Combined somatosensory and motor training to improve upper limb recovery after stroke

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STATEMENT OF ORIGINALITY

I hereby certify that the work embodied in the thesis is my own work, conducted under normal supervision.

The thesis contains no material which has been accepted, or is being examined, for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made. I give consent to the final version of my thesis being made available worldwide when deposited in the University's Digital Repository, subject to the provisions of the Copyright Act 1968 and any approved embargo.

Signed:

Name: Urvashy Gopaul

Date: 31st December 2018

ACKNOWLEDGMENT OF AUTHORSHIP

I hereby certify that the work embodied in this thesis contains published papers/scholarly work of which I am a joint author. I have included as part of the thesis a written declaration endorsed in writing by my supervisor, attesting to my contribution to the joint publications/scholarly work.

Chapters 1 and 2 were written with editorial support of my supervisors.

For Chapter 3, I conducted a systematic scoping review and write the first draft. This was followed by editorial support from my supervisors.

For Chapters 4, 5 and 6, I designed all aspects of the projects in collaboration with my supervisors. I conducted all outcome measures for Chapter 6, analysed all data for Chapter 5 and 6 and wrote the first draft of all three chapters. This was followed by editorial support from my supervisors.

Chapter 7 was written with editorial support of my supervisors.

By signing below I confirm that Urvashy Gopaul contributed to the following publications as stated above:

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Last but not least, I dedicate this thesis to my lovely mother, who has taught me the true meaning of being strong and resilient. My passion and determination for improving care for any patient, I owe that to you Mum. I think you would have been proud of me.

PUBLICATIONS ARISING FROM THIS THESIS

This thesis is presented with the inclusion of four papers. I am the lead author on all papers. At the time of submission, one of these papers (Chapter 3) has been accepted in a peer-reviewed journal and another paper (Chapter 4) has been published in a peer-reviewed journal. At the time of submission, the other two chapters (Chapters 5 and 6) are being prepared for submission to peer-reviewed journals.

Manuscripts in peer-reviewed journals: Published

Gopaul U, van Vliet P, Callister R, Nilsson M & Carey L. COMbined Physical and somatoSEnsory training after stroke: Development and description of a novel intervention to improve upper limb function. *Physiotherapy Research International*. 2018;0(0):e1748.

Manuscripts in peer-reviewed journals: In press

Gopaul U, Carey L, Callister R, Nilsson M & van Vliet P. Combined somatosensory and motor training to improve upper limb function following stroke: a systematic scoping review. *Physical Therapy reviews.* DOI: 10.1080/10833196.2018.1553668

PRESENTATIONS ARISING FROM THIS THESIS

During my candidature, I presented results arising from this thesis at 6 conferences. This resulted in 4 oral platform presentations, 1 oral poster and 2 poster presentations. I was also invited to present at one research seminar.

Conference presentations

Gopaul U, Carey L, Callister R, Nilsson M & van Vliet P. Feasibility of the Combined Physical and somatoSEnsOry (COMPoSE) training to improve arm function after stroke: A single-case experimental study. *Presented at:*

World Stroke Congress Oct 2018, Canada. Oral presentation

Stroke Aug 2018, Australia. Oral poster presentation

Gopaul U, van Vliet P, Carey L, Hudson & Nilsson M. Description of a novel ''Combined Physical and SEnsOry training'' (COMPoSE) intervention to improve arm function after stroke, using TIDIER checklist. *Presented at:***World Confederation of Physical Therapy** July 2017, South Africa. Oral presentation.

Combined Stroke Conference Aug 2016, Australia. Oral presentation.

Gopaul U, Carey L, Callister R, Nilsson M & van Vliet P. Combined interventions for improving sensory-motor function of the upper limb (UL) post-stroke: a systematic review. *Presented at:*

Smart Stroke conference Aug 2017, Australia. Oral presentation.

Stroke Society of Australasia conference Aug 2017, New Zealand. Poster presentation.

Gopaul U, Carey L, Callister R, Nilsson M & van Vliet P. Feasibility of TactArray: A novel method for evaluating and retraining of sensorimotor control of finger forces post-stroke: a case report. *Presented at:*

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Research seminars

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PUBLISHED ABSTRACTS FROM THIS THESIS

- **Gopaul U**, Callister R, Carey L, Nilsson M, Sampson C, P vV. Feasibility of TactArray: A novel method for evaluating and retraining of sensorimotor control of finger forces post-stroke: a case report. International Journal of Stroke 2017;12(3S):3–59.
- **Gopaul U**, Van Vliet P, Carey L, Hudson I, M N. Description of a novel ‘‘Combined Physical and SEnsOry training’’ (COMPoSE) intervention to improve arm function after stroke, using TIDIER checklist. International Journal of Stroke. 2016; 11(1S): 3–31.
- **Gopaul U**, Carey L, Hudson I, Nilsson M, Callister R, P vV, editors. Description of a novel COMbined Physical and SEnsory training (COMPoSE) intervention to improve arm function after stroke, using Tidier checklist. World Confederation of Physical Therapy Congress 2017 conference proceedings; 2017; Capetown, South Africa: World Confederation of Physical Therapy.
- **Gopaul U**, Callister R, Carey L, Nilsson M, van Vliet P. Combined interventions for improving sensorymotor function of the upper limb following stroke: A systematic review. International Journal of Stroke,. 2017;12(2S).
- **Gopaul U**, Carey L, Callister R, Nilsson M, van Vliet P. World Stroke Congress Abstracts, 2018. International Journal of Stroke. 2018;13(2_suppl):3-217.

AWARDS

Throughout my candidature, I have been supported by a University of Newcastle Research Scholarship and University of Newcastle Top-up Scholarship.

In 2015, I was successful in acquiring a travel scholarship(AUD 5,000) from the National Health and Medical Research Council Centre of Research Excellence in Stroke Rehabilitation and Brain Recovery. I also won a research equipment grant (AUD 4,000) from the School of Health Sciences. I was also successful in acquiring a Research Higher Degree student exchange grant (AUD 4,500).

In 2016, I contributed to a successful Linkage pilot research grant (AUD 9,600) from the University of Newcastle as a co-investigator.

In 2017, I was awarded a Research Support grant (AUD 5,735) and a Clinical Research Design, Information Technology and Statistical Support grant (AUD 2,500) from the Priority Research Centre For Stroke And Brain Injury.

In 2018, I won travel a Travel Support Grant (AUD 2,000) from the Priority Research Centre for Stroke and Brain Injury.

CONTRIBUTION STATEMENT

The body of work presented in this thesis has produced four papers. I was the sole PhD student responsible for this project and was involved in all aspects of this project. A summary of my contributions and involvement is outlined at the beginning of each chapter.

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COMMON ABBREVIATIONS

Abbreviation	Meaning
ARAT	Action Research Arm Test
BBT	Box And Block Test
CI	Confidence interval
CV	Coefficient of variation
COMPoSE	COMbined Physical and somatoSEnsory training
FAS	Fatigue Assessment Scale
FMT	Fabric Matching Test
FMA-UL	Fugl Meyer assessment upper limb
FTORT	Functional Tactile Object Recognition Test
ICC	Intraclass correlation coefficient
MAL-AS	Motor Activity Log-Amount Scale
MAL-HW	Motor Activity Log-How Well
MOCA	Montreal Cognitive Assessment
MTS	Modified Tardieu Scale
RCT	Randomised Controlled Trial
RTG	Reach-to-grasp
PVAS	Pain visual analogue scale
PPS	Pressure Profile Systems
SD	Standard deviations
SIS	Stroke Impact Scale
SFVAS	Stanford fatigue visual analogue scale
SPSS	Statistical Package For The Social Sciences
TDT	Tactile Discrimination Test
UL	Upper limb
WFMT	Wolf Motor Function Test
WPST	Wrist Position Sense Test

THESIS ABSTRACT

Background

Stroke is a leading cause of disability worldwide. Upper limb motor and somatosensory impairments are common following stroke, making performance of everyday tasks difficult. Interventions directed at motor deficits have traditionally been separated from interventions directed at somatosensory deficits. By treating motor and somatosensory impairments separately, the potential beneficial effects of combining somatosensory training to further enhance sensorimotor function and action are not utilised. Hence, there is a critical need for the development of new and more effective treatments addressing both somatosensory and motor function to improve long-term disability after stroke. Also, there is a lack of objective outcome measures with good responsiveness to evaluate sustained grasp performance in people with stroke indicating a need for new outcome measures to quantify grasp deficits after stroke.

Overall aim

This thesis aimed to investigate whether combined somatosensory and motor training improves upper limb recovery after stroke.

Objectives

This thesis studied the effects of combining somatosensory and motor training to improve upper limb recovery after stroke. This thesis also investigated the reliability of measures of maximal tactile pressures and forces during grasping using the TactArray device in healthy people and people with stroke. There are four distinct but complementary studies included in this thesis to address these research objectives.

Methods

Study 1: A systematic scoping review was conducted to identify combined somatosensory and motor training interventions for the upper limb and their training components, and to review the efficacy of the combined interventions.

Study 2: This report describes the rationale and development of a new upper limb stroke rehabilitation intervention known as COMPoSE: "COMbined Physical and somatoSEnsory training" and, designed to improve somatosensory and motor deficits in the upper limb after stroke. A standardised training matrix was developed to facilitate intervention delivery.

Study 3: A trial was conducted to assess the feasibility of the COMPoSE trial using a single-case experimental study design. The outcomes from this feasibility trial included: 1) feasibility of the recruitment of participants; 2) review of intervention protocol and feasibility of study design; 3) acceptability of the intervention and trial; 4) appropriateness of data collection procedures; and the 5) evaluation of resources required. The preliminary impact of the COMPoSE intervention on somatosensory and motor deficits and upper limb function after stroke were also assessed.

Study 4: A test-retest reliability study was conducted to evaluate the reliability of measures of maximal tactile pressures and forces during sustained grasping using the TactArray device in healthy participants and participants with stroke.

Results

Study 1: Ten studies (n= 219) were included and the interventions consisted of combinations of tactile stimulation/discrimination, proprioceptive stimulation/discrimination, haptic object discrimination/recognition, movement training, and functional training. Only one group study (n=45), a non-randomized controlled study with multiple active components and the largest dose of treatment (72 hours), found significant improvements in fine motor and somatosensory measures.

Study 2: The essential features of COMPoSE include: combined somatosensory-motor training variables (grasp pressure, distance, object size, crushability, surface texture and friction),

feedback using a haptic device providing measures of grasp pressure, and high dose repetitive task practice with and without vision. It was planned for ten treatment sessions to be delivered over three weeks, using a standardised matrix for treatment delivery.

Study 3: Findings from this feasibility trial (n=5) indicated that training with the combination of somatosensory and motor variables synchronously, i.e., within the same task, was feasible. The delivery of the COMPoSE intervention using the standardised training matrix was feasible, however modifications to allow more specific tailoring to participant deficits is recommended. This trial identified components of the COMPoSE intervention such as the combinations of somatosensory-motor variables, amount of practice, and the duration of treatment, that would need to be modified in order to maximise improvement of upper limb function after stroke. Additionally, operational aspects of the trial methods, such as the number of outcome measures and timing of outcome measures were identified that would need to be addressed prior to subsequent trials.

Study 4: The TactArray device demonstrates satisfactory reliability for measures of maximal tactile pressures during complete grasp duration of 8s (from finger contact to grasp release) for within-day and between-day testing sessions using an average of three trials with and without vision, in healthy people and those with stroke. Measures of maximal tactile forces are less reliable than maximal tactile pressures.

