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ASSOCIATIONS BETWEEN BODY FUNCTIONS, ACTIVITIES AND HEALTH-RELATED QUALITY OF LIFE FROM ONSET UNTIL 18 MONTHS AFTER STROKE

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To my collegues.

ABSTRACT

Introduction and aims: In planning rehabilitation services for patients with stroke, it is important to know the frequency of the impairments and activity limitations presented by the patients and also how each body function and activity is associated with other body functions and activities, as well as the patients' health-related quality of life (HRQL) at different time-points after stroke. The overall aims of the thesis were to describe body functions, activities and HRQL in patients with stroke and to analyse the associations between those variables, in the first week and at three and 18 months after stroke onset.

Patients and methods: This thesis is based on two samples of consecutively recruited patients, presented in four papers.

The patients presented in Paper I, II and IV were assessed in the first week (N=109) as well as at three (N=95) and 18 months (N=66) after stroke with reference to: occurrence of stereotyped mass patterns of movement (Brunnström's hemiplegic limb synergies); muscle tone (Modified Ashworth Scale); muscle stiffness (self-report); tendon reflexes (physical examination); motor performance (Lindmark Motor Assessment Scale); fine hand use (Nine Hole Peg Test); grip strength (Vigorimeter); somatosensory functions (light touch and Thumb Localizing Test); mobility (Rivermead Mobility Index); self-care, i.e. activities of daily living, ADL (Barthel Index); and HRQL (SF-36).

For Paper III, 115 patients, ≥65 years, were assessed five days after stroke with reference to: somatosensory, perceptual (Line- and Letter Cancellation Tasks and Kohs Block Design Test); and cognitive functions (Mini Mental State Examination); depressive symptoms (Montgomery-Åsberg Depression Rating Scale); mobility; and self-care.

Results: Three months after stroke, the voluntary movements of 13% of hemiparetic stroke patients were restricted to the hemiplegic limb synergies, all of which displayed spasticity (Paper I).

Eighteen months after stroke, 20% of all patients and 34% of the hemiparetic patients, displayed spasticity (Paper II). Both spasticity and the hemiplegic limb synergies were associated with impaired movements and activity limitations although severe disabilities were seen both in patients with and without these impairments (Papers I and II). Hemiparetic patients without spasticity had significantly better HRQL on one of the eight SF-36 health scales, than patients with spasticity (Paper II).

Multivariate analyses showed that normal proprioceptive function was significantly associated with better mobility, five days after stroke onset. Normal perceptual and touch functions were significantly associated with better self-care (Paper III).

Seventy percent of all patients had limited fine hand use in the first week, 41% at three months and 45% at 18 months after stroke. The strength of the associations between fine hand use and touch function, upper extremity movement function and self-care, respectively, was moderate to high but decreased over time. In general, fewer patients improved from limited fine hand use compared to other disabilities (Paper IV).

Conclusions: The assessment of hemiplegic limb synergies, as presented by Brunnström, may only be suitable for a small fraction of hemiparetic patients—namely, those displaying spasticity.

The current exaggerated focus on reflex-mediated spasticity in stroke care seems to overestimate its clinical importance, not for the single patient, but from a population-based perspective.

It is of specific importance to consider somatosensory and perceptual functions, respectively, in the rehabilitation of older patients in the acute phase after stroke, since these functions significantly affect the patients' mobility and self-care levels.

Limited fine hand use is common after stroke. With time after onset, patients with stroke seem to become less dependent on fine hand use when performing upper extremity movements and self-care activities.

SAMMANFATTNING

Introduktion och syfte: Vid planering av rehabilitering och val av rehabiliteringsmetoder för patienter med stroke är det viktigt att känna till hur vanligt förekommande olika funktionshinder är samt hur olika kroppsfunktioner och aktiviteter är relaterade till patienternas funktionstillstånd och hälsorelaterade livskvalitet (HRQL) vid olika tidpunkter efter insjuknandet. Avhandlingens syfte var att beskriva kroppsfunktioner, aktiviteter och HRQL hos patienter med stroke och att analysera sambanden mellan dessa variabler, första veckan samt tre och 18 månader efter insjuknandet.

Patienter och metoder: Avhandlingen baseras på två urval av konsekutivt rekryterade patienter med stroke, presenterade i fyra delarbeten.

Patienterna presenterade i delarbete I, II och IV undersöktes den första veckan (N=109) samt tre (N=95) och 18 månader (N=66) efter insjuknandet avseende: förekomst av stereotypa massrörelser (Brunnströms hemiplegisynergier); muskeltonus (modifierad Ashworth skala); muskelstelhet (självrapportering); senreflexer (fysisk undersökning); rörelseförmåga i övre och nedre extremiteterna (Lindmark Motor Assessment Scale); handens finmotorik (Nine Hole Peg Test); greppstyrka (Vigorimeter); somatosensorisk funktion (ytlig beröring och Thumb Localizing Test); förflyttningsförmåga (Rivermead Mobility Index); personlig ADL, det vill säga aktiviteter i dagliga livet (Barthel Index); och HRQL (SF-36).

För delarbete III, undersöktes 115 patienter, ≥65 år, fem dagar efter insjuknandet avseende: somatosensorisk, perceptuell (Line och Letter Cancellation Tasks och Kohs Block Design Test), och kognitiv funktion (Mini Mental State Examination); depressiva symptom (Montgomery-Åsberg Depression Rating Scale); förflyttningsförmåga; och personlig ADL.

Resultat: Tre månader efter insjuknandet i stroke var rörelserna hos 13 % av de hemiparetiska patienterna med stroke begränsade till Brunnströms hemiplegisynergier. Patienterna vars rörelser var begränsade till hemiplegisynergierna uppvisade alla spasticitet (delarbete I).

Arton månader efter stroke uppvisade 20 % av alla patienter och 34 % av de hemiparetiska patienterna spasticitet (delarbete II). Både spasticitet och hemiplegisynergierna var associerade med nedsatt rörelseförmåga och aktivitetsbegränsning även om svåra funktionshinder sågs både hos patienter med och utan dessa funktionsnedsättningar (delarbete I och II). Hemiparetiska patienter utan spasticitet hade signifikant bättre HRQL på en av de åtta hälsoskalorna i SF-36 (delarbete II).

Multivariata regressionsanalyser visade att normal proprioceptiv funktion var signifikant relaterat till bättre förflyttningsförmåga, fem dagar efter insjuknandet i stroke. Normala perceptuella funktioner och beröringsfunktioner var signifikant relaterade till en bättre förmåga att utföra personlig ADL (delarbete III).

Sjuttio procent av alla patienter hade nedsatt finmotorik den första veckan, 41 % vid tre månader och 45 % vid 18 månader efter stroke. Styrkan på sambanden mellan handens finmotorik och beröringsfunktion, rörelseförmåga i övre extremiteten respektive personlig ADL var moderat till stark men minskade med tiden efter insjuknandet. Generellt sett förbättrades färre patienter avseende handens finmotorik jämfört med rörelseförmåga och förmåga att utföra personlig ADL (delarbete IV).

Slutsats: Undersökning av rörelseförmåga i enlighet med Brunnströms hemiplegisynergier, förefaller endast vara lämpligt att utföra på en liten del av alla patienter med stroke – nämligen de som uppvisar spasticitet.

Dagens fokus på spasticitet i strokerehabilitering förefaller överskatta spasticitetens kliniska betydelse, inte för den enskilda patienten, men ur ett populationsbaserat perspektiv.

Somatosensoriska och perceptuella funktioner är viktiga att ta hänsyn till vid rehabilitering av äldre patienter med stroke eftersom dessa funktioner signifikant påverkar patienternas förmåga att förflytta sig och utföra personlig ADL.

Nedsatt finmotorik är vanligt efter stroke. Med tiden efter insjuknandet förefaller patienter med stroke bli allt mindre beroende av handens finmotorik vid utförandet av rörelser i övre extremiteten och vid personlig ADL.

LIST OF PUBLICATIONS

The thesis is based on the following papers, which will be referred to in the text by their roman numerals:

I. Welmer AK, Widén Holmqvist L, Sommerfeld DK. Hemiplegic limb synergies in stroke patients. Am J Phys Med Rehabil. 2006;85:112-119

II. Welmer AK, von Arbin M, Widén Holmqvist L, Sommerfeld DK. Spasticity and its association with functioning and health-related quality of life 18 months after stroke. Cerebrovasc Dis. 2006;21:247-253

III. Welmer AK, von Arbin M, Murray V, Widén Holmqvist L, Sommerfeld DK. Determinants of mobility and self-care in older patients with stroke: importance of somatosensory and perceptual functions. Phys Ther. 2007;87: [ahead of print]. This is not the final edited version.

IV. Welmer AK, Widén Holmqvist L, Sommerfeld DK. Limited fine hand use after stroke and its association with other disabilities: a longitudinal study. Submitted.

CONTENTS

LIST OF ABBREVIATIONS

ADL	Activities of daily living
BI	Barthel Index
CI	Cerebral infarction
CI	Confidence interval
CIMT	Constraint-induced Movement Therapy
DS	Danderyd Hospital
DSM IV	Diagnostic and Statistical Manual of Mental Disorders, 4th edition
HRQL	Health-related quality of life
ICF	International Classification of Functioning, Disability and Health
ICH	Intracerebral haemorrhage
IQR	Interquartile range
LMAS	Lindmark Motor Assessment Scale
LR	Likelihood ratios
MADRS	Montgomery Åsberg Depression Rating Scale
MAS	Modified Ashworth Scale
MMSE	Mini-Mental State Examination
NHPT	Nine Hole Peg Test
NPV	Negative predictive value
OR	Odds ratio
PPV	Positive predictive value
QoL	Quality of life
RMI	Rivermead Mobility Index
SAH	Subarachnoidal haemorrhage
SD	Standard deviation
SF-36	Swedish Short Form 36
SSS	Scandinavian Stroke Scale
TIA	Transitory ischemic attack
UMN	Upper motor neuron
WHO	World Health Organization

1 INTRODUCTION

1.1 BACKGROUND

Stroke is a dramatic event, which may affect many aspects of a person's life. No two patients with stroke present identical symptoms; the consequences are, thus, different for each individual. The consequences of a stroke may be physical, psychological and/or social and the symptoms presented by the patients depend on the brain structures affected by the stroke (1, 2). Through rehabilitation, patients with stroke can regain some of their lost abilities (3) or learn to compensate for the loss (4). The need for rehabilitation services is not homogenous in the stroke population, but is likely to vary depending, for example, on the extent of impairments and activity limitations.

In planning rehabilitation services for patients with stroke, it is important to know the frequency of the impairments and activity limitations presented by the patients and also how each body function and activity is associated with other body functions and activities, as well as the patients' health-related quality of life (HRQL) at different time-points after stroke.

Impaired control of voluntary movements of the extremities on one side, so-called hemiparesis, has been reported to be present in about 80% of all patients with stroke (5). Other examples of impairments after stroke are: spasticity, abnormal synergies, somatosensory and mental (perceptual, cognitive and depressive) impairments (2). Abnormal synergies are stereotyped mass patterns of movement resulting in an inability to move a single joint without simultaneously generating movements in other joints (6).

The assessment and rehabilitation of patients with movement disabilities, for example after a stroke, are greatly influenced by the therapist's theories concerning motor control (2). Motor control is the ability to regulate or direct the mechanisms essential to movement. Theories of motor control describe viewpoints regarding how movement is controlled. Some theories of motor control (the reflex and hierarchical theories) focus on the role of the nervous system, suggesting that reflexes are the building blocks of complex behavior (7). Other theories focus on central motor patterns, which can be activated by both external and internal forces (2). Further theories assume that movement can emerge as a result of interacting elements without the need of specific commands within the nervous system or that movements are specific for the task and the environments in which they are being performed (2). As no theory is totally comprehensive, it has been suggested that the best theory of motor control is one that combines elements from all of the theories presented (2). Further, it has been suggested that normal movements emerge as an interaction between many systems (2).

The most commonly employed physiotherapy approaches are based on the reflex and hierarchical theories and the assumption that abnormal reflexes, associated with spasticity and abnormal synergies, are the most troublesome contributors to hemiparesis after stroke (8). Some studies have suggested that task-specific training might be more effective than the above-mentioned approaches, although the data supporting those results are meagre (9). Thus, the assumption that hemiparesis after

stroke is characterized by spasticity and abnormal synergies still remains as a theoretical base for stroke rehabilitation and assessment (2, 8, 10-12). It has, however, not yet been established to what extent the voluntary movements of hemiparetic stroke patients in a consecutive sample are restricted to these abnormal synergies: nor has the relation of hemiplegic limb synergies to spasticity and activity limitations been elucidated in a consecutive sample. The occurrence of spasticity and its impact on functioning in the acute phase and three months after stroke was recently investigated in the same sample of patients as evaluated in the present thesis (13). Of the 95 patients studied, 18 (19%) exhibited spasticity three months after stroke. The extent to which patients exhibit spasticity 18 months after stroke – i.e., at a time when their disabilities are thought to be in a stable phase – has been poorly documented. Nor has the impact of spasticity on functioning and HRQL in the stable phase after stroke received adequate attention.

Compared to spasticity and abnormal synergies, much less emphasis in stroke rehabilitation literature has been placed on the impact of somatosensory and mental (perceptual, cognitive and depressive) functions on activity after stroke. Indeed, according to a recent survey, a majority of files on patients with stroke in Swedish hospitals lack information on those functions (14). This lack of information may be important if the information has a predictive function. Activity limitations five days after acute stroke, in the same sample of patients as evaluated in the present thesis, have been shown to exert a negative impact on discharge destination and length of hospital stay (15). It is, therefore, important to explore whether somatosensory and mental impairments are associated with activity limitations five days after stroke onset. If these impairments are associated with activity limitations, they should be clearly assessed and the results noted in the patient's file, since they are not always obvious and so may easily be overlooked.

Older age, compared to younger, has been shown to be associated with worse post-stroke mental impairments and self-care limitations (16). Functioning among older patients with stroke is, however, not as well described as among younger patients. Therefore, it is important to describe functioning among the former group of patients.

It has been shown that 50% of all patients with stroke retrieve independent walking ability (17) and 79% of the patients attain full ability to perform upper extremity self-care activities (18). Data concerning the percentage of all patients with stroke who recover from limited fine hand use or concerning the degree of recovery that occurs are, however, scarce (19). Furthermore, little is known about the long-term outcome of fine hand use in these patients.

