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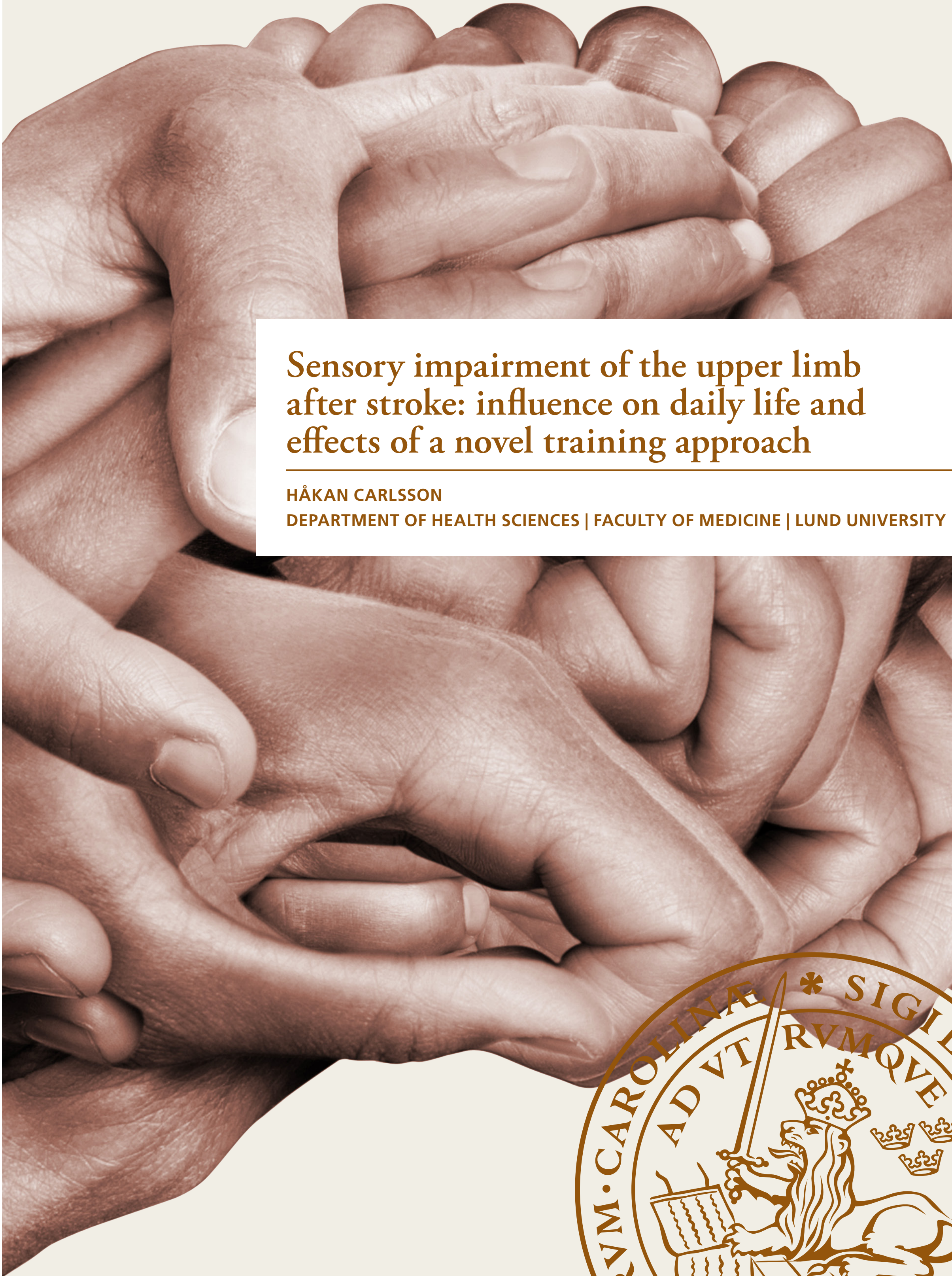

Sensory impairment of the upper limb after stroke: influence on daily life and effects of a novel training approach

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Sensory impairment of the upper limb after stroke: influence on daily life and effects of a novel training approach

Håkan Carlsson

DOCTORAL DISSERTATION

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Title: Sensory impairment of the upper limb after stroke: influence on daily life and effects of a novel training approach

Abstract: Sensory impairments in the upper limb are common after stroke. Different sensory modalities can be affected such as sense of touch, pressure, pain, temperature and proprioception. The sensory impairments can negatively affect motor function, dexterity and the ability to perform daily activities. Despite these problems limited attention is paid to sensory impairments in stroke rehabilitation.

The overall aim of this thesis was to increase knowledge about the consequences of sensory impairments of the upper limb after stroke, and to evaluate the effects of a novel training approach.

The thesis comprises four studies. In study I, 15 participants aged 35-78 years were interviewed individually about their experiences of sensory impairment in the upper limb after stroke. Data were analysed by inductive content analysis. In study II, factors associated with dexterity were evaluated by linear regression models among 75 participants with mild to moderate stroke. Dexterity was the dependent variable and age, gender, affected hand, social situation, vocational situation, grip strength, spasticity, sensory function, and pain were independent variables. In study III, 27 participants were randomized to either sensory relearning in combination with task-specific training (intervention group, n=15) or task-specific training only (control group, n=12). Both groups trained 2.5 hours per day, twice weekly for 5 weeks. Primary outcome was sensory function of the upper limb , and secondary outcomes were dexterity, ability to use the affected hand in daily activities and perceived participation. An independent assessor conducted all the assessments at baseline, post-treatment and at 3 months follow-up. In study IV, the 15 participants who had underwent sensory relearning in combination with task-specific training in study III were interviewed about their experiences and perceived effects.

The results showed that an impaired sensory function in the upper limb after stroke had a great impact on personal tasks and on everyday activities and leisure activities. Despite this, specific training to improve sensory function was lacking and had not been a part of the participants´ rehabilitation (study I). Sensory function in terms of discriminative touch was a major contributing factor to dexterity in persons with mild to moderate stroke explaining 46% of the variance in dexterity (study II). After sensory relearning in combination with task-specific training there was a significant between group difference in touch detection ($p = 0.007$) in favour of the intervention group but not in any other outcomes. A significant improvement ($p<0.05$) within the intervention group was found regarding use of the affected hand in daily activities, movement quality and with satisfaction with performance in meaningful activities. The control group significantly improved ($p<0.05$) their performance to use the hand in meaningful activities. The training was well-tolerated and performed without any adverse events (study III). Sensory relearning in combination with task-specific training was experienced meaningful but strenuous by the participants. They appreciated the feedback from the therapist and to train in groups, and home training was challenging to perform. Small improvements in sensory function were reported but an increased movement control and improved ability to use the affected hand in daily activities was also reported (study IV).

In conclusion, this thesis has shown that sensory impairments in the upper limb had a highly negative impact on activities in daily life, but specific rehabilitation for the upper limb is lacking. Sensory function in terms of active discriminative touch seems to be a major contributing factor to dexterity. Sensory relearning in combination with task-specific training was experienced as a strenuous but inspiring and meaningful training method. It may be a promising and feasible intervention to improve upper limb sensorimotor function after stroke.

Key words: Stroke, Upper limb, Sensory impairments, Rehabilitation, Qualitative research, Activies of daily living, Dexterity

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To my family

Table of Contents

Abstract

Sensory impairments in the upper limb are common after stroke. Different sensory modalities can be affected such as sense of touch, pressure, pain, temperature and proprioception. The sensory impairments can negatively affect motor function, dexterity and the ability to perform daily activities. Despite these problems limited attention is paid to sensory impairments in stroke rehabilitation.

The overall aim of this thesis was to increase knowledge about the consequences of sensory impairments of the upper limb after stroke, and to evaluate the effects of a novel training approach.

The thesis comprises four studies. In study I, 15 participants aged 35-78 years were interviewed individually about their experiences of sensory impairment in the upper limb after stroke. Data were analysed by inductive content analysis. In study II, factors associated with dexterity were evaluated by linear regression models among 75 participants with mild to moderate stroke. Dexterity was the dependent variable and age, gender, affected hand, social situation, vocational situation, grip strength, spasticity, sensory function, and pain were independent variables. In study III, 27 participants were randomized to either sensory relearning in combination with task-specific training (interventions group, n=15) or to task-specific training only (control group, n=12). Both groups trained 2.5 hours per day, twice weekly for 5 weeks. Primary outcome was sensory function of the upper limb, and secondary outcomes were dexterity, ability to use the affected hand in daily activities and perceived participation. An independent assessor conducted all the assessments at baseline, post-treatment and at 3 months follow-up. In study IV, the 15 participants who had underwent sensory relearning in combination with task-specific training in study III were interviewed about their experiences and perceived effects.

The results showed that an impaired sensory function in the upper limb after stroke had a great impact on personal tasks and on everyday activities and leisure activities. Despite this, specific training to improve sensory function was lacking and had not been a part of the participants´ rehabilitation (study I). Sensory function in terms of discriminative touch was a major contributing factor to dexterity in persons with mild to moderate stroke explaining 46% of the variance in dexterity (study II). After sensory relearning in combination with task-specific training there was a significant between group difference in touch detection ($p = 0.007$) in favour of the intervention group but not in any other outcomes. A significant improvement ($p<0.05$) within the intervention group was found regarding use of the affected hand in daily activities, movement quality and with satisfaction with performance in meaningful activities. The control group significantly improved ($p<0.05$) their performance to use the hand in meaningful activities. The training was well-tolerated and performed without any adverse events (study III).

Sensory relearning in combination with task-specific training was experienced meaningful but strenuous by the participants. They appreciated the feedback from the therapist and to train in groups, and home training was challenging to perform. Small improvements in sensory function were reported but an increased movement control and improved ability to use the affected hand in daily activities was also reported (study IV).

In conclusion, this thesis has shown that sensory impairments in the upper limb had a highly negative impact on activities in daily life, but specific rehabilitation for the upper limb is lacking. Sensory function in terms of active discriminative touch seems to be a major contributing factor to dexterity. Sensory relearning in combination with task-specific training is a strenuous but inspiring and meaningful training method. It may be a promising and feasible intervention to improve upper limb sensorimotor function after stroke.

List of papers

This thesis is based on the following papers.

I. Carlsson H, Gard G, Brogårdh C. Upper limb sensory impairments after stroke: Self-reported experiences of daily life and rehabilitation. J Rehabil Med 2018; 50: 45-51. doi: 10.2340/16501977-2282

II. Carlsson H, Ekstrand E, Brogårdh C. Sensory Function, Measured as Active Discriminative Touch, is Associated With Dexterity after Stroke. PM R. 2019; 11:821-827.

III. Carlsson H, Rosén B, Björkman A, Pessah-Rasmussen H, Brogårdh C. Efficacy and feasibility of SENSory relearning of the UPPer limb (SENSUPP) in people with chronic stroke: A pilot randomized controlled trial. PM R. 2022; 1-13.

IV. Carlsson H, Lindgren I, Rosén B, Björkman A, Pessah-Rasmussen H, Brogårdh C. Experiences of SENSory relearning of the UPPer limb (SENSUPP) after Stroke and Perceived Effects: A Qualitative Study. Int. J. Environ. Res. Public Health 2022, 19, 3636.

Svensk sammanfattning

Nedsatt känsel i arm och hand är vanligt efter stroke. Känseln innefattar förmågan att kunna uppfatta ytlig beröring, kyla- värme, tryck och smärta men även att kunna tolka beröring, att känna en leds position och hur en rörelse utförs. En nedsatt känsel medför ofta svårigheter att utan synens hjälp kunna identifiera ytor, form, storlek och föremål och att kunna känna skillnad på temperaturer. Känselåterkopplingen från handen till hjärnan är viktig för att kunna styra handens rörelser och därigenom kunna använda den påverkade handen på ett ändamålsenligt sätt i vardagliga aktiviteter. En nedsatt känsel kan även påverka förmågan att spontant använda handen i olika aktiviteter med ökad risk för inlärning av ett icke användande av handen.

Det övergripande syftet med denna avhandling var att öka kunskapen om konsekvenserna av en känselnedsättning i arm och hand efter stroke, och att utvärdera effekterna av ett nytt träningsprotokoll.

I studie I, som var en kvalitativ studie intervjuades 15 personer om deras upplevelser av en nedsatt känsel i arm och hand efter stroke. Datan analyserades med innehållsanalys. I studie II undersöktes vilka faktorer (ålder, kön, drabbad hand, social situation, yrkesutbildning situation, greppstyrka, spasticitet, känsel och smärta) som har betydelse för finmotoriken efter stroke. Sjuttiofem personer testades vid ett tillfälle enligt ett standardiserat protokoll och datan analyserades med linjära regressions modeller. I studie III undersöktes effekten och genomförbarheten av specifik känselträning i kombination med uppgiftsspecifik träning jämfört med enbart uppgiftsspecifik träning. Tjugosju deltagare genomförde träningen; 15 i interventionsgruppen (känselträning i kombination med uppgiftsspecifik träning) och 12 i kontrollgruppen (uppgiftsspecifik träning). Deltagarna tränade 2.5h 2 ggr/vecka under 5 veckor. Primärt utfallsmått var känseln i den påverkade armen och sekundära utfallsmått var finmotorik, förmåga att använda den påverkade handen i dagliga aktiviteter och upplevd delaktighet. En oberoende bedömare genomförde alla bedömningar före träningen, direkt efter träningen och vid en 3 månaders uppföljning. I studie IV intervjuades de 15 deltagare som genomfört känselträningen i kombination med uppgiftsspecifik träning i studie III om sina erfarenheter och upplevda effekter.

Deltagarna i studie I beskrev en förändrad känsel i form av domningar, stickningar och köldkänsla. De beskrev också svårigheter med rörelsekontroll i arm och hand, vilket ledde till svårigheter att använda handen i många dagliga aktiviteter. De uppgav olika strategier för att övervinna svårigheterna, såsom att använda synen vid aktiviteter och att kompensera med den icke-påverkade handen. Få hade fått någon specifik träning för att förbättra känseln. Studie II visade att diskriminativ beröringsförmåga var en bidragande faktor och förklarade 46% av variationen i finmotoriken hos personer med mild till måttlig stroke. Studie III visade att efter specifik känselträning i kombination med uppgiftsspecifik träning, fanns det en signifikant skillnad mellan grupperna ($p = 0.007$) avseende förmågan att uppfatta beröring till förmån för interventionsgruppen, men ingen skillnad i andra utfallsmått. Interventionsgruppen förbättrade signifikant ($p < 0.05$) förmågan att använda den påverkade handen i dagliga aktiviteter både vad gäller hur mycket och rörelsekvalitet. Kontrollgruppen förbättrade signifikant ($p < 0.05$) förmågan att använda handen i dagliga aktiviteter. Träningen tolererades väl och genomfördes utan några allvarligare negativa händelser. Studie IV visade att deltagarna uppskattade träningen men att den var ansträngande och krävde mycket koncentration. Stödet från terapeuten var viktigt och att träna i grupp var positivt. Hemträningen upplevdes svår att genomföra på grund av brist på support, tid och motivation. Deltagarna angav små förbättringar av känseln men en förbättrad rörelsekontroll och förmåga att använda den påverkade handen i vardagliga aktiviteter.