Conclusion

Findings from this thesis makes an important contribution to advancing our understanding of various factors that influence the effects of combined somatosensory and motor training interventions. So far, there is little consistency across "combined somatosensory and motor training" interventions to improve upper limb function after stroke. The individual studies in the systematic scoping review and the COMPoSE trial provide preliminary evidence that combined somatosensory and motor training interventions have the potential to improve upper limb recovery after stroke, if they incorporate the appropriate active ingredients and dosage. Findings from this thesis identified research questions still to be answered with regards to active ingredients, recruitment capability, responsiveness of outcome measures for people with severe deficits after stroke, individualised somatosensory-

motor training, dosage and intensity of intervention. Furthermore, results from this thesis indicated that it could be beneficial to deliberately train for somatosensory and motor training synchronously to improve upper limb recovery after stroke. Additionally, a novel means of measuring maximal grasp pressures during a sustained grasp using the TactArray device has been evaluated, which can be further explored in larger trials. Recommendations have been provided on optimisation of the intervention contents and study design of the COMPoSE intervention and trial in the future.

CHAPTER 1: INTRODUCTION

1.1 OVERVIEW

This introductory chapter provides a rationale for focusing on combining somatosensory and motor training to improve upper limb recovery after stroke. It provides a brief description of the aetiology of stroke, followed by the epidemiology of stroke. The cost implications of stroke are also summarised. An overview of the post-stroke impairments is presented along with a description of mechanisms of recovery. Limitations of existing upper limb rehabilitation interventions are reported that relate to the overall research question of this thesis. This chapter also provides an outline of the research questions, aims and hypotheses and presents the overall structure of this thesis.

1.2 BACKGROUND

1.2.1 Aetiology of stroke

The World Health Organisation (WHO) defines stroke as "a syndrome of rapidly developing signs of focal (or global) disturbance of cerebral function, lasting longer than 24hours (unless interrupted by death) with no apparent non-vascular cause"[1]. This disruption in cerebral blood flow arising from ischaemic stroke (blockage of a cerebral artery)[2] or haemorrhagic stroke (from vessel bleeding) interrupts the supply of oxygen and nutrients to a part of the brain[3] leading to subsequent tissue damage[2] resulting in neurological deficits[4].

1.2.2 Epidemiology of stroke

Stroke is a leading cause of chronic adult disability worldwide[5]. Every year, 15 million people suffer a stroke, of which 5 million are left permanently disabled[6]. It is predicted that the prevalence of stroke survivors will climb to 77 million by 2030. Stroke burden is associated with 43.7 million lost disability-adjusted life years (DALYs) yearly worldwide[7] and is anticipated to rise to 61 million DALYs by 2020[6]. According to the Global Burden of Disease study for the period 2002-2030, it is anticipated that stroke would be ranked seventh amongst the leading causes of DALYs[8]. In Australia, stroke represents 75% of cerebrovascular disease

related deaths[9]. Over 437,000 people were living with the effects of stroke in 2014 in Australia and this number is projected to increase to 709,000 in 2032 (2.4% of the population)[10].

The risk of stroke increases with ageing, with the incidence doubling each decade after the age of 45 years[11]. In the 35-44 years age group, the incidence of stroke ranges between 30-120 per 100,000 per year whereas for adults aged 65-74 years, the incidence rises to 670-970 per 100,000 per year[12]. The lifetime risk of stroke has been estimated to be 1 in 6 men and 1 in 5 women, with increased risks in younger men and older women[13]. Given the high prevalence and incidence of stroke, these epidemiological findings emphasise the importance of stroke rehabilitation trials to address residual impairments.

1.2.3 Cost implications associated with stroke

Stroke is a global epidemic and is a primary concern for public health. Given the large prevalence of stroke, it is not surprising that the global economic burdens of stroke are high. Stroke imposes a substantial socioeconomic constraint on the patients, families and society at large[14,15]. An international comparison of stroke cost-analysis studies showed that about 0.27% of gross domestic product was spent on stroke by national health systems. Additionally, stroke care accounted for approximately 3% of total health care expenditures[16]. In Australia, the financial impact of stroke was estimated at $45 billion (AUD) in 2012. Health-related costs represented $881 million (AUD)[9] with in-patient rehabilitation accounting for 28% of these healthcare costs[17].

The economic impact of loss in productivity due to stroke is also significant. Many stroke survivors who do not fully recover and work less than people without stroke. Productivity is therefore lost as a result of reduced employability, increased absenteeism from work or reduced effectiveness in their jobs[17]. Seventy-five percent of stroke survivors have a residual disability that affects their employability [18]. The cost of lost income due to stroke was estimated at $975 million (AUD) in 2012 for individuals of working age in

Australia[10]. Consequently, stroke survivors earn a significantly reduced income which imposes a financial constraint on themselves and their families.

The financial constraints of stroke patients are exacerbated by personal costs associated with their healthcare. In 2012, the "out-of-pocket" (non-reimbursed) costs in the stroke healthcare expenditure system were estimated at 44% ($5229) of the total cost per stroke survivor in Australia. Personal costs become more important with time as people with stroke continue to require rehabilitation services throughout their lifetime that impose out-of-pocket costs[17]. Hence, there is a critical need for more cost-effective rehabilitation strategies to reduce the long-term disabling consequences after stroke, to enhance quality of life, and reduce the costs associated with stroke care and rehabilitation.

1.2.4 Motor and somatosensory deficits after stroke

Upper limb impairments after stroke are the primary causes of functional limitations[19]. More than 85% of stroke survivors suffer from residual upper limb movement deficits due to incomplete motor recovery[20], and one in two stroke survivors have deficits in somato (body) sensations[21].

Common motor upper limb impairments after stroke include muscle weakness[22-25], mass synergistic movements[22], and abnormal muscle tone[26]. These impairments are associated with impaired ability to activate muscles[22-25], altered mechanical and physiological properties of motor units[27,28], abnormal activation of agonist motor units[29,30], and deficits in the ability to regulate stretch-reflex threshold excitability[31].

Somatosensory deficits such as impairment of tactile sensations (2-point discrimination and texture discrimination), loss of proprioception (inability to know where the body is in space is) and astereognosis (impaired recognition of objects through touch) are common post-stroke[32]. Additionally, the level of processing can be impaired which impacts on the detection of cues, and discrimination of somatosensory information as well as its integration across the sub-modalities[33]. Controlled motor performance or action of the upper limb relies on the accurate processing and interpretation of somatosensory input before and

during movement execution[34,35]. Given associations between motor and somatosensory impairments[36], impaired somatosensation limits the exploration of the immediate environment and affects execution of daily tasks such as grasping and manipulation of objects[37].

1.2.5 Stroke recovery and upper limb interventions

According to the Glasgow Outcome Scale, good recovery post-stroke involves a "resumption of normal activities even though there may be minor neurological and psychophysical deficits"[38]. Based on this definition, any improvement in functional independence would indicate some recovery[39,40]. However, stroke recovery is a complex process that occurs through three main mechanisms: restoration, substitution and compensation of functions[41,42]. To enhance upper limb recovery after stroke, it is essential for rehabilitation interventions to drive processes of neuroplasticity and recovery of the nervous system after stroke[43]. According to the International Classification of Functioning, Disability and Health classification, somatosensory and motor recovery could take place at neuronal (health condition), impairment (performance) and functional (activity) levels[44]. Current upper limb rehabilitation interventions have demonstrated limited benefits on functional outcomes[45]. This lack of improvement could result from insufficient dosage or inappropriate interventions[46]. This could result from a lack of understanding about the active ingredients that can optimise an intervention, the interactions between them, their targets and mechanisms of action so as to enhance upper limb recovery post-stroke[47]. Hence, it is unclear what constitutes optimal training strategies.

Priming strategies have been proposed as a restorative means of targeting neural mechanisms to reduce impairments in neurological conditions[48]. Movement-based priming[49] and sensory priming[50] are strategies that influence neural mechanisms to enhance changes in motor function. For instance, movement-based priming includes any type of repetitive movements such as unilateral wrist or elbow flexion and extension[51]. Moreover, stroke rehabilitation interventions are encouraged to combine various training approaches including global motor rehabilitation and multisensory interaction, amongst others[52].

Combined somatosensory and motor training could be a potential means of optimising upper limb recovery after stroke. Sensory based priming has previously prioritised the use of peripheral electrical stimulation, muscle vibration or deafferentation[53], which do not emphasise the active exploration of touch by the upper limb. Few studies have focused on sequentially combining motor training with somatosensory training that actively involved the upper limb (Chapter 3). Moreover, few interventions integrated tasks combining somatosensation and motor function (Chapter 3). Additionally, the use of haptic devices such as the TactArray pressure distribution system to provide online feedback have not yet been applied to upper limb interventions post-stroke (Chapter 5). Therefore, investigations are required to characterise these combined interventions and evaluate their effects so as to inform the design of novel interventions addressing somatosensory and motor function of the upper limb after stroke.

1.2.6 Framework for the development of rehabilitation interventions

The Medical Research Council (MRC) (UK) framework advocates a stepwise and systematic approach for the development and evaluation of complex interventions. The complexity of an intervention is determined by a combination of several components that act independently or inter-relate with each other to influence outcomes[54]. The process involves the systematic development of the intervention by identifying the evidence base, establishing the theoretical basis of the intervention, then the development of the intervention, followed by a feasibility and piloting phase, an evaluation phase, and an implementation phase[54]. This thesis focuses on the early stages of the development of a new intervention, particularly the development of the intervention, and the feasibility and piloting aspects (figure 1.1).

The development phase explores the conceptual basis of the intervention through review of pertinent literature. This is followed by determining and assembling the components of the intervention, as well as providing a rationale for how this training approach might achieve its goal[54]. The feasibility and piloting phases are critical in understanding the feasibility of delivering an intervention, in determining the feasibility of conducting an intervention trial, and in optimising the design and evaluation of a subsequent trial[54-56]. Additionally, a series of feasibility and pilot trials could identify key factors and flaws

that may impact on the methodological rigour of the design and conduct of the trial. If outcomes are different from anticipated results, feasibility and pilot trials could help to identify the limitations of the trial design that impact on outcomes. Moreover, feasibility and pilot trials are recommended for better understanding of the underlying theory and mechanisms underpinning interventions by exploring the interactions between components of the intervention[55]. In rehabilitation interventions, the feasibility and piloting phases serve to evaluate the preliminary responses of participants to the intervention, which may contribute to a better understanding of the mechanisms underlying motor learning-related neuroplasticity[57-60]. Thus, feasibility and pilot trials are required to explore novel interventions combining somatosensory and motor training to improve upper limb recovery after stroke.

The effects of an intervention can be compromised by limitations in its design or by poor implementation[61]. The importance of feasibility and pilot trials in the development process of a complex rehabilitation intervention has been poorly emphasised in stroke rehabilitation trials often resulting in either ineffective or suboptimal interventions or interventions that cannot be recommended clinically. Systematic reviews with meta-analyses on upper limb rehabilitation trials post-stroke have shown that a large number of randomised controlled trials (RCTs) tend to be negative, inconclusive or show small effects[45,62,63]. Therefore, a comprehensive and systematic approach to the development of rehabilitation interventions will reduce research waste and better inform clinical practice[64].

Small exploratory studies can be conducted using single-case experimental designs to determine the individual responses to a novel intervention over time. Single-case experimental designs are characterised by repeated measures over time from the baseline to the intervention phase. The initial baseline phase acts as a control such that data recorded across the baseline can be compared with any change in the intervention phase[65,66]. One limitation of single-case study designs with baseline-intervention phases is their weak internal validity such that they cannot necessarily demonstrate a cause-effect relation between the change in outcome measures and a particular treatment. The generalisability of the results from single-case study designs could therefore be significantly increased by the accumulation

of results across participants. A causal relationship can eventually be established if a predictable trend and consistent results are obtained if and the intervention effects are replicated in at least three to four single-case experimental studies[67].

The overall outcome of a trial investigating feasibility of a novel intervention would inform the decision about step-wise progression with a trial as follows:

(i) Stop because the main study is not feasible;

(ii) Continue, but protocol needs to be modified to be feasible;

(iii) Continue without modifications, but close monitoring is required to ensure feasibility; and

(iv) Continue without modifications[68].