It has been suggested that a simple movement of active finger extension is associated with recovery from arm impairments and activity limitations (20). Fine hand use requires finger extension and good proximal control to place and hold the hand in the correct position. In addition, fine hand use consists of more complex tasks, and might, therefore, be influenced by the patient's cognitive functions, including perception and control of action (21). The importance of fine hand use for upper extremity movements and self-care has, however, not been described. It has been suggested that the passage of time accounts for more of the recovery of upper extremity movements and self-care

than it does for the recovery of fine hand use (22). It has, however, not been elucidated whether the associations between limited fine hand use and other disabilities change with time, after stroke.

1.2 STROKE – GENERAL ASPECTS

Stroke is a clinical syndrome, defined by the World Health Organization (WHO) as "rapidly developed clinical signs of focal, or global, disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than of vascular" (23). Transitory ischemic attacks (TIAs) imply that the symptoms disappear within 24 hours (24). Cerebral infarctions (CI) are responsible for approximately 85% of all strokes, intracerebral haemorrhage (ICH) for 10% and subarachnoidal haemorrhage (SAH) for 5%. Stroke severity is generally higher in patients with ICH than those with CI but patients with ICH show better recovery ratios (25).

Approximately 30 000 people suffer stroke every year in Sweden, of whom 20 000 for the first time (24). About 80% of the patients with first-ever stroke are expected to survive the first month (26). Approximately the same number of women as men suffer a stroke (24). More than 80% of the people who suffer a stroke in Sweden are over 65 years of age. The mean age for stroke onset is 76 years, 78 for women and 74 for men (24). The number of stroke victims is expected to rise significantly in the future as the percentage of senior citizens in the country increases (27).

In Sweden, stroke is the most common cause of neurological disability in adults and the third most common cause of death (9). Approximately one third of the patients suffer severe stroke, another third moderate stroke and one third suffer mild stroke (28). More than half of all survivors have persisting disabilities after stroke (28). With nearly one million health-care days per year, stroke is the somatic disease accounting for most health-care days (9) and the total direct and indirect cost of stroke in Sweden is approximately SEK 14 billion, yearly (24).

Stroke is an acute condition and patients with stroke symptoms, for example sudden weakness in arm or leg or aphasia, should be taken to hospital as fast as possible (9). One reason for this is that some patients may need thrombolytic therapy. The percentages of patients receiving thrombolytic therapy in Sweden were 0.9% in 2003 and 3.5% in 2006 (24). In hospital, patients with acute stroke symptoms are assessed to exclude differential diagnoses, to chart the patients' neurological symptoms and disabilities as well as their need for rehabilitation (9).

Since the late 60s, the survival rates among stroke patients have increased manifold (5). It has been suggested that stroke has become a less lethal and disabling, though no less common, disease, resulting in an increased prevalence of stroke in the older population (5). One reason for the increasing survival rates among stroke patients might be the improved stroke care. For example, the number of patients treated in stroke units has increased during recent decades (27). Riks-stroke, the Swedish national quality register on stroke care, shows that outcome is better in patients treated in stroke units than in general wards, not only in randomized trials but also in routine stroke care (29). A stroke unit is an organized institutional care unit that exclusively or almost exclusively

treats patients with stroke and is managed by a multi-professional team competent in stroke care (24).

1.3 PARADIGMS WITHIN PHYSIOTHERAPY

Research paradigm is the term used to describe a model in which a community of scientists generates knowledge. The different models quoted in physiotherapy and health care literature are: The biomedical model, in which disease and disability are thought to reflect deviations from what is considered as normal and illness and disease are thought to exist outside cultural and historical limits (30). The social model, which builds on the concept of disability as being socially determined rather than belonging to an individual disabled person (30). Holism, which contradicts the biomedical model by claiming that certain wholes are greater than the sum of their parts and that one should look at the whole first to make sense of the parts (30). The biopsychosocial model is a further development of holism. It divides human beings into three inter-related entities – a biological being, a psychological being and a social being – examining all three and then adding them together to make a whole (30).

1.4 INTERNATIONAL CLASSIFICATION OF FUNCTIONING, DISABILITY AND HEALTH

In rehabilitation literature, a uniform language for the classification of disability is often missing. The International Classification of Functioning, Disability and Health (ICF) (31) is based on the biopsychosocial model and provides a standardized language and framework for the description of health and health-related states. The ICF was presented by the WHO in 2001 (31). The domains within the ICF are classified from body, individual and societal perspectives. The classification consists of two parts, each with two components. The first part is: functioning with the components: body functions and structures, and activities and participation. The other part is: contextual factors with the components: environmental and personal factors. Functioning is an umbrella term encompassing all body functions, activities and participation; similarly, disability is an umbrella term for impairments, activity limitations and participation restrictions. The interactions between the components described within the ICF work in two directions; just as the health condition may modify the disabilities, the presence of disability may also modify the health condition itself. The ICF is used as a theoretical framework for the present thesis because it provides a standardized language and a compound view of health without any assumptions regarding causality (31).
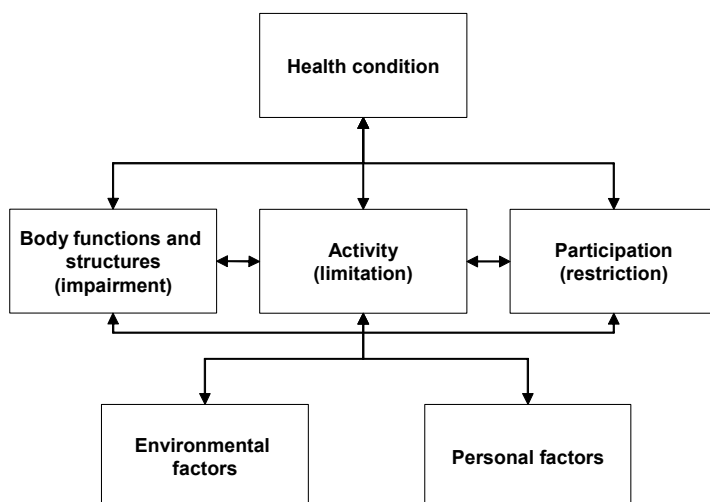
Figure 1. The theoretical model of the interactions between health condition and the components of the ICF.

1.4.1 Definition of the components of the ICF

Body functions are physiological functions of body systems (including psychological functions), and body structures are anatomical parts of the body. Impairments are problems in body function or structure such as a significant deviation or loss. Activity is the execution of a task or action by an individual. Activity limitations are difficulties that an individual may have in executing activities. Participation is involvement in a life situation and participation restrictions are problems that an individual may experience in such situations. Environmental factors make up the physical, social and attitudinal environment in which people live and conduct their lives. Personal factors include factors that influence how disability is experienced by the individual.

The terms health, health condition and well-being are not included in the ICF, although they are related to the model and are therefore briefly described here: Health is defined by the WHO as "a state of complete physical, mental and social well-being and not merely the absence of disease and infirmity" (32). Health condition is an umbrella term for acute or chronic disease, disorder, injury or trauma. Well-being is a general term comprising all human life areas, including physical, psychological and social aspects of what can be called "a good life" (31).

1.4.2 Body functions and impairments after stroke – associations with other body functions, activities and health-related quality of life

As a stroke can affect any part of the brain, a large number of body functions and structures, activities as well as participation and contextual factors are considered relevant for patients with stroke (33). Many terms used in stroke literature are not ICF terms. To allow comparison with other studies, some terms used in this thesis are not

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ICF terms. All terms are however sorted according to the ICF. Below follow descriptions of functioning and disabilities after stroke as well as contextual factors that are discussed in the thesis, starting with body functions and impairments.

1.4.2.1 Mental functions

In the literature cognitive functions are defined as all the mental activities associated with thinking, knowing and remembering (34). Impaired cognitive functions are reported to be present in more than 30% of patients with stroke (35, 36). Some studies have shown an association between impaired cognitive functions and activity limitations after stroke (35, 37), whereas another study did not show any association between those variables (38). The conflicting results are probably due to a diversity of assessment tools, diagnostic criteria and time point of assessment in the different studies. The above studies all assessed cognitive functions more than two weeks after stroke onset.

Perceptual function is defined as the mental functions of recognizing and interpreting sensory stimuli (31). Impaired perceptual function is common after stroke although the reported frequency varies in different studies (39). One study has shown an association between impaired perceptual functions and activity limitations one to four days after stroke onset (40), whereas another study did not show any association between those variables in the first week after stroke (41).

Depression after stroke might occur at the same time as the neurological impairments, or develop slowly, although still clearly connected to the stroke (9, 42). The percentage of patients who develop depression after stroke has been reported to be 30-40% (43). During the in-patient hospital stay, 15% of the patients have been shown to suffer from depression (44). The most common symptoms in people with depression are depressed mood, i.e. sadness, decreased interest, loss of appetite, changed sleep patterns, changed motor function, physical and mental fatigue, self-accusation and feelings of guilt, difficulties in concentrating and making decisions and suicidal thoughts (45). For a medical diagnosis of major depression, according to the Diagnostic and Statistical Manual of Mental Disorders (DSM IV), to be made, at least five of the above-mentioned symptoms should have been present daily over the past two weeks, with the two cardinal symptoms, sadness and loss of interest, always being present (46). Further, the depressive symptoms should not be due to a medical condition (46). When diagnosing depression in patients with stroke, exceptions can be made from the above criteria as well as from the time criteria (44). As rather few patients meet the criteria for a diagnosis of depression in the first week after stroke, an alternative is to screen for depressive symptoms. Indeed, it has been recognized that two questions about the DSM-IV core symptoms (sadness and loss of interest) are equally effective in detecting depression as more time-consuming instruments (47). It has been suggested that depression influences physical and cognitive impairments after stroke negatively (48). Depression after acute stroke has also been shown to be associated with activity limitations, and to exert a negative effect on rehabilitation, for a multitude of theoretical reasons, many not yet clearly defined (42, 49).

1.4.2.2 Sensory functions and pain

Somatosensory impairments, including touch and proprioceptive impairments, have been reported to be prevalent in up to 60% of patients with stroke (50). It has been shown that normal somatosensory function is associated with high activity levels 10 days after acute stroke (51). However, impaired somatosensory function is an uncertain indicator of negative outcome (51).

1.4.2.3 Neuromusculoskeletal and movement-related functions

Impairments resulting from damage to the upper motor neuron (UMN), often referred to as the UMN syndrome, including lesions in the pyramidal and parapyramidal tracts, exhibit positive and negative features (52). The negative features are: weakness and loss of dexterity. Dexterity can be described as skill in generating appropriate spatial and temporal muscle activation patterns that conform to environmental demands (53). Loss of dexterity has been shown to be a specific negative impairment that can exist independently of the other impairments of the UMN syndrome (53). Weakness and impaired dexterity have both been shown to be associated with physical disability after stroke (54). Grip strength has been shown to be associated with upper extremity functioning (55, 56). It has been acknowledged that the negative features of the UMN syndrome are often more troublesome for the patient than the positive features (57).

The positive features of the UMN syndrome are characterized by muscle over-activity, either excessive muscle contraction or some sort of inappropriate muscle activity (58). They can be divided into three main categories (58). The first is spinal reflexes, the second is efferent drives and the third category is the various disorders of voluntary movement (58). Spinal reflexes are afferent-dependent, relying on sensory feedback from the periphery, such as pain, cutaneus stimulation or muscle stretch (58). Stretch reflexes are proprioceptive reflexes, and are either phasic or tonic. The phasic stretch reflex or the tendon jerk arises from a short muscle stretch. The tonic stretch reflex arises from a sustained muscle stretch and is the cause of spasticity (58). Spasticity is defined as a velocity-dependent increase in tonic stretch reflexes experienced by a clinician attempting to flex or extend a limb in patients with UMN lesions (59). It is caused by abnormal processing of proprioceptive input in the spinal cord, not by hyperactive muscle spindles (58). The period of shock which often follows a lesion to the UMN is suggested to be due to sprouting of neural afferent axons or to changes in receptor sensitivity (58). Spasticity may be exacerbated by muscle contracture because, when a muscle and its spindles shorten due to contracture, a stretch of the muscle may increase the size of the tonic stretch reflex (52). Contracture is caused by immobility and is considered to be an adaptive feature of the UMN syndrome, i.e. a consequence of the impairments caused by the stroke (58). The tonic stretch reflex, i.e. the neuronal component of spasticity, has been shown to reach its peak one to three months after stroke, while the phasic stretch reflex continues to increase during the first year after stroke (60, 61). Lesions to the cortex or the internal capsule may give rise to some spasticity, hyper-reflexia, and clonus, while lesions to the dorsal reticulospinal tract, in the brain stem or spinal cord, produce marked spasticity, hyper-reflexia and flexor and extensor spasms (Figure 2) (58).

As mentioned in the background, a previous study, conducted on the same sample of patients as evaluated in the present thesis, found that 19% of all patients exhibit spasticity three months after stroke (13). Another study found that as many as 39% of stroke patients suffer from spasticity 12 months after first-ever stroke (62); in that study, however, non velocity-dependent resistance to passive stretch i.e. shortened muscle length was also regarded as evidence of spasticity.

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┌──────────────────┐
│  Motor areas of  │
│   the cortex     │
└──────────────────┘
        │ Internal capsule
(excitatory)│

┌──────────────┐  ┌──────────────┐  ┌──────────────────┐
│ Ventromedial │  │ Bulbopontine │  │ Vestibular nucleus│
│  reticular   │  │  tegmentum   │  │                  │
│  formation   │  │              │  │                  │
└──────────────┘  └──────────────┘  └──────────────────┘
Dorsal            Medial            Vestibulo-
Reticulo-         Reticulo-         spinal
spinal            spinal tract      tract
tract             (excitatory)      (excitatory)
(inhibitory)

         ┌──────────────┐
1a-afferent│ α-motorneuron│
         └──────────────┘
Muscle stretch    Muscle contraction
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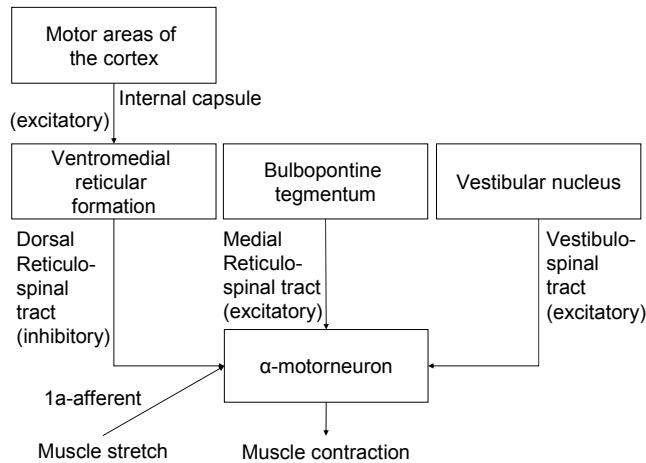
Figure 2. The major descending pathways controlling spinal reflex excitability: theoretically adopted from Sheean G. (58).