Sammanfattningsvis visar studierna i denna avhandling att känselnedsättning i arm och hand efter stroke har en mycket negativ inverkan på rörelsekontroll och en påverkan på genomförandet av aktiviteter i det dagliga livet. Känseln i form av diskriminativ beröring är betydelsefull för finmotoriken och därigenom viktig att bedöma och behandla i rehabiliteringen av övre extremitet efter stroke. Specifik känselträning i kombination med uppgiftsspecifik träningen upplevdes som ansträngande men inspirerande och meningsfull. Deltagarna beskrev förbättringar i rörelsekontroll och förmågan att använda den påverkade handen i olika vardagliga aktiviteter.

Abbreviations

ADL	Activities of Daily Living
BBT	Box and Block Test
CG	Control Group
CIMT	Constraint-Induced Movement Therapy
CNS	Central Nervous System
COPM	Canadian Occupational Performance Measure
EmNSA	Erasmus modification of Nottingham Sensory Assessment
FMA-UE	Fugl-Meyer Assessment Upper Extremity (sensory section)
ICF	International Classification of Functioning, Disability and Health
IG	Intervention Group
M1	Primary motor cortex
MAL	Motor Activity Log
MAS	Modified Ashworth Scale
mSHFT	mini Sollerman Hand Function Test
NHPT	Nine Hole Peg Test
NSA	Nottingham Sensory Assessment
PMC	Premotor Cortex
PNS	Peripheral Nervous System
PPC	Posterior Parietal Cortex
RASP	Rivermead Assessment of Somatosensory Performance
S1	Primary somatosensory cortex
S2	Secondary somatosensory cortex
SIS	Stroke Impact Scale
SMA	Supplementary Motor Area
STI	Shape Texture Identification test
SWM	Semmes-Weinstein Monofilament
SU	Stroke Unit
UL	Upper Limb

Thesis at a glance

Aims	Methods	Results	Conclusions
Paper 1: To describe stroke survivors experiences of sensory impairment in the upper limb, the influence of such impairment on daily life, coping strategies used, and sensory training for the affected hand.	Fifteen participants with stroke and sensory impairments in their affected upper limb were interviewed. A semi-structured interview guide was used and the material was analysed with an inductive content analysis.	Five categories emerged from the analyses. 1. Changed and varied perception of the sensation, 2. Affected movement control, 3. Problems to use the upper limb in daily life, 4. Various strategies to cope with the upper limb disability and 5. Lack of sensory training.	Sensory impairment of the upper limb after stroke has a highly negative impact on daily life, but specific sensory rehabilitation for the upper limb is lacking. These findings imply that the clinical management of sensory impairment after stroke requires more attention.
Paper 2: To evaluate how several factors are associated with dexterity after stroke.	Seventy-five participants with sensorimotor impairments of the upper limb were recruited. Dexterity and potentially associated factors (age, gender, affected hand, social situation, vocational situation, grip strength, spasticity, sensory function and pain) were evaluated by regression models.	Sensory function in terms of active discriminative touch had the strongest association with dexterity, explaining 46% of the variance. When spasticity and grip strength were added the explained variance increased to 57% in the final multivariable model.	Sensory function in terms of active discriminative touch seems to be a major contributing factor to dexterity in persons with mild to moderate stroke whereas spasticity and grip strength may be of lesser importance.
Paper 3: To evaluate the efficacy of sensory relearning in combination with task-specific training compared to task-specific training only, for people with sensory impairments in the upper limb after stroke and to evaluate the feasibility of the training.	Twenty-seven participants were randomized to an intervention group (n=15) or to a control group (n=12). Both groups received training twice a week, in 2.5 hours sessions for 5 weeks. Primary outcome was sensory function. Secondary outcomes were motor function, ability to use the hand in daily activities and perceived participation. Feasibility was evaluated by a questionnaire.	There was a significant change between groups in touch tresholds in favor of the sensory relearning. There were no significant differences in changes in any of the other primary outcomes or secondary outcomes. Significant changes in the ability to use the hand were seen in the intervention group and partly for the control group. The sensory relearning was well tolerated and performed without any adverse events.	Combined sensory relearning and task-specific training may be a promising and feasible intervention to improve upper limb sensorimotor function after stroke.
Paper 4: To explore how persons with impaired sensory function of the UL after stroke experienced the SENSUPP protocol and its effect.	The 15 participants who were randomized to the sensory relearning group were interviewed. A semi-structured interviewguide was used. The data was analysed with inductive content analysis.	One overall theme 'Sensory relearning was meaningful and led to improved ability to perform daily hand activities' and two categories 1. The outpatient training was inspiring but strenous, while the hometraining was a struggle, and 2. Overall small effects on sensory function but improved ability to use the hand.	Sensory relearning was experienced as a strenuous but inspiring and meaningful training method. Individualized structured training combined with guidance and feedback from a therapist and to train in groups were appreciated. The training led to small improvements in sensory function, but an increased movement control and ability to use the hand in daily life. The home training was a challenge to complete.

Introduction

The importance of somatosensory function

The somatosensory function in the upper limb (UL) is well developed in humans. With our hands we can easily identify the character of different objects and materials without help from vision. For example, we can determine the size of a coin we have in our pocket, and with a well-adjusted grip strength pick a grape without crushing it. The somatosensory function in UL enable the interaction with the surrounding world and is vital for our non-verbal communication with other people (1).

In addition, feedback from the sensory system is important for how we perceive our body parts in space and body image, and it can alert us about potential dangers in our environment (2). Somatosensory information from skin, muscles and joints are sent to the brain where it is processed. Part of this processed information is used for motor control. The somatosensory and motor systems are closely interconnected. This connection is imperative for well-coordinated arm and hand movements. Through this process we can perform complex motor tasks that are important in everyday life, work and in leisure activities (3).

The nervous system

The human nervous system can be divided into the central nervous system (CNS), comprising the brain and spinal cord, and the peripheral nervous system (PNS) including the peripheral nerve and receptors (4). The brain is anatomically divided into different areas based on structure, but it is also divided into areas based on function. The sensory system and the motor network are examples of functional systems within the CNS. The CNS and the PNS, act together with integration of sensory information, motor control and cognitive functions (5).

The sensory system

The somatosensory system can detect a wide range of different modalities of stimuli such as touch, discriminative touch, proprioception and stereognosis. The most basic modality is touch detection defined as an awareness of a specific sensation such as touch, pressure, thermal or pain. Touch discrimination is our ability to discriminate between different textures, shapes, sizes and weights and e.g. if there is one or two things touching the skin. The most complex level of touch is tactile object recognition also referred to as stereognosis or tactile gnosis, which often is required for active hand movements. Stereognosis defines our ability to manipulate and identify objects in the hand without vision (4) and is commonly used for the assessment of injuries in the CNS. Tactile gnosis, on the other hand, is often used to assess injuries in the PNS. Finally, proprioception is our ability to recognize position and movements in the hand and other joints without the support of vision (6). In addition there are other terms in the literature for example haptic object recognition which is a broader perceptual concept that involves a combination of tactile information and proprioception in order to identify common objects (7), however this definition is similar to tactile object recognition. Throughout this thesis the terms sensory function will be used, which includes the following modalities: touch detection, active touch discrimination, tactile object recognition and proprioception.

Sensory receptors in the hand

There are four different types of mechanoreceptors in the hand. Meissner's corpuscles have small receptive fields, adapting rapidly to stimuli and are sensitive to light touch, Merkel's discs have small receptive fields, adapting slowly to stimuli and are sensitive to vibration, Pacinian corpuscles have large receptive fields, adapting rapidly and are sensitive to pressure and vibrations. Ruffini's endings have large receptive fields, adapting slowly to stimuli and are sensitive to stretching of the skin. Activation of this mechanoreceptors provide us with valuable sensory information about objects and surfaces in the hand (7). Ruffini's endings are also important together with muscle spindles, Golgi tendon organ in the junction between the muscle and tendon and joint receptors (4) responsible for our ability to recognize position and movements of the limbs (proprioception). Finally, free nerve endings within the skin are sensitive to pain, crude touch, and temperature changes. The sensory information from the mechanoreceptors and free nerve endings are mediated by the peripheral nerves to the dorsal root ganglia located adjacent to the spinal cord and via the dorsal root, sensory nerve impulses are led into the spinal cord. In the spinal cord the nerve signals are transmitted by two different pathways to the brain, the dorsal column-medial lemniscus system (touch and proprioception) and the anterolateral system (pain, crude touch, and temperature). The pathways cross the midline at various levels in the spinal cord in CNS and the afferent input is sent to the thalamus, where the sensory information is further processed. The nerve signals are then projected to primary sensory cortex (S1) in the parietal lobe (8).

The hand is represented with a large number of neurons in S1, that solely process afferent stimuli from the hand (Figure 1).

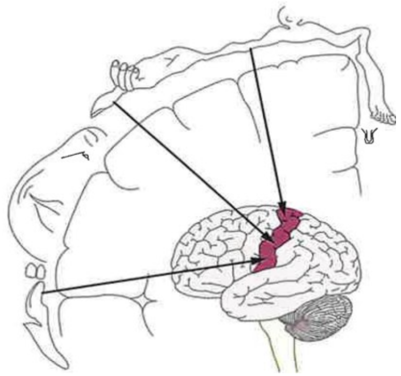

Figure 1. A description of the proportions of neurons devoted to processing sensory information from specific skin areas. With permission from Typoform AB.

The sensory information in S1 is sent to the secondary somatosensory cortex (S2) and higher order regions such as the posterior parietal cortex (PPC). The sensory information is also transferred to regions in the motor system which in turn conveys feedback projections to somatosensory cortical areas (8, 9).

The motor system

The motor system consists of the primary motor cortex (M1) in the frontal lobe just anterior to central sulcus, as well as the premotor cortical areas such as the supplementary motor area (SMA) and the premotor cortex (PMC). Together with the information from the sensory system, the visual system, cerebellum and basal ganglia (7) the motor system produces a motor plan for the intended movement (8). An output signal with the motor plan information is passed through the internal capsula. Before entering the spinal cord, 90% of the axons pass to the contralateral side to form the lateral corticospinal tract and 10% continue to the spinal cord to form the anterior corticospinal tract and decussate at segmental levels . Thereafter, the signal is passed on in the spinal cord to the lower motor neurons in the anterior horn. From here efferent signals are sent via the peripheral nerve to the skeletal muscles (4).

Sensorimotor control

Sensorimotor control is a complex process involving many systems in the brain (10). There are various theories of sensorimotor control and how the brain learns to perform a specific movement (5). Makino defines sensorimotor learning as an "improvement in one's ability to interact with the environment by interpreting the sensory world and responding to it with the motor system" (11). Sensory information from peripheral receptors are crucial for our ability to control movement (12), to adjust the grip-force, (13) and for learning new motor skills (14). One skill that requires a high degree of sensorimotor control is dexterity, which is defined as the ability to grip and release an object, perform precision grip, coordinate finger movements, and manipulate objects (15).

Prior studies have shown that sensory feedback is processed at different levels within the CNS and has an important role for the control of coordinated movements, motor learning and error modifications (16), and in the planning and performance of voluntary movements (17).

Cerebellum is also involved in sensorimotor control, it receives feedback from the sensory system (5), is responsible for modulation and correction of movements and thus produce smoothly and well-coordinated movements (4). Cerebellum has also a central role for motor learning and automatic movements (8). Another area important for our sensorimotor control is the basal ganglia (18), which receives input from motor, sensory and association areas in the brain. It is responsible for initiating and coordinating movements for targeted goals, filtering and inhibiting unwanted movements and is also contribute to motor learning (8) (Figure 2).

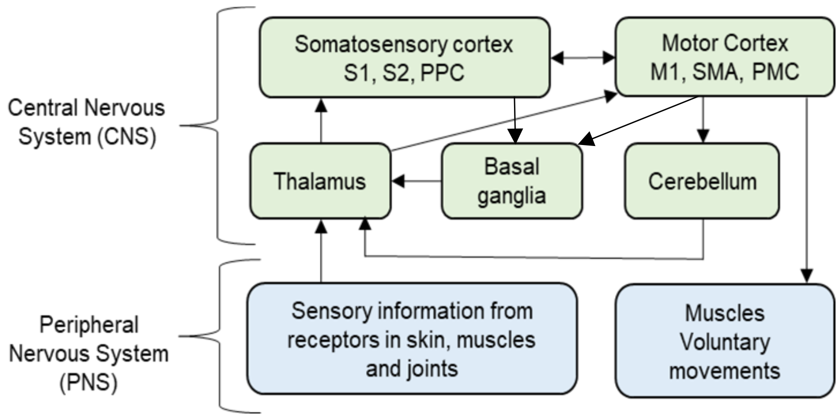

Figure 2. A description of the afferent sensory information to CNS, the senorimotor process in the CNS, and the efferent signal from the motor cortex to the muscles.

Following a stroke an impaired sensory function is common (6) and due to the close connection between sensory function and motor skills the sensorimotor control is often affected, which can have a great impact on the person's daily life.

Stroke

Stroke is one of the most common causes of disability in adults worldwide (19) In Sweden, approximately 25400 persons suffered a stroke during 2020 with a mean age of 75 years (20). Two-thirds of these persons suffer a stroke for the first time. Stroke is caused by a disruption of the blood supply to the brain causing damage in the brain. Ischemic stroke accounts for approximately 85% and occurs through an obstruction of a cerebral artery leading to a focal ischemia in the surrounding brain tissue. Haemorrhagic stroke accounts for approximately 15% and occurs by either an intracerebral bleeding within the brain tissue (10%) or a subarachnoid bleeding (5%) between cerebral meninges.

In recent years, the incidence in stroke has declined due to an improved primary prevention and an improved management to prevent recurrent stroke (21). Advances in the medical treatment in the acute phase with endovascular thrombectomy and thrombolysis, as well as specialized stroke unit (SU) care where all personnel have special knowledge of stroke have increased functional independence (22). Despite the advances in medicine and care, up to 100 000 persons live with stroke in Sweden and are facing its consequences.