1.2.7 Overarching research question

Considering the need for systematic development and evaluations of interventions combining motor and somatosensory training for the upper limb post-stroke in future trials, this thesis incorporates identifying the existing evidence, determining the contents of the intervention, followed by the feasibility and piloting phase, which address the overarching research question:

> ***"Can combined somatosensory and motor training improve upper limb recovery after stroke?"***

1.3 RESEARCH QUESTIONS

Four specific research questions are proposed to address this overarching research question:

Research Question 1:

What interventions combining both somatosensory and motor training currently exist for the treatment of upper limb function in stroke and which of these combined interventions are effective in improving upper limb function after stroke?

Research Question 2:

What are the essential features of a novel intervention combining somatosensory and motor training to improve upper limb function after stroke and what is the rationale for these features?

Research Question 3:

Is it feasible to conduct a trial of a combined somatosensory and motor training intervention to improve upper limb recovery in people with chronic stroke?

Research Question 4:

Are measures of tactile pressures or forces during sustained grasping using a TactArray device reliable amongst healthy people and stroke survivors?

1.4 RESEARCH AIMS

The four research questions above correspond to my thesis aims (figure 1.1):

Aim 1: To conduct a systematic scoping review of interventions combining somatosensory and motor training to improve upper limb function after stroke

Aim 2: To describe the rationale for and development of a combined somatosensory and motor training intervention to improve upper limb function after stroke

Aim 3: To evaluate the feasibility of the combined somatosensory and motor training intervention on improving upper limb recovery after stroke in a trial and gather preliminary data on the impact of the intervention

Aim 4: To assess the test-retest reliability of maximal tactile pressures and forces of a sustained grasp task using the TactArray device and determine which measures of maximal tactile pressures or forces are most reliable in both healthy people and those with stroke.

1.5 HYPOTHESIS

The overarching hypothesis of this thesis is that combining somatosensory and motor training can improve upper limb recovery after stroke.

In this thesis, it is anticipated that the upper limb recovery process post-stroke would primarily occur through neural repair i.e., restitution[41].

1.6 THESIS STRUCTURE

This thesis is presented as a series of four manuscripts in the main text that address the above aims. At the time of submission, two of these papers (Chapters 3 and 4) have been published in peer-reviewed journals and the other two papers (Chapters 5 and 6) are being prepared for submission to peer-reviewed journals. Figure 1.1 illustrates the thesis structure showing pertinent stages of the 2008 MRC (UK) framework together with the activities undertaken in the intervention development process. Given the structure of this thesis and the inter-relationships between the chapters, it is acknowledged that there is some

duplication of information. This is purposeful so that the chapters that have been and those that will be published can be viewed independently of other chapters. Ideally the study described in Chapter 6 would have preceded the study in Chapter 5, however they were conducted in parallel. The study in Chapter 6 was important for establishing that the device used to provide grasp pressure feedback during training and outcome measures in Chapter 5 was reliable.

Chapter 2: Literature Review

This chapter provides a brief description of the motor and somatosensory systems controlling the upper limbs. This chapter summarises deficits in reaching and grasping after stroke and addresses the existing evidence underlying upper limb recovery after stroke with regards to neuroplasticity underlying somatosensory and motor recovery, coupling action between somatosensation and motor function, and the literature on current interventions that combine somatosensory and motor training. This chapter also provides an overview of objective and sensitive outcome measures to evaluate grasp deficits after stroke.

Chapter 3. Combined somatosensory and motor training to improve upper limb function following stroke: a systematic scoping review.

This chapter presents the results of a systematic scoping review of studies that combined somatosensory and motor training to improve upper limb function after stroke. Of 2813 non-duplicate titles identified, 132 full-text articles were assessed for eligibility and 10 articles were included. Two review authors (UG and PvV) independently assessed the methodological quality of the studies using the Structured Effectiveness Quality Scale (SEQES) and graded the level of evidence according to the Oxford Centre for Evidence Based Medicine Levels of Evidence system. The findings of this systematic scoping review addressed thesis aim 1, i.e., to conduct a systematic scoping review of interventions combining somatosensory and motor training to improve upper limb function after stroke.

Chapter 4. COMbined Physical and somatoSEnsory training after stroke: Development and description of a novel intervention to improve upper limb function

This chapter describes a new upper limb stroke rehabilitation intervention known as COMPoSE: "COMbined Physical and somatoSEnsory training" and describes the rationale and development of the intervention, designed to improve somatosensory and motor recovery in the upper limb after stroke. The key features and content of this intervention are reported. The findings of this chapter addressed thesis aim 2, i.e., to describe the rationale for and development of a combined somatosensory and motor training intervention to improve upper limb function after stroke.

Chapter 5. The COMbined Physical and somatoSEnsory (COMPoSE) training to improve upper limb recovery after stroke: A feasibility study

This chapter presents findings from a trial to evaluate the feasibility of the COMPoSE training intervention on improving upper limb recovery and to gather preliminary data on the impact of the COMPoSE intervention using a single-case experimental study design. The outcomes from this trial included: 1) feasibility of the recruitment of participants; 2) review of the COMPoSE intervention protocol and feasibility of the study design; 3) acceptability of the intervention and trial; 4) appropriateness of data collection procedures; 5) resources required; and 6) the measures of preliminary impact on participants using laboratory measures (maximal tactile pressures) and clinical motor and somatosensory measures. The findings from this study addressed thesis aim 3, i.e., to evaluate the feasibility of the combined somatosensory and motor training intervention on improving upper limb recovery after stroke in a trial and gather preliminary data on the efficacy of the intervention.

Chapter 6. Reliability of maximal tactile pressures and forces of a sustained grasp task using a TactArray device in healthy people and in people with stroke

This chapter presents the results of an exploratory study, which investigated the reliability of maximal tactile pressures and forces using a TactArray device in healthy people and in people with stroke. Reliability was determined using changes in mean, coefficients of

variation and intraclass correlation coefficients. Both arms were tested in within-day sessions and between-day sessions, with vision and without vision. Measures of maximal tactile pressures and forces were measured for the complete grasp duration (8s) and for the plateau phase (5s) and were reported using the highest value amongst the three repetitions, the mean of two repetitions and the mean of three repetitions. The findings from this study addressed thesis aim 4, i.e., to assess the test-retest reliability of maximal tactile pressures and forces of a sustained grasp task using a TactArray device and determine which measures of maximal tactile pressures or forces are most reliable in both healthy people and those with stroke.

Chapter 7. General discussion

A synthesis of findings is presented in this chapter with regards to the research aims of this thesis. The strengths and limitations of the research are reported. The implications for clinical practice and research are discussed and recommendations for future research are also provided.

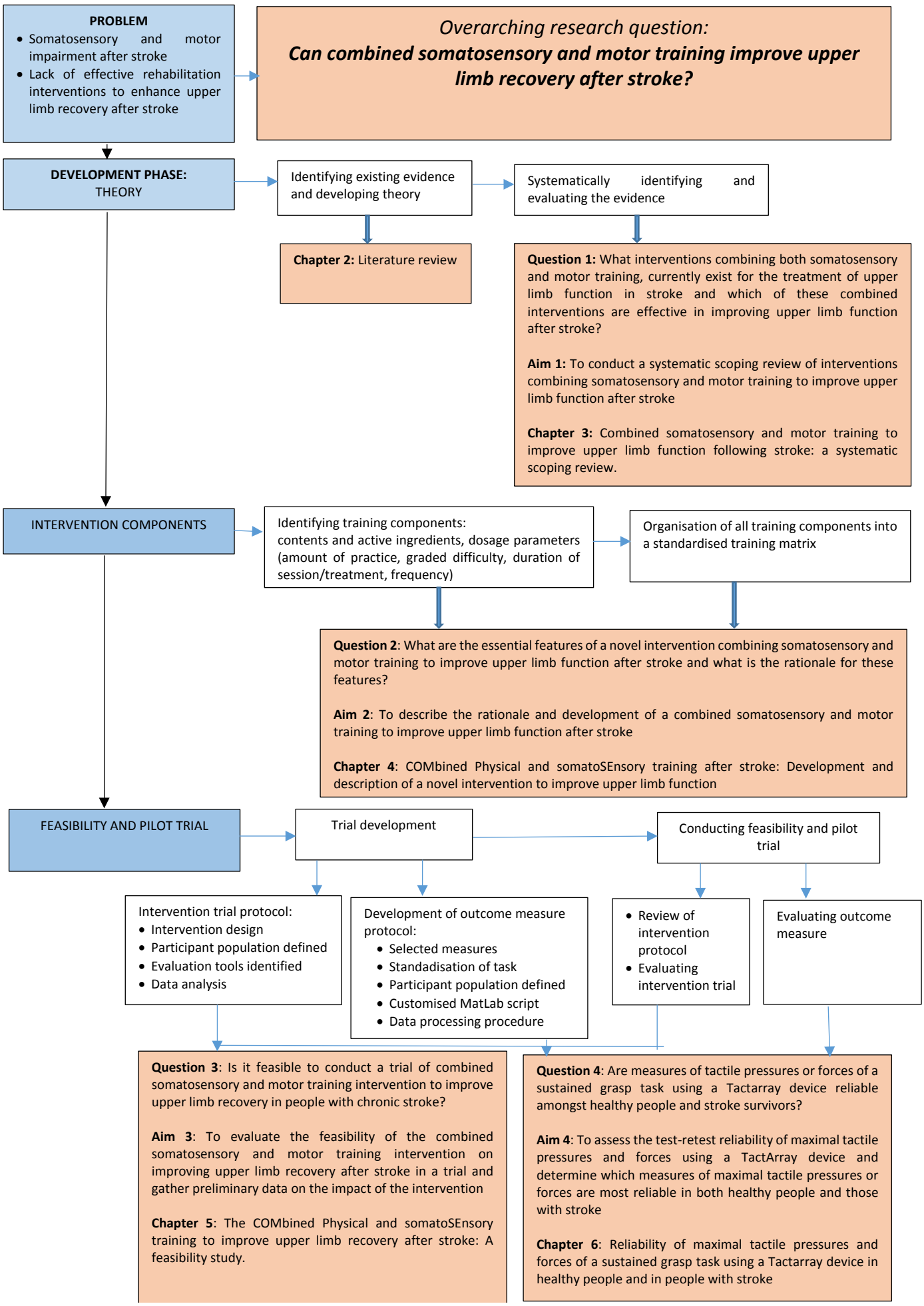

Figure 1.1 Structure of thesis from overarching research question, specific research questions, thesis aims and thesis chapters

CHAPTER 2: LITERATURE REVIEW

2.1 OVERVIEW

This chapter provides a review of literature pertaining to the overarching research question of this thesis. The first section of this chapter provides a brief description of the motor and somatosensory systems controlling the upper limbs. Reach-to-grasp (RTG) behaviours and the relationship between these reaching and grasping components in healthy individuals are summarised, followed by deficits in reaching and grasping after stroke. An overview of the timing of recovery post-stroke is presented along with a description of neuroplasticity processes underlying somatosensory and motor recovery. A summary of strategies proposed to optimise upper limb recovery after stroke are also reported. The second section of this chapter provides an overview of outcome measures used to evaluate grasp deficits after stroke and their limitations. The methods used to evaluate the reliability of outcome measures are also presented. This chapter concludes by highlighting the gaps identified in this review of the literature.

2.2 MOTOR AND SOMATOSENSORY SYSTEM OF THE UPPER LIMB

2.2.1 Upper limb motor system

Performing common activities of daily life requires precise control of our upper limbs. The corticospinal system is the main motor neural system responsible for controlling movements that require advanced skill and flexibility[69-71]. It mediates movement of distal extremities and primarily fine motor activities of the hand[69,70,72]. The corticospinal system connects the frontal and anterior parietal lobes with the grey matter of the spine[73]. It runs from the cortex through the deep white matter to the brain stem. The corticospinal tract decussates from one side to the other in the lower brain stem and descends in the contralateral white matter of the cord (lateral corticospinal tract). The lateral corticospinal tract controls the muscles involved in fine movements[69,74]. To regulate tactile and proprioceptive information that is generated during movement, the corticospinal system also projects from the somatic sensory cortex to somatic sensory processing centres in the dorsal horn and brain stem demonstrating an overlap in the somatic sensory and motor/premotor

cortex in the deeper part of the dorsal horn[75]. Therefore, the corticospinal tract has a dominant role in selecting the somatosensory input from the spinal cord coming from cutaneous and proprioceptive somatosensory afferents[76-78], which are essential for motor control and the appropriate execution of movements[79].