The third category of the positive features of the UMN syndrome is disordered control of voluntary movements (58). One example of this is co-contraction, i.e. the simultaneous contraction of agonist and antagonist muscle groups (58). It is suggested that co-contraction results from an activation of tonic stretch reflexes in combination with an inability to control reciprocal inhibition of agonist and antagonist muscle groups (58). An inability to control reciprocal inhibition can also result in excessive reciprocal inhibition, which can produce the appearance of weakness. For example, if a muscle is contracted by spasticity, then the muscle on the opposite side of the joint may be strongly inhibited (58). In addition to co-contraction and excessive reciprocal inhibition, biomechanical factors might contribute to impaired voluntary movements. Inability to control individual joints are often referred to as abnormal synergies (6, 63). For patients moving within abnormal synergies, the muscles are so strongly linked that movement outside of the fixed pattern is often not possible (6). According to Brunnström, a pioneer of physiotherapy, recovery after stroke is reflected by the capacity to move outside of abnormal synergies, the so called hemiplegic limb synergies (6). Recovery is said to occur in six sequential stages (Table I), but may become arrested at any stage (6). Two kinds of synergy patterns are described by Brunnström; flexion and extension synergies. In the upper extremity, a full flexor synergy is characterized by scapular retraction and elevation, shoulder abduction and external rotation, elbow flexion, forearm supination and wrist and finger flexion; and a full extensor synergy is characterized by scapular protraction, shoulder adduction and internal rotation, elbow extension, forearm pronation and wrist extension. In the lower extremity, a full flexor synergy is characterized by hip flexion, abduction and external

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rotation, knee flexion, ankle dorsiflexion and inversion and toe dorsiflexion; and a full extensor synergy is characterized by hip extension, adduction and internal rotation, knee extension, ankle plantar flexion and inversion and plantar flexion.

Table I. Brunnström's six stages of recovery after stroke

Stage	Movement	Evaluation method
1	None	No voluntary movement is present
2	Weak associated movements in synergy; little or no active finger flexion	When movement is attempted, there are associated movements in synergy
3	All movements are in synergy; mass grasp in hand	Full upper-extremity synergy; hip, knee and ankle flexion are coupled in either sitting or standing
4	Some deviation from synergies; lateral grasp and semi-voluntary finger extension	The patient can place his hand behind his back; flex at the glenohumeral joint with his elbow extended; pronate/supinate his forearm with the elbow flexed; sit and dorsiflex the foot while keeping the heel on the floor; and sit and slide the leg past 90 degrees
5	Almost free from synergies; palmar grasp and voluntary mass extension of digits	The patient can perform the tests for stage 4 with greater ease and abduct the glenohumeral joint with the elbow extended; flex the glenohumeral joint more than 90 degrees with the elbow extended; pronate/supinate the forearm with the elbow extended; flex the knee and extend the hip in standing position; and dorsiflex the ankle with the knee extended in the standing position
6	Free of synergy	In the present thesis, if the hemiparetic patient cannot fully perform a certain movement (because of weakness, for example), but can isolate movements and master individual joint movements, without activating synergistic movements, the patient is considered to be moving outside the synergies.

Laboratory studies have demonstrated a limited ability in hemiparetic patients with stroke to activate muscles outside of the hemiplegic limb synergies (10, 64-66). In contrast, other laboratory studies have shown that stroke patients have equally impaired movements, regardless of whether they are moving within or outside a particular hemiplegic limb synergy (67-69). Despite these contradictory results, the existence of abnormal synergies after stroke is often taken for granted in rehabilitation literature (12, 70, 71). Brunnström's sequential stages of recovery also serve as a theoretical base for two commonly used scales for assessment of voluntary movements after stroke, the Chedoke McMaster Stroke Assessment and the Fugl-Meyer stroke scales (11, 72, 73). The hemiplegic limb synergies, as described by Brunnström, are also used to assess the control of voluntary movements after stroke both clinically and in research (12, 70, 71).

Studies that use hemiplegic limb synergies to assess the control of voluntary movements after stroke usually feature selected samples of patients recruited from rehabilitation settings (11, 12, 70, 71).

1.4.3   Body structures – structures and impaired structures of the brain

The brain structures affected by the stroke may influence the symptoms, as patients with right- versus left-sided lesions may present different symptoms. Lesions to the left hemisphere may for example cause aphasia, while spatial deficiencies are more common after lesions to the right hemisphere. It has been suggested that initial stroke severity predicts recovery from movement impairments and of self-care activities similarly for right- and left-hemisphere strokes, but lesion side may modify the association between initial stroke severity and outcome on depressive and cognitive measures (74).

1.4.4   Activities and participation after stroke – associations with body functions, other activities and length of hospital stay

Activities and participation are not separate according to the ICF but constitute one list (31). Mobility and self-care scales have, however, been suggested as suitable outcome measures for activity, while it is suggested that scales assessing HRQL mainly assess the participation category (75, 76).

1.4.4.1   Mobility

About 50% of all patients with stroke are estimated to have mobility limitations (manipulation of objects not included) one year after stroke (77). In this thesis, mobility is defined as moving by changing body position or location or by transferring from one place to another, by walking, running or climbing, or by using wheelchairs, i.e. transportation (31). Mobility scores in the acute phase after stroke have been shown to predict recovery of disabilities and length of hospital stay (15, 28).

According to the ICF, *fine hand use*, i.e. manipulating objects, is included in the definition of mobility (31). Fine hand use is a complex activity, requiring many body functions such as dexterity (as defined in section 1.4.2.3) and somatosensory-, perceptual- and cognitive functions (21, 78). There are about 30 muscles in the hand, which need to be coordinated in order to perform skilled hand movements (78). Proximal muscles are also important for stabilizing the hand (78). Many parts of the brain are involved in the neural control of the hand, and the pyramidal fibers play an important role (78). A study on a group of severely disabled patients with stroke shows that 38% had regained some fine hand use and 12% had regained complete fine hand use six months after stroke onset (79).

1.4.4.2   Self-care

According to the ICF, self-care is defined as caring for oneself, washing and drying oneself, caring for one's body and its parts, dressing, eating and drinking, and looking after one's health, i.e. personal activities of daily living (ADL) (31). Independence regarding self-care is of paramount importance for all individuals. The frequency of

dependence in self-care activities after stroke is difficult to estimate since the definitions vary between studies. About one third of all patients with stroke are, however, estimated to be dependent regarding self-care six months after stroke onset (80). Self-care scores in the acute phase after stroke have been shown to predict recovery of disabilities and length of hospital stay (15, 28).

1.4.5 Environmental factors

It has been suggested that an enriched environment, including social interaction and physical activity significantly improves functional outcome after stroke (81). Environmental factors are not explicitly described in the present thesis although they may have influenced the patients' functioning.

1.4.6 Personal factors

Personal factors include characteristics such as age, gender, lifestyle, upbringing, coping ability, social background, education and life experience. These factors are considered to play a very important role in the patients' functioning (33). The only personal factors included in this thesis are the patient's gender and age. It has been suggested that female gender is associated with a less favourable outcome after stroke (82) and women are also generally older than men at the time of stroke onset. The risk of suffering a stroke increases with age (9). Older age, compared to younger, has also been shown to be associated with a worse pre- to post-stroke cognitive decline, more dementia, as well as a worse pre- to post-stroke decline in physical function, self-care and social functioning (16). It has, however, been suggested that functional recovery depends more on the extent of the initial disability than on age (83, 84).

1.5 HEALTH-RELATED QUALITY OF LIFE

1.5.1 Quality of life and health-related quality of life

The WHO defines quality of life (QoL) as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns". It is a broad-ranging concept affected in a complex way by the person's physical health, psychological state, level of independence, social relationships, and their relationship to salient features of their environment (85). For practical reasons, QoL is often restricted to HRQL (86). HRQL is a narrower concept than QoL and measures of HRQL concentrate on the functional effect of an illness as perceived by the patient (87). The term "health status" is a limited element of HRQL, referring to "self-rated health" and "functional ability" (88). HRQL is not a part of the ICF. Post et al (87) have, however, suggested a conceptual model, where the concept of quality of life is integrated with the ICF. In their model, quality of life is seen as an overall concept, incorporating all levels of the ICF. The terms health or health status are used to indicate the total profile of all body functions, activities and participation. Finally, overall well-being, or happiness, is given a separate place in the model, where well-being cannot be seen as part of health but rather, health is one of the possible determinants for well-being (87).

1.5.2 Health-related quality of life after stroke

HRQL, two years after stroke, has been shown to be very poor in a substantial proportion of stroke survivors (89). In another study (90), 66% of the patients reported a deterioration in life situation compared to the pre-stroke level. The patients' HRQL also deteriorated over a 12-month period after stroke onset (90). In contrast, a population-based case-control study from New Zealand (91) reports that the HRQL appears to be relatively good for the majority of patients as much as six years after stroke. The authors suggest that, despite physical disability, patients with stroke appear to adjust well psychologically to their illness with time after stroke onset (91). The conflicting results may be due to different time points for the assessments.

Factors that influence HRQL after stroke negatively are, for example, physical impairments and activity limitations (89, 92), depression (89), cognitive impairment (93), female sex (92, 93), and low socioeconomic status (89, 92, 93). The influence of age on HRQL after stroke shows conflicting results (89, 92, 93).

1.6 PHYSIOTHERAPY

The World Confederation for Physical Therapy describes the nature of physiotherapy as "providing services to people and populations to develop, maintain and restore maximum movement and functional ability throughout the lifespan. Physical therapy includes the provision of services in circumstances where movement and function are threatened by the process of aging or that of injury or disease. Full and functional movement is at the heart of what it means to be healthy" (94). Further it is stated that "Physical therapy is the service only provided by, or under the direction and supervision of a physical therapist and includes assessment, diagnosis, planning, intervention and evaluation" (94).

The Swedish National Board of Health and Welfare and the European Stroke Initiative recommend that practically all patients who suffer a stroke should be admitted to acute hospital care and be assessed by physiotherapists (9). For patients in need of rehabilitation, treatment should be initiated at an early stage after stroke (9, 95).

1.6.1 Physiotherapy and stroke rehabilitation

The therapist's perception of the extent to which each impairment and activity limitation may affect functioning and the HRQL of the patients may influence their choice of rehabilitation methods and, hence also, the outcome of the rehabilitation. So far there is no consensus on what disabilities cause the activity limitations in patients with stroke or on what physiotherapy treatment to use (8). Some of the available physiotherapy approaches are briefly described below.

As mentioned in the background, many of the most commonly employed physiotherapy approaches are based on the assumption that abnormal reflexes, constraining the patient's ability to move normally, are the most troublesome contributors to hemiparesis after stroke (8). The most common of these, so-called neurodevelopmental approaches, is the Bobath concept (8, 63).

Carr and Shepherad developed the motor relearning model for rehabilitation (96). The training emphasizes the importance of the task and the context to avoid the problem of transfer to real life. This approach assumes that movements emerge as an interaction between many systems and that patients learn by actively attempting to solve the problems of a functional task rather than repetitively practising normal movements. Carr and Shepard suggest a therapeutic model for rehabilitation developed from a theoretical base (96).

A therapy that has been shown to be effective for improving control of voluntary movements and activities, including dexterity, especially of the upper extremity, by means of evoking brain plasticity, is Constraint Induced Movement Therapy (CIMT) (97). CIMT includes intensive repetitive training of "real world tasks" by shaping, i.e. constantly increasing the challenge of the task, and a constraint of the non-affected upper extremity. This therapy has proved to be effective even months and years after stroke onset (97, 98). However, only a small percentage of all patients with stroke meet the inclusion criteria for CIMT (97, 98).

So far, there is insufficient evidence to prove that any treatment is superior to another (8, 9). Some studies have suggested that task-specific training might be more effective than the neurodevelopmental approaches, although the data supporting those results are meagre (9, 99). It has been suggested that if physiotherapists are to practice evidence-based stroke rehabilitation, their own attitudes will have to shift away from the use of compartmentalised approaches to assessing the scientific and research base for each treatment technique (8).

The main goals of rehabilitation for patients with stroke are set at the level of activity and participation (100). Impairments may however limit the patient's ability to perform activities and should therefore be considered while teaching the patients to perform an activity. Although, treatment of specific impairments is not always conducted by physiotherapists, the documented effectiveness of these treatments is described here in order to give a comprehensive picture of the impairments discussed in the thesis.

There is some evidence suggesting that cognitive training improves alertness, sustained attention, memory and, possibly, self-care activities after stroke (101, 102). Further, there is some evidence suggesting that rehabilitation of perceptual impairments by visual scanning improves physical function and, possibly, self-care activities after stroke (101, 103). Depression after stroke is mainly treated pharmacologically (9). A longitudinal study has shown that post-stroke depression improved irrespective of whether the patients had received antidepressant medication or placebo (44). A positive effect of the antidepressant medication was, however, observed in QoL (44). It has been suggested that a programme aiming at improving somatosensory impairment, including, for example, exercises on recognizing and distinguishing sensory stimuli, is effective for patients with pure sensory strokes (104). It has also been suggested that, for some patients with somatosensory impairment, vision is an effective compensatory mechanism when performing finger manipulation tasks (105). Resistance training has been shown to increase muscle strength after stroke, although it has not been clearly established whether strength training leads to improved activity levels (106). Spasticity is sometimes treated, for example, by movement exercises or splints although there are

no scientific data supporting such treatments (9). Maintaining muscle length by active and passive movements is, however, important to prevent muscle shortening, as muscle shortening may be an important contributor to spasticity (52). Pharmacological treatment or intramuscular injections of Botulinum toxin is currently used for treatment of spasticity (9). Alleviation of spasticity in stroke patients by injection of Botulinum toxin in combination with therapeutic interventions, most of which were forms of physiotherapy, has been shown to reduce activity limitations (107, 108). At present, however, there is no evidence that suppression of spasticity improves motor function (109).