Consequences following stroke

The clinical characteristics and severity after a stroke vary widely depending on the extent of the lesion and/or lesion site. Common consequences following a stroke are however hemiparesis, sensory impairments, reduced balance, spasticity, vision deficits, impaired swallowing, problems with communication and cognition such as attention, memory, and executive functions. All these impairments can have a large influence on activities and participation in daily life such as indoor and outdoor walking, personal daily activities for example ability to dress, eat, and perform households' activities. The impairments can also have an impact on work ability, social roles, leisure activities and reduce quality of life (23). A framework that can be used to describe the consequences following a stroke is the International Classification of Functioning, Disability and Health (ICF) (24) The ICF covers aspects of impairments, activity limitations and participation restrictions, as well as personal and environmental factors. Impairments include problems in body function and structures, activity refers to execution of a task or action by an individual and participation is defined as an engagement in life situations. Personal factors are aspects that influences the person´s functioning and environmental factors could be equipment and aids that facilitate an activity. The ICF can be used both in the clinic and in research Figure 3.

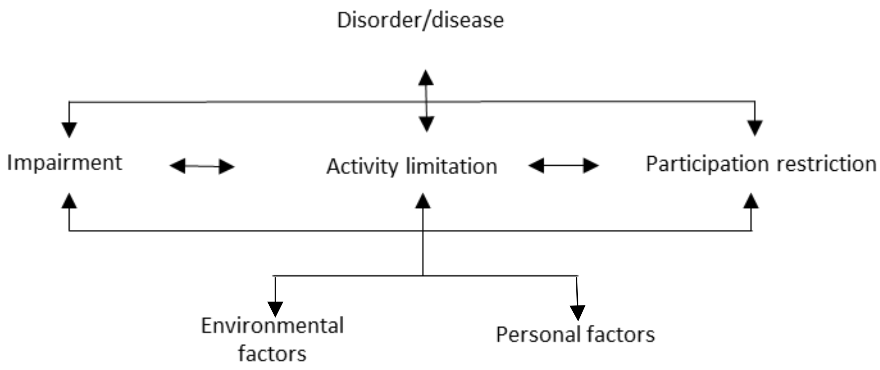

Figure 3. International Classification of Functioning, Disability and Health (ICF)

Sensory impairments and recovery

Sensory impairments can vary from only a slightly impaired touch detection to complete loss of both touch and proprioception. Studies have shown an association between impaired sensory function and motor skills such as fine motor control, object manipulation and grasp force (25, 26) and independence in activities of daily living (ADL) (27, 28). Furthermore, an association between impaired proprioception and motor function (29), and between impaired touch, proprioception and motor recovery, ADL difficulties and social roles are reported (30, 31).

The incidence of sensory impairments vary between 25-85% (32). In the acute phase, there is often an underestimation of the incidence due to limited time to examine the sensory function (33). In the subacute phase (1 to 3 months after stroke onset) it is reported that between 47% and 66% had a reduced touch, and that between 28% and 49% had a reduced proprioception (27, 34). Possible explanations for the large variability may be due to different definitions of sensory impairment, various assessment methods used, sensory modalities tested, and heterogeneity of study populations (16, 31).

Regarding recovery of sensory impairments longitudinal studies have revealed that there is a spontaneous recovery of the UL the first months depending primarily on neural mechanisms (35, 36), so called spontaneous neurological recovery. A fixed proportional sensory recovery during the first 6 months after stroke has been suggested, that is, a strong proportional relation between initial impairment and recovery especially for those with mild to moderate initial impairments (37). Other longitudinal studies have however shown that the recovery of sensory function in the UL varies during the first 3-12 months. In a prospective study, 70 participants were assessed on admission and 2, 4 and 6 months after stroke. Of these, 53% had an impaired touch in the hand in the acute phase, and 63% had a reduced proprioception (28). Touch improved up to 4 months while proprioception improved up to 6 months. In another study, 101 persons with an ischemic stroke were assessed in the acute phase, and after 3 and 12 months. In the acute phase, 56 % had sensory impairments in at least one modality with light touch as the most common; that declined to 39% at 12 months. Recovery of sensory function was seen for all modalities, mainly within the first 3-month and small further improvements at 12 months (6).

Consequences of sensory impairments in the upper limb

The sensory impairments in the UL could affect the ability to discriminate textures, weights, shapes, and sizes, but also to control the level of grip force, and to reach, grasp and manipulate objects. This can, in turn, lead to reduced ability to perform bimanual tasks in everyday life (32, 38-40) and to participate in meaningful activities (33).

Another consequence of sensory impairments is that lack of sensory feedback from the affected UL can contribute to development of "learned non-use phenomenon, which means that even if the motor function is good, the actual use of the UL is much less than the potential ability (41). Thus, sensory function has shown to be a strong predictor of the amount of use of the more affected arm in daily activities (42). It can also be difficult to maintain attention on activities with the affected hand due to sensory impairments which further can contribute to the non-use phenomenon (1).

Only a few qualitative studies have described the impact of sensory impairments of the UL following stroke. In one study by Doyle et al the participants expressed difficulties in personal and instrumental tasks such as eating, dressing and meal preparation, and in leisure and work-related activities (43). The participants in that study mentioned a mentally and emotional fatigue when trying to adapt to the sensory impairments. In another study by Connell et al the participants described difficulties to understand the sensory impairment and its impact on daily activities (44). The awareness of the sensory impairments could however increase along with motor recovery (43). When the person started to use their affected hand in daily activities, they better understood the close connection between sensory function and motor skills (45). However, despite that sensory impairments in their UL are common, limited attention is often paid to these problems in rehabilitation (43, 44). Taken together, previous studies have shown that sensory impairments in the UL are common after stroke and can have significant consequences on the person's independence in everyday activities, participation and quality of life. Efficient rehabilitation interventions targeted these deficits are therefore warranted.

Rehabilitation for upper limb after stroke

The WHO (46) defines rehabilitation as 'a set of interventions designed to optimize functioning and reduce disability in individuals with health conditions in interaction with their environment'. Since recovery has proven to be largest during the first 3 months after stroke this time-window has been proposed for rehabilitation (47). However, the optimal time window for interventions after stroke onset is still not fully clarified (48) and studies have shown that improvements can occur up to 12 months after a stroke (49, 50). Therefore there is a need for rehabilitation for persons with stroke even in the long-term.

A well-coordinated multidisciplinary approach is a key factor in stroke rehabilitation and the process should begin with an assessment of the patients' stroke related impairments, activity limitations and participation restrictions (51). Thereafter, goal setting is important involving the patient and family (52). To achieve meaningful goals, the rehabilitation interventions should be designed aiming at improving body functions and increasing the ability to perform activities, as well as participate in society (47) (Figure 4).

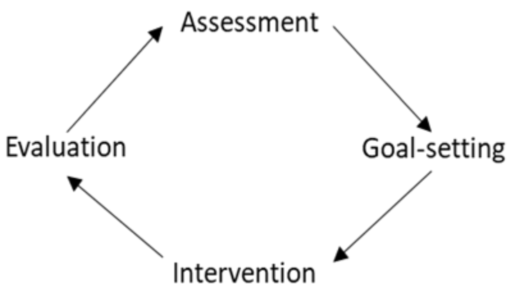

Figure 4. Description of the rehabilitation process.

There are a variety of interventions described in the literature to improve UL functioning after stroke (52). Evidence-based interventions for UL are for example constraint-induced movement therapy (CIMT), mirror therapy, virtual reality, interventions for sensory impairment and a relatively high dose of repetitive task-specific practice (53).

Task-specific training for improving motor performance in the UL is recommended in the stroke rehabilitation (54, 55). The training involves exercises of gross and fine motor function in goal-directed and meaningful tasks (56) with the purpose to improve performance (53, 57), by intensive, repetitive and varied practice (58). In addition, intermittent feedback is also important during the training (59). Previous studies regarding task-specific training have shown a faster improvement on function (60) and on activity performance. Moreover, a review has concluded that there is a moderate evidence that additional 20 hours of repetitive task training seems to be efficient for improving UL function after stroke. However, the authors called for more high-quality randomized controlled trials to increase the evidence.

Interventions to improve sensory function in the upper limb

Historically, less attention has been paid to specific sensory training for the UL (38) despite that sensory impairment in the UL affects more than 50% of those who have had a stroke (34). Overall, there seems to be an uncertainty among therapists about evidence-based interventions (61) and there is a need for more knowledge regarding the management of sensory impairment of UL after stroke (2).

Sensory rehabilitation can be divided into either active sensory training (i.e. manual exploration of different textures, figures and objects with the hand and fingers, and spatial detection of limb position) or passive sensory training including exposure to different sensory stimuli by vibration, icing and rubbing, electrical stimulation, thermal stimulation with hot or cold packs and pneumatic compression (62). In a systematic review of 13 studies with 467 individuals (2) the effects of sensory training of the upper limb were evaluated. The authors found some evidence that mirror therapy can improve light touch, pressure, and temperature, and that thermal stimulation and intermittent pneumatic compression can improve light touch and proprioception. In the largest to date randomized controlled trial (RCT, n=50) ‘sensory relearning’ in terms of an active sensory discrimination training, including texture discrimination, limb position sense, and tactile object recognition was investigated. The authors found a significant improvement in touch discrimination, proprioception, and tactile object recognition in favour for the sensory relearning group compared to a control group that received passive sensory training (34). However, the effect of ‘sensory relearning’ on activity and participation was not investigated in that study and still unexplored at the time of the planning of my thesis.

Sensory relearning

Sensory relearning is defined as *”the gradual and progressive process of reprogramming the brain through the use of cognitive learning techniques such as visualization and verbalization, the use of alternate senses such as vision or hearing* *and the use of graded tactile stimuli designed to maintain and/or restore sensory areas affected by nerve disorder to improve tactile gnosis"* (63). Sensory relearning for persons with peripheral nerve injuries was developed in the 70s by Wynn-Parry and Dellon (64) and then further developed by Rosén et al (65). During the 90s, Carey developed sensory training for the UL after stroke influenced by principles of learning (66).

Learning principles are important components in rehabilitation and to apply these principles for persons with UL sensorimotor impairments after stroke is essential (66). Important aspects in sensory relearning are intensive, repetitive practice with increasing difficulty, attentive exploration of the sensory attributes with closed eyes, as well as feedback in terms of intrinsic feedback of the impaired sensory function via vision or the unaffected hand (66), or extrinsic feedback by verbal guidance from the therapist (5). Other important learning principles are variable practice (67), meaningful and goal-oriented activities (52), and motivation. Based on these learning principles neural plasticity can be stimulated and contribute to recovery (68). The brain has the ability to change based on experience and learning through neuroplasticity (69). Cramer defined neuroplasticity as: "the ability of the nervous system to respond to intrinsic or extrinsic stimuli and reorganizing its structure, function, and connections"(70). This means that the brain has the ability to reorganize in response to training (71) and neural plasticity is suggested to be the basis for learning and recovery after injury (72) and provides a solid foundation for motor (68) and sensory relearning after stroke (66).

Combined sensory relearning and task-specific training

Although it is well known that the sensory input plays an important role for motor function after stroke (73), rather few studies have investigated the effect of combined sensory- and motor training aiming at improving sensorimotor control of the UL after stroke. There is some evidence that training of tasks that require active use of the hand and sensory discrimination, can improve both sensory and motor function (74, 75), and that sensory training can improve motor ability (33). In a review by Yilmazer et al, in which nine studies were included, the authors found that active sensory training significantly improved motor function, even though the level of evidence was low (76). In another review of combined sensory and motor training the authors concluded that there were limited evidence of its effect on sensorimotor function and UL functioning (77). Possible reasons could be the large variation in study design, stroke severity, dosage of the training, how the training was combined and a lack of sensitivity of outcome measures used. Thus, to be able to assess the degree of sensory impairments appropriately, as well as the consequences in daily life and the effect of interventions, standardized and reliable outcome measures are needed.

In this thesis, we have used a training protocol where sensory relearning and task-specific training are combined, the so called SENSUPP protocol (78).

Outcome measures to assess sensory function

There is limited knowledge about which outcome measures that are the most appropriate to use when assessing sensory function after stroke. A Cochrane review, including 13 studies, revealed that 36 outcome measures were used to assess sensory function and that 13 outcome measures were used to assess UL functioning (2). It is described that light touch and proprioception is most often measured in clinical settings (32), and if other sensory modalities are not assessed (79), it may lead to an underestimation of the sensory impairments (33). Moreover, the assessments are often performed using unstandardized protocols (79).

There are a few screening tools that can be used to assess sensory impairments. One is the Nottingham Sensory Assessment (NSA), which later on was slightly modified and renamed to Erasmus modification of NSA (EmNSA). The EmNSA includes assessments of light touch, pressure, pinprick, proprioception, sharp/blunt and two-point discrimination (80). Another measure is the Rivermead Assessment of Somatosensory Performance (RASP), which assesses pressure, surface localization, temperature, proprioception and sharp-blunt discrimination (81). In the Fugl-Meyer Assessment of Upper Extremity there is a sensory subscale including light touch and proprioception showing good inter-rater reliability but has a significant ceiling effect (32). Most tests are performed in a passive manner and there is a need when it is possible to complement the examination with an active sensory test (82). Such test is the Shape-Texture Identification test (STI™), which has been developed to assess active discriminative touch including the ability to identify shapes and textures with the affected hand (83).

Rationale

Although impaired sensory function in the UL is common after a stroke and can have a major impact on the person's ability to carry out everyday activities and thereby affect participation and quality of life, there was at the time of the start of this thesis limited knowledge about how stroke survivors with impaired sensory function experience their difficulties. Thus, there was a need for a more thorough understanding about stroke survivors' experiences of an impaired sensory function in the UL after stroke, its consequences and how they handle daily life.

Moreover, dexterity is shown to be a crucial factor for the ability to perform daily hand activities. Therefore, it is essential to understand which factors are associated with dexterity after stroke. This knowledge is important to be able to plan appropriate rehabilitation interventions for the UL after stroke.

Sensory relearning has been shown to improve touch discrimination and proprioception in UL after stroke. However, knowledge about the effect on sensorimotor function and the ability to use the hand in daily activities was limited. Only a few studies had evaluated the combination of sensory and task-specific training with inconclusive results. Therefore, there was a need for increased knowledge about the effect of such training as well as of how the participants' experience the training and possible effects.

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

Aims

Overall aim

The overall aim of this thesis was to increase knowledge about the consequences of sensory impairments of the upper limb after stroke, and to evaluate the effects of a novel training approach. The specific aims were:

Specific aims

- To describe stroke survivors' experiences of sensory impairment in the UL, the influence of such impairment on daily life, coping strategies used, and sensory training for the affected hand.
- To evaluate how several factors (age, gender, affected hand, social situation, vocational situation, grip strength, spasticity, sensory function, and pain) are associated with dexterity after stroke.
- To evaluate the efficacy of sensory relearning in combination with task-specific training compared to task-specific training only, and the feasibility of the training in chronic stroke.
- To explore how persons with impaired sensory function of the UL after stroke experienced sensory relearning in combination with task-specific training and perceived effects of the training.