The parietal lobe is a key brain area responsible for processing information regarding RTG coordination[80,81]. In the parietal cortex, there are two neural circuits that contribute to the control of reach and grasp between the parietal lobe and the premotor cortex. For proximal muscles participating in the transport phase, the medial circuit is involved in object location. For distal muscles involved in grasp, the lateral circuit is concerned with the size and shape of the object. Both circuits also partially overlap and converge to the dorso-medial pathway[82]. The parietal cortex has a primary role in processing somatosensory information. It is responsible for converting somatosensory input into motor commands and for integrating somatosensory information with previous and ongoing motor commands. This allows a person to be continuously informed about the state of their arm in order to plan for present and for future movements[83].

2.2.2 Upper limb somatosensory control

The somatosensory system is responsible for interpretation of somatosensory messages received by somatosensory receptors in the body. These somatosensory receptors are primarily found in the skin, tissues and joints, the nerve cell tracts in the body and spinal cord and in the brain centres that are involved in processing somatosensory information[84]. The major somatosensory regions include: the primary somatosensory cortex (SI), the secondary somatosensory cortex (SII), the thalamus, the insula, the posterior parietal cortex and the cerebellum.

The SI involves Broadmann Areas (BA) 3a, 3b, 1 and 2 and processes somatosensory information, in particular feature detection. Functional MRI analyses of the somatosensory-motor cortex on healthy adult adults have shown that BA 3a and BA 2 process information

about limb positioning[85,86] while BA 3b, BA 1 and BA2 receive information from skin receptors about texture[87], size and shape[88,89]. Studies on somatosensory perception in healthy individuals have also shown that along with activation of SI, other areas of the brain such as SII, the motor cortex and the supplementary motor area are simultaneously activated, suggesting connections between SI and these brain areas[87]. The contribution of SII in texture discrimination and tactile object recognition has been demonstrated in monkeys[90]. SII shares connections with SI[91], motor regions e.g premotor cortex[92] and the thalamus[93]. The supramarginal gyrus, located next to the SII contributes to conscious proprioceptive perception and processing of spatial stimuli[94].

The thalamus relays touch information from the periphery to the contralateral SI and SII regions[91]. These connections help to optimise the detection of new stimuli or stimuli that are hard to sense[95]. The insula is primarily responsible for perceptual recognition and learning, particularly interoceptive information processing[96]. The posterior parietal cortex processes information for both perception and action. SI, SII and the thalamus project into posterior parietal cortex, which in turn projects back to SII and premotor cortex. The posterior parietal cortex has an important role in integrating somatosensory information with other senses, especially vision, to guide motor action[96].

Besides modulation of motor action, cognition[97] and adaptive motor skill learning[98], the cerebellum also contributes to processing of somatosensory information[99] regarding RTG coordination[81]. A study measuring cerebellar evoked magneto-encephaloraphic (MEG) responses in humans showed elicitation of cerebellar activity when attention was drawn towards the somatosensory stimuli[100]. The cerebellum also has a role in the cross talk between somatosensory and motor cortices. This has been demonstrated in animal models (rats) where excitability of the contralateral motor cortex during somatosensory stimulation was reduced when input from the cerebellum was blocked[101,102]. In animal studies, as in man, the cerebellum is also involved in the comparison of temporal and spatial information for detection of sequences[97]. This was further supported by an fMRI study investigating tactile and visual stimulation in humans which showed that the inferior olivary complex of the

cerebellum conveys temporal information about somatosensation[103]. The cerebellum therefore has a distinct role in providing information about an internal state of somatosensory predictions used during online motor control of movements[104], which enables coordination of actions between the eye, hand and arm[104]. The estimate of somatosensory predictions also allows adjustment of the relative strength and timing of muscle activation corresponding to the effector move[105]. The cerebellum is also responsible for making quick adjustments in response to perturbations by adjusting automatic movements that is reliant on visual and somatosensory input[106].

Activation of the precentral and postcentral gyrus was observed during active motor tasks[107] and somatosensory discrimination tasks[108], which illustrated the anatomic overlaps between the motor and somatosensory cortices. This argument was further supported by functional MRI analyses, which showed motor and somatosensory responses in the hand in the precentral and postcentral regions, suggesting that motor and somatosensory hand cortices overlap and that the central sulcus does not strictly divide these two regions. Mixed motor and somatosensory responses were limited in the middle part of the central sulcus[109]. This study further supported previous animal studies that found extensive connections linking the precentral and postcentral gyrus[110]. Since the precentral gyrus corresponds to the primary motor cortex and the postcentral gyrus corresponds to the primary somatosensory cortex, the widespread connections between these two areas suggest a strong anatomic link between the somatosensory input and motor output in the somatosensory-motor cortex[111].

2.3 REACH-TO-GRASP IN HEALTHY INDIVIDUALS

The ability to reach, grasp and manipulate objects has been chosen as a representative movement task in this thesis because these are essential upper limb movements required during functional activities of daily living[112]. RTG and manipulation involve a complex interplay between coordinated movements of several upper limb segments and somatosensation in the upper limb[113].

The temporal planning of reaching and grasping involve two distinct components: a) reaching (the transport phase), which brings the hand towards the object, and b) the grasp component, which adjusts the hand configuration and grasp aperture according to object shape and orientation[114,115].

2.3.1 Transport phase

For the transport component, the velocity profiles are approximately bell-shaped, starting with an initial acceleration phase, followed by a deceleration phase. The mean and peak velocities increase linearly with increasing object distance such that transport time remains constant[115,116]. Changes in object velocity affect the temporal relations between the acceleration and deceleration phases. For a shorter transport distance, the duration of the deceleration phase decreases with increasing object velocity[117].

Fitts' Law further elaborated motor control theories of reach-to-grasp[118]. Fitts' Law described the formal relationship that models movement speed and accuracy tradeoffs in relation to human motor control behaviour[118]. Even though Fitts' experiments measured pointing movements, similar precision is required in RTG movements[119]. Movement time is a function of the combined effects of movement amplitude and target width, referred to as Fitts' index of difficulty. The index of difficulty that quantifies the difficulty of motor tasks is given by $\log_2(2A/W)$, where A is the amplitude of movement and W is target width[118]. The relationship between movement time and index of difficulty was formulated by a linear function[118]:

Movement time $= a + b(\text{Index of difficulty}) = a + b \log_2(2A/W)$

- Where a and b are empirically determined constants, that are device dependent.
- A is the distance (or amplitude) of movement from start to target centre
- W is the width of the target, which corresponds to accuracy

The index of performance is the amount of information that the human can process per unit of time and is given by the ratio ID (in bits) to movement time (in seconds). The index

of performance is a measure for the processing ability for the motor system in one-dimensional tasks[120].

Fitts' Law states that the time needed to move as quickly as possible between two targets is determined by the width of the targets and the distance separating them. Consequently, either increasing movement distance or decreasing the width of the targets increases movement time in a predictable way. Similarly, when applied physically, Fitts' law states that reaching for large targets at close distance are acquired faster than small targets at a further distance[118]. Fitts' Law is reflected in a study investigating how the size of stimuli affect transport during reach-to-grasp[121].The participants were instructed to reach and grasp two objects of sizes 2 and 4 cm, identical in shape. For the smaller object, the transport time was greater and peak velocity was attained earlier compared with the larger object. This implies that a smaller stimulus size imposes greater task demands requiring more accuracy. Another study supporting these findings demonstrated that increased object width reduces the spatial accuracy demands during the transport phase, thus allowing a faster movement to develop. Grasp aperture concurrently increases so as to compensate for subsequent directional errors that may occur[122]. Additionally, in the absence of visual information, accuracy is decreased causing compensatory hand opening[123].

It is noteworthy that the Fitts' Law presents with some limitations. For instance, Fitts' law accounts only for the accuracy component of the movement task. This is because whilst Fitts' paradigm states that movement time can be predicted based on the index of difficulty (if movement distance and width of target are controlled experimentally), the movement is performed as fast as possible such that the resultant difficulty of the movement task remains constant across all index of difficulty values[118]. On the other hand, based on the Fitts' Law equation, it is unclear whether the index of difficulty is the best predictor of movement time over variations of the speed and accuracy of movements[124]. Therefore, extending Fitts' Law, it is suggested that by maintaining movement distance and size of object constant and not imposing a defined movement time, increasing speed of reach leads to increased movement

difficulty and therefore increased planning demands on the human motor system. Consequently, accuracy is reduced with increased compensation by larger grasp aperture[124].

Since upper limb interventions in stroke rehabilitation primarily aim for reacquisition of RTG movements, Fitts' Law can be used to provide information about the capacity of an individual's motor system by assessing the quality of movement[125-127]. Fitts' Law has also been validated as a mechanism to adapt task difficulty and can therefore be integrated into exercises for upper-extremity rehabilitation[128]. Therefore, in this thesis, Fitts' index of difficulty is used to express difficulty of tasks in a novel intervention.

2.3.2 Grasp phase

Grasping consists of two manipulation phases, namely grip formation followed by actual grasping. Grip formation involves increasing finger extension and thumb abduction, leading to maximum grip aperture which is proportional to object size. Actual grasping involves closure of the fingers on the object[114]. In healthy individuals, peak grasp aperture occurs within 60-70% of the duration of hand transport, followed by closure of the fingers until contact with the object[114]. The start time of finger opening for grasp correlates with the start time of hand transport toward an object. Additionally, the time of maximum grasp aperture correlates with the time of peak deceleration of the hand[114,115].

Peak grasp aperture is also tightly scaled to the size of the object to be grasped, implying that the peak grasp aperture will be larger for a larger object size. Grasp aperture usually exceeds the actual object size by approximately 20%[114,116,129]. When reaching for objects of different geometry, the fingers move so as to gradually pre-shape the entire hand in order to approximate the object contours as the hand approaches the object[130,131] and occurs without the need for continuous visual feedback[132]. This is because the movement is guided by stored information from previous observations (memory-guided reaches). The ability to correctly position the thumb in opposition to the other fingers is essential for effective use of the hand[133]. Grasp aperture is not influenced by object distance[114].

For visually guided RTG movements, it has been proposed that the transport of reaching and grasp components are controlled by temporal synchronisation of independent visuomotor channels[134]. However, even though two separate and parallel processing streams have been identified, one for reach and one for hand positioning and preshaping the hand to grasp the target[135], other studies have suggested that the reaching and grasping components are not independent of each other but are temporally coupled[136,137]. It was further argued that a higher-order control system is responsible for the integration of the temporal coupling between the transport and grasp components[138].

A stable grasp involves successfully selecting the finger positions on the grasped object, followed by the ability to modulate finger forces so as to prevent slip, tilt and to resist any perturbation whilst grasping[139,140]. The grasp needs to be adequately strong to prevent accidental slips with appropriate scaling of finger force to allow fragile objects to be handled gently[141]. During 5-digit multifinger prehension tasks, the index and little finger are more involved in torque control during rotational tasks whereas the middle and ring fingers are more involved in loading[142,143]. To ensure grasp stability, the thumb opposes the total force produced by the fingers[144]. However, it is not well understood how the total force exerted by all fingers is shared among each finger (force sharing pattern)[144]. It is noteworthy that the grip forces exerted by each finger during a multifinger prehension grip tend to fluctuate such that the forces need to be controlled and coordinated temporally[145].