1.6.2 Rationale for the thesis

In planning rehabilitation services, it is important to know the frequency of the impairments and activity limitations presented by the patients and also how each body function and activity is associated with other body functions and activities, as well as with the patients' HRQL at different time points after stroke. Further it is important to know whether the associations between functioning change with time after stroke. Knowledge concerning this might be of assistance in setting priorities, planning rehabilitation resources and choosing rehabilitation strategies at different time points after stroke onset. This knowledge is important in order to give each patient the best possible rehabilitation according to their individual needs.

Recovery from disability occurs in most patients within three months from stroke onset (110), although, in some patients, recovery continues long after the onset of stroke (111). The time course of recovery from impairments and activity limitations is however strongly related to initial stroke severity (110). Therefore, functioning among some patients in the present thesis is described in the first week and also three months after stroke. Further, these patients were followed up at 18 months after stroke. The 18-month follow-up was chosen since few data exist in the literature, describing functioning among patients with stroke more than one year after onset. On the other hand, a longer follow-up would probably have resulted in too large a number of dropouts.

Functioning in the other sample of patients in the present thesis is described at five days after stroke onset. The rationale for assessing functioning at that time point is that a decision on the most proper subsequent level of care usually has to be made five days after stroke onset at Danderyd Hospital (DS). Further, as mentioned in the background, activity limitations five days after acute stroke, in the same patients as evaluated in the present thesis, have been shown to exert a negative impact on discharge destination and length of hospital stay (15). The changes in functioning between five and 10 days after stroke, in those patients, were small in contrast to the rapid recovery pattern often seen during the first days after stroke (15). Also, the mean time for inpatient stroke care at many hospitals in large cities in Sweden is less than 10 days (24).

2 AIMS

The overall aims of the thesis were to describe body functions, activities and HRQL in patients with stroke and to analyse the associations between those variables in the first week and three and 18 months after stroke onset.

The specific aims were to describe and analyse:

I. The extent to which the impaired voluntary movements of hemiparetic stroke patients are restricted to the hemiplegic limb synergies described by Brunnström, and the extent to which the synergies are related to impairments and activity limitations, in the first week and at three months after stroke

II. The frequency of spasticity, 18 months after stroke, and its association with impairments, activity limitations and HRQL

III. The association between somatosensory (touch and proprioceptive), perceptual and cognitive functions, as well as depressive symptoms, as independent variables, and mobility and self-care, respectively, as dependent variables five days after acute stroke in older patients (≥65 years)

IV. Whether assessment of somatosensory functions will also provide information on perceptual functions in older patients with acute stroke

V. The recovery from limited fine hand use and its association with somatosensory functions, grip strength, upper extremity movements and self-care in the first week and at three and 18 months after stroke, and whether the strength of the associations changes over time

VI. The recovery from limited fine hand use compared to the recovery from other impairments and activity limitations

3 PATIENTS AND METHODS

3.1 PATIENTS

All patients were recruited from the stroke unit at DS in Stockholm, Sweden. The hospital serves an area of approximately 250 000 inhabitants in the Stockholm area. About 600 patients with stroke were treated at DS, in the year 2002, and, of those, more than 80% were treated at the stroke unit. Since SAH is considered to have a different etiology from that of CI and ICH, and patients with SAH present more global symptoms, patients with SAH are not included in this thesis. About 2% of all patients with stroke suffer cerebellar stroke, also presenting a specific syndrome (112). Patients with cerebellar stroke are not included in this thesis, either.

This thesis is based on four papers, carried out on two different samples of patients. Papers I, II and IV are carried out on one sample and Paper III on another. Twenty-five patients were included in both samples. None of the patients in the thesis received thrombolytic therapy.

3.1.1 Patients included in Papers I, II and IV

For Papers I, II and IV, consecutive patients with stroke were recruited (unless presenting at weekends or public holidays) from the stroke unit of DS between June 2001 and March 2002. Patients ultimately enrolled in the study were those residing in Stockholm who presented with an acute, first-ever stroke, in the absence of other diagnoses affecting muscle tone, who were conscious and who agreed to participate in the study. For patients with communication problems, proxy consent was obtained. Examples of other diagnoses affecting muscle tone are neuromuscular diseases, Parkinson's disease, multiple sclerosis and spinal cord injuries.

Initially, 109 patients were enrolled in the study, although one patient suffered a second stroke in the first week. During the three-month follow-up, three patients suffered a second stroke, four died, five claimed to be fully recovered and declined further participation, and one could no longer be located. At the 18-month follow-up, an additional 29 patients had been excluded, for the following reasons: nine had suffered a second stroke; 15 had died; four declined further participation (including one who claimed to be fully recovered); and one could no longer be located.

The patients were assessed initially, i.e. when admitted to the stroke unit and diagnosed with a first-ever stroke, as well as three and 18 months after stroke. Paper I includes the patients who presented with hemiparesis and were assessed initially and three months after stroke. Paper II evaluates the patients' functioning at the 18-month follow-up, and Paper IV evaluates the patients' functioning at all three occasions. Paper I includes 64 patients—39 women and 25 men, with a mean age at recruitment of 79 years (range 44 to 90)—who were hemiparetic three months after stroke. Papers II and IV include 66 patients—44 women and 22 men, with a mean age at recruitment of 76 years (range 44 to 93). Table II shows an overview of the three assessment occasions and the papers including data from each assessment occasion.

Table II. Sample of patients recruited between June 2001 and March
2002 and included in Papers I, II and IV.

	Paper I	Paper II	Paper IV
Assessment time (Number of patients)			
First week after stroke (N=109)	X		X
Three-month follow up (N=95)	X		X
Eighteen-month follow up (N=66)		X	X

3.1.2 Patients included in Paper III

For Paper III, patients were recruited from the Stroke Unit at DS from September 1999 to May 2002. Patients with acute stroke were eligible for the study if they were 65 years or older, still in hospital five days after stroke onset and had movement-related impairments, i.e. ≤17 points on the Scandinavian Stroke Scale (SSS) (arm, hand, leg, maximal score 18 points), or limitations in mobility or self-care, i.e. ≤11 on the Rivermead Mobility Index (RMI) or ≤65 on the Barthel Index (BI) and agreed to participate in the study. For patients with communication problems or impaired consciousness, proxy consent was obtained. After examination and treatment conducted by all members of the team, about 50% of the patients at the stroke unit are discharged and sent home within five days after stroke onset. We excluded patients dependent on personal care assistance prior to the current stroke; patients with diagnosed dementia or severe confusion preventing them from living at home; and patients with non-stroke-related major disorders that considerably affected their activity level. One hundred and fifteen patients—52 men and 63 women, mean age 81 (range 65-96) years were included according to the inclusion and exclusion criteria.

3.2 DATA COLLECTION PROCEDURE

The assessments in Papers I, II and IV were conducted by four physiotherapists and the assessments in Paper III were conducted by five physiotherapists and three occupational therapists co-trained for the purpose. To improve inter-rater reliability between the therapists involved, at least 15 of the patients in Paper III were assessed by all the therapists and more than one third of the assessments in Papers I, II and IV were performed by at least two of the physiotherapists. When more than one therapist assessed a patient, one of the therapists conducted the actual assessment and the other therapist/therapists noted the scores. The score noted represented a consensus reached by the therapists involved in the assessment. All assessments were made in a predefined order. The assessments were performed either in the hospital or in the patient's home.

3.3 REGISTERED DATA

Table III includes an overview of the clinical scales used in the thesis.

Table III. Clinical scales (possible ranges of score) in Papers I-IV.

Clinical scale (possible range of scores)	Paper I	Paper II	Paper III	Paper IV
Mini-Mental State Examination (MMSE) (0-30 points)			X	
Line Cancellation Task (0-36 points)			X	
Letter Cancellation Task (0-29 points)			X	
Kohs Block Design Test (0-7 points)			X	
Montgomery Åsberg Depression Rating Scale (MADRS)				
Item 2, reported sadness (0-6 points)			X	
Item 4, reduced sleep (0-6 points)			X	
Item 5, reduced appetite (0-6 points)			X	
Item 7, lassitude (0-6 points)			X	
Touch function (Normal/Impaired)			X	X
Thumb Localizing Test (Normal/Impaired)			X	X
Modified Ashworth Scale (MAS) (0, 1, 1+, 2, 3 or 4 points)	X	X		
Self-reported muscle stiffness (Yes/no)		X		
Tendon reflexes (Increased/not increased)		X		
Vigorimeter (Air pressure in kPa)				X
Lindmark Motor Assessment Scale (LMAS)				
Active movements, upper extremities (0-57 points for each side)	X	X		X
Active movements, lower extremities (0-36 points for each side)	X	X		
Rapid movements, upper extremities (0-6 points for each side)	X	X		
Rapid movements, lower extremities (0-6 points for each side)	X	X		
Brunnström's hemiplegic limb synergies (1-6 points)	X			
Scandinavian Stroke Scale (SSS) (0-18 points [Arm, hand, leg])	X			
Rivermead Mobility Index (RMI) (0-15 points)	X	X	X	
Nine Hole Peg Test (NHPT) (Time in seconds)	X	X		X
Barthel Index (BI) (0-100 points)	X	X	X	X
Swedish Short Form 36 (SF-36) (0-100 points for each health scale)		X		

3.3.1 Assessment of body functions and impairments

Cognitive functions were screened via the Mini-Mental State Examination (MMSE) (113), five days after stroke in Paper III. The scale ranges from 0-30 points and a normal range has been established at 24-30 points (114). The MMSE was chosen for

assessment of cognitive functions because it is widely used in studies of patients with stroke (73). The MMSE can however be criticized for being a rough measure of cognitive function with low sensibility (115). Patients with interrupting aphasia or dysarthria were not assessed by the MMSE. The MMSE is considered to show acceptable validity in detecting cognitive dysfunction at an early stage after stroke in older patients (116) and to be reliable (117).

Perceptual space function was assessed using the Line (118) and Letter Cancellation Tasks (119), five days after stroke in Paper III. Possible score ranges are 0-36 and 0-29, respectively. The patients were allowed unlimited time to complete the tests. The score represents the number of targets cancelled. In assessment of the Line Cancellation Task, four lines at the centre of the page are used for demonstration, leaving 36 lines to cancel. The patients were asked to cancel the remaining lines, ruled in a standard fashion on a sheet of Paper. The suggested normal value is 32-36 cancelled lines (120). In assessment of the Letter Cancellation Task, the patients were asked to cancel 29 of 30 target "A"s among 120 distracting letters, displayed at random on a sheet of Paper. One "A" at the centre of the page was used for demonstration. No normal value has been established. We used the same percentage definition of normal as in the Line Cancellation Task, i.e. 26-29 cancelled targets. At least two different cancellation tests are recommended to identify all patients with impaired attention. These cancellation tests are widely used and are considered valid tests of perceptual space function (121) but have not been tested for reliability.

Perceptual functions were further evaluated with respect to colour sense and visuospatial construction, using the Kohs Block Design Test (122), five days after stroke in Paper III. Possible range of scores is 0-7 points. There are 16 cubes with one red, one white, one blue, one yellow, one red-white and one blue-yellow side. The colours divide the two-coloured sides diagonally. Four cubes are used in tests 1 to 4; nine cubes in tests 5 and 6; and 16 cubes are used in test 7. One point is given for each construction. The test leader demonstrated the task by building two constructions from given designs, presented on pictures. The patients were allowed unlimited time to complete the test. No normal value has been established. We chose the cut-off 0/>0, to minimize the skewed distribution towards the less impaired patients. The Kohs Block Design Test is considered valid (123) and reliable (124) in evaluating everyday spatial function.

Selected depressive symptoms were assessed, five days after stroke in Paper III, from the Montgomery Åsberg Depression Rating Scale (MADRS) (125): item 2, reported sadness; item 4, reduced sleep; item 5, reduced appetite; and item 7, lassitude (0-6 points for each item. A higher score indicates a more severe symptom). Item 2, reported sadness, was chosen since it represents a core depressive symptom, equivalent to the first of the two cardinal symptoms in the DSM-IV depression diagnostic criteria (46). Item 4 and 5, reduced sleep and reduced appetite were chosen in order to depict the autonomic situation of the patient. Item 7, lassitude, was chosen since it is a common depressive symptom which is associated with the second of the two cardinal symptoms in the DSM-IV depression diagnostic criteria (46). Item 2 was observed by the staff, while the remaining items were reported by the patient. The MADRS is considered valid and reliable also for individual items (125).

Touch function was determined by testing the ability to perceive pinprick (metal pin) and light touch (cotton wool) on the upper arm, forearm, dorsal hand, thigh, calf and dorsal foot, five days after stroke in Paper III; and by testing the ability to perceive light touch on the upper arm, forearm and palm of the hand, in the first week as well as at three and 18 months after stroke, in Paper IV. If the patient was unable to perceive pinprick and/or light touch in one location or more on the affected side with his or hers eyes closed, the test was defined as impaired touch function. A dichotomous outcome was chosen since this rough grading is considered more reliable than a fine-graded scale (126). The tests for touch function have not been tested for validity but are commonly used by physiotherapists and are considered reliable for grading into normal or impaired touch function (126).

Proprioceptive function of the affected upper limb was tested by the Thumb Localizing Test (127), five days after stroke in Paper III; and in the first week as well as at three and 18 months after stroke, in Paper IV. The upper limb of the affected side is positioned passively and the patient is asked to pinch the thumb of that limb with the opposite thumb and index finger, repeated four times. Proprioceptive function is considered normal if the patient is able to locate the thumb on the affected side in three of the four tests with his or her eyes closed. The test is considered valid (127) but has not been tested for reliability.