Methods

Study designs

This thesis is based on four studies with different designs including two qualitative studies (study I and study IV), one cross-sectional study (study II) and one pilot randomized controlled trial (pilot RCT, study III). An overview of the study designs, participants, data collection and data analysis for all studies is shown in Table 1.

Table 1. Overview of study design, participants, data collection and data analysis for the four included studies.

Study	I	II	III	IV
Study design	Qualitative	Cross-sectional	Pilot randomized controlled trial	Qualitative
Participants	N=15 (8 men and 7 women) Mean age 62 years (SD ± 10) Time since stroke median 62 months (min-max 6-132)	N=75 (54 men and 21 women) Mean age 66 years (SD ± 8) Time since stroke median 33 months (min-max 4-116)	N=27 randomized to sensory relearning and task-specific training N=15 (10 men and 5 women) or to task-specific training N= 12 (10 men and 2 women) Mean age 59 years (SD ± 11) Time since stroke median 16 months (min-max 6-96)	N=15 (10 men and 5 women) from the sensory relearning group in study III Mean age 59 years (SD ± 12) Time since stroke median 15 months (min-max 7-96)
Data Collection	A semi-structured interview with questions how the participants perceived the impaired sensory function, how it affects daily life, coping strategies used and experiences of sensory training.	Data from medical records regarding characteristics and demographics of the participants. Performance-based measures for sensory function, dexterity, grip strenght, spasticity, and pain.	Assessments of sensory function, dexterity, ability to use the affected hand in daily life and participation were performed at baseline, post-intervention and at 3-month follow-up.	A semi-structured interview with questions about the participants' experiences of the training and perceived effects.
Data analysis	Inductive content analysis.	Descriptive statistics, uni- and multivariable linear regression.	Descriptive statistics, Mann-Whitney U test, Friedmann test, Wilcoxon signed rank test, effect sizes with rank biserial correlations.	Inductive content analysis.

Participants

All participants in the four studies (study I-IV) had received initial medical care at the stroke units in Malmö or Lund, Department of Neurology, Rehabilitation Medicine, Memory Disorders and Geriatrics, Skåne University Hospital. After discharge from the stroke units, some continued with inpatient rehabilitation at the hospital, whereas others were discharged to their homes and continued rehabilitation in outpatient healthcare settings specialized in stroke rehabilitation. Physiotherapists and occupational therapists working with stroke rehabilitation in these units were helpful in recruiting participants to the studies and in identifying persons with sensorimotor impairments of UL after stroke. All participants were mildly to moderately affected by their stroke, had remaining sensorimotor impairments in their affected UL and were able to walk with or without an assistive device.

In study I, 47 potential participants with mild to moderate impairments of the UL after stroke were identified (Figure 5). The inclusion criteria to participate in the study were sensory impairment of the affected UL, measured with Shape-Texture - Identification test (STI™), ability to grasp and release an object, ability to understand verbal and written information and to communicate verbally, age younger than 85 years, and at least 6 months since stroke onset.

To gain diversity regarding gender, age, time since stroke, hand dominance and degree of sensory impairment 24 potential participants were selected. They received written information about the study and were contacted after 1-2 weeks by phone by HC for further oral information and asked if they were willing to participate in the study. Six persons declined to participate, and three persons did not respond. Thus, a sample of 15 persons were included in study I.

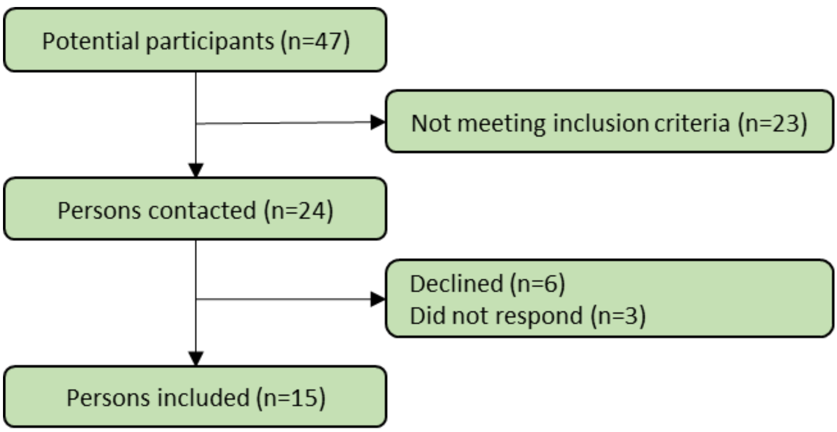

Figure 5. Flow-chart of the recruitment process in study I.

Of the 15 participants, eight were men and seven women. Their mean age was 62 years (35 to 78 years), and time since stroke was on average 62 months (6 months to 11 years). Ten of the participants were affected in their dominant side, and all of them had an impaired sensorimotor function in their affected side.

In study II, 270 potential participants with sensorimotor impairment of the UL following stroke were identified (Figure 6). The inclusion criteria to participate in the study were: at least 4 months after stroke and having mild to moderate impairments of the affected UL (i.e., ability to place the palm to the forehead and ability to grasp and release an object with the hand). Exclusion criteria were: inability to follow instructions due to aphasia or cognitive deficits, and other neurological or musculoskeletal conditions affecting function of the UL. In the first step, 92 persons did not meet the inclusion criteria and thus 178 persons were contacted. Of these, 44 did not meet the inclusion criteria, 51 declined to participate and eight did not respond. Thus, a total of 75 persons were included in study II.

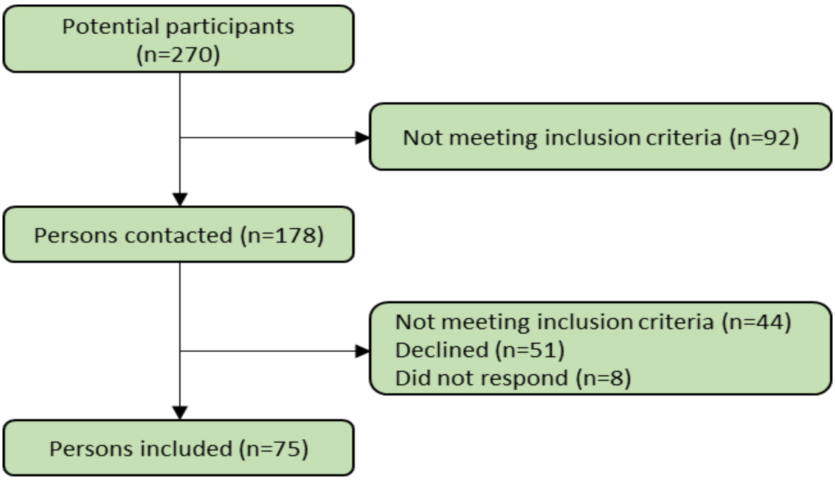

Figure 6. Flow-chart of the recruitment process in study II.

The participants were on average 66 years (44 to 85 years), 72% were male and time since stroke was on average 33 months (4 months to 116 months). In Table 2, the characteristics of the participants are presented.

Table 2. Demographics and characteristics for the 75 participants in study II.

Variabels	
Age, years mean (± SD; min-max)	66 (± 8; 44 to 85)
Gender (male), n (%)	54 (72)
Time since stroke, months mean (± SD; min-max)	33 (± 26; 4 to 116)
Vocational situation (not working), n (%)	62 (83)
Stroke type, n (%)	
Ischemic	58 (77)
Hemorrhagic	17 (23)
Side of paresis (right), n (%)	37 (49)
Affected hand (dominant), n (%)	39 (52)
Social situation (living alone), n (%)	25 (33)

In the pilot RCT (study III), 47 potential participants were identified for eligibility to participate in the study. The inclusion criteria for participation were: sensory impairments of the UL (≤5 points in Shape-Texture Identification test, STI™), ability to grasp and release an object, ability to understand oral and written information, 18-80 years of age, at least 6 months since stroke onset, and ability to walk with or without an assistive device. The exclusion criterion was sensory impairments in the UL due to other diagnosis than stroke. Of the 47 potential participants, 20 persons were excluded due to not meeting inclusion criteria, were working and had other diseases. Finally, 27 participants were recruited and randomized to either an intervention group (sensory relearning in combination with task-specific training) or to a control group (task-specific training).

In the qualitative study (study IV), the 15 persons who were randomized to the intervention group were interviewed. Characteristics of the participants are presented in Table 3.

Table 3. Characteristics of the participants in the intervention group (study III and IV) and the control group (study III).

Variables	Intervention group (n=15)	Control group (n=12)
Age, years, Median (min-max)	64 (28-74)	60 (32-72)
Gender, Male/Female	10/5	10/2
Time since stroke (months), Median (min-max)	15 (7-96)	18 (6-84)
Type of stroke, ischemic/hemorrhage	11/4	6/6
Side of paresis, Right/Left	9/6	7/5
Affected hand dominant, Yes/No	9/6	8/4

Data collection and outcomes

Experiences of sensory impairments of the upper limb (Study I)

In study I, all individual interviews were conducted between May and December 2015 at the Department of Neurology and Rehabilitation Medicine at Skåne University Hospital. The first author (HC) conducted all the interviews, which lasted between 15 and 70 minutes with an average time of 38 minutes. To cover different aspects of the UL sensory impairments and consequences in daily life, an interview guide based on the components of the ICF model was used with the following topics: perception of the impaired sensation of the UL; how it affects daily life, how to cope with UL disability; and experiences of sensory training for the affected UL. To obtain as rich and comprehensive description as possible of the participants' experiences feedback questions such as "can you give an example" and "please describe" were used. All interviews were recorded and transcribed verbatim.

Factors associated with dexterity (Study II)

The 75 participants in study II were recruited from April 2012 to August 2015. Functioning of UL was assessed on one occasion by a physiotherapist with long experience in neurological rehabilitation (EE). The assessment was performed in a separate room at the hospital and to standardize the test procedure all assessments were performed in the following order: pain; spasticity; sensory function (light touch and proprioception); fine manual dexterity; sensory function (touch discrimination) and grip strength. Dexterity was assessed by the mini Sollerman Hand Function Test (mSHFT), grip strength with a digital dynamometer (Grippit), spasticity of the UL was assessed by the Modified Ashworth Scale (MAS), sensory function by two different tests: the Fugl-Meyer Assessment of the Upper Extremity sensory section (FMA-UE) and the Shape-Texture Identification test (STI^{TM}). These outcome measures are presented in Table 4 and described under the heading 'Outcome measures'.

Each test took about 10 minutes to perform, and a short rest was allowed between the tests. Other variables that were collected were age, handedness, social situation (if they lived alone or with another person), vocational situation (not working or in work at least 20 hours per week), time since stroke onset, type of stroke (ischemic or haemorrhagic), side of paresis and pain.

Outcome measures (Study II and III)

An overview of the outcome measures used in study II and III is shown in Table 4. A variety of outcome measures were used to capture participants' sensorimotor function, activity and participation according to ICF. The outcome measures in paper III are also described in a study protocol (84).

Table 4. Overview of the outcome measures used in study II and III.

	Outcome measure	Variable	Study II	Study III
Sensory function	Semmes-Weinstein monofilament (SWM)	Touch detection thresholds		x
	Shape-Texture- Identification test (STI^{TM})	Touch discrimination	x	x
	Fugl-Meyer Assessment Upper Extremity (FMA-UE) sensory section	Light touch and proprioception	x	x
	Daily or almost daily pain in more affected upper limb (present or not)	Pain	x	
Muscle function	Modified Ashworth Scale (MAS)	Spasticity	x	
	Grippit dynamometer	Grip strength	x	
Dexterity	Box and Block Test (BBT)	Gross manual dexterity		x
	mini Sollerman Hand Function Test (mSHFT)	Fine manual dexterity	x	x
Activity	Motor Activity Log (MAL)	Difficulties in daily activities		x
	Canadian Occupational Performance Measure (COPM)			x
Participation	Stroke Impact Scale (SIS) Participation domain	Perceived participation		x

Touch detection thresholds: The Semmes-Weinstein Monofilament (SWM) pocket version was used to assess touch thresholds of the hand. The test includes five standardized nylon filaments giving a pressure from 0.07 gram (thinnest filament) to 279 grams (largest filament) (Touch Test® Sensory Evaluators, North Coast Medical Inc.) (85, 86).

Touch discrimination: The STI-test™ (www.sensory-tests.com) was used (study II and III) to measure 'active discriminative touch' i.e., the ability to discriminate between different shapes (cube, cylinder or hexagon) and textures (one, two or three raised metal dots placed in a row) by active movements of the index finger (Figure 7). The score ranges from 0 to 6 points per hand, where 6 indicates normal active discriminate touch. The STI™-test was originally developed to assess functional outcome for people with peripheral nerve injury (83). The STI-test™ has been tested on people with stroke and shown to be reliable in persons with mild to moderate impairments of the UL after stroke (87).

Figure 7. Measurement of active discriminative touch with the Shape-Texture Identification test (STI™).

Light touch and proprioception: The Fugl-Meyer Assessment Upper Extremity (FMA-UE) sensory section was used to measure light touch and proprioception (88) (study II and III). To assess light touch the participants were asked if they could detect the touch from a cotton swab on the upper arm/ forearm and the palmar side of the hand/ fingers. Proprioception was assessed with passive movements of the wrist, and interphalangeal joint of the thumb. The score ranges from 0 to 4 points for each subtest, with a maximum score of 8 points. The FMA-UE sensory section has been shown to be a clinically useful and robust instrument in persons with sensory impairment after stroke (89).

Pain: was assessed by asking if the participants perceived daily or almost daily pain in their more affected UL (study II).

Muscle tone: Spasticity in the muscles in the elbow, wrist, or fingers was assessed by the Modified Ashworth Scale (MAS) (90) (study II).The assessment ranges from 0 (no increase in muscle tone) to 4 points (affected part rigid in flexion or extension). Spasticity was classified as present if the participant had a score equal to or greater than 1 point. The MAS has been shown to have high intrarater reliability of the UL for persons with stroke (91).

Grip strength: was measured with the Grippit dynamometer (Catell AB, Hägersten, Sweden, www.catell.se) (study II) and was measured three times; each contraction lasted 3 seconds with a 60-second rest between the trials and the highest value was recorded (in Newton, N). Grip strength has been shown to be reliable in persons with mild to moderate impairment of the UL after stroke and to be a representative measure of the entire UL muscle strength after stroke (92).

Gross manual dexterity: The Box and Block Test (BBT) was used to assess gross manual dexterity. During 1 minute as many wooden blocks as possible should be transported from one compartment to the other (93). The BBT has been shown to be reliable in persons with mild to moderate disability after stroke (94).