Somatosensory function has a critical role in motor control of grasp and is tightly coupled with action. An effective grip force is the result of a complex interplay of somatosensory feedback signals and modulated muscle activity in the hand and arm[139,146]. Somatosensation contributes to the ability to control pinch grip[139], to sustain and adapt appropriate grip force without vision[115], to manipulate objects[147], to discriminate between different surfaces[148], and to adjust to conflicting somatosensory conditions, e.g., to a rough surface[149]. The appropriate selection of grip forces is therefore largely determined by the object property including weight, slipperiness, shape and the weight distribution and also the magnitude, direction and points of application of these grip forces[150].

Cutaneous mechanoreceptors are critically important in providing the necessary somatosensory feedback on this somatosensory information in order to accurately adjust the grip force to the weight and surface friction of the object[139,146]. Four main types of tactile mechanoreceptors are found in the glabrous skin of the grasping fingers. These are Merkel cells, Meissner corpuscles, Ruffini endings, and Pacinian corpuscles, each responding to a specific mechanical stimulus. These can be categorised as slow-adapting receptors that respond to sustained static stimuli and rapid-adapting receptors that respond to dynamic stimuli. The slow-adapting receptors include Merkel cells that detect static pressure distribution while the Ruffini endings detect slips at the fingertips. The rapid-adapting receptors include Meissner corpuscles that detect light touch, grip control and texture discrimination while Pacinian corpuscles detect movement between the skin and an object and play a determinant role to perception of surface texture[151]. When an object is handheld, cutaneous surface deformations are sensed by these mechanoreceptors which precondition the release of motor commands to adjust the manipulative actions.

Cutaneous mechanoreceptors in the hand provide explicit information about the kinematics and position of the hand and fingers and the grip forces exerted during grasping and object manipulation[152]. Visual information about the physical properties of the object may also aid to adjust the appropriate grip force[150]. In healthy individuals, grip force is appropriately modulated such that it always exceeds the minimum force required to prevent slippage by approximately 20%[153]. Somatosensation also contributes to combining component parts of movement such as transport and grasp. A lack of tactile somatosensation impairs the control of grasp and in particular, the kinematics of finger-opening phase resulting in increased duration of finger opening and increased maximum finger aperture. It was also found that tactile input affects the reaching component with an increase in variability in hand path. However, the total extent of hand path, the spatial relations between the finger aperture and closure phase were not influenced by a lack of somatosensation[113]. Additionally, the duration of the finger closure phase was least affected. These findings emphasise the use and need for somatosensory information in a motor task.

2.4 DEFICITS IN REACH-TO-GRASP AFTER STROKE

After stroke, RTG movements are disrupted as a result of various residual motor and somatosensory impairments[154]. Upper extremity movements are slower, less coordinated, and less efficient after stroke compared to healthy individuals[154,155]. Deficits are evident in the reaching phase, i.e., the transport phase (involving more proximal muscles of the arm) and grasp (involving more distal muscles of the arm and hand) components of the task[156]. These motor impairments can be precisely quantified during forward reach in survivors of stroke using kinematic motion analysis (end point error, peak velocity, movement time, reach extent) and movement quality variables (ranges of shoulder flexion, shoulder abduction, elbow extension, and elbow-shoulder cross-correlation) as these provide insight into motor control challenges of the upper limb after stroke[157].

2.4.1 Deficits in the transport phase (reach)

Kinematic studies have found that movement durations of the shoulder, arm and elbow are longer, with end-point trajectories being more segmented and variable in stroke survivors as compared to healthy controls. Ranges of angular motion in the elbow also decreased after stroke such that there is a strong association between the level of motor function and motor performance of the elbow and shoulder[154]. Further kinematic analyses of RTG found that movement duration was longer in stroke survivors, peak velocity was lower[158]with an increased variability of size and timing of peak velocity[159] compared to healthy individuals. Peak deceleration occurs in an earlier phase of the movement[158], with reduced movement smoothness characterised by an increased in the number of peaks in the velocity curve), compared to healthy adults[160].

2.4.2 Deficits in grasp phase

The relative time to maximal grip aperture occurs earlier in people with stroke compared to healthy individuals. However, when grasping a small object, both people with stroke and healthy individuals perform maximal grip aperture earlier than with a larger object[158,161]. People with stroke having mild to moderate hemiparesis tend to open their fingers excessively, resulting in greater maximal grip aperture compared to healthy

individuals[156]. Stroke survivors with severe hemiparesis may also have difficulty in accurately opening their fingers when approaching the object to be grasped[162]. This is due to a disruption in the coordination and time activation of finger muscles involved in the grasp aperture part and activation of proximal muscles involved in the hand transport. Difficulty in activating extensor muscles of the fingers and coordination of muscle activity between finger flexor and extensor causes grasp aperture to be inconsistent[162]. Additionally, stroke individuals with severe hemiparesis tend to initiate formation of grasp aperture in the deceleration phase of hand transport[139]. Significant reduction in independent finger movements has also been found in humans with lesions of the corticospinal tract following stroke[163]. For instance, volitional control of finger and thumb extension is affected after stroke, contributing to deficits in hand shaping during grasping and incorrect positioning of fingers for effective hand use[164].

2.5 IMPACT OF DEFICITS IN TACTILE SOMATOSENSATION ON GRASP

The ability to discriminate surface friction depends on the ability to detect and interpret tactile cues that arise when the object moves against the skin. The extent of slip between object and skin sends tactile cues to correctly adapt the grip force. Consequently, the amount of grip force required for a successful grasp is largely determined by the friction between the object and the skin[139,165].

Impaired tactile somatosensation after stroke makes it difficult to perform everyday tasks such as picking up a coin, holding an object without dropping it or crushing it. This includes difficulty in discriminating different physical properties of objects such as texture (rough, smooth), hardness (rigid, crushable) and extent of friction (slippery and non-slippery)[21]. As a result, the ability of the fingers and the hand to appropriately scale grip force for effective object handling, lifting and manipulation is impaired[165]. Impaired discrimination of surface friction contributes to pinch grip deficit after stroke[166]. Kinetic analyses of grip forces showed discoordination between grip and lift forces and inefficient scaling of grip forces in stroke survivors resulting in poor grip force control during object handling[156]. It also takes longer to reach the maximum grip force and larger grip forces during the preload phase as compared to healthy people[167,168]. Thus, impaired touch discrimination severely

compromises function to a larger extent than motor deficits alone[169] and adversely affects reacquisition of skilled movements of the upper limb[115,170]. In the absence of vision, poor friction discrimination results in longer latency of grip-lift and grip force dysregulation[166]. Therefore, in an attempt to compensate for somatosensory loss, people with stroke rely on their vision to gauge the force required in object grasping[171].

2.6 FUNCTIONAL RECOVERY AND RESIDUAL IMPAIRMENTS POST-STROKE

Recovery of upper limb function after stroke is a complex process that involves the combination of spontaneous recovery and learning-dependent processes through restitution, substitution and compensation[41,42]. The chronicity of the phases of stroke are characterised as acute (<1 month), subacute (1 month to 6 months) and chronic (>6 months)[172,173]. The timing of rehabilitation interacts with the spontaneous recovery processes during the acute and sub-acute phases and the learning processes involved in the chronic phase in stroke recovery. While the recovery process is greatest during the first 3 months after stroke[42], improvements are most significant in the first month following stroke[174]. Between 3 and 6 months, the functional gain is small[174], such that 50% of ischaemic stroke survivors (> 65 years) have hemiparesis at 6 months post-stroke[11]. At 6 months post-stroke, 11.6% stroke survivors achieve full functional recovery while 62% of individuals with stroke failed to regain dexterity[20]. In the chronic phase, up to 45% of people with stroke had persistent deficits in the upper limb[175-178]. Even though the extent of recovery declines with time, improvements are still possible in the chronic phase[42]. This was demonstrated by a study investigating factors predicting functional potential of the upper limb after stroke using transcranial magnetic stimulation and functional MRI. This study found meaningful improvements in upper limb function in people who showed the presence of motor-evoked potential responses to TMS at 3 years post-stroke[179]. Given the potential of functional recovery in the chronic phase, rehabilitation exercises should be pursued throughout life after stroke for interventions targeting upper limb recovery.

Initial severity is considered the best predictor of long-term motor outcomes, though it is limited in people who present with initial severe impairment after stroke[180]. Alternatively,

the viability of the corticospinal tract correlates with initial upper limb impairment and also accounts for upper limb outcomes beyond initial severity[181]. When combined with the National Institutes of Health Stroke Scale score, the viability of the corticospinal tract may be an efficient predictor for long-term upper limb recovery post-stroke as their predictions were accurate in 75% of patients with stroke[182]. It is noteworthy that this biomarker-based algorithm is limited to people within a few days post-stroke. Amongst stroke survivors with intact corticomotor integrity, upper limb motor impairments are expected to improve by 70% of their maximal recovery potential[183]. Those with a fractional anisotropy asymmetry of > 0.25 are likely to have poor improvements in the upper limb function, low functional potential and poor recovery of upper limb function[179,183]. It is therefore important to consider the effect of corticospinal tract damage on upper limb impairment when predicting potential recovery after an intervention.

2.7 NEUROPLASTICITY UNDERLYING SOMATOSENSORY AND MOTOR RECOVERY

Following stroke, the damaged brain attempts to recover through neuroplasticity by reorganising its structure, function and connections. Neuroplasticity refers to "the ability of neurons, neural circuits, and the brain itself to be modified and to reorganise both physically and functionally". This includes, but may not be limited to, changes in the strength of synaptic connections, the formation and elimination of synapses, dendrites, and axons as well as changes in the synaptic vesicular pool and content[184-189].

Seminal studies in animals provide preliminary evidence supporting the functional reorganisation of somatosensory and motor systems following motor or somatosensory tasks. One study investigated the relationship between manual dexterity tasks and activation of specific motor areas in monkeys during a pellet-retrieving task training using digits and wrist movements[190]. After 12 days of pellet-retrieving task training, an increase in digit representation in the motor cortex was observed, demonstrating reorganisation of movement representations in primary motor cortex following a motor task.

Another pioneering study investigated the relationship between somatosensory input and activation of the somatosensory cortex in monkeys[191]. Tactile stimulation was delivered which consisted of the distal part of the digits maintaining contact for 10-15 seconds with a rotating disc having raised and lowered surfaces. This study found that somatosensory tactile stimulation training resulted in functional reorganisation of primary somatosensory cortex[191]. Plasticity of the somatosensory cortex was also found during recovery of motor skills in adult monkeys following stroke[192]. This implies that somatosensory stimulation induces neuroplasticity in the somatosensory cortex which could result in improvement in motor function.

Besides the effect of somatosensory training on the somatosensory cortex, tactile stimulation was found to also improve motor recovery in adult rats following cortical injury[193]. Those receiving tactile stimulation significantly improved their motor performance compared to the control group that did not receive tactile stimulation, indicating that tactile stimulation enhanced motor recovery after stroke. The resulting improvement in both somatosensory and motor function following somatosensory stimulation demonstrates that somatosensory and motor functions are tightly coupled[193]. A study of neural mechanisms involved in developing novel motor skills amongst cats found highly specific projections from the somatosensory to the motor cortex, suggesting that these corticocortical projections have a role in providing the necessary feedback to neural modulation during learning of new motor tasks[194].

Functional reorganisation in the somatosensory and motor cortices have been evidenced following upper limb somatosensory or motor tasks in stroke survivors[195-202]. Furthermore, in people with chronic stroke, MRI analyses have shown increased activation responses in the somatosensory-motor cortical area, including the hand region of the pre-central gyrus, the post-central gyrus, the ventral post-central gyrus, the secondary somatosensory cortex and the supplementary motor area following tactile stimulation[203]. Based on the effect of somatosensory stimulation on reorganisation of the somatosensory cortex and the motor cortex, this may suggest that there is a need to couple somatosensory

training with motor interventions in order to obtain significant improvement in somatosensory-motor function of the upper limb after stroke. Given the connections between somatosensory deficits and motor impairments, it is hypothesised that if volitional muscle activity is coupled with enhanced somatosensation, this will result in increased activation of integrated motor and somatosensory brain networks. Stronger connections may be formed between the somatosensory cortex and the functionally related motor cortex to boost neuroplasticity. Coupled movement and somatosensory training replicates the way motor and sensory functions are jointly integrated in tasks are performed in everyday life. It is expected that combined movement and somatosensory interventions will maximise improvement in upper limb function to a larger extent than if movement and somatosensory interventions were delivered separately. A few studies of upper limb interventions in stroke rehabilitation have attempted to train somatosensation and movement in the same treatment session (Chapter 3). However, their efficacy on somatosensory and motor impairments and functional deficits have not been reviewed.