Muscle tone function—spasticity, defined as velocity-dependent resistance to passive stretch, was assessed by the Modified Ashworth Scale (MAS) (128), in the first week and at three months after stroke, in Paper I; and at 18 months after stroke, in Paper II. The MAS is regarded as one of the best clinical measures of spasticity (129). The scale grades the resistance of a relaxed limb to passive stretch from 1 to 4, where 1+ constitutes the modification. The muscle groups evaluated were, in the upper extremity: arm adductors, elbow flexors and extensors, wrist flexors and extensors, and finger flexors (tested in the sitting position, if possible); and, in the lower extremity: hip adductors, knee flexors and extensors, and plantar flexors (tested in the supine position). If a patient's score was greater than 0 on the MAS for any of the muscle groups tested, he or she was deemed to exhibit spasticity. The highest score for the upper or lower extremities was used in the statistical analysis and the MAS was computed to a scale ranging from 0 to 5. The validity of the MAS can be questioned because the scale does not distinguish between neural and peripheral contributions to the resistance to stretch (130). The MAS is considered fairly reliable (131).

Muscle stiffness was assessed by asking the patient whether he or she experienced increased muscle stiffness anywhere in his or her body at the time of the assessment (Yes or No), 18 months after stroke, in Paper II. If the patient answered, yes, he or she was asked to describe where, verbally or by pointing. The answers were documented as right or left, upper or lower extremity. Self-rated muscle stiffness has been found to be associated with the MAS scores in patients with spinal cord injuries (132) although the rating has not been tested for validity or reliability.

Tendon reflexes were tested using a reflex hammer on the biceps and triceps tendons of the upper extremities and on the patellar and Achilles tendons of the lower extremities, 18 months after stroke, in Paper II. Plantar-flexor tone was also evaluated by counting

the number of clonic beats. The tendon reflexes were rated as normal or increased. Ratings of tendon reflexes are considered to be moderately reliable (133).

Grip strength was assessed by means of the Vigorimeter, which measures air pressure in a rubber bulb, three and 18 months after stroke, in Paper IV. The pressure in the bulb is registered on a manometer via a rubber junction tube and expressed in kiloPascals (kPa). The medium-sized bulb was used for women and the large bulb for men. The Vigorimeter is considered valid and reliable (134).

Control of voluntary movements was assessed using parts 1 and 2 of the 7-part Lindmark Motor Assessment Scale (LMAS) (135) (upper extremity movements 0-57 points, upper extremity rapid movements 0-6 points; lower extremity movements 0-36 points, lower extremity rapid movements 0-6 points; the higher the score, the better). The LMAS was assessed in the first week and at three months after stroke, in Paper I; at 18 months after stroke, in Paper II; and in the first week as well as at three and 18 months after stroke, in Paper IV. The LMAS was chosen for assessment of bilateral voluntary movements since it is not based on any assumptions of motor recovery (135). It consists of simple movements and assesses both the paretic and the non-paretic side. The LMAS is considered reliable and valid (135, 136).

The *occurrence of stereotyped movements* was assessed by Brunnström's hemiplegic limb synergies (stages 1 to 6), hereafter referred to as the synergies (6) (Table I), in the first week and at three months after stroke, in Paper I. The patients' movements were considered to be restricted to the synergies, i.e., to be "within the synergies" if they exhibited the patterns described by Brunnström in stages 2 to 3 and partly restricted to the synergies, hereafter also referred to as "within the synergies," if they exhibited the patterns described by Brunnström at stages 4 to 5. If a hemiparetic patient is able to initiate isolated movements, he is considered to be moving "without clinically evident synergies", i.e. stage 6. Further, if the hemiparetic patient cannot fully perform a certain movement, because of weakness, for example, but can isolate movements and master individual joint movements, without activating synergistic movements, the patient is deemed to be moving without clinically evident synergies. The synergies have not been tested for validity or reliability.

3.3.2 Body structures – structures and impaired structures of the brain

Previous stroke and lesion side was registered in study III. Type of lesion (CI or ICH) was registered in Paper II.

3.3.3 Assessment of activities and activity limitations

Mobility was assessed by the Rivermead Mobility Index (RMI) (137) (possible range 0-15 points; 0 or 1 point on each of 15 items). The RMI was assessed in the first week and at three months after stroke, in Paper I; at 18 months after stroke, in Paper II; and five days after stroke, in Paper III. There is no obvious floor or ceiling effect of the RMI, although the test can be criticized for not giving information about the quality of the activities included. We chose the cut-off ≥4/ <4 for RMI because an RMI score <4 shortly after acute stroke has been found to exert a negative influence on the recovery

of activities, discharge destination and length of hospital stay (28, 84). The RMI is considered valid and reliable for patients with stroke (137).

Fine hand use was assessed by the Nine Hole Peg Test (NHPT) (138), in the first week and at three months after stroke, in Papers I and IV and at18 months after stroke, in Papers II and IV. In Papers I and II, the NHPT was used only to decide whether the patients were hemiparetic or not (see section 3.3.5.). The NHPT has been suggested to be one of the best clinical measures of hand functioning after stroke (126). There is, however, no consensus in the literature on what cut-offs to use for disability, although the task includes putting nine pegs in holes on a wooden board as fast as possible. In the statistical analyses, patients who were unable to pick up a peg or unable to participate in the test were given the lowest possible score. This cut-off was chosen as patients, who were non-assessable according to the NHPT, form a homogenous group, where the inability to be assessed acts as a common indicator of low mobility and self-care scores. The cut-off for the second worst score was chosen according to the ability to place all the pegs within 60 seconds. Finally, the last cut-off for limited fine hand use was based on the ability to perform the test within normal values (the mean value plus two standard deviations, SD) because 95% of all healthy individuals perform the test within two SD from the mean value adjusted for age, gender and affected side (139). The NHPT is considered valid and reliable for evaluating fine hand use (138).

Self-care was assessed by the Barthel Index (BI) (140) (possible range 0-100 points; 0, 5, 10 or 15 points on each of 10 items; 5 is the maximum score for two items, 10 for six items and 15 for two items). The BI was used in Papers I, II, III and IV and was assessed at all assessment times. The BI has been proposed as a standard index for clinical and research purposes (141). Although the BI is a quite rough measure of self-care, it was chosen because it is widely used and results can be compared with other studies. Further, the BI was chosen since it is designed to assess improvement, is sensitive to change (142), can be used on all patients and can be used to predict outcome after stroke (143). We chose the cut-off ≥35/ <35 for BI because a BI score <35 shortly after acute stroke has been found to constitute a negative influence on the recovery of activities, discharge destination and length of hospital stay (28, 84). The BI is considered valid and reliable for patients with stroke (140, 144).

3.3.4 Personal factors

The patients' age and gender were registered in all studies.

3.3.5 Definition of hemiparesis

To avoid subtle differences lacking clinical significance, the patients were regarded as hemiparetic only if they fulfilled ≥ 1 of the following criteria: ≥ 5-point difference in scores between the affected and the non-affected side for the upper or lower extremities on the active-movement dimension of the LMAS; ≥ 2-point difference in scores between the affected and the non-affected side for the upper or lower extremities on the rapid-movement dimension of the LMAS; ≥ 5-second difference in scores between the affected and the non-affected hand on the NHPT (138). Reference values for the NHPT of the right and the left hand (139) were subtracted from measured values; the adjusted

value for the non-affected hand was then subtracted from the adjusted value for the affected hand to establish the difference between sides. Papers I and II.

For patients unable to actively participate in the LMAS or the NHPT in the first week after stroke, the presence of hemiparesis was assessed by the Scandinavian Stroke Scale (SSS) (145), which is an observational scale. The motor items of the SSS range from 0-18 points; ≤12 points were considered to indicate hemiparesis. The SSS is considered valid and reliable (146). Paper I.

3.3.6 Assessment of health-related quality of life

HRQL was assessed by the Swedish Short Form 36 health-survey questionnaire (SF-36) (147), at 18 months after stroke, in Paper II. The survey consists of 36 items grouped into the following eight health scales: physical functioning, role limitations due to physical problems, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems and mental health. Possible scores are 0-100 for each scale. A higher score indicates a better HRQL. All patients received the questionnaire by mail in advance of the assessment. They were asked to return the answer to the examiner at the time of the assessment. Patients who were unable to independently answer the survey were interviewed in accordance with the survey. On the SF-36, a difference of five points or greater between compared groups has been suggested to reflect a clinically and socially relevant difference in HRQL (148). Both the original version and the Swedish version of the SF-36 are considered valid and reliable measures of physical and mental health after stroke (149, 150).

3.4 STATISTICAL METHODS

Table III includes an overview of the statistical methods used in the thesis.

Table III. Statistical methods used in Papers I-IV.

	Paper I	Paper II	Paper III	Paper IV
Descriptive statistics				
Medians, interquartile ranges (IQRs) and ranges	X	X	X	X
Analytical Statistics				
Mann-Whitney U test	X	X	X	
Power analysis of group size		X		
Wilcoxon matched pairs test		X		
Spearman rank-order correlation		X		X
Likelihood ratios			X	
Predictive values				X
Chi-2 test				X
Fisher's exact test				X
Univariate logistic regression analyses			X	X
Multivariate logistic regression analyses (forward stepwise)			X	
Bonferroni correction	X	X	X	

Data in all papers were analysed using STATISTICA 6.1 or 7.0 for Windows. Descriptive statistics were used in all papers and the significance levels were set at 0.05. Correlation coefficients with absolute values less than 0.5 are referred to as low; between 0.5 and 0.75, as moderate to good; and coefficients with values greater than 0.75, as high (151).

In Paper I, the Mann-Whitney U test was used to compare scores between patients moving within, or partly within, the synergies and, respectively, patients unable to move their affected side and patients moving without clinically evident synergies, at three months after stroke, according to the MAS, the RMI and the BI.

In Paper II, the Mann-Whitney U test was used to compare assessment results in hemiparetic patients with and without spasticity. When a non-significant difference of 5 points or greater on the SF-36 was found between groups, a power analysis was performed to establish the number of patients needed to reach an alpha value of 0.05 with a power of 80%. Wilcoxon matched pairs test was used to compare the scores of the patients with age- and gender-matched median scores on the SF-36 health scales for the general Swedish population (152). Spearman rank-order correlations were used to establish the associations of the MAS with the LMAS, the RMI, the BI, and the SF-36.

In Paper III logistic regression analyses were conducted to examine possible associations between touch, proprioceptive, perceptual, and cognitive functions; and depressive symptoms as independent variables, and respectively, mobility and self-care as dependent variables; with age, gender, previous stroke and brain lesion side as covariates. Univariate models assessed the unadjusted odds ratios (OR) and 95% confidence intervals (CI). Multivariate models (forward stepwise) assessed the adjusted OR and 95% CI. Using the Mann-Whitney U test, we compared mobility and self-care scores for patients who were able to complete the body function tests with those who were not. In order to establish whether assessment of somatosensory functions will also give information on perceptual functions, Likelihood Ratios (LRs) for positive values were calculated.

In Paper IV, Spearman rank-order correlations were used to establish the correlations between fine hand use and other functioning scores in the first week as well as at three and 18 months after stroke. The differences in the number of patients with impaired scores who improved from limited fine hand use compared to the number of patients who improved from other disabilities, were calculated using the Chi-2 test and Fisher's exact test. Positive and negative predictive values for improvements in impaired grip strength and somatosensory impairment to parallel improvements in fine hand use were calculated. Positive and negative predictive values for improvements in fine hand use to parallel improvements in movement function and self-care scores were also calculated.

3.5   ETHICAL APPROVAL

All studies included in this thesis were approved by the Ethics Committee of Karolinska University Hospital or the regional ethical review board in Stockholm.

4 RESULTS

4.1 PAPER I

The first week after stroke, two (3%) of all 64 hemiparetic patients moved within the synergies for the lower extremities but none did for the upper extremities. One of the patients moving within the synergies exhibited spasticity. Ten patients were non-assessable because of an inability to follow instructions.

Three months after stroke, these two patients and an additional six patients (i.e., eight patients in all [13%] of the 64 patients) moved within the synergies for the upper or lower extremities. Of all 64 patients, 63 were hemiparetic in the upper extremity, 35 in the lower extremity, and 34 in both the upper and lower extremities. Of the 63 patients who were hemiparetic in the upper extremity, seven (11%) moved within the synergies for the upper extremities; 48 patients (76%) moved without clinically evident synergies; and eight (13%) were unable to move their affected upper extremity. Of the 35 patients who were hemiparetic in the lower extremity, six (17%) moved within the synergies for the lower extremities; 23 patients (66%) moved without clinically evident synergies for the lower extremity; and six (17%) were unable to move their affected lower extremity. A total of 18 patients (28%) exhibited spasticity three months after stroke; all eight patients (44%) who moved within the synergies were found among these 18 patients.

Comparison, three months after stroke, between patients unable to move their affected side, patients moving within the synergies, and patients moving without clinically evident synergies as assessed by the MAS, the RMI and the BI are shown in Figures 3 and 4. Patients moving within the synergies had significantly worse scores, for both the upper extremity and lower extremities, on the MAS (upper and lower extremity $p<0.01$), the RMI ($p<0.01$) and the BI ($p<0.05$) than patients moving without clinically evident synergies, although severe disabilities were seen in both of these groups (Figures 3 and 4). Patients moving within the synergies had significantly better scores, for the BI ($p<0.01$), than patients unable to move their affected side, but not for the MAS or the RMI.

