min sida (t ex läsning eller samtal med andra människor).
5
6 Jag kan överhuvudtaget inte koncentrera mig på någonting.

6. Initiativförmåga

Här ber vi dig försöka värdera din handlingskraft. Frågan gäller om du har lätt eller svårt för dig att komma igång med sådant du tycker du bör göra, och i vilken utsträckning du måste övervinna ett inre motstånd när du skall ta itu med något.

0 Jag har inga svårigheter med att ta itu med nya uppgifter.
1
2 När skall jag ta itu med något, tar det emot på ett sätt som inte är normalt för mig.
3
4 Det krävs en stor ansträngning för mig att ens komma igång med enkla uppgifter som jag vanligtvis utför mer eller mindre rutinmässigt.
5
6 Jag kan inte förmå mig att ta itu med de enklaste vardagssysslor.

7. Känslomässigt engagemang

Här ber vi dig ta ställning till hur du upplever ditt intresse för omvärlden och för andra människor, och för sådana aktiviteter som brukar bereda dig nöje och glädje.

0 Jag är intresserad av omvärlden och engagerar mig i den, och det bereder mig både nöje och glädje.
1
2 Jag känner mindre starkt för sådant som brukar engagera mig. Jag har svårare än vanligt att bli glad eller svårare att bli arg när det är befogat.
3
4 Jag kan inte känna något intresse för omvärlden, inte ens för vänner och bekanta.
5
6 Jag har slutat uppleva några känslor. Jag känner mig smärtsamt likgiltig även för mina närmaste.

8. Pessimism

Frågan gäller hur du ser på din egen framtid och hur du uppfattar ditt eget värde. Tänk efter i vilken utsträckning du ger självförebråelser, om du plågas av skuldkänslor, och om du oroat dig oftare än vanligt för t ex din ekonomi eller din hälsa.

0 Jag ser på framtiden med tillförsikt. Jag är på det hela taget ganska nöjd med mig själv.
1
2 Ibland klandrar jag mig själv och tycker jag är mindre värd än andra.
3
4 Jag grubblar ofta över mina misslyckanden och känner mig mindervärdig eller dålig, även om andra tycker annorlunda.
5
6 Jag ser allting i svart och kan inte se någon ljusning. Det känns som om jag var en alltigenom dålig människa, och som om jag aldrig skulle kunna få någon förlåtelse för det hemska jag gjort.

9. Livslust

Frågan gäller din livslust, och om du känt livsleda. Har du tankar på självmord, och i så fall, i vilken utsträckning upplever du detta som en verklig utväg?

0 Jag har normal aptit på livet.
1
2 Livet känns inte särskilt meningsfullt men jag önskar ändå inte att jag vore död.
3
4 Jag tycker ofta det vore bättre att vara död, och trots att jag egentligen inte önskar det, kan självmord ibland kännas som en möjlig väg.
5
6 Jag är egentligen övertygad om att min enda utväg är att dö, och jag tänker mycket på hur jag bäst skall gå tillväga för att ta mitt eget liv.

Lägg samman poängen från *båda sidor* av formuläret och ange summan i rutan

Wyeth AB

EQ - 5D

Hälsoenkät

Svensk version
(Swedish version)

Markera, genom att kryssa i en ruta i varje nedanstående grupp (så här ☑), vilket påstående som bäst beskriver Ditt hälsotillstånd i dag.

Rörlighet

Jag går utan svårigheter ☐

Jag kan gå men med viss svårighet ☐

Jag är sängliggande ☐

Hygien

Jag behöver ingen hjälp med min dagliga hygien, mat eller påklädning ☐

Jag har vissa problem att tvätta eller klä mig själv ☐

Jag kan inte tvätta eller klä mig själv ☐

Huvudsakliga aktiviteter *(t ex arbete, studier, hushållssysslor, familje- och fritidsaktiviteter)*

Jag klarar av min huvudsakliga sysselsättning ☐

Jag har vissa problem med att klara av min huvudsakliga sysselsättning ☐

Jag klarar inte av min huvudsakliga sysselsättning ☐

Smärtor/besvär

Jag har varken smärtor eller besvär ☐

Jag har måttliga smärtor eller besvär ☐

Jag har svåra smärtor eller besvär ☐

Rädsla/nedstämdhet

Jag är inte orolig eller nedstämd ☐

Jag är orolig eller nedstämd i viss utsträckning ☐

Jag är i högsta grad orolig eller nedstämd ☐

Till hjälp för att avgöra hur bra eller dåligt ett hälsotillstånd är, finns den termometer-liknande skalan till höger. På denna har Ditt bästa tänkbara hälsotillstånd markerats med 100 och Ditt sämsta tänkbara hälsotillstånd med 0.

Vi vill att Du på denna skala markerar hur bra eller dåligt Ditt hälsotillstånd är, som Du själv bedömer det. Gör detta genom att dra en linje från nedanstående ruta till den punkt på skalan som markerar hur bra eller dåligt Ditt nuvarande hälsotillstånd är.

Ditt nuvarande hälsotillstånd