2.8 STRATEGIES TO OPTIMISE UPPER LIMB INTERVENTIONS

In order to optimise upper limb recovery after stroke, somatosensory and motor interventions have traditionally focused on learning-based strategies such as repetitive practice[204-207] and augmented feedback[157].

2.8.1 Intensive repetitive practice

Intensive repetitive practice is strongly recommended in stroke rehabilitation guidelines internationally to induce neuroplastic changes driving recovery of upper limb function[204-207]. A recent meta-analysis explored the dose-response relationship in stroke rehabilitation and found a positive relationship between time scheduled for therapy and improvement in motor therapy for adults after stroke[208]. This review concluded that large doses of therapy lead to clinically meaningful improvements. Although the optimal dose of therapy time and repetitions in stroke rehabilitation is yet to be determined, it is feasible for stroke survivors to complete at least 300 repetitions of task specific training of the upper limb in 1 hour[209]. This is in stark contrast to therapy delivery in actual clinical practice whereby

upper limb therapy sessions last between 0.9 and 7.9 minutes, with an average of only 32 repetitions completed[210]. Furthermore, the concept of intensive repetitive practice differs between motor and somatosensory training. Traditionally, motor training has prioritised high volume repetitions as a key active ingredient to induce cortical reorganisation[211] in order to improve motor learning[212] and motor functions[62]. On the other hand, somatosensory retraining strategies have focused on duration of exposure to the stimuli to improve somatosensory functions[213]. Therefore, it is recommended that people with stroke perform high numbers of repetitions as well as being sufficiently exposed to a target stimuli during therapy to improve their upper limb function.

2.8.2 Augmented feedback

The addition of feedback to upper limb training to enhance somatosensory-motor learning and skill acquisition is widely acknowledged[214,215]. Feedback involves provision of somatosensory and motor information provided during or after a task performance. Feedback can be classified as either intrinsic or extrinsic. Intrinsic feedback involves the individual's own somatic information (e.g touch, proprioception, vision) obtained as a result of the task being performed. Extrinsic (or augmented) feedback relates to the environment and is provided by an external source. Augmented feedback is provided in addition to intrinsic feedback or can substitute for it. Augmented feedback is categorised as knowledge of results or knowledge of performance. Knowledge of results is 'externally presented information about the outcome of performing a skill or about achieving the goal of the performance'. Knowledge of performance is "information about the movement characteristics that led to the performance outcome"[216]. Augmented feedback can be verbally directed to focus attention on body movements (internal focus of attention, e.g., open your fingers more), or on the effects of the movement on the environment (external focus of attention, e.g., move closer to the jar)[217]. Augmented feedback provided during motor training (e.g., task specific training, virtual reality, robot-mediated therapy) enhances improvement in motor performance[218].

Kinematic feedback, which often involves a graphical display of results as a source of information feedback to the learner has been found to be effective in the acquisition of

bimanual skills[219]. Amongst stroke survivors, external focus feedback contributed to shorter movement durations and increased peak velocities during a RTG task[220]. Moreover, the beneficial effects of external focus feedback were enhanced when preceded by internal focus feedback amongst stroke patients[215]. This is because the use of implicit information is impaired after stroke[221], such that explicit information is integrated using internal focus feedback, which is in turn used to enhance implicit processes when external focus feedback is provided[222].

There is limited evidence primarily from Carey's team on the integration of feedback in somatosensory interventions after stroke. In one randomised controlled trial (n= 50), somatosensory feedback has been integrated in somatosensory training for stroke individuals resulting in significant improvement in texture discrimination, limb position sense, and tactile object recognition[213]. Feedback was provided: a) on the accuracy of response by allowing the client to see the correct response, the therapist telling the client or by exploration of the stimulus by the client with the other hand[223,224]; b) on the actual somatosensation and critical difference of the somatosensory attribute being trained[223]; c) movements that are most optimal to explore the somatosensory attribute e.g. static contact, lateral motion, contour following[225]; and d) using calibration which involves comparison of the somatosensation with the other hand[223].

Online concurrent feedback is still under development in stroke rehabilitation. There is preliminary evidence that online augmented kinematic feedback regulated by vision has been found to improve the velocity, acceleration, and jerk during transport as well as grasp aperture amongst healthy individuals[226]. No evidence has been found on the use of online concurrent somatosensory feedback in upper limb rehabilitation after stroke. In clinical practice, feedback on motor performance relies on observable production of motor movements. Similarly, feedback on somatosensory performance relies on interpretation of somatosensory stimulation. It can therefore be expected that provision of online concurrent motor and somatosensory regulation using visual feedback can further enhance somatosensory-motor learning and improve upper limb function.

The feedback delivery schedule can be continuous (provided on every trial), summary (after a fixed trial number), faded (initially every trial, then after several trials) or bandwidth (provided on trials where errors are outside the band of correctness)[157]. However, feedback provided too frequently can compromise motor learning by making the learner more dependent on the feedback[227,228]. Alternatively, faded feedback has been recommended to improve motor learning in stroke survivors[229]. However, there is a lack of evidence on optimal reduced feedback schedule in people with stroke[157,230]. It is also unclear whether all stroke survivors will equally benefit from reduced feedback frequency[157].

The next section of this chapter reviews the literature on assessment tools used to evaluate grasp deficits and the reliability of these measures. Currently, there is a lack of objective and reliable measures to evaluate grasp deficits post-stroke. This thesis addresses the development of a novel outcome measure to evaluate grasp forces (Chapter 6), which was a key component evaluated in the COMPoSE trial (Chapter 5).in line with the recommendations of the Stroke Recovery and Rehabilitation Roundtable[231].

2.9 EVALUATION OF GRASP DEFICITS

Analysis of grip strength or force is necessary to unmask subtle deficits in the efficiency of grasps. Grip strength is widely used to characterise muscle weakness after stroke[232,233]. Grip dynamometry is a standard method of measuring grip strength which quantifies the amount of force that the hand can squeeze around a dynamometer[234]. Grip dynamometry is quick to administer to stroke survivors[235], making it readily usable in research and clinical settings[236].

Dynamometers can be classified as hydraulic (e.g Jamar), pneumatic (e.g Martin Vigorimeter), mechanical (e.g Harpenden dynamometer) and electronic devices (e.g Isometric Strength Testing Unit)[236]. Amongst grip dynamometers, the Jamar hand dynamometer is the most commonly used[237-241]and is accepted as the gold standard[242]. Also, the Jamar dynamometer has excellent test-retest reliability in healthy adults (ICC 0.82)[243] and in people with stroke (ICC 0.80-0.89)[244]. To detect a genuine change in grip strength with the Jamar, a change of more than 6Kg[245] is required for healthy adults[245] and a change of 4.7-6.2 kg is required for people with stroke[236]. Consequently, the Jamar dynamometer lacks responsiveness to detect to changes in people with severe loss of grip strength post-stroke who are unable to achieve a genuine change[246]. Moreover, the Jamar dynamometer requires frequent calibration to maintain its reliability[247]. In addition, considerable heterogeneity has been found between the measurement protocols used with regards to body position, encouragement provided, and intervals between measurements, which limits comparisons across studies[236,241].

Measurement of grip strength is commonly performed in stroke trials[248]. In people with stroke, grip strength correlates closely with higher levels of independence in activities of daily living[249] and improvements in grip strength are associated with upper limb functional recovery[250,251]. Maximal grip strength is used as a representative measure of upper limb recovery in stroke rehabilitation due to its moderate to high correlations with upper limb function and performance[244,252,253]. While the relevance of maximal grip strength measurements has been clearly recognised[244,252], a recent overview of systematic reviews (2004-2014) on upper limb outcomes after stroke found insufficient psychometric robustness of grip strength with regards to reliability, validity, responsiveness or amount of change and therefore limited its clinical utility[254]. Additionally, using grip dynamometry to evaluate maximal grip strength over a short duration does not provide insight into possible variation of grip strength throughout the duration of the grip[255]. Alternatively, the analysis strength data versus time curves during a sustained grasp was useful in characterising motor or functional limitations after stroke[195,256].

Sensor-based devices can be used to evaluate grip force based on strength-time profiles. However, little attention has been paid to their use despite their higher sensitivity. Kinetic measures such as force and torque trends can be used to evaluate paresis[257]. These measures have been advocated in stroke trials by the Stroke Recovery and Rehabilitation Roundtable as they facilitate the distinction between behavioural restitution and compensation post-stroke, though the specific kinetic parameters are yet to be established[231]. Several studies have reported the use of sensors to measure unidirectional forces produced by individual fingers[258-260]. Advanced sensor-based technologies such as Interlink FSR® [261], Peratech QTC™[262], Tactilus® [263], Sensitronics® [264] and Tekscan grip pressure mapping system (South Boston, MA, USA)[265]have been used to sense pressure in hand or grip evaluations[266-271]. These sensors are based on piezoresistive sensing technology and are stiff and frail, though they have good sensitivity[272,273]. The TactArray pressure distribution system (Pressure Profile System, Los Angeles, CA, USA)[274] is another sensor-based technology that uses capacitive tactile pressure sensing which is amongst the most sensitive techniques to detect small variations in pressure with the fingers[275].

Because of its high sensitivity, TactArray has been used in surgical robots for tissue palpation[276] and in robotic hands to detect slippage in dextrous tasks[277]. These studies indicate that pressure sensors could be an objective and sensitive means to evaluate grip deficits in stroke. However, prior to the application of a sensor-based device in stroke trials, its psychometric properties need to be assessed.

Psychometric properties provide guidance to the selection of an appropriate outcome measure. Several psychometric properties influence the clinical utility of an outcome measure, namely the reliability, the validity, the responsiveness and the minimal clinically important difference. Reliability is defined as the repeatability or reproducibility of a measure[278]. Validity concerns to the extent to which an instrument measures what it intends to measure[278]. Responsiveness refers to the ability of a measure to detect change over time[279]. The minimal clinically important difference is the smallest amount a measurement must change to be meaningful to patients[280]. As part of the development of an outcome measure, this thesis explores the evaluation of reliability of grasp forces measured with the Tactarray (Chapter 6) which was used as an outcome measure in the COMPoSE trial (Chapter 5).

2.10 EVALUATION OF TEST-RETEST RELIABILITY

To evaluate the test-retest reliability of a measure, retest correlations have been commonly used to estimate the magnitude of association between repeated measures[281]. Pearson correlation coefficients and intraclass correlation coefficients (ICCs) are the most common techniques to assess reliability. However, the use of the Pearson correlation is limited as it cannot assess systematic bias and is largely dependent on the range of values in the sample[282]. The ICC which is an agreement index between repeated measures (only the variance between participants) is also limited as it also depends on the rank of the participants in the sample. The ICC is preferred to the Pearson correlation as the latter overestimates the true correlations for small sample sizes (<15)[283,284].

Another limitation of the ICC is that the value of the correlation is sensitive to sample heterogeneity[281,283] which consequently has several implications. Firstly, the reliability ICCs should be compared only if they have been estimated from the same population[285], implying that it is not meaningful to compare the reliability between healthy participants and those of patients. Moreover, it could be argued that a measure that shows poor reliability in healthy participants is unlikely to be better in a patient population due to larger variability within and between patients. Therefore, findings from the healthy group could assist the selection of a reliable measure and improve the design of longitudinal studies involving patients[286]. Secondly, a heterogeneous sample could yield high ICC values even if the within-subject variation was large[281]. This implies that two sets of data could be highly correlated but not necessarily repeatable and this error would not be detected by the ICC. It is therefore recommended to provide additional measures of reliability using absolute estimates of reliability such as the percentage change in mean and the typical error to prevent erroneous estimation of reliability[281,283,284] as reinforced by other reliability studies[287-291].