Three months after stroke, severe activity limitations were defined as an RMI or BI score lower or equal to the lower quartile for all 64 patients, i.e. 4 and 45 points, respectively. These limitations were present in four hemiparetic patients moving their upper and lower extremities within the synergies, in five hemiparetic patients moving their upper extremity without clinically evident synergies and in four hemiparetic patients moving their lower extremity without clinically evident synergies. Severe movement impairments, three months after stroke, were defined as an LMAS score lower or equal to the lower quartile for all 64 patients, i.e. 30, for the upper extremity part and 21, for the lower extremity part. These impairments were present in six hemiparetic patients moving their upper extremity within the synergies, in three hemiparetic patients moving their upper extremity without clinically evident synergies, in five hemiparetic patients moving their lower extremity within the synergies and in

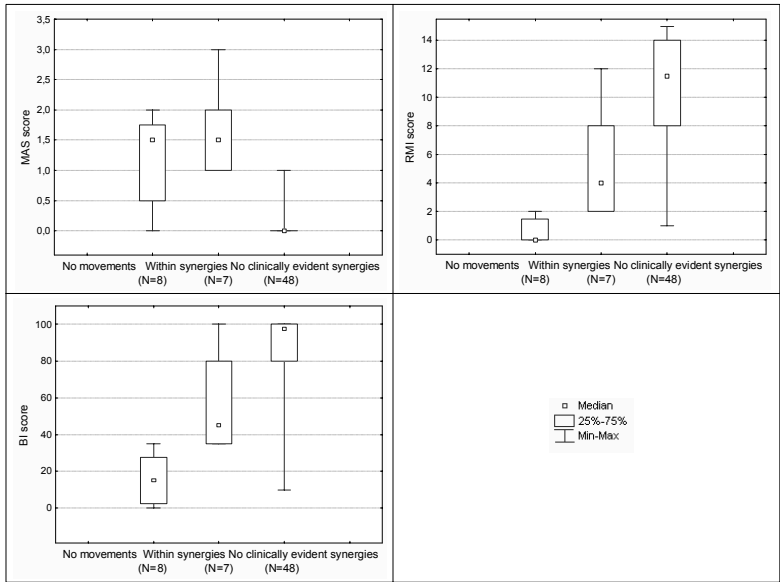six hemiparetic patients moving their lower extremity without clinically evident synergies.

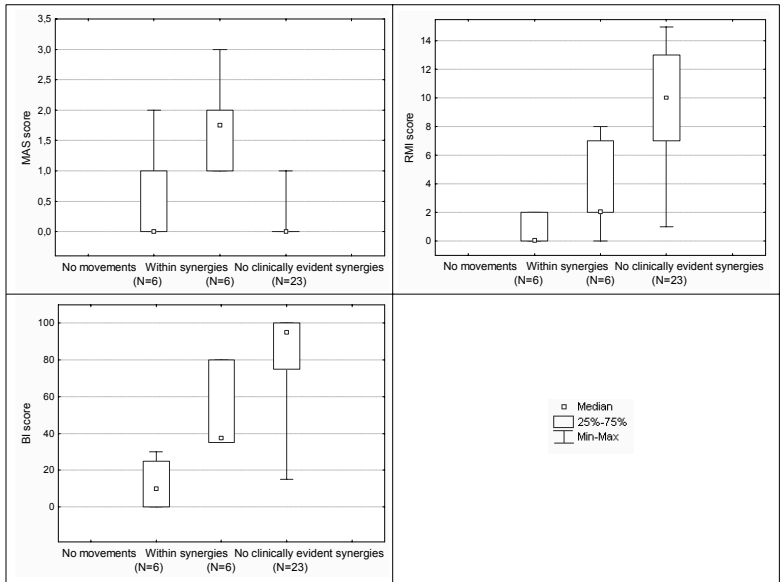Figure 3. Patients with upper extremity hemiparesis.

Figure 4. Patients with lower extremity hemipareis.

4.2   PAPER II

The numbers of patients with spasticity (a score greater than 0 on the MAS), self-reported muscle stiffness, hyperreflexia, and clonic beats of the plantar flexors, 18 months after stroke, are shown in Figure 5. Of the 66 patients investigated, 38 (58%)

were hemiparetic, and 13 of these (20% of all patients; 34% of hemiparetic patients) displayed spasticity, 18 months after stroke. Of these 13 patients, 10 displayed spasticity in both the upper and lower extremities, and three in the upper extremities alone. Of the 13 patients displaying spasticity, five (38%) reported muscle stiffness; 10 (77%) exhibited hyperreflexia; and six (46%) exhibited clonic beats. Of the 13 patients with spasticity three months after stroke (Figure 5), and who still remained in the study at the 18-month follow-up, nine (69%) still displayed spasticity 18 months after stroke, while four (31%) did not. (Prior to the 18-month assessment, one patient in the latter group received injections with botulinum toxin in the elbow and wrist flexors. Between the three-month and 18-month follow-ups, the patient's score on the active-movement dimension of the LMAS improved [from 34 to 45, maximum 57], while his score on the scale's rapid-movement dimension remained the same [4, maximum 6].)
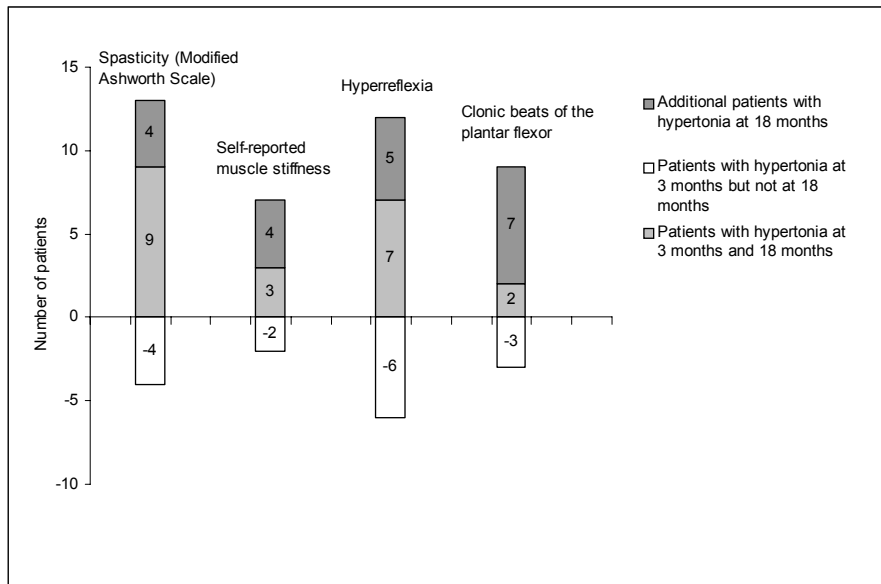
Figure 5. Muscular hypertonia (spasticity, self-reported muscle stiffness, hyperreflexia, or clonic beats of the plantar flexors) in the 66 patients assessed 18 months after first-ever stroke.

Significant correlations, for all patients, between MAS scores for the upper extremities and scores on the LMAS, the RMI, and the BI, and between MAS scores for the lower extremities and scores on the LMAS, were moderate to good (with correlation coefficients between 0.51 and 0.65). Low correlations were observed between MAS scores for the lower extremities and the RMI and the BI (r<0.5), and between MAS scores for the upper and lower extremities and the physical-functioning scale of the SF-36 (r<0.4). Correlations between MAS scores and the other six SF-36 health scales were not statistically significant. Four patients (including three who were hemiparetic, two of whom displayed spasticity) were unable to answer the survey despite assistance. For each of the SF-36 health scales, except for bodily pain (p=0.3) and general health (p=0.2) the median scores of all the investigated patients (N=62) were statistically significantly lower than scores for the general Swedish population.

Compared to patients with spasticity, patients without spasticity had statistically significantly better functioning scores and statistically significantly better scores on the physical-functioning scale of the SF-36. However, both patients with and without spasticity showed quite wide ranges of scores. Median scores for patients with and without spasticity differed by less than five points on the following scales of the SF-36: bodily pain, social functioning, and mental health. Median scores on four additional scales—role limitations due to physical problems, general health perceptions, vitality, and role limitations due to emotional problems—differed by five points or more. Power analyses for group size showed that we would have required sample sizes of 80, 198, 72, and 148 hemiparetic patients, respectively, to achieve statistical significance.

Six of the 66 patients had a BI score less than 35, at 18 months after stroke; four of these six patients displayed spasticity. The first week after stroke, 17 of the 66 patients had a BI score less than 35; at 18 months after stroke, 10 of these 17 patients exhibited spasticity. BI scores were significantly worse in these 10 patients, 18 months after stroke, than in the seven patients without spasticity (p<0.05). Three months after stroke, patients with spasticity were significantly younger than patients without spasticity (p<0.05) but this was not the case at 18 months after stroke (p=0.4).

4.3   PAPER III

Of all 115 patients, 23 had had a previous stroke. Fifty-six patients showed right-sided; 54, left-sided and one, bilateral movement-related symptoms; and four had no such symptoms but did have activity limitations. Unadjusted ORs and 95% CIs for the association between the somatosensory and mental functions as independent variables and, respectively, the RMI and BI, as dependent variables, are shown in Table IV.

Some patients were non-assessable according to the body function tests, i.e. the tests for somatosensory and mental functions (Table IV), in most cases due to an inability to follow instructions. These patients showed significantly poorer mobility and self-care scores than the patients in whom the assessment of body functions was possible (p<0.001). This was true for all body function tests. No significant differences were found between the assessable and the non-assessable patients regarding age or gender.

Multivariate logistic regression, with the RMI as a dependent variable, showed that normal proprioception according to the Thumb Localizing Test was significantly associated with better mobility according to the RMI (OR 3.4, 95% CI 1.1-10.6). Normal perceptual function according to the Kohs Block Design Test tended to be significantly associated with better mobility according to the RMI, p=0.08 (OR 3.3, 95% CI 0.9-12.7). The sensitivity of the model, i.e. patients with a true low mobility level, was 39%.

Multivariate logistic regression, with the BI as a dependent variable, showed that normal perceptual function according to the Kohs Block Design Test (OR 7.3, 95% CI 1.8-29.0) and normal touch function in the lower extremities (OR 3.9, 95% CI 1.0-15.3) were independently associated with a better self-care score, according to the BI. Not having had a previous stroke tended to be significantly associated with a better self-care

score according to the BI, p= 0.06 (OR 4.5, 95% CI 0.9-22.3). The sensitivity of the model was 58%. No interaction effects were found.

Table IV. Unadjusted Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for the association between all independent variables and the RMI and BI, respectively.

Independent variables (number of assessable patients)	Dependent variables OR (95% CI)			
	RMI $\geq$ 4	P	BI $\geq$ 35	P
Categorical variables				
Touch function; upper extremity (N=84)	1.6 (1.0-2.5)*	0.030	2.4 (1.4-4.1)*	<.001
Touch function; lower extremity (N=84)	2.0 (1.3-3.2)*	0.003	3.0 (1.7-5.3)*	<.001
The Thumb Localizing Test (N=81)	1.9 (1.4-2.7)*	<.001	2.6 (1.5-4.3)*	<.001
The Line Cancellation Task (N=81)	4.0 (1.3-12.5)*	0.019	7.0 (2.2-22.0)*	<.001
The Letter Cancellation Task (N=80)	2.4 (1.0-6.2)*	0.058	4.6 (1.7-12.4)*	0.002
The Kohs Block Design Test (N=76)	3.9 (1.4-11.4)*	0.011	10.1 (3.2-31.7)*	<.001
Mini-Mental State Examination (N=62)	0.8 (0.3-2.3)*	0.658	1.0 (0.3-3.1)*	0.954
Ordinal variables				
Montgomery Åsberg Depression Rating Scale				
Item 2, reported sadness (N=97)	1.2 (0.9-1.6)†	0.260	1.4 (1.0-2.0)†	0.027
Item 4, reduced sleep (N=98)	1.2 (0.8-1.8)†	0.370	1.1 (0.8-1.7)†	0.541
Item 5, reduced appetite (N=94)	1.9 (0.9-4.0)†	0.084	1.8 (0.9-3.4)†	0.089
Item 7, lassitude (N=84)	1.2 (0.8-1.8)†	0.363	1.4 (0.9-2.2)†	0.101

*Normal versus impaired; †A better versus a worse score.

The LRs for positive results of the somatosensory tests in determining the status of the perceptual tests ranged from 1.5 to 8.6. The highest LR (8.6) was seen for the Thumb Localizing Test in indicating the outcome of Kohs Block Design Test.

4.4 PAPER IV

Of the 66 patients followed up at 18 months, the numbers of patients who were unable to pick up a peg or unable to participate in the test were: 25 in the first week, 11 at three months and 10 at 18 months. The numbers of patients who could place some pegs but were unable to place all the pegs within 60 seconds were: 15 in the first week, six at three months and eight at 18 months. Furthermore, the numbers of patients who could

place all the pegs within 60 seconds although the time exceeded the normal value plus two SD, were: six in the first week, 10 at three months and 12 at 18 months. Thus, 46 (70%) of the 66 patients had limited fine hand use in the first week, 27 (41%) at three months and 30 (45%) at 18 months after stroke.

Between the first week and three months after stroke, 43 of all 66 patients improved their fine hand use and six deteriorated. Between three and 18 months after stroke, 25 patients improved their fine hand use and 22 deteriorated.

The patients who were non-assessable according to the NHPT showed significantly poorer upper extremity movement function and self-care scores than the patients in whom the assessment of fine hand use was possible ($p<0.001$). This was true for all three time points.

Moderate to good correlations were observed between fine hand use and grip strength at three and 18 months. Between fine hand use and the somatosensory tests, moderate to good correlations were observed in the first week and at three months, and low correlations at 18 months after stroke. High correlations were observed between fine hand use and upper extremity movement function, in the first week and at three months, and moderate to good correlations at 18 months after stroke. Between fine hand use and self-care, moderate to good correlations were observed at all time points although the strength of the correlations decreased from 0.69 to 0.54 from the first week to 18 months after stroke. The strength of the correlations between fine hand use and somatosensory functions, movement function and self-care, respectively, decreased over time. All correlations were statistically significant.

Significantly fewer patients improved from limited fine hand use compared to impaired movement function of the upper extremity and self-care limitations between the first week and three months. No other significant difference in improvement was seen between limited fine hand use and other impairments or activity limitations, although the difference in improvement between limited fine hand use and impaired movement function of the upper extremity between three and 18 months tended to reach statistical significance.

Table V shows the positive and negative predictive values for improvements in impaired grip strength and somatosensory impairment to parallel improvements of fine hand use, as well as for improvements in fine hand use to parallel improvements in movement function and self-care scores, between the first week and 18 months after stroke.

Table V. The Positive (PPV) and Negative (NPV) Predictive Values for improvements in grip strength and somatosensory function to parallel improvements in fine hand use and for improvements in fine hand use to parallel improvements in upper extremity movement function and self-care, between the first week and 18 months after stroke.

Body functions/activities	Fine hand use	
	PPV	NPV
Grip strength	53.6%	73.7%
Touch function	70.0%	44.4%
Proprioceptive function	80.0%	75.0%
Upper extremity movement function	100.0%	50.0%
Self-care	100.0%	18.8%

5 DISCUSSION

5.1 FINDINGS

The present thesis describes body functions, activities and HRQL in patients with stroke and analyses the associations between those variables, in the first week and at three and 18 months after stroke onset. The ICF was used as a conceptual framework to describe functioning although, as pointed out elsewhere, in order to allow comparison with other studies, some terms used in the thesis are not ICF terms. Sorting the variables according to the ICF, however, provides a structure which is of assistance when analysing the association between the variables.