Fine manual dexterity: The mini Sollerman Hand Function Test (mSHFT) (PROcare ApS, www.procare.dk) was used to assess fine manual dexterity (study II and III). The mSHFT contains of three selected tasks that correlate strongly with the 20 tasks in the original SHFT (95, 96). The three tasks include picking up four coins of different sizes from a purse, putting four nuts of decreasing sizes on bolts, and buttoning four buttons of decreasing sizes (Figure 4). The time to complete the task and the quality of the selected grasp is assessed on a 5-point scale (0 to 4 points) and summarized into a total score (0-12 points) where 12 indicate normal dexterity (97). The mSHFT has been shown to be a valid and reliable measure for persons with mild to moderate impairment of the UL after stroke (94) (Figure 8).

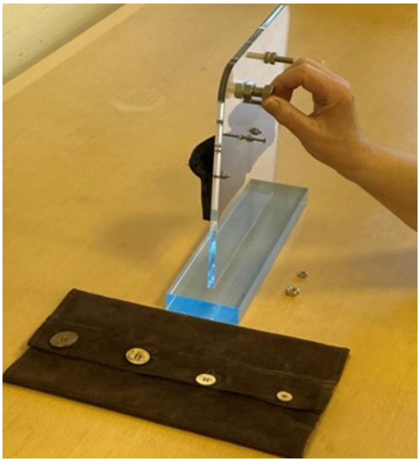

Figure 8. Measurement of fine manual dexterity with mini Sollerman Hand Function test (mSHFT).

Activity: The Motor Activity Log (MAL) was used to evaluate use of the more affected UL in daily activities (98). The test consists of a structured interview where the participants were asked to assess their perception of how much (amount of use; AOU) and how well (quality of movement; QOM) they used their affected hand in 30 daily activities (99, 100).

The Canadian Occupational Performance Measure (COPM) was used to capture participants' self-perceived performance (COPM-P) and satisfaction (COPM-S) of activities in self-care, productivity and leisure activities (101). COPM has been used in rehabilitation studies (58, 102) and has shown moderate to good test-retest reliability in persons with stroke (103).

Participation: was assessed by the Stroke Impact Scale, perceived participation domain (SIS-Participation) (104). SIS is commonly used in stroke research (105) and has shown to be reliable, valid and sensitive to change in persons with mild to moderate stroke (106, 107).

Sensory relearning (Study III)

In the pilot RCT (study III), the 27 participants with sensory impairments in the UL were randomized either to an intervention group (sensory relearning in combination with task-specific training n=15) or to a control group (task-specific training only n=12).

The training consisted of 2.5 hours of training, twice a week for 5 weeks for both the intervention group and the control group at the outpatient clinic. The intervention group performed 60-70 minutes of sensory relearning and 60-70 minutes of task-specific training and were also instructed to train at home daily for 30 minutes. The control group performed 60-70 minutes of task-specific training and 60-70 minutes of strength training, movement exercises and self-stretching. Two experienced physiotherapists were involved in the training. During the first and second training sessions both therapists participated to find the optimal training level for each participant. Thereafter, only one physiotherapist supervised most of the training sessions. The training was individualized depending on the participants' sensorimotor capacity.

Primary and secondary outcomes

Primary outcome in study III was sensory function examined with three measures (see Table 4) covering different sensory modalities such as touch thresholds, touch discrimination and proprioception. Touch thresholds were assessed by the Semmes Weinstein Monofilament (SWM), discriminative touch was assessed by the Shape-Texture Identification test (STI^{TM}) and light touch and proprioception were assessed by the Fugl-Meyer Assessment of the Upper Extremity, sensory section (FMA-UE).

Secondary outcomes were dexterity measured with the Box and Block Test (BBT) and mini Sollerman Hand Function Test (mSHFT), the ability to use the affected hand in daily activities measured with Motor Activity Log (MAL) and Canadian Occupational Performance Measure (COPM). Stroke Impact Scale (SIS) was used for perceived participation. An independent assessor conducted all the assessments at baseline (T1), post-treatment (T2) and at 3 months follow-up (T3).

Training for the intervention group

The sensory re-learning, i.e., the SENSUPP protocol consisted of four components: sensory relearning, task-specific training, home training and learning principles (Figure 9). The training is described in detail in a TIDieR protocol (78), and summarized below.

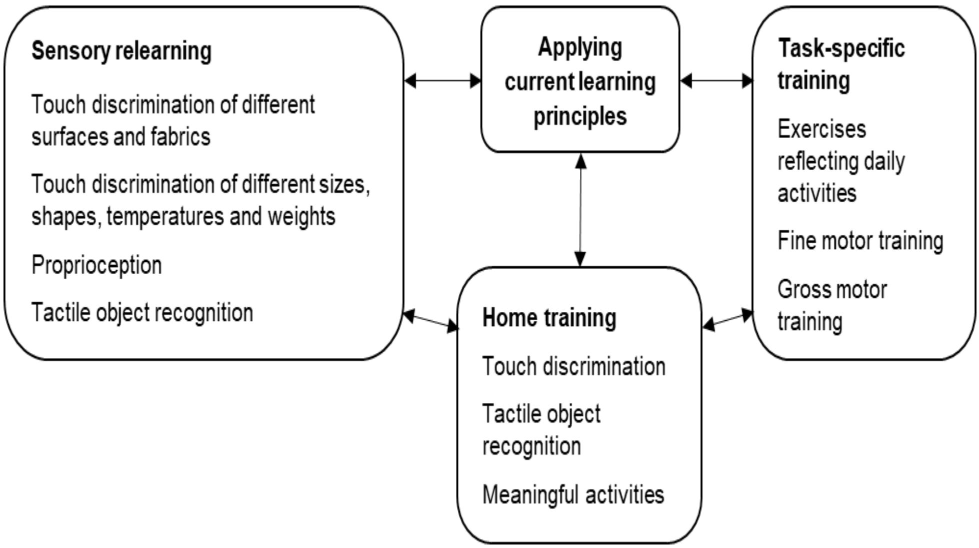

Figure 9. A description of the components in the SENSUPP study

Sensory relearning

The sensory relearning was influenced by Carey et al. (34), and by Rosén and Lundborg (65). It was based on active hand movements since active movements have been found to activate the sensory cortex more compared to passive movements (108). Sensory relearning includes the following components: touch discrimination, proprioception and tactile object recognition. Touch discrimination was trained by exploring different surfaces (Figure 10), different materials, weights and temperatures, identification of objects of different sizes and shapes.

Figure 10. Touch discrimination of different surfaces without vision (A), then calibration with the non-affected hand (B), finally calibration with vision (C).

The main principle during the sensory relearning was to start blind-folded (without vision), then feel the surface or object with the non-affected hand followed by feeling the surface or object with the affected hand and at the same time looking at the hand (Figure 10 and 11).

Proprioception was trained in two different ways. First, the therapist placed the participant's affected thumb in different positions and asked him/her to locate the thumb with the non-affected hand. Secondly, the therapist placed the participant's affected UL in different positions and asked the person to place the non-affected UL in the same position. Tactile object recognition was trained by trying to identify various everyday objects with the affected hand. If participants had difficulties to identify an object, they were encouraged to describe the different properties of the object regarding size, shape, material, and temperature (Figure 11).

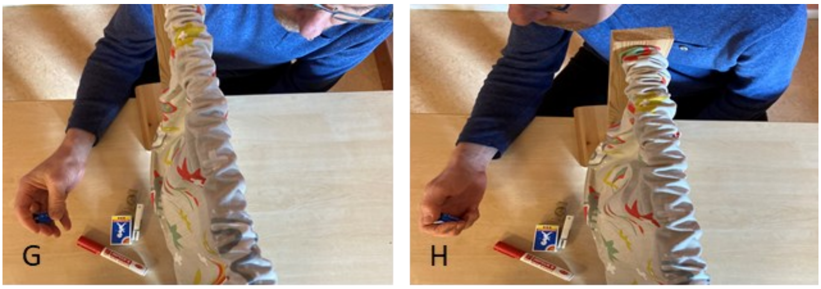

Figure 11. Tactile object recognition first without vision (G), then calibration with vision (H).

Task-specific training

The task-specific training included both gross and fine motor training in meaningful and functional tasks (56). The training consisted of various exercises such as 'whole reach-to-grasp task' or broken down to 'part of the whole task' depending on the participant's sensorimotor capacity (78). Examples of gross motor training were reaching and moving objects up and down shelves at different heights using various grasps depending on the object's weight, size and shape; and throwing a tennis ball to the floor or against a wall and catching it again with the affected hand. Examples of fine motor training were picking up coins, buttons, clips and nuts from cans or a flat surface, stacking wooden rods, shuffling, dealing and turning cards, moving coins and marbles from the palm to the fingertip, and manipulating two spheres in the hand.

Examples of tasks in daily activities were tying shoelaces, doing buttons, pulling up a zipper and using cutlery, assembling and disassembling various nuts and bolts, putting on and removing a bottle cap and jar lid, as well as pouring water into and out of a cup or bottle (Figure 12). During the exercises, the participants were encouraged to reflect on their sensory experiences.

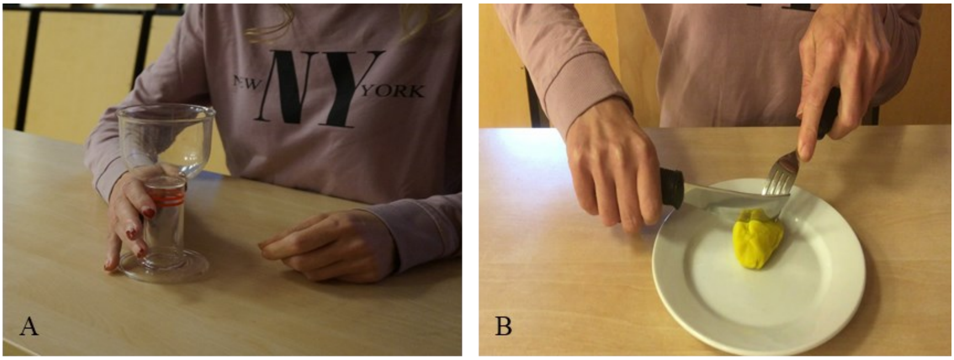

Figure 12. Illustrations of the task- specific training, (A) drinking from a glass, and (B) practicing the use of cutlery.

Home training

The participants were also encouraged to train daily at home for 30 minutes. They brought material home to practise either exercises focusing on touch discrimination or object recognition depending on their sensory and motor impairments. The participants were also encouraged to use the affected hand as much as possible during everyday activities and to focus on a meaningful task they perceived problematic and wanted to improve. They were also encouraged to reflect on their sensory experience when they used the affected hand in daily activities.

Learning principles

During the training current neurobiological learning principles were applied to promote neural plasticity and recovery (66). Key components in sensory relearning to promote learning and sensorimotor recovery were intensive and repetitive practice (105), variation in training tasks (67) with gradually increased degree of difficulty (55), and attentive exploration of a stimuli with focus on the sensory properties (109). Another important aspect was feedback by the physiotherapists provided intermittently both verbally and manually during the execution of a task.

Training for the control group

The task-specific training included the same type of exercises as the intervention group received but without any focus on the sensory component. The strength training consisted of exercises in a gym machine and using free weights with focusing on strengthening arm and shoulder muscles. Movement exercises included active arm movements and ball exercises such as throwing, catching and bouncing a ball. Stretching was performed as self-stretching for arm and shoulder muscles. The participants in the control group did not receive any instruction for home training but were encouraged to use their affected UL as much as possible in everyday activities.

Feasibility and experiences of sensory relearning (Study III and IV)

The feasibility of the SENSUPP protocol in study III was evaluated at the end of the 5-weeks training period. The participants answered a questionnaire about their experiences of the training both at the clinic and the home-training. In addition, the therapists' experiences how the intervention had been carried out and reports of any adverse events were also included in the feasibility evaluation.

In study IV, where participants' experience and perceived effects of sensory-relearning were explored, the 15 participants from study III were interviewed in connection with their 3-months follow-up. A physiotherapist not involved in the training (IL) conducted all the interviews according to a semi-structured interview guide. The interview guide covered questions about the participants' experiences of the sensory relearning at the outpatient clinic (such as tasks, intensity, duration, and support from the therapists), experiences of the home training and perceived benefits of the training. The interviews were audio-recorded, ranged between 24-51 minutes and were transcribed verbatim.

Data analyses

Qualitative analyses

An inductive qualitative content analysis approach was used both in study I and IV to describe the participants' experiences of sensory impairment in the upper limb (study I) and the participants' experiences of sensory relearning and perceived effects (study IV). An inductive approach is suitable when there are few earlier studies describing the phenomenon (110) and is characterised by a description close to the text derived in coded categories and in varying levels of interpretation (111). The analyses in both studies were performed according to Graneheim & Lundman (112), and consisted of several steps. The analyses started with reading all the interviews several times to gain a sense of the text in its entirety, and to identify meaning units derived from the text that answered the research questions. Next step was to condensate the meaning units without losing the core meaning of the text, and then the meaning units were labelled with preliminary codes. The codes were compared and based on their similarities and differences organized into subcategories and categories. In study IV an overall theme was also identified. Throughout the coding process all authors discussed and refined the findings.

Statistical analyses

In study II and III descriptive statistics were used for the participants' demographics and clinical characteristics as well as for appropriate variables, by calculating frequencies, means and standard deviations (±) or medians with minimum and maximum (min-max) values. All analyses were performed using IBM SPSS Statistics version 23 or 26 (IBM Corporation, Armonk, NY, USA).

In study II, the association between the dependent variable dexterity and the independent variables age, gender, social situation, vocational situation, affected hand, grip strength, spasticity, sensory function included both light touch and proprioception and discriminative touch, and pain were evaluated by linear regression models. First, a univariable regression analysis was applied to evaluate each independent variables association with dexterity. Secondly, a forward stepwise selection strategy was used adding the most significant variables one after the other in multivariable regression models. This procedure was continued until the P-values for the included independent variables were $P \leq 0.20$. In the final multivariable model only variables with a $P < 0.05$ were retained.

In study III, a non-parametric statistic approach was chosen since most of the data were on ordinal scale levels and not normally distributed. Mann-Whitney U-test was used to analyse between-group differences of changes between baseline and post-intervention (T1), between post-intervention and 3 month follow-up (T2) and between baseline and 3 month follow-up (T3). The Friedman test was used to analyse within-group differences between the different time-points (T1-T2, T2-T3 and T1-T3, respectively).