The change in mean reflects the random and systematic changes in the mean value between two consecutive testing sessions. The random change in the mean accounts for random errors of measurement that can make the mean for each testing session vary, such as fatigue. The systematic change in the mean accounts for non-random changes in the mean value between 2 testing sessions applicable to all participants, such as a learning effect[283,285].

The typical error reflects the random changes in the mean which result from biological variations in individuals and mechanical variations in the assessment tool[283]. In order to keep biological variations small, the length of time between two testing sessions should preferably be short[285]. The typical error is a better index of reliability than ICC because it is independent of sample size[283,284]. The typical error can be expressed as a coefficient of variation (%CV)[283,284]which reflects the variability of scores from trial to trial for specific individuals. Therefore, the typical error and coefficient of variation are independent of where the individuals rank in a sample, unlike the ICC[281]. Exploration of heteroscedasticity, i.e., presence of variation of typical error is also encouraged to determine whether the data should be log-transformed prior to evaluating reliability[281].

2.11 CONCLUSION

Stroke survivors suffer from motor and somatosensory deficits that severely impair their ability to perform tasks of daily living. Further studies need to be conducted to evaluate interventions combining somatosensory and motor training to improve upper limb recovery after stroke. There is also a need to develop objective and sensitive outcome measures to better characterise grasp deficits after stroke.

CHAPTER 3: COMBINED SOMATOSENSORY AND MOTOR TRAINING TO IMPROVE UPPER LIMB FUNCTION FOLLOWING STROKE: A SYSTEMATIC SCOPING REVIEW

Preface

This chapter presents the results from a systematic scoping review investigating thesis Aim 1 (i.e., to conduct a systematic scoping review of interventions combining somatosensory and motor training to improve upper limb function after stroke). This study was conducted to investigate Research Question 1 (What interventions combining both somatosensory and motor training, currently exist for the treatment of upper limb function in stroke and which of these combined interventions are effective in improving upper limb function after stroke?).

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Contribution statement:

I was responsible for leading all stages of this systematic scoping review. I devised and ran the search strategy, and conducted the title, abstract and full-text screening assisted by Professor Paulette van Vliet. I was responsible for leading and conducting the data extraction, quality appraisal and synthesis of results for included articles with the support of my supervisors. I drafted the full manuscript which has been approved by my supervisors.

3.1 ABSTRACT

Title: Combined somatosensory and motor training to improve upper limb function following stroke: a systematic scoping review

Purpose: The purpose of this systematic scoping review was to 1) identify combined somatosensory and motor training interventions for the upper limb and their training components, and 2) review the efficacy of the combined interventions.

Methods: Participants were adults post-stroke with somatosensory and/or movement deficits in the upper limb. All studies with interventions combining somatosensory and motor training and targeting the affected upper limb were included. Outcome measures were assessments of somatosensory and/or motor impairment and upper limb function.

Results: Ten studies (n= 219) were included, comprising three randomized controlled trials, two pre-post studies with non-randomized comparison groups, three single-case experimental studies, and two case reports. There was heterogeneity across studies with regards to intervention contents and dosage, participant characteristics, and outcome measures. The interventions included combinations of tactile stimulation/discrimination, proprioceptive stimulation/discrimination, haptic object discrimination/recognition, movement training, and functional training. Only one group study, a non-randomized controlled study with multiple active components and the largest dose of treatment, found significant improvements in fine motor and somatosensory measures. Some improvements were found in case studies.

Conclusion: There was little consistency across "combined somatosensory and motor training" interventions and few have been rigorously tested for efficacy across somatosensory, motor and functional outcomes.

Key words: stroke, somatosensory, motor, arm, hand, upper limb, rehabilitation

Combined somatosensory and motor training to improve upper limb function following stroke: a systematic scoping review

3.2 INTRODUCTION

3.2.1 Background

Together somatosensory and motor functions are important for goal directed action of the upper limb (UL)[292]. Movement execution is important for reach, grasp and release, and contributes to functional use of the UL. Somatosensation also plays a critical role in arm and hand function, and is essential for successful object recognition and manipulation[293]. Seminal studies on motor and sensory representations in the sensorimotor cortex demonstrated that controlled motor performance, or action of the UL, relies on the accurate processing and interpretation of somatosensory input before and during movement execution. Thus functionally, somatosensory and motor networks are tightly coupled[34,35].

Following stroke, more than 85% of individuals suffer from residual UL movement deficits due to incomplete motor recovery[20] and one in two stroke survivors have deficits in somato (body) sensations[21]. Somatosensory deficits impact functional loss in the UL[21] and are associated with reduced arm use[294] and return to previous life activities[295]. To date, UL training has typically focused on motor function, often to the exclusion of sensory rehabilitation[296], and interventions are usually targeted to either motor or somatosensory deficits. Ignoring the contribution of sensory systems to skilled tasks could result in interventions with submaximal efficacy regarding the somatosensory[213]and motor re-learning underlying functional recovery post-stroke[297]. It is proposed that purposefully combining somatosensory training with motor training may lead to greater improvements in the stroke-affected UL than if only somatosensory *or* motor training is provided or if they are provided at different times. It is suggested that this added benefit may occur by eliciting greater focal and/or functionally-connected brain activation in the motor *and* somatosensory networks during *combined* sensorimotor training, i.e., training that provides combined and temporally integrated use and feedback of *both* somatosensory and motor functions during use of the UL.

Three systematic reviews[45,62,63], two with meta-analyses[62,63], and one scoping review[298] have investigated the effects of somatosensory *or* motor interventions alone on sensorimotor outcomes and/or UL function after stroke. High-level evidence for specific interventions addressing somatosensory or motor impairments is limited, except for positive effects of constraint-induced movement therapy based on meta-analyses[62,63]. Though summary effect sizes for sensory rehabilitation of the UL indicate positive outcomes for somatosensory functions, outcomes were non-significant for motor functions[63]. Overall, there is moderate level evidence for high intensity task-oriented and task-specific training[63]. Combined somatosensory and motor interventions were not included in these reviews.

A previous scoping review[299] synthesized the research describing the effects of sensorimotor interventions on UL function in various UL conditions, however this review included evidence from only two studies with a stroke population. Thus, to date there has been neither comprehensive review nor synthesis of the evidence from "combined somatosensory and motor training" interventions on UL function for people after stroke.

3.2.2 Objectives

The primary objective of this systematic scoping review was to identify existing literature reporting the use of "combined somatosensory and motor training" interventions to improve UL function after stroke and characterize the training components and combinations used. A secondary objective was to review and synthesize the efficacy of these combined interventions to improve somatosensory and motor impairments and UL function after stroke.

3.3 METHODS

For the primary objective, this systematic scoping review adhered to the methodological framework of a scoping review suggested by Arksey and O'Malley[300] and

Levac et al.[301]. The methods for searching, screening and reviewing abstracts were conducted in a systematic way[302]. For the secondary objective, this review adhered to the standards of reporting efficacy of the interventions for systematic reviews[303](PROSPERO 2015 CRD42015017288). Currently there are no standardized guidelines to report scoping reviews though The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)-extension for Scoping Reviews (PRISMA-ScR) is currently being developed[304]. As the studies included complex interventions consisting of two types of UL training[305], thePRISMA checklist for Complex Interventions(PRISMA-CI)[306,307] was used to guide the reporting of this systematic scoping review.

3.3.1 Identification of studies

The search strategy was developed using a combination of controlled vocabulary (MeSH) and free text terms for MEDLINE and modified to suit other databases. The key terms included: stroke, cerebrovascular disorder, hemiplegia, upper extremity, rehabilitation, physiotherapy, occupational therapy, somatosensory and motor. The search terms can be found in Appendix 3.1, Supplementary Material. The electronic databases used were: MEDLINE (1950 to September 2018), Cochrane Central Register of Controlled Trials (CENTRAL), EMBASE (1980 to September 2018), CINAHL (1982 to September 2018), AMED (1985 to September 2018), Johanna Briggs Institute library, Cochrane Database of Systematic Reviews and Cochrane Controlled Trials Register, Database of Abstracts of Reviews of Effect. Grey literature databases accessed were dissertations through ProQuest and full paper conference proceedings. Stroke-specific online databases such as the Stroke Engine and the Evidence-Based Reviews for Stroke Rehabilitation were searched. Hand searching of journals and bibliographies of relevant systematic reviews and other narrative reviews, as well as web searching on the internet, were also performed. The search was limited to publications in English. Studies were excluded if only an abstract was available.

3.3.2 Inclusion criteria

3.3.2.1 Design of Studies

All study designs with interventions combining both somatosensory and motor trainingof the affected UL were included. The studies had to have a specific design objective to improve somatosensory and/or motor impairments and UL functions.

3.3.2.2 Types of Participants

Participants were adults (18 years and older) with stroke[308]. Participants must have had a somatosensory or motor deficit in the UL, or both.

3.3.2.3 Interventions

The interventions had to include at least one somatosensory and one motor training component targeted at treatment of the UL and delivered within the same treatment session. Focus was on active somatosensory and motor training. Training approaches incorporating only passive stimulation were excluded (Table 3.1). Studies with adjunct activities in addition to the “combined somatosensory and motor training” were included.

Table 3.1. Inclusion and exclusion criteria of somatosensory and motor training components

Somatosensory	*Inclusion: Active somatosensory training* • Training tasks designed specifically to train somatosensory function in the context of active exploration with the involved hand *Exclusion: Solely passive somatosensory stimulation/discrimination* • Invasive or non-invasive stimulation (e.g., weight-bearing tasks, thermal stimulation, pneumatic compression, vibration training, peripheral magnetic stimulation, acupuncture, electrical stimulation, brain stimulation techniques to produce activation of cutaneous nerves in the absence of active and voluntary muscle contraction) • Non-specific passive stimulation (e.g., rubbing the limb with an object or material with a specific texture, icing, or mirror therapy)
Motor	*Inclusion: Active motor training* • Exercises designed to train motor function, and to involve voluntary muscle contraction initiated by the central nervous system • Robotic components, if the robot assisted active movements • Electrical stimulation coupled with active exercises *Exclusion: Solely passive motor training* • Generating a muscle contraction but not physiologically triggered by the central nervous system (e.g., electrical stimulation, non-invasive cortical stimulation) • Not generating any active muscle contraction (e.g., passive movements, robotics where the upper limb is moved passively by the robot, motor imagery)

3.3.2.4 Outcome measures

To determine the efficacy of interventions, any measurement of somatosensory and/or motor impairment or function of the paretic UL was included.

3.3.3 Selection of studies

Two authors (UG and PvV) independently screened the titles, abstracts and full text articles against the inclusion criteria. If there was disagreement, consensus was reached through discussion.

3.3.4 Assessment of methodological quality

The methodological quality of the included studies was assessed using a 24-item scale; The Structured Effectiveness Quality Scale (SEQES)[309]. The level of evidence of each study was graded according to the Oxford Centre for Evidence Based Medicine Levels of Evidence system[310,311]. Two review authors (UG and PvV) independently assessed the methodological quality of the studies and the level of evidence. An intra-class correlation coefficient and 95% confidence intervals were used to assess inter-rater reliability of total SEQES scores using SPSS 24 (SPSS Inc, Chicago, IL) based on average measures, absolute-agreement, and 2-way random-effects model. Weighted kappa was used to assess and interpret the inter-rater agreement between the two raters for each study[312].

3.3.5 Data extraction and management

Data extraction was carried out independently by the two reviewers (UG and PvV) and entered into a standardized data extraction form. The following data were summarized: description of the "combined somatosensory and motor training" interventions, dosage of intervention, the outcome measures for somatosensory and motor impairments and UL function, participant characteristics and study design.