The results showed that, three months after stroke, only eight patients moved within the synergies, i.e. 13% of the 64 hemiparetic patients and 44% of the 18 patients with spasticity. Eighteen months after stroke 20% of the 66 patients investigated—34% of the hemiparetic patients—exhibited spasticity. Both the synergies and spasticity were associated with impaired control of voluntary movements and limitations of activity. Spasticity was however only associated with one of the eight health scales on the SF-36. Between three and 18 months after stroke, spasticity appeared for the first time in four patients (Figure 5). Since the tonic stretch reflex has been shown to reach its peak one to three months after stroke (60, 61), it is reasonable to assume that, rather than being reflex-mediated, the late-developing spasticity, in those four patients, was due to intrinsic muscle changes (52). This is in line with the theories of the ICF, where the components described work in two directions; just as the body functions may modify the activities, the presence of activity limitations may also modify the body functions (31). In this case, activity limitations—and the resulting immobility—may have given rise to spasticity, as assessed by the MAS.

Other results show that normal somatosensory and perceptual functions and lack of, or only a low severity rate/grading of reported sadness, respectively, were associated with better mobility and self-care in older patients with acute stroke. In the case of patients with unimpaired proprioceptive function assessed by the Thumb Localizing Test, this test seems to indicate not only normal proprioceptive function but also normal perceptual function. The analyses were cross-sectional, which does not allow us to examine the cause-effect relationship between the somatosensory and mental functions and, respectively, mobility and self-care. In line with the ICF, it is therefore reasonable to assume that although, for example, reported sadness might have contributed to the activity limitations, the activity limitations may also have contributed to the sadness. These associations may, however, give an indication of the importance of somatosensory and mental functions for activities after stroke and, thus, for the patients' prognoses (15, 28).

Further results show that limited fine hand use is common after acute stroke. Although many patients recover from limited fine hand use, about 40% of the patients have remaining limitations in fine hand use at three months and slightly more patients at 18 months after stroke. The strength of the associations between fine hand use and somatosensory functions, upper extremity movements and self-care activities decreased

over time. Further, more improvements seem to occur in upper extremity movements and self-care activities than in fine hand use with the passage of time after stroke. The decreasing association levels suggest that, with time, patients with stroke seem to become less dependent on fine hand use when performing upper extremity movements and self-care activities and on somatosensory function when performing activities requiring fine hand use. In line with the above discussion however, it is also reasonable to assume that the causality may be reversed so that, for example, just as the patients may depend on somatosensory function when performing activities requiring fine hand use, the recovery of somatosensory function may also depend on the amount of hand use.

We chose to examine some selected functioning in this thesis. All papers included assessments of activities, since these are considered the most important outcome after stroke (100). The selection of body functions, that may affect the ability to perform the activities was made on the basis of earlier studies, of our own interests and experiences as well as on the basis of what we believe was missing in the stroke literature. The present thesis does not give a complete picture of body functions, activities, or HRQL of patients with stroke. Other body functions and constructs, for example fatigue, anxiety, coping and motivation may play an important role for the patients' activity levels and HRQL. Further studies are needed to describe how body functions and activities affect recovery of activities as well as HRQL for patients with stroke.

When comparing groups, group assignment was not made randomly but on the basis of certain impairments, for example the presence of spasticity. Thus, the possibility that some other confounding factor might have affected the comparison cannot be eliminated, which presents a threat to the internal validity. Another threat to the internal validity includes the possibility that the content of the rehabilitation given to the patients differed between the groups. In Paper III, the patients' age, gender, previous stroke and lesion side were used as covariates in the multivariate analyses, which strengthens the internal validity of the study.

The present thesis does not explicitly describe motor control, i.e. how movements are controlled (2), although it describes the extent to which some selected body functions and activities are associated with for example movements and activities. We assessed the patients' performance of movements and activities (2). Motor performance has to be separated from motor learning, i.e. learning new strategies for sensing and moving. The performance of a task is however a first step towards learning the task (2). The associations between the functioning of the patients described in the thesis may, therefore, be used to create theories on how functioning affects learning and, thus, the recovery of movements and activities for patients with stroke.

5.1.1 Hemiplegic limb synergies and spasticity—associations with functioning

Our results show that few patients exhibited spasticity after stroke and even fewer patients showed abnormal synergies. Although, as pointed out elsewhere, the negative features of the UMN syndrome are often more troublesome for the patients than the positive features, much focus is still placed on the role of spasticity by physiotherapists

working with patients with stroke (8). In addition, spasticity is currently treated by for example intramuscular injections of Botulinum toxin (9), although at present there is no evidence that suppression of spasticity improves motor function (109). Our results show that spasticity is associated with impaired control of voluntary movements and limitations of activity, although the causal relations are not clear. Further, the results indicate that the current exaggerated focus on reflex-mediated spasticity in stroke care overestimates its clinical importance from a population-based perspective. The result showing that very few patients exhibited synergies, together with previous studies questioning the validity of the synergies (67-69), suggests that abnormal synergies should not be used as a theoretical base for assessment of voluntary movements for patients with stroke, in general. Our results indicate, however, that, for some patients with spasticity, assessment based on Brunnström's hemiplegic limb synergies may be appropriate and add some information.

A plausible explanation for the focus on spasticity and abnormal synergies in stroke literature may be that it remains among physiotherapists, for traditional reasons. Since the time when the neurodevelopmental approaches were developed, stroke has become a less disabling disease and the prevalence of stroke has increased in the older population (5). It has been suggested that tendon reflexes decrease with age (153). If this decrease were attributable to tonic reflexes, the differences in stroke populations might contribute to the discrepancies between the results in the present thesis and the observations which are the basis for the neurodevelopmental approaches, including Brunnström's synergy stages.

The physiological mechanism underlying abnormal synergies is still unknown. It has, however, been argued that they arise from changes at the level of the spinal cord due to a loss of descending corticospinal input and a subsequent greater influence of bulbospinal input, i.e. of excitatory descending pathways (Figure 2) (66). It has been suggested that the coactivation of abductor and flexor muscles can be explained by the collateralization of the pathways for these muscles (66). It has also been suggested that the link between adduction and extension may be explained by an increase in the activity of the vestibular system, which, for example, elicits triceps brachii activity (66). The vestibular system is sensitive to biomechanical constraints, which change with body movements (66). Thus, according to this hypothesis, the adduction synergy is only present in some body positions.

Spasticity and abnormal synergies are both positive features of the UMN syndrome (58). According to the above hypothesis, the synergies arise from lesions similar to those which cause spasticity. As the physiological mechanism underlying abnormal synergies is still unknown, the possibility that abnormal synergies can exist without the presence of spasticity cannot be eliminated.

In Paper II, four of the 13 patients with spasticity at three months after stroke and who remained in the study at the 18-months follow up, did not display spasticity at 18 months. Since reflex-mediated spasticity has been shown to reach its peak one to three months after stroke (60, 61), these results may be explained by diminished tonic stretch reflexes. Further, we found predominantly moderate to high correlations between the MAS scores and other functioning scores. In our earlier study based on the same study

population assessed three months after stroke, correlations between the MAS and the functioning scores were mostly low (13). The higher correlations at 18 months may merely be due to the immobilization of affected limbs in patients with low scores on the movement and activity scales.

There is a possibility that spasticity may have been advantageous for some patients in the present thesis and disabling for others. Indeed, it has been suggested that spasticity may help patients to support body weight during gait (154), implying that spasticity might be advantageous for some patients. Considering the above, there is a possibility that the correlations between spasticity and other functioning scores in this thesis would be misleading if the correlations are positive for some patients and negative for others.

5.1.2 Health-related quality of life after stroke and its association with spasticity

The patients in the present thesis had significantly lower SF-36 scores on all the subscales, except for bodily pain and general health, than the general Swedish population. These findings are partly in accordance with Mayo et al. (155) who found that all the subscales of the SF-36, except for bodily pain, were affected by stroke. The fact that we did not find a difference between our patients and the general Swedish population on the general health scale may for example be explained by a lack of validity for older respondents. Indeed, the SF-36 has been criticized for not being completely relevant for older respondents (156, 157). Our patients were in general eight years older than the patients in the study by Mayo et al. (155). Further explanations may be put down to a decreased ability for patients with cognitive impairments to answer the survey or that some patients may have had a lack of insight into their health. It has also been noted that there is a considerable variation in subjective interpretation of items (156). Our experience gained from interviewing patients, in accordance with the survey, show that many patients had difficulties in interpreting the questions, which may limit the validity of the survey and, thus, the validity of the study. Our results, however, mainly confirm those of earlier studies, suggesting that HRQL is negatively affected by stroke (89, 90).

Correlations between spasticity and the SF-36 were mainly low. Moreover, only the physical functioning scale attained a statistically significant difference between patients with spasticity and those without spasticity. We uncovered clinically significant differences between patients with and without spasticity – in most cases, in favor of the patients without spasticity – for the following four SF-36 scales: role limitations due to physical problems, general health perceptions, vitality, and role limitations due to emotional problems. Our sample was too small, however, for these differences to attain statistical significance. Four patients, including two patients with spasticity, were unable to answer the survey; the exclusion of these patients may have led to overrepresentation in the sample of less impaired patients, especially in the group of patients displaying spasticity.

The findings in the present thesis suggest that spasticity does not have a major impact on HRQL in patients with stroke. Our findings support those of Childers et al. (158) who found that alleviation of spasticity by Botulinum toxin in patients with stroke only

improved one of the eight subscales of SF-36. Since spasticity is a physical impairment and HRQL is influenced by a broad variety of variables, such as physical and mental impairments as well as social factors (89, 93, 159), these findings seem plausible. In view of the focus put on spasticity in stroke rehabilitation, it is important to assess not only the possible impact of spasticity on movements and activities but also on the patient's HRQL. The SF-36 was chosen since it has been suggested to be a suitable outcome measure for participation after stroke (76).

5.1.3 Somatosensory and mental functions – associations with functioning

In Paper III, we investigated the associations between somatosensory and mental functions and activity after stroke. In accordance with other studies we found that normal somatosensory functions were associated with better activity scores (51). This was true also in the multivariate analyses. In line with the findings of Desrosiers et al. (160), we also found that impaired lower extremity touch function seems to be more associated with activity limitations than impaired upper extremity touch function is. A plausible explanation may be that it is easier to compensate for impairments in the upper than in the lower extremity, since, for example, walking requires the use of both legs.

We found no relationship between cognitive functions, as assessed by the MMSE, and activity. Our result agrees with the findings of Hajek et al. (38) who report no association between those variables in patients with stroke. Indeed, it has been suggested that some basic behaviour activities, such as walking and stair climbing, are unaffected by cognitive dysfunction, in contrast to more complex activities (161). Another interpretation of our findings might be that the mobility and self-care scales have been constructed in a way that underestimates the importance of the cognitive functions required for activity tasks; or that the MMSE is too rough a measure of cognitive function. However, since some patients were non-assessable according to the MMSE, mainly due to an inability to follow instructions, it is possible to assume that these patients had a poorer cognitive function than the patients who were assessable. These non-assessable patients showed poorer activity scores than the assessable patients. Therefore, no ultimate conclusion can be drawn that no association exists between cognitive function and activity in older patients with acute stroke.

Normal perceptual functions were significantly associated with better mobility and self-care, although the association between perceptual function and mobility was not quite significant in the multivariate analyses. The difficulties for patients with perceptual impairments when performing mobility and self-care activities may result from failure to take account of aspects of the situation necessary for performance of complex sequences of actions such as eating and dressing. Our results confirm those reported by Paolucci et al. (162), in which perceptual function is more strongly associated with self-care than with mobility in patients assessed five weeks after stroke.

Mobility and self-care were more strongly associated with visuospatial construction, as assessed by the Kohs Block Design Test, than with perceptual space function, as assessed by the cancellation tasks, after acute stroke. This is perhaps because

visuospatial construction requires not only perceptual space function but also flexibility in the use of spatial reference systems (163).

The likelihood ratios for the Thumb Localizing Test in indicating the status of the Kohs Block Design Test, suggest that, in the case of patients with unimpaired proprioceptive function assessed by the Thumb Localizing Test, this test seems to indicate not only normal proprioceptive function but also normal perceptual function. Since the Thumb Localizing Test is more quickly and easily performed than the Kohs Block Design Test, this information may be clinically useful.

It has been suggested that the severity of depressive symptoms is related to activity limitations (42). We found that, of the selected items, only the first of the two DSM-IV core symptoms, i.e. reported sadness, was significantly associated with dependence regarding self-care, in the univariate analysis. A lower score, i.e. a less pronounced sadness, of the MADRS, item 2: reported sadness, increases the chance of achieving a better self-care score. This finding confirms that of Ramasubbu et al. (49) who found global self-rated depression related to dependence regarding self-care. Although the association between sadness and self-care, in our study, was not significant in the multivariate analysis, it nevertheless seems important to assess sadness since it indicates that depression should be assessed, and the diagnosis verified or ruled out according to DSM-IV diagnostic criteria. If the patient is found to be depressed, treatment may positively influence the patient's activity levels (44).

The patients included in Paper III were quite disabled, which was evident from the fact that about 40% of the patients suffered from urinary incontinence, as shown by a previous thesis conducted on the same sample of patients (15). The patients who were non-assessable according to any of the tests for somatosensory, perceptual and cognitive functions or for depressive symptoms, form a homogenous group, where the inability to be assessed acts as a common indicator of low mobility and self-care scores. The fact that these patients were not included in the analyses skews the results towards the less impaired patients in this generally impaired sample.

As movement function obviously affects mobility and self-care after stroke (37), inclusion of this variable in the multiple analyses would most probably have affected the results. It is, therefore, a limitation for the study that movement function was not included in the analyses. Indeed, the sensitivity of the multivariate analyses was quite low, indicating that other variables than those assessed affect the patients' ability to perform mobility and self-care activities.