To determine at which time point significant changes had occurred post-hoc analysis with Wilcoxon signed rank test were performed. Adjustment for multiple tests was performed with the Bonferroni correction and the statistical significance was set at $P < 0.017$ ($0.05/3 \approx 0.017$). To calculate the effect sizes, rank biserial correlations were used with the formula $r = 1 - (2U) / (n1 * n2)$ for the Mann-Whitney U-test and for the Wilcoxon signed rank test we used the formula r = positive ranks/total ranks – negative ranks/total ranks. The effect sizes were interpreted as small ($r = 0.2$), medium ($r=0.5$) and large ($r=0.8$) effects according to Kerby et al (113).

Ethical considerations

All studies were approved by the Regional Ethical Review Board in Lund Sweden and had the following number: Dnr 2015/296 (study I), Dnr 2012/591 (study II) and Dnr 2017/8 (study III and IV). All studies were conducted in accordance with the Declaration of Helsinki. In addition, study III was registered on 8 November 2017 at the Clinical Trials.gov: NCT03336749.

All participants were informed that participation in the studies was voluntary and that they could withdraw participation at any time, which did not affect further contacts with the health care. Before inclusion all participants received detailed information about the studies, both verbally and written. Verbal and written informed consent were obtained from all the participants prior to inclusion in the studies.

In the qualitative studies (study I and IV) the persons provided experiences and information about themselves. The questions asked in the interviews were about how they experienced their altered sensory function in the UL after a stroke (study I), and how they experienced the sensory relearning approach and possible effects (study IV). The questions during the interviews were not considered to be of such a nature that they violated the privacy of individuals in an unpleasant or harmful manner. All data from the interviews were treated confidentially, and only the people involved in the project had access to the code key. The data was presented in such a way that no individual could be identified.

In study II and III outcome measures that are commonly used both clinically and in research after stroke were used. The assessment of these tests from an ethical perspective was that the nature of these outcome measures was considered to entail only a very small risk of discomfort. However, in study II, the participants performed several different tests, which may lead to an increased fatigue. They were therefore offered the opportunity to take a short rest between the tests.

In study III, the participants performed tests at three different time points that approximately took 2 hours to complete. The assessor continuously asked the participants if they needed to take a break and they were also offered light beverages. The participants in study III also performed a five-weeks intervention with training two days/week, 2,5 hours at each session. The training had a high intensity and required focus and concentration which contributed to varying degrees of increased fatigue. If necessary, the participants had the opportunity to take short breaks during the training. However, no participant had to interrupt the training due to fatigue.

Results

Experiences of sensory impairments of the upper limb

The participants in study I with an impaired sensory function in their upper limb described a wide range of impairments and disabilities, various coping strategies used and lack of sensory training. The qualitative analysis of the interviews resulted in five categories; (1) Changed and varied perception of the sensation, including three subcategories, (2) Affected movement control, including two subcategories, (3) Problems using the upper limb in daily life, including three subcategories, (4) Various strategies to cope with upper limb disability and (5) Lack of sensory training. The categories and subcategories are described in Table 5. A description of the main findings is presented below.

Table 5. An overview of the categories and subcategories in study I.

Categories	Subcategories
(1) Changed and varied perception of the sensation	Numbness and tingling Changes in temperature sensitivity Increased senstivity to touch and pain
(2) Affected movement control	Difficulty adjusting the grip force Proprioceptive and perceptual difficulties
(3) Problems using the upper limb in daily life	Personal care and dressing difficulties Difficulty with cooking and eating Difficulty performing leisure activities
(4) Various strategies to cope with the upper limb disability	
(5) Lack of sensory training	

Changed and varied perceptions of the sensation

Numbness and tingling in the hand and fingers were commonly reported by the participants. Other impairments described were a burning sensation, a feeling of heaviness and a feeling that the fingers were asleep. Many expressed that the affected hand was perceived as cold and that they had difficulty to determine how hot something was. Some also described unpleasant feelings of hypersensitivity when someone touched their affected UL or when they touched an object.

Affected movement control

The impaired sensory function in the UL also led to difficulties in performing movements and using the hand in various daily activities. The participants described for example difficulties when grasping objects, and when adjusting the grip force in relation to the object's properties.

> *I can't adjust it... portion that force... it becomes firm, don't drop it, hold it firmly*

In order not to risk dropping an object, many used more force and concentration when handling objects in their affected hand. Another aspect that affected movement control was that they had difficulty perceiving the position of the arm and hand which made it difficult to perform movements with timing and precision.

Problems using the upper limb in daily life

Participants also described difficulties in everyday life when performing personal care such as washing, cutting nails, brushing teeth and combing the hair because of their sensory impairments. Dressing difficulties were also described, for example tying shoelaces, pulling up zips and buttoning shirts.

> *I don't feel the buttonhole so [that] I can hold it with my left hand and take the button with my right, but I don't feel it*

Some household activities were also experienced as difficult, for example grasping and lifting objects, chopping or cutting food and eating with cutlery. Leisure activities such as gardening, playing the piano, boules and tennis and applying the brakes on a bicycle were other problems that participants mentioned. Another difficulty was driving a car, such as finding the safety belt or the gear stick without looking for it or managing the cruise control and indicators. Handling technical products such as remote controls, using a mobile phone, typing on a computer and taking pictures with a camera could also be difficult.

Various strategies to cope with the upper limb disability

To overcome and cope with the difficulties the participants used a variety of strategies. Many had to compensate with an increased concentration and use of vision when performing everyday activities. Others mentioned that they did not use the affected hand in activities, that they did not rely on the arm, especially in activities that require fine motor skills. Another compensatory strategy for being able to use the affected hand in everyday life was to adapt shoes, clothes and household utensils in different ways that facilitated the performance.

Lack of sensory training

Regarding rehabilitation, the participants said that specific sensory training for the affected UL was uncommon. A few participants described attempts to sensory training such as electrical stimulation, acupuncture and touch training. However, the purpose of the training was not very well communicated by the therapists, and therefore the participants were not fully aware if it was the sensory function they trained. Generally, the training for the UL was focused on gross and fine motor skills as well as strength training. Many had also received information to use the affected UL as much as possible in everyday activities.

Factors associated with dexterity

In Table 6, participants' clinical characteristics from study II are described.

Table 6. Clinical characteristics for the 75 participants in study II.

Dependent variable	
Dexterity† total score (0-12 points), mean (±SD)	5.4 (±3.3)
Independent variables	
Grip strength** (Newton, N), mean (±SD)	198 (±110)
Spasticity± of upper limb, (present), n (%)	23 (31)
Light touch and proprioception‡, mean (±SD), median (min-max)	7.0 (±1.7), 8 (1-8)
Active discriminative touch*, mean (±SD), median (min-max)	3.8 (±2.2), 5 (0-6)
Pain in upper limb (present), n (%)	32 (43)
Abbreviations: †mini Sollerman Hand Function Test, **Grippit dynamometer, ± Modified Ashworth Scale, ‡ Fugl-Meyer Assessment Upper Extremity sensory section, *Shape-Texture Identification test™	

Dexterity was the dependent variable and age, gender, affected hand, social situation, vocational situation (see Table 2), as well as grip strength, spasticity, sensory function, and pain were the independent variables.

In the univariable linear regression analyses, the strongest associated variable with dexterity was active discriminative touch explaining 46% ($p<0.001$) of the variance. The regression coefficient (β) of active discriminative touch showed that a one point increase in the STI™-test will give an improvement of 1.03 points in dexterity (mSHFT). Light touch and proprioception was also included as independent variable of sensory function and explained 15% of the variance ($p<0.001$). Spasticity, grip strength and age also fulfilled the criteria of being included in the multivariate model building ($p\leq0.2$) However, light touch and proprioception and age were not retained in the final multivariate model.

Thus, active discriminative touch ($p<0.001$), spasticity ($p<0.001$) and grip strength ($p<0.024$) were included in the final multivariate model and together they explained 57% of the variance, Table 7. The β for active discriminative touch changed from

1.03 to 0.86 in the multivariate model and the corresponding change for spasticity was 3.33 to 1.9 and for grip strength 0.12 to 0.06.

Table 7. Variables associated with dexterity† in the final multivariable linear regression model for the 75 participants with stroke.

Independent variables	β-values (95% CI)	P-value
Active discriminative touch*	0.86 (0.62-1.10)	<0.001
Spasticity of upper limb± (not present vs present [ref])	1.90 (0.75-3.04)	<0.001
Grip strength** (newton, per 10 units increase)	0.06 (0.00-0.10)	0.024
Explained variance††	46 % (active discriminative touch) 55% (+spasticity) 57% (+grip strength)	
Abbreviations: †mini Sollerman Hand Function Test, *Shape-Texture Identification test™, ± Modified Ashworth Scale, **Grippit dynamometer, †† Cumulative explained variance after succesive addition of variables to the final multivariabel model. Ref = reference group indicate the category to which the other category is compared.		

Sensory relearning

Baseline characteristics in study III for both the intervention group and the control group are presented in Table 8. At baseline, there was a significant difference in discriminative touch (STI™) in favor for the control group (p=0.04).

Table 8. Baseline clinical characteristics for the intervention group and the control group.

	Intervention group	Control group
Variables	**Median (min-max)**	**Median (min-max)**
SWM (0-25 p)	13 (2-21)	17 (0-22)
STI™ (0-6 p)	0 (0-4)	2.5 (0-5)
FMA-UE sensory (0-8 p)	5 (2-8)	6.5 (0-8)
BBT (number of blocks/min)	28 (1-48)	28.5 (10-63)
mSHFT (0-12 p)	3 (0-10)	3.5 (0-11)
MAL AOU (0-5 p)	2.1 (0.8-4.5)	2 (0.5-4.9)
MAL QOM (0-5 p)	1.7 (0.6-4.3)	1.8 (0.5-4.4)
COPM P (0-10 p)	3.5 (1-7)	3.6 (1-6.7)
COPM S (0-10 p)	3.2 (1-10)	3.25 (1-7.5)
SIS (0-100 %)	44 (21-75)	45.5 (12-100)
Abbreviations: SWM=Semmes-Weinstein monofilament, STI™=Shape-Texture Identification test, FMA-UE=Fugl-Meyer Assessment-Upper Extremity sensory section, BBT=Box and Block Test, mSHFT=mini Sollerman Handfunction Test, MAL AOU=Motor Activity Log Amount Of Use, MAL QOM=Motor Activity Log Quality Of Movement, COPM P=Canadian Occupational Performance Measure Performance, COPM S=Canadian Occupational Performance Measure Satisfaction, SIS=Stroke Impact Scale perceived participation		

Effects of the training

Between-group differences

Regarding the primary outcome there was a significant difference in changes in touch detection in favour of the intervention group from pre-intervention (T1) to post-intervention (T2), (median difference 4 points; P=0.007, r=0.61), but no significant difference in changes between the groups at 3 months follow-up. In the other primary outcomes, such as touch discrimination (STI^{TM}) and light touch and proprioception (FMA-UE sensory section) there were no significant differences in changes between the groups at any time point (Table 9). Regarding differences in changes in the secondary outcomes between the groups there were no significant differences at any time point.

Table 9. Between-group differences in changes (T1-T2, T2-T3, T1-T3) of the primary outcomes.

Primary outcomes		**SWM (0-25p)**	**STI (0-6p)**	**FMA-UE (0-8p)**
Time point				
T1-T2	IG (Md diff)	6.0	0	1.0
	CG (Md diff)	-2.0	-1.5	0
	P-value	**0.007***	0.116	0.126
	Effect size#	0.61	0.30	0.32
T2-T3	IG (Md diff)	-2.0	0	0
	CG (Md diff)	-1.5	-0.5	-1.0
	P-value	0.230	0.580	0.898
	Effect size#	0.27	0.11	0.03
T1-T3	IG (Md diff)	4.0	0	1.0
	CG (Md diff)	-3.5	-2.0	-1.0
	P-value	0.06	0.345	0.149
	Effect size#	0.42	0.19	0.31

Abbreviations: Md diff= Median differences, IG= Intervention Group, CG= Control Group, SWM= Semmes-Weinstein-Monofilament, STI= Shape-Texture-Identifcation test, FMA-UE= Fugl-Meyer Assessment Upper Extremity sensory section. *Significant differences are indicated in bold. #Effect size according to rank biserial correlation.

Within-group differences

For the primary outcome, the intervention group showed a significant improvement in touch detection (SWM) from pre-intervention (T1) to post-intervention (T2), change in median was 13 to 19 points (P= 0.008, r= 0.80) (Figure 13). There were no significant changes within the intervention group or within the control group for any of the other primary outcomes.

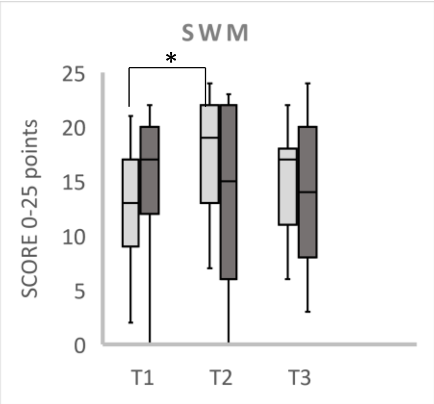

Figure 13. Box-plots with medians and min/max values for the intervention group (IG, light grey) and the control group (CG, dark grey) in the primary outcome Semmes Weinstein Monofilament (SWM) before (T1), post-intervention (T2), and at 3-month follow-up (T3). * significant difference after correction for multiple comparison p<0.017.

For the secondary outcomes the intervention group showed significant improvements in the ability to perform daily activities (assessed by the Motor Activity Log). The amount of use changed in median from 2.1 to 2.6 points (P=0.001, r=0.96) and quality of movement changed in median 1.7 to 2.0 points (P=0.004, r=0.85) from pre-intervention (T1) to post-intervention (T2). There was also a significant improvement in how satisfied the participants were with the performance in self-selected daily activities (assessed by the COPM S) from pre-intervention (T1) to the 3 months follow-up (T3); the median changed from 3.2 to 5.7 points (P=0.004, r=0.94) (Figure 14).

The control group showed a significant improvement in self-perceived performance in daily activities (assessed by the COPM P) from pre-intervention (T1) to post-intervention (T2), the median changed from 3.6 to 4.6 points (P=0.017, r=0.86), (Figure 14).

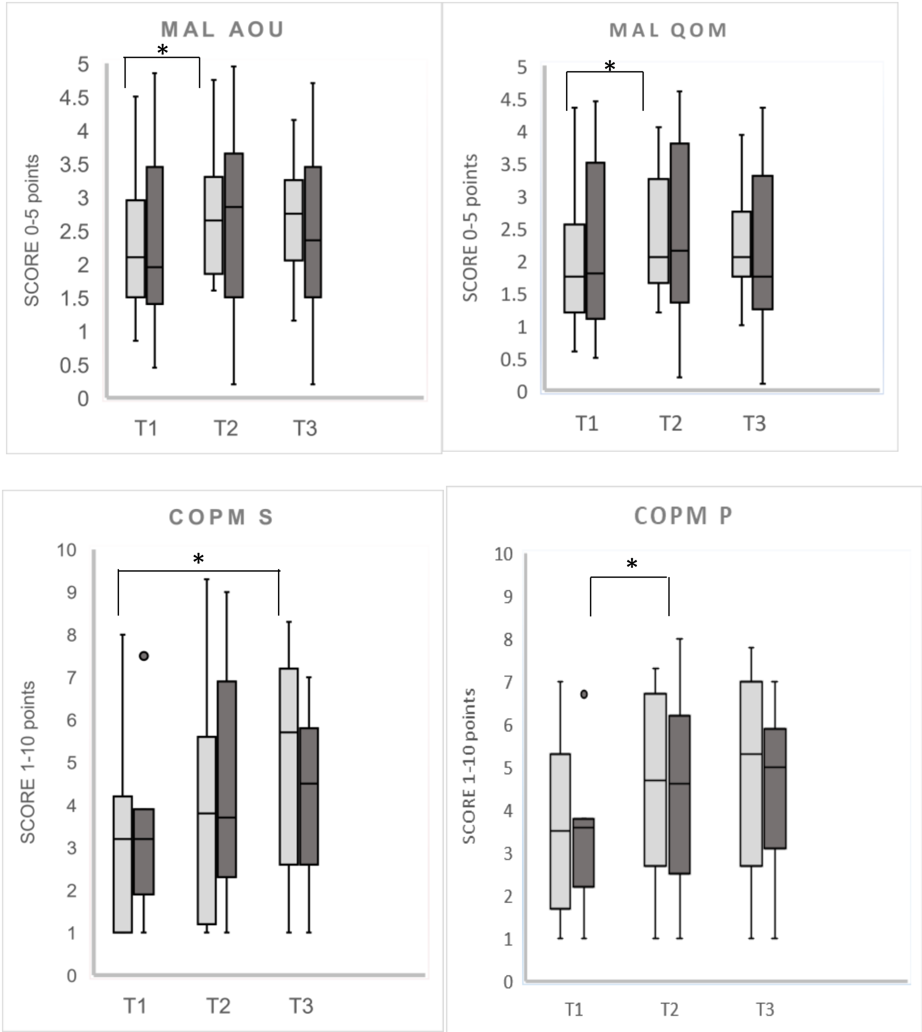

Figure 14. Box-plots with medians and min/max values for the intervention group (IG, light grey), and the control group (CG, dark grey) in the secondary outcomes. Motor Activity Log Amount of use (MAL AOU), Motor Activity Log Quality of movement (MAL QOM), Canadian Occupational Performance Measure Satisfaction (COPM S) and Canadian Occupational Performance Measure Participation (COPM P) before (T1), post-intervention (T2), and at 3-month follow-up (T3). Outliers are denoted with (●). * Significant difference after correction for multiple comparisons p= 0.017.

Feasibility and experiences of the training

Regarding the feasibility of the SENSUPP protocol (study III), the participants in the intervention group who completed the 5-weeks protocol were positive and appreciated the training. They all completed 10 training sessions according to the protocol and the duration and length of the training sessions were well tolerated, even though the training was perceived strenuous, intensive, and required a high degree of concentration. The sensory relearning was performed without any adverse events. The participants appreciated the group training and felt that they received good support from the therapist. They had become more aware of their ability in how to use their affected hand and had learned to use the hand at home in various activities. The therapists' experiences were that participants were highly motivated and positive to the training.

When analysing the participants' more in-depth experiences of the training (study IV) one overall theme emerged 'Sensory relearning was meaningful and led to improved ability to perform daily hand activities'. Two categories were also found (1) 'The outpatient training was inspiring but strenuous, while the home training was a struggle' including three subcategories and (2) 'Overall small effects on sensory function but improved ability to use the hand' including three categories. The theme, categories and subcategories are described in Figure 1. A description of the main findings is presented below.

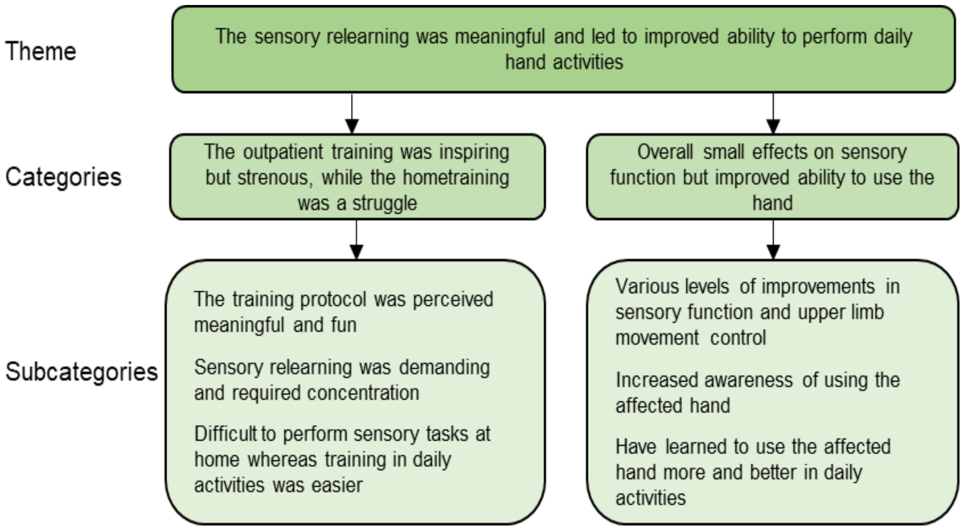

Figure 15. An overview of the overall theme, categories and subcategories.

Experiences of the sensory relearning

The sensory relearning was appreciated by many of the participants. They thought it to be inspiring and stimulating to come to the outpatient clinic to exercise. One aspect that contributed to the appreciation of the training was the feedback and support which they received from the therapist during the training. Many found it also positive to train with another person, and to meet a person in a similar situation gave them the opportunity to exchange thoughts and experiences.

> *...I thought it was fun, it was fun to come here these days and then [do] the same at home. You feel like you have to keep it up… It was stimulating for the entire psyche and everything, it was…*

Most participants thought that training twice a week for five weeks was appropriate, even if some expressed a desire for a longer training period. Overall they thought that the training was well-structured and adapted to their difficulties and that there was a progression in difficulty as they made improvements.

> *Some exercises were more difficult than others and the level of difficulty gradually increased. As I managed the exercise a bit better, they increased it, so it was always at a level… challenging enough to try to feel what kind of object it was.*

The participants described that to concentrate and to focus were important during the training. For some, this led to increased fatigue, and some had to take short breaks during the training. A common strategy among the participants were to rest when they got home after the training.

Many experienced difficulties in identifying materials and objects without the help of vision, and they became aware of the importance of being able to manipulate the object properly in order to be able to feel something. This caused frustration for some participants especially when they noticed how easily they could feel an object with the unaffected hand.

> *...I got to have different objects in my hand without seeing what it was and had to try to identify what it was. It's really difficult when you can't manipulate the objects around in your hand and feel it.*

Completing the home training was difficult for several participants. Without a written training program, it was difficult to perform the training. They also reported a lack of time, motivation and feedback. However, many expressed that they tried to use their affected hand in daily activities at home.

Perceived effects of the sensory relearning

Most participants felt that their sensory function was unchanged after sensory relearning, even though some perceived that they could more easily identify larger objects. Many expressed however an improved movement control. They described improved timing in gross motor function and improved ability to adjust the grip force in the affected hand. This meant that they could better use their affected hand in daily activities such as opening and closing a door and handle cutlery.

> *Now, when I'm at a restaurant cutting and such, I don't need to think that much about how I'm cutting. But at first [before the sensory training], I just ripped it [the piece of meat] apart. ...So, something about the training has made me feel like I have better control of how hard to grasp things…*

For many participants the sensory relearning had led to an increased awareness of how they could use the affected hand in various daily activities. However, they still needed to concentrate on the task and many also expressed that they compensated with vision to be able to perform everyday activities with the affected hand. Some expressed that they consciously used their affected hand more in daily activities but that they had to remind themselves to do so, it was not on an automatic level.

Several mentioned that they had learned to use their affected hand more in meaningful daily activities. They also expressed an improved ability to use the UL in personal care, for example when washing and combing the hair, in household activities when emptying the dishwasher, vacuuming, making the bed, and hanging laundry, and at meals when cutting food, using cutlery and drinking from glasses.

> *...I get things out from the dishwasher, have started combing my hair [with the affected hand], I'm vacuuming with both my hands… I've started eating with cutlery in both hands… this thought hadn't even struck me before, even trying these things.*

Discussion

The overall aim of this thesis was to increase knowledge about the consequences of sensory impairments of the upper limb after stroke, and to evaluate the effects of a novel training approach.

Various research methodologies and theoretical frameworks, such as the ICF and the theory of sensorimotor control were used in this thesis to address the research questions in the papers.

The results showed that an impaired sensory function in the UL limb after stroke had a great impact on personal tasks and on everyday activities and leisure activities. Despite this, specific training to improve sensory function was lacking and had not been a part of the participants´ rehabilitation. Sensory function in terms of discriminative touch was a major contributing factor to dexterity. After sensory relearning in combination with task-specific training a significant between-group difference in touch detection in favour of the intervention group was found, but not in any other outcomes. Within the intervention group, a significant improvement was found regarding the use of the hand in daily activities and in movement quality after the training. Within the control group, a significant improvement in performance of using the hand in daily activities was found after the training. The participants tolerated the training well, and it was performed without any adverse events. Those who were randomized to the intervention group appreciated the training in the SENSUPP protocol and thought that it was meaningful but strenuous. They appreciated feedback from the therapist and to train in groups. Small improvements on sensory function was reported but an increased movement control and improved ability to use the affected hand in daily activities.

Below are the findings from each study discussed in more detail.

Experiences of sensory impairments of the upper limb

In study I, the participants with sensory impairments in the UL described a variety of consequences according to the ICF-model, i.e., impairments, activity limitations, participation restrictions but also aspects related to personal and environmental factors. They perceived a changed sensation in the hand such as numbness, tingling and difficulties in temperature senses such as cold sensitivity, but also a perception of a rigid and clumsy arm. These experiences are in agreement with other studies where the participants reported strange sensations of heaviness and coldness (43) (45) which affected their performance in daily activities (114). Another aspect that our participants mentioned was an increased sensitivity when touching objects or being touched by someone else which could be uncomfortable. This is in line with another study describing that an impaired touch limited the person's intimate relationships (115). All these aspects are important to consider in the management of persons with stroke as an impaired sensory function can affect the person's body image and also the relationship with other people.

Regarding activity limitations our participants perceived difficulties in controlling the arm and adjusting the grip force when performing daily activities. These difficulties caused problems to carry out many activities, for example in the household, personal care, and leisure activities. Other studies have reported similar problems in household activities and hobbies, as well as personal tasks and leisure activities (43), among people with impaired sensory function (43), or a more general disability in the arm after stroke (116). Not being able to perform personal tasks and maintain meaningful leisure activities can have a negative impact on independency and well-being contributing to a less active social participation and a reduced quality of life (117).

Furthermore, our participants related that when they tried to use their affected hand in various activities, especially in those that required dexterity, they had to increase their concentration. This effort was described as tiring and may be a contributing factor to post-stroke fatigue. Our findings are consistent with other studies, where participants have described how exhausting it was when they had to focus and concentrate on every movement during reaching and grasping, and when they have lost their automatically movements (118). This indicates that there is a potential risk that persons with sensory impairments of the UL after stroke (41, 44) will not use their affected hand in activities to the extent they could, which may contribute to a 'learned non-use' behaviour (50). This emphasizes the importance to encourage persons with sensory impairments of the UL as early as possible after stroke to use their affected hand in everyday activities in order to improve recovery and to prevent decline in functioning.

Another important problem that our participants described was the difficulty to use various technical products in daily life because of their UL sensory impairment, for example handling the remote controls, touch screens and mobile phones. To be able to perform such activities is crucial for participation in many parts of contemporary life such as managing personal banking and maintaining contact with friends via social media. This underscores the need to develop technical products that are suitable for people with UL disabilities.

To facilitate the performance of various activities different strategies to handle the difficulties were described. One strategy to compensate for the impaired sensory function was to use vision when performing activities more constantly. However, there may be conditions when this is difficult for example in reduced lightning and to identify objects in a pocket. Other strategies were to make practical adaptations to clothes and household utensils, and to compensate with the unaffected hand in daily activities. One possible risk to focus too much on compensatory strategies might be that the person will miss potential improvements in the affected hand. In the study by Doyle et al (43) the participants expressed that the rehabilitation for the UL was focused on compensatory strategies rather than on sensory impairments. Similar experiences were noticed among our participants with limited focus on sensory training. This implies that both sensory assessment and sensory training needs an enhanced attention in the rehabilitation of the UL after stroke.

Factors associated with dexterity

The findings in study II showed that sensory function in terms of active discriminative touch had the strongest univariable association with dexterity. Active discriminative touch explained 46% of the variance compared to when sensory function was measured in a passive way (by light touch and proprioception) which explained 15% of the variance in dexterity. One possible explanation to the difference between the two sensory tests (STI™ and FMA-UE sensory section) may be that an active sensory test can better detect difficulties in fine motor skills compared to a passive sensory test (82). In other studies where the sensory function was measured in a passive way, sensory function contributed only to a small extent to the variance in dexterity. Furthermore, the dexterity (dependent variable) was measured with mSHFT, which is a reliable test after stroke (94) including three tasks that involves both sensory and motor function of the hand (119). Other studies have most often used BBT and NHPT (120, 121) to assess dexterity. Our findings suggests that persons with a better active discriminative touch have in general a better ability to perform dexterity tasks and that sensory impairments can have different impact on motor function depending on the task that should be performed. Thus, a thorough assessment of sensorimotor function of the hand should include a measure of active touch discrimination.

In the final multivariable regression model, active discriminative touch was included and explained 46% of the variance. Together with spasticity that added 9%, and grip strength that added another 2% to the explained variance, the final model explained 57% of the variance in dexterity. This indicates that those without spasticity and better grip strength performed better in the dexterity test. It is well-known that spasticity may impede motor and activity performance (122). About one-third of the participants (31%) in study II had spasticity, which is in line with another study showing that 28% of persons with hemiparesis had spasticity at 3 months (122). Thus, it is important to assess the level of spasticity appropriately and to initiate treatment for those where spasticity affects the motor function and performance in daily activities.