5.1.4 Fine hand use after stroke – associations with functioning

Paper IV, describes the recovery from limited fine hand use between the first week and three months and between three and 18 months after stroke onset. Seventy percent of the 66 patients followed up at 18 months had limited fine hand use in the first week, 41% at three months and 45% at 18 months after stroke. An earlier population-based study has shown that 79% of the patients with stroke attain full ability to perform upper extremity self-care activities (18). However, in that study, patients were allowed to compensate using their unaffected extremity when performing the activities. We found that only 59% of the patients attained full fine hand use three months after stroke onset.

To our knowledge, no earlier study has described fine hand use more than one year after stroke in a sample of consecutive patients. We found that between three and 18 months after stroke, a few more patients improved than deteriorated regarding fine hand use. However, according to our definition of limited fine hand use, slightly more patients had limited fine hand use at 18 than at three months.

We found moderate to good correlations between fine hand use and grip strength and somatosensory functions respectively, but the correlation between fine hand use and somatosensory functions decreased with time after stroke. A plausible explanation for the decreased correlation is that some patients learn to compensate for their impaired somatosensory function.

We found high correlations between fine hand use and upper extremity movement functions and moderate to good correlations between fine hand use and self-care activities in the first week after stroke. These correlations all decreased with time after stroke onset. It has been suggested that the improvements in self-care are greater and occur faster compared to improvements in upper extremity movements (160). We found that more patients recovered from impairments in upper extremity movement functions and self-care activities compared to limited fine hand use. The high positive predictive values for fine hand use, in predicting the recovery of upper extremity movement impairments and self-care limitations, indicate that all patients who recover from limited fine hand use also recover from upper extremity movement impairments and self-care limitations. The low negative predictive values indicate that many patients recover from upper extremity movement impairments and self-care activity limitations without recovering from limited fine hand use. A plausible explanation for our results might be that patients develop compensatory strategies for upper extremity movement impairments and self-care limitations to a higher extent than for limited fine hand use. It is probably easier to develop compensatory strategies for upper extremity movements and self-care activities since they consist of more gross motor tasks than fine hand use does, thus requiring less precise movements. Self-care activities can also be performed by involving the non-paretic hand (4). The use of the affected upper extremity may be negatively reinforced by its ineffectiveness in carrying out activities (97). Although limited fine hand use is less associated with other impairments and activity limitations at three and 18 months after stroke than in the first week, limited fine hand use might still cause great inconvenience to the patients affected and should, therefore, be treated adequately, for example by Constraint Induced Movement Therapy (98).

The NHPT was selected for the study because it assesses distal movements of the upper extremity, which have been shown to be related to recovery from arm and hand disabilities after stroke (20). Moreover, the NHPT was used because it assesses an activity requiring movements of the whole upper extremity as it depends on good proximal control to place and hold the hand in the correct position. In addition, the test consists of complex movements, for example fast eye-hand coordination, and may, therefore, be influenced by the patient's cognitive functions (21). Fine hand use may not be the most important contributor to upper extremity functioning in patients with stroke. Our results however suggest that the NHPT provides clinically valuable information on fine hand use and upper extremity functioning in patients with stroke.

5.2 METHODOLOGICAL CONSIDERATIONS

5.2.1 Samples of patients

For Papers I, II and IV patients were recruited consecutively when admitted to the stroke unit at DS. All patients fulfilling the inclusion criteria were included except those admitted and discharged during the same weekend or public holiday. Exclusion of patients with earlier stroke or other diagnoses affecting muscle tone may, however, have biased our sample towards the less disabled patients. Those patients were excluded because we wanted to assess only the stroke-related disabilities arising from a first-ever stroke. Thus the sample can only be generalized to patients with first-ever stroke. The mean ages of the patients included in Papers II and IV, i.e. 76 years, were equivalent with the mean age for the general Swedish stroke population (24), while the mean age for the patients in Paper I was higher (79 years). This might limit the external validity of Paper I.

In Paper III, we focused on older patients with stroke (≥65 years). The rationale for focusing on older patients is that functioning among them is not as well described as among younger patients. Further, older patients have proved to differ from younger patients in terms of a worse pre- to post-stroke mental and physical decline (16). In Paper III, we only included patients with movement-related impairments or limitations in mobility or self-care. The patients who are still in hospital five days after stroke generally constitute a quite disabled sample of patients since about 50% of all patients have already been discharged to their homes by that time. We excluded patients dependent on personal care assistance prior to the current stroke; patients with diagnosed dementia or severe confusion preventing them from living at home; and patients with non-stroke-related major disorders that considerably affected their activity level. This was done because we wanted to, as far as possible, examine only the stroke-related disabilities.

There were more women than men in all studies, which limits the external validity, since the same number of women as men suffer from stroke in Sweden (24). Further, it has been suggested that patients with a higher socioeconomic status have lesser stroke severity (164). Since DS serves people living in the north of Stockholm, including some areas of high socioeconomic status, this may also have affected our results. Other limitations to the external validity include the relatively small sample sizes as well as the decreased sample size at each measurement time for the sample of patients in Papers I, II and IV, leading to a less representative sample of the initial population.

5.2.2 Data collection

A strength of this thesis is that we predominantly used quickly and easily performed tests, which may be administered one-to-one and may be performed in the patient's home. Limitations of the thesis, associated with the assessments, include roof- and floor effects of some scales, lack of validity or reliability testing of some of the administered tests for patients with stroke, some rough measures, and the fact that it was not possible to assess all the patients with all tests. There are a lot of tests available for assessment of disability after stroke. We chose the best tests available for the functioning we

wished to assess. The tests administered are currently used in clinical and research settings as outcome measures for stroke rehabilitation, which makes our results comparable to other study results and also clinically useful. The chosen cut-offs for the different scales may have affected our results. This is always a potential cause of varying study results and constitutes a cause of difficulties when comparing studies.

To assure the inter-rater reliability, the assessments were performed by physiotherapists and occupational therapists, co-trained for the purpose. In many of the assessments, more than one of the therapists were involved and the score noted represented a consensus reached by the therapists involved in the assessment. We did not compute actual tests of inter-rater reliability, which is a limitation to the thesis. However, the co-training and the consensus during the assessments give some credibility to the inter-rater reliability of the assessments.

For assessment of cognitive functions, we chose the MMSE. Although the test is commonly used in studies of patients with stroke (73), it can be criticized for being too rough a measure of cognitive function (115). Perceptual function may be hard to assess at an early stage after stroke with the clinically available tests as they demand much attention from the patients. For assessment of perceptual functions, we chose some of the most commonly used tests: the Line and Letter Cancellation Tasks and Kohs Bloch Design Test.

The tests for touch function, included in the thesis, are commonly used by physiotherapists (126). Although, a dichotomous outcome is a rough measure of touch function, this grading was chosen since it is considered more reliable than fine graded scales (126). The Thumb Localizing Test was chosen since it is easy to carry out both for the examiner and the patient. It is closely linked with, although not equal to, tests of joint position and movement (127). The test examines the relative position of a passively fixed thumb in relation to the body axis as measured by motor tasks of the contralateral reaching limb (127).

The validity of the MAS can be criticized because the scale does not distinguish between neural and peripheral contributions to the resistance to stretch (130). Regardless of the cause, the exact influence of spasticity on disability in stroke patients is difficult to assess, because the degree of spasticity may change with body position and with the task being performed (165). The MAS is, however, regarded as one of the best clinical measures of spasticity (129).

The LMAS was chosen for assessment of bilateral voluntary movements since it is not based on any assumptions of motor recovery such as abnormal synergies (136). Since the LMAS has the advantage of assessing both the paretic and the non-paretic side, it was used to decide whether the patients were hemiparetic or not. Our definition of hemiparesis can, however, be criticized because the movement impairments in patients with bilateral impairments may have been underestimated.

Brunnström's hemiplegic synergies have not been tested for validity or reliability, which is a potential limitation to the synergies and to our study. When a patient could not perform a certain movement (because of weakness, for example), but could isolate their small movements and master individual joint movements, without activating

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synergistic movements, the patients was deemed to be moving without clinically evident synergies. It is possible that some emerging synergistic movements may have been missed. It is also possible that some of the 10 patients who were non-assessable the in first week after stroke may have moved within the synergies. Further, the patients were not assessed continuously, thus it is not known to what extent their recovery confirmed to the synergy stages described by Brunnström.

The advantages of mobility and self-care scales are that data can be equally reliably collected from the patient or from others; thus, there is little risk of missing data (100). Indeed, mobility was assessed in three papers and self-care was assessed in all four papers in the thesis and there were no missing data for these measures. Limitations of the RMI and the BI are that they are quite rough measures. An advantage of the RMI is that it has no obvious floor or ceiling effect. The BI on the other hand has obvious ceiling effects.The BI is, however, sensitive to change (142), can be used to predict outcome after stroke (143) and is widely used both clinically and in research (141).

The NHPT was used to assess fine hand use. An advantage of the test is its simplicity. The NHPT has however obvious floor effects, which is a limitation to the test and the thesis. To diminish this limitation and to avoid dropouts, we chose to include the non-assessable patients and gave them the lowest score in the statistical analyses. This is a potential limitation to the study. These patients showed however significantly lower activity scores than the assessable patients.

The SF-36 was chosen for assessment of HRQL since it is widely used in studies of patients with stroke (76). The scale was chosen in preference to other scales predominantly assessing "health status", for example the Nottingham Health Profile, the stroke adapted version of the Sickness Impact Profile and the Stroke Impact Scale (76). It has been suggested that the SF-36 has a well-demonstrated validity compared to other scales (76), although the validity for older respondents can be questioned (156, 157). Although, cognitive impairments are common after stroke (35, 36), the validity of the SF-36 has not been tested for patients with cognitive impairments.

5.2.3 Statistical considerations

Descriptive statistics have been used in all papers because they are a simple way of helping the reader to obtain an overview of the data. Because most scales used in the thesis are ordinal scales, we predominantly used non-parametric statistical methods to analyse the data. This was done because statistical methods for data from rating scales must take account of the rank-invariant properties of ordinal data, which means that the methods must be unaffected by re-labelling, i.e. changing the numbers, although not the order, of the scale categories (166). When performing non-parametric analyses, for example of group differences, as done in all papers, the tests do not take into account the size of the differences, which has to be considered when interpreting the results. The power analyses in Paper II were made to get an indication of whether the non-significant differences between the groups were primarily due to a too small sample or if they truly reflected no differences between the groups. When dichotomizing variables, as done in Papers III and IV, a limitation is that small differences near the cut-off may be exaggerated and large differences may be taken too lightly. Bonferroni corrections were used to reduce the risk of Type 1 errors, i.e. the risk of getting an

incorrect statistically significant difference between groups. A downside of these corrections is that the corrections may be too large, thus increasing the risk of Type 2 errors, i.e. the risk of getting an incorrect statistically non-significant difference between groups. The various sensitivities of the scales, as well as ceiling effects, may have affected comparisons between scales. A small improvement in a scale does not necessarily represent a clinically relevant improvement. One might argue that an improvement in a rough scale is more clinically relevant than an improvement in a more sensitive scale, because it requires a larger change in functioning.

5.2.4 Ethical considerations

In line with the principle of autonomy (167), informed consent was obtained from all patients after they had received written and oral information about the studies. For patients with communication problems or impaired consciousness, proxy consent was obtained. The patients could choose to decline any further assessments at any time during the study. The methods used in the studies are currently used in clinical practice and are, therefore, not considered harmful to the patients, which is in line with the principle of non-malfeasance, i.e. not to harm (167). The follow-up assessments could potentially have been experienced as time-consuming by the patients. Our experience of the follow-ups, however, shows that patients with stroke were very willing to be assessed and to share with the investigators, their experiences of having a stroke. This experience, together with the knowledge gained from the study, is in line with the principles of beneficence and utility, i.e. to promote welfare and try to bring about the greatest benefits and the least harm (167). The patients were allowed to choose the time for the assessment that best suited them. An ethical dilemma, however, is that the patients assessed may not be the same as those who may benefit from the research. Another ethical dilemma during the follow-up assessments involved discovering disabilities in the patients without treating them. To minimize these negative aspects of the assessments, the investigator informed each patient where he or she could turn for professional support. Just as there is harm associated with research, there is also harm associated with not conducting research. The knowledge gained from the assessments will hopefully contribute to improving the rehabilitation and, thus, the living situation for patients with stroke in general.

6 CONCLUSIONS

Since few of the hemiparetic patients moved within the synergies three months after stroke and they all displayed spasticity, the assessment of hemiplegic limb synergies, as presented by Brunnström, may only be suitable for a small fraction of hemiparetic patients—namely, those displaying spasticity. Further, since few patients are expected to display spasticity, the current exaggerated focus on reflex-mediated spasticity in stroke care seems to overestimate its clinical importance, not for the single patient, but from a population-based perspective. Somatosensory and perceptual impairments and reported sadness, respectively, are of specific importance to consider in the rehabilitation of older patients in the acute phase after stroke, since they significantly affect the patients' mobility and self-care levels. In the case of patients with unimpaired proprioceptive function, assessed by the Thumb Localizing Test, this test seems to indicate not only normal proprioceptive function but also normal perceptual function. Limited fine hand use is common after stroke. With time after onset, patients with stroke seem to become less dependent on fine hand use when performing upper extremity movements and self-care activities and on somatosensory function when performing activities requiring fine hand use. The ICF was found useful in providing a structure and a scientific base when studying the associations between the variables included in the thesis.

6.1 CLINICAL IMPLICATIONS

- Assessment of movement function for the majority of patients with stroke should not be based on any assumption of motor recovery, for example of abnormal synergies.

- A neurodevelopmental approach, based on the assumption that spasticity is the most troublesome contributor to movement impairments after stroke, should not be used as a base in physiotherapy assessment or rehabilitation as most patients with stroke will not develop spasticity.

- Although, the majority of patients with stroke are not expected to show spasticity, our results emphasize the importance of maintaining soft-tissue extensibility in patients with stroke by passive and active stretching in exercise and training.

- While teaching the patients to perform an activity, it is important to consider somatosensory and perceptual functions. If these functions are impaired, the activities should be performed to challenge the patient's somatosensory and perceptual functions, since these may affect the performance of the activities.

- It is important to be aware of sadness in patients with stroke at an early stage after onset because this is a treatable impairment, which may negatively affect the patient's performance of activities.

- Rehabilitation of fine hand use seems warranted, especially active training of fine hand use in self-care activities at an early stage after stroke, to prevent learned non-use.

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