Regarding grip strength, another study has shown that it explained 54% of the variance in dexterity with BBT as the dependent variable, and 36% of the variance in dexterity with NHPT as the dependent variable (120). Moreover, in another study pinch force explained 22% of variance in the BBT (121). A possible explanation for the difference in the grip strength's association to dexterity may be that dexterity was measured with mSHFT in our study. The tasks in the mSHFT reflects daily activities where fine manual dexterity is used while BBT may be associated with more gross manual dexterity.

Taken together, the findings in study II showed that sensory function in terms of active touch discrimination was highly associated with dexterity and has contributed to the knowledge of the close relation between the sensory and motor function of the hand. Thus, this factor is important to consider in UL rehabilitation after stroke, both to assess and when planning appropriate interventions to improve dexterity and UL functioning.

Sensory relearning

Effects of the training

In study III, sensory function in terms of touch thresholds, touch discrimination and proprioception was the primary outcome. There was a significant difference in touch thresholds between the groups after the training, in favour of the sensory relearning group, but not in touch discrimination or proprioception. Previous studies have shown a significant effect of sensory training on touch discrimination (34), as well as on proprioception and tactile object recognition (109). In the interviews (study IV) our participants also reported small effects on the sensory function after the training. A possible reason for the result might be that several of the participants in the intervention group had severe sensory impairments in terms of touch discrimination. Previous studies show somewhat conflicting results; one study reported that those with mild to moderate sensory impairments improve to a greater extent than those with severe sensory impairment (123), while Turville et al reported improvements in touch discrimination after sensory training for those with severe sensory impairments (124). It is not entirely clear how the severity of sensory impairment influences the outcome of active sensory training and therefore further studies are needed.

Furthermore, the results in study III regarding the secondary outcomes showed no significant differences between the groups in motor function, the ability to use the affected hand in daily activities and perceived participation. There was also no difference in motor function within the groups after the training, even though the 5-weeks training contained a lot of motor practice training. One explanation to the result could be that persons with mild to moderate sensory impairments seem to improve their motor function more than those with severe sensory impairments, which is in line with our study (125). On the other hand, in study IV our participants who participated in the intervention group (sensory relearning group) perceived a better movement control and better control of the grip force. This may be due to an optimization of the performance of the task without any improvement of the underlying neurological impairments since there was no difference in objective outcome measures in motor function.

In study IV, many participants expressed that they had become more aware of their ability to use the affected hand and that they had learned what they could do with the hand in various daily activities. In study III, the same participants in the sensory relearning group significantly improved their ability to use the affected UL in daily activities (medium to large effect sizes, r= 0.72-0.96) and they were more satisfied with the performance and movement quality as measured with the self-reported outcome measures COPM and MAL. Also the control group made some improvements in their ability to use their affected hand in daily activities. The results indicate that a high focus on the affected UL in the training is beneficial and that encouragement to try to use the affected hand may lead to overcoming the learned non-use phenomenon . Previous studies have also shown improvement in the use of the affected hand in daily activities after sensory training (126) or combined sensory and motor training (74, 127). These findings indicated that there is a possibility for improvements even in the chronic phase after stroke. This also showed the importance of focusing on the affected UL in the rehabilitation after stroke.

Feasibility and experiences of the training

The participants in the intervention group (i.e., the sensory relearning group) in study III appreciated and were positive to the training. Also, the interviews in study IV revealed that the participants thought that the training was meaningful and well-adapted to their difficulties. In the rehabilitation it is important to analyse the person's difficulties and to modify the activities in accordance with the participant's goal and capacity (128), which enables the person to succeed when performing the activity. To feel that the training is meaningful, clearly related to everyday activities (129, 130) and that there is an opportunity to complete the task is related to the level of motivation, which is an important factor in sensorimotor learning. To increase the motivation among the participants in study III, COPM was used as an outcome measure where the participants identified meaningful activities that they wanted to improve. This test is considered a valuable tool in person-centered rehabilitation.

The participants in study III and study IV described the training in the SENSUPP protocol to be demanding and strenuous and that the task required a lot of concentration. This led to transient fatigue and by taking short breaks during the training everyone managed to complete the training according to the protocol. A common strategy that they used were to take a rest when they returned home after the training. Our findings that the participants manage to perform intensive training despite experiencing fatigue are in line with other studies (131, 132). However, to achieve a sufficient level of intensity in the training with regard to the person's needs and capacity is important to consider in the rehabilitation of the UL after stroke to increase the motivation.

Another important factor in UL rehabilitation and to promote learning is to give sufficient feedback. Feedback should be given on the performance of the task and when the task becomes more difficult (128). The participants in study IV described that it was important to get feedback from the therapist about the performance during the training. Similar findings are reported in other studies showing that feedback and encouragement from the therapist can enhance motivation and adherence to the rehabilitation (133, 134) as well as a sense of good performance (135). A positive relationship between the professional and the participant is therefore emphasized as an important factor in rehabilitation (132, 136).

An aspect that probably contributed to that the participants experienced the training as positive was the training in groups. To support and learn from each other and to have contact with a person in a similar situation was perceived important and contributed to the appreciation of the training. The gains of training in groups have been described previously (135, 137). It is reported that observing others that take part in comparable task practice is positive (133), and that group training enhance motivation (138). However, even in a group setting, it is important to meet the person's own goals and expectations. These aspects are essential to consider in the planning and implementation of sensory relearning of the UL after stroke.

A challenging part of the SENSUPP protocol was the home-training. Participants reported that the home exercises focusing on improving sensory function did not feel so meaningful, and the exercises were hard to perform without support from the therapist. Instead they focused on using the affected hand as much as possible in everyday activities. They said that a written training program would facilitate the home-training. Other studies have also reported difficulties for participants to perform the home training (75) and to motivate themselves to do the exercises (139). These findings emphasize that activities at home should focus on meaningful tasks used in everyday life based on the participant’s own goals, with continuous support from professionals. To increase adherence and motivation to home training is important and a way to increase the training dose and time spent in meaningful activities (140). More studies should therefore focus on developing meaningful training for the UL in the home environment. A possible way may be to use new technical products for training and support.

When and how should sensory relearning be provided for best possible outcome?

In study III, participants were included in the chronic stage after stroke so that the spontaneous neurological recovery would not affect the result. There are some evidence that the training should start earlier after stroke with the idea to support the spontaneous neurological recovery in the early time window (141, 142). However, the optimal timing to start rehabilitation after stroke is currently unknown (48). In one study at least 6 weeks post-stroke the participants improved in touch discrimination and proprioception after sensory relearning (34). In another study the participants were included within 8 weeks and no significant changes were found in somatosensory measures (125). De Diego et al reported improvements in touch discrimination and proprioception for participants in the chronic phase after stroke (127). Similar results were reported in studies were they combined sensory and motor training with an improvement in the chronic phase but not in the subacute phase with same intervention, however there were differences in severity of motor impairment (77) which could explain the result.

This thesis has shown that the SENSUPP protocol was well tolerated regarding dose, frequency and duration. The total amount of training in study III with 25 hours was based on previous studies (34, 127), comprising 16-20 hours of training. A difference was that we chose to have longer training sessions (2.5 hours vs 1 hour) compared to other studies (74, 125, 127), in order to gain a high intensity with repetitive practice during the training since this are important for learning after stroke. On the other hand, we had fewer training sessions per week, 2 times/week compared to 3-4 times/week as is described in other studies (34, 109). There are some evidence that increased time in therapy leads to larger improvements in motor function after stroke (143-145), but not necessarily in activity measures. Regarding combined sensory and motor training it has been suggested that the training should be at least 30 hours in total (77). However, currently there is limited knowledge about the optimal training protocol regarding frequency and duration of exercises in a sensory relearning approach to promote improvement on sensorimotor function and ability to use the affected hand in daily life.

Furthermore, the SENSUPP protocol was focused on touch discrimination, proprioception and tactile object recognition in combination with task-specific training with the hypothesis that an active training may activate both the sensory and motor areas in the brain. The participants were encouraged to reflect on the objects' sensory characteristics during the training and a challenge was to include tasks that challenged both the sensory and motor function, for example regulate the grip force. The ambition was to start the training based on the participant's sensory level and with gradual progression. A challenge was to increase the difficulty of the proprioception training, as it is not entirely clear how this should be done. An alternative might be to use robot-based proprioceptive training which can deliver high-intensity training with continual assessment of changes in performance (146).

However in the clinical setting there is often limited access to more advanced equipment.

Methodological considerations

Strengths

In study II and III several standardized, reliable and valid outcome measures were used covering various domains in the ICF to assess functioning and disabilities of the UL after stroke. In both studies one therapist conducted the assessments either on one test occasion (study II) or on several test occasions (study III). The assessments in both studies were in accordance with a standardized test procedure. Also, in study III all assessments were performed by a blinded assessor not involved in the training. In study II, 75 participants were included which was considered sufficient to be able to examine the association between dexterity and the independent variables. All participants in study III completed the 5-week intervention according to the SENSUPP protocol without any adverse advents and participated in the 3-months follow-ups.

In the two qualitative studies (study I and IV) an inductive content analysis was used according to Graneheim and Lundman (112). The purpose with this analysis approach was to obtain a deeper understanding of the persons' experiences of sensory impairments in the UL after stroke (study I) and to explore experiences of a new novel training approach (study IV). In qualitative research trustworthiness should be considered in terms of credibility, dependability, confirmability and transferability (111). Efforts were made to strengthen trustworthiness in study I and IV. The participants were interviewed individually, and semi-structured interview guides were used. In study I, the author of this thesis (HC) conducted all interviews. Since the author (HC) supervised the training in study III an independent co-author (IL) not involved in the training conducted the interviews in study IV, which we believe made it easier for the participants to talk more open-minded about their experiences.

Another strength in study I was that the participants differed regarding, age, gender, time since stroke, hand dominance and level of sensory impairment in their affected UL. Fifteen participants were included, and the number of participants was considered appropriate to obtain sufficient information based on our research questions. In study IV it was not possible to have a purposive selection of the participants as they participated in the intervention group in study III. However, when analysing their characteristics we found that there was a spread in terms of age, gender, time since stroke, type of stroke, side of paresis and hand dominance among the participants. Another strength was that all authors continuously discussed the subcategories and categories during the analysis process until consensus was reached about the interpretation of the results and quotations that illuminated the findings were presented. Also, in study IV the authors had different professions and pre-understanding of the patient group and sensory relearning which enriched the interpretation of the results.

Transferability refers to the extent whether the findings can be applied to other groups or settings. Since the participants both in study I and IV were in a chronic phase post-stroke the findings cannot be generalized to persons in the early phase after stroke, but maybe to other persons with neurological conditions and mild to moderate UL sensorimotor impairments.

Limitations

There are also some limitations in the studies of this thesis. In all four studies the participants were slightly younger compared to the whole stroke population. Also, more men than women participated in the studies, but it is consistent with the fact that more men than women experience stroke. In study I, III and IV the participants were in the chronic phase after stroke and in study II in the subacute to chronic phase after stroke. People older than 80 years, with cognitive impairments or difficulties to communicate were excluded. This makes it difficult to generalize the results to the entire stroke population and for those in an early phase post-stroke.

In Study I, some interviews were quite short due to the participants' difficulties in providing comprehensive answers. However, the material was judged sufficient and did not affect the overall analysis.

In study II, the cross-sectional design limits the ability to establish causality between the included variables in the univariable and multivariable regression models. There might also be other important variables not included in our multivariable analysis such as neglect, vision impairments and fatigue which may be relevant for dexterity.

The intention in study III was to recruit 30 participants. However, since there were difficulties in the recruitment rate, because of the COVID-19 pandemic and limited time frame to finish the thesis, the inclusion was ended after 27 participants. We believe that the sample size is sufficient for a pilot RCT.

The participants in study IV were interviewed in connection with the three-month follow-up, and some of the participants may have had some difficulties in recalling their experiences of the training protocol.

Conclusions

- Persons with sensory impairment of the UL after stroke experienced a changed and varied perception of the sensation leading to a highly negative impact on many daily activities. They also expressed a lack of specific sensory rehabilitation for the UL.
- Sensory function in terms of active touch discrimination was a major contributing factor to dexterity in persons with mild to moderate stroke, whereas spasticity and grip strength were of lesser importance.
- In the pilot RCT the differences in outcomes between the intervention group (sensory relearning group) and the control group were discrete. There were significant improvements in more outcome measures within the intervention group than the control group, regarding both sensory function and the ability to use the hand in daily activities. Thus, combined sensory relearning and task-specific training may be a promising and feasible intervention to improve UL sensorimotor function after chronic stroke.
- The SENSUPP protocol was experienced as a strenuous but inspiring and meaningful. It was well tolerated by the participants without any adverse events. Individualized structured training combined with guidance and feedback from a therapist and to train in groups were appreciated. The home training was challenging due to lack of support, time, and motivation. Small improvements in sensory function were perceived, whereas increased movement control and ability to perform daily hand activities were reported.

Clinical implications

- The clinical management of sensory impairment of the UL after stroke requires more attention.
- In the rehabilitation of UL after stroke there is a need to identify and assess the extent of sensory impairments and their impact on movement control and to perform everyday activities.
- Sensory function in term of active discriminative touch of the hand is an important factor for dexterity and should be thoroughly assessed in rehabilitation of the UL after stroke.
- The assessment of the sensory function in the UL should include both active and passive sensory tests.
- When evaluating the effect of sensory relearning it is important to use psychometrically sound outcome measures including various domains of ICF.
- The SENSUPP protocol is well tolerated and could be used as outpatient training for persons with UL sensorimotor impairments after stroke.
- The home training in the SENSUPP protocol needs to be further developed including sensory training in meaningful daily activities, with regular follow-ups and an exercise diary to register the training.
- Important factors to consider in sensory relearning are individualized training, gradual increased in difficulty, guidance and feedback from the therapist and to train in small groups.

Future research

- Further research should focus on giving recommendations of appropriate outcome measures to assess sensory function/sensorimotor function of UL after stroke.
- Future studies are warranted to find the optimal time to start the training, to find the optimal dose, frequency and duration to promote learning and recovery of the sensorimotor function in the UL after stroke.
- Longitudinal studies are warranted to investigate how other potential factors influence dexterity in persons with mild to moderate impairment of UL after stroke.
- If an impaired sensory function in the hand contributes to a reduced hand function, it is important to both assess and integrate the sensory component in the motor training. There is a need to find optimal sensorimotor tasks which places demands on both the sensory and motor components.
- There are reasons to believe that persons with mild to moderate sensory impairments of UL can conduct sensory relearning compared to those with more severe sensory impairment. However, future studies should identify persons with an impaired sensory function in the UL after stroke who will benefit most from a combined sensorimotor approach.
- There is a need for future studies to develop the home training and to include new technology such as smartphone apps and internet-based wearable systems to provide feedback, education, treatment and regular follow-ups.

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