3.3.6 Data synthesis

Descriptive statistics (means and standard deviations) were used to summarize the findings. Effect sizes (standardized mean differences) were calculated as Cohen's d for each study comparing post-intervention outcomes with baseline measures where sufficient data were reported for pre- and post-intervention mean scores[313]. Reporting and interpretation of effect sizes adhered to guidelines recommended by Durlak[314]. For controlled trials, the effect size of the difference between pre- and post-intervention within-groups and between-groups were calculated. Effect size calculations were adjusted for non-randomized controlled trials (non-RCTs) to correct for non-randomized differences between the study groups in the outcome measures at baseline and differences in sample sizes of the study groups[314]. Cohen's d values were converted to Hedges's g for between-group comparisons in controlled trials to correct for bias due to small sample sizes ($n<20$)[315]. For single-case experimental studies[316] and case reports[316], effect size estimates for changes in individual participants were reported as the raw difference in means between pre- and post-tests within each individual, as well as the percentage change from pre to post-test[317]. The formulas to calculate effect size for each type of study design are summarized in Appendix 3.2, Supplementary Material. To interpret the effect sizes, these were described as follows: small, d=0.2, medium, d=0.5, or large, d=0.8 based on standards suggested by Cohen[313].

3.4 RESULTS

The selection process for the inclusion and exclusion of trials is summarized using the PRISMA flow diagram (figure 3.1). Of 2813 non-duplicate titles identified, 132 full-text articles were assessed for eligibility and 10 articles were included[318-327].

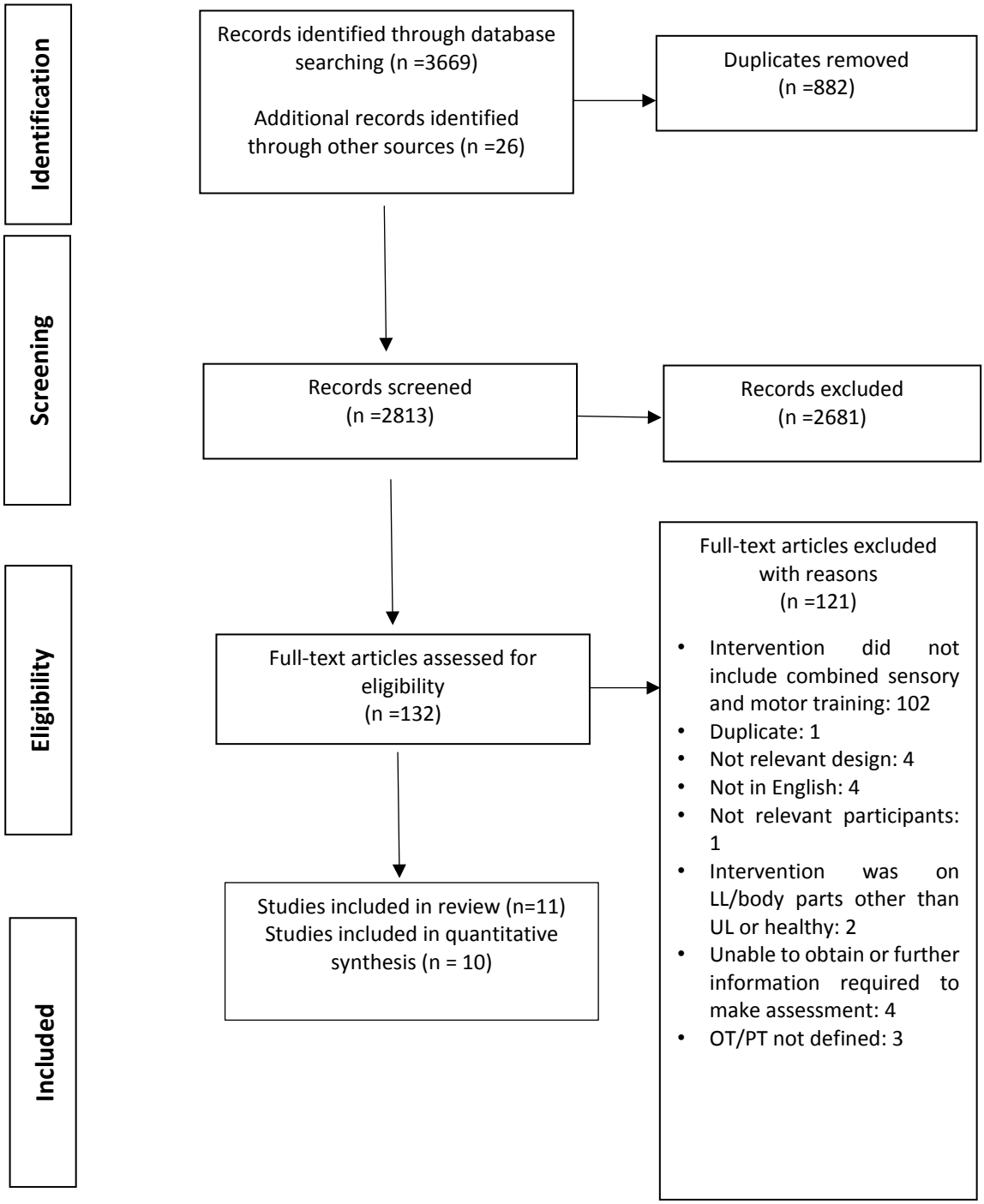


Figure 3.1. PRISMA flow diagram of study selection

3.4.1 Study designs

The experimental designs varied across studies. One intervention was evaluated in three clinical trials: two single-case experimental studies, one in sub-acute[322] and one in chronic[327] stroke participants, and one 4-arm RCT[323] in people with sub-acute stroke. Two other RCTs were conducted in people with acute[319] or chronic stroke[321]. One study[318] was a post-hoc dose-response analysis of a prior 3-arm study. One pre-post study[326] compared the effects of their intervention in two groups of stroke participants with sensorimotor deficits and neglect, respectively; only findings from the sensorimotor deficit group were included in this review. The remaining studies were a single-case experimental study[325] and two case reports[320,324].

3.4.2 Methodological quality scores (SEQES) and level of evidence

The methodological quality scores (SEQES), level of evidence and weighted Kappa scores are summarized in Table 3.2. Six studies were high quality (SEQES 33-45, level of evidence 2-4)[318,319,321-323,327], three moderate quality (SEQES 22-27, level of evidence 3-4)[324-326] and one low quality (SEQES 9, level of evidence 4)[320]. High inter-rater reliability was obtained between the two independent raters (ICC= 0.98; CI: 0.92-1.00). The values of weighted kappa across the 24 SEQES items ranged from 0.56 to 1.00. The kappa agreement was very good in six studies, good in three studies and moderate in one study.

Table 3.2. Methodological quality scores (SEQES) and Oxford level of evidence

Study	Study question	Study design							Subjects				Intervention			Outcomes			Analysis					Recommendations	Total (48)[a]	SEQES grading[b]	Oxford level of	Weighted Kappa[c]	Kappa agreement
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24					
Hunter et al. (2011)[323]	2	2	2	2	2	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2	45	High	2	0.83	Very good
Chanubol et al. [319]	2	2	2	2	2	1	1	2	2	2	2	2	2	2	2	2	2	1	2	2	1	2	2	2	44	High	2	1.00	Very good
Hunter et al. (2008)[322]	2	1	2	2	0	1	1	0	2	2	1	2	2	2	2	2	1	2	2	0	2	2	1	2	36	High	4	0.68	Good
Byl et al. (2008)[318]	1	1	2	2	1	1	1	2	1	2	1	1	2	2	2	2	2	1	2	1	1	0	1	2	34	High	3	0.56	Moderate
Diego et al. (2013)[321]	2	2	2	2	2	1	1	2	1	2	0	2	2	1	2	1	1	1	2	0	1	1	0	2	33	High	2	0.94	Very good
Winter et al. (2013)[327]	2	1	2	2	1	1	1	0	2	2	1	2	2	0	2	1	1	1	2	0	1	2	2	2	33	High	4	0.75	Good
Song et al. (2013)[326]	1	2	2	2	0	1	1	0	1	2	0	2	1	1	2	1	1	1	2	0	1	1	0	2	27	Moderate	3	0.95	Very good
Smania et al. (2003)[325]	2	0	2	2	0	1	1	0	2	2	0	2	2	0	0	1	1	2	2	0	1	2	0	2	27	Moderate	4	0.91	Very good
Molier et al. (2011)[324]	1	0	2	2	0	1	1	0	1	2	0	2	2	1	0	1	1	1	0	0	0	2	0	2	22	Moderate	4	0.86	Very good
Dannenbaum (1988)[320]	2	0	0	1	0	1	0	0	0	0	0	2	1	0	0	0	0	0	0	0	0	1	0	1	9	Low	4	0.79	Good

Study question

1. Was the relevant background work cited to establish a foundation for the research question?

Study design

2. Was a comparison group used?
3. Was patient status at more than one time point considered?
4. Was data collection performed prospectively?
5. Were patients randomized to groups?
6. Were patients blinded to the extent possible?
7. Were treatment providers blinded to the extent possible?
8. Was an independent evaluator used to administer outcome measures?

Subjects

9. Did sampling procedures minimize sample/selection biases?
10. Were inclusion/exclusion criteria defined?
11. Was an appropriate enrolment obtained?
12. Was appropriate retention/follow-up obtained?

Intervention

13. Was the intervention applied according to established principles?
14. Were biases due to the treatment provider minimized (i.e., attention, training)?
15. Was the intervention compared with the appropriate comparator?

Outcomes

16. Was an appropriate primary outcome defined?
17. Were appropriate secondary outcomes considered?
18. Was an appropriate follow-up period incorporated?

Analysis

19. Was an appropriate statistical test(s) performed to indicate differences related to the intervention?
20. Was it established that the study had significant power to identify treatment effects?
21. Was the size and significance of the effects reported?
22. Were missing data accounted for and considered in analyses?
23. Were clinical and practical significance considered in interpreting results?

Recommendations

24. Were the conclusions/clinical recommendations supported by the study objectives, analysis, and results?

[a]SEQES scale: Each item is given a score of 2, 1, or 0 based on comparison with specific descriptors, with 2 indicating the highest item score.

[b]Rating of SEQES score: low (scores 1–16), moderate (scores 17–32), high quality (scores 33–48) [309]

[c]Rating of agreement based on Kappa value: poor (<0.20), fair (0.20 to 0.40), moderate (0.40 to 0.60), good (0.60 to 0.80) or very good (0.80 to 1.00)[312]

3.4.3 Participants

A summary of the participant characteristics is presented in Table 3.3. Across the 10 studies that delivered an intervention, a total of 219 participants with stroke were included. Participant mean ages ranged from 51.8 to 74.8 years. The mean time post-stroke varied from < 2 weeks to 60.7 months. One study enrolled participants with acute stroke (<2 weeks post-stroke)[319], two included participants with sub-acute stroke (> 2 weeks and <6 months post-stroke)[322,323], and five studies included participants with chronic stroke (>6 months post-stroke)[318,320,321,324,327]. Two studies included a mix of subacute and chronic stroke participants[325,326].

3.4.4 Experimental interventions

1) Training components combined

The somatosensory and motor training components incorporated in the combined interventions varied considerably across the studies. To facilitate reporting, five categories were used to summarize the training components: 1) tactile stimulation/discrimination; 2) proprioception stimulation/discrimination; 3) haptic object discrimination/recognition; 4) movement components/whole movements; and 5) functional UL training (Table 3.4). Tactile stimulation/discrimination, proprioceptive stimulation/discrimination training and haptic object discrimination/recognition are forms of somatosensory training[225]. Training of whole movements or movement components are forms of motor training[328]. Functional UL training typically refers to training in the context of functional tasks[329].

Table 3.3. Participant characteristics, description of training protocols and results

Studies	Training protocol of experimental group	Dosage and Adjunct exercise	Outcome measures and Results
Hunter et al. (2011)[323] Single-blind RCT N: 76 Range time post-stroke:0.27-2.8 Mo Subacute stroke Stroke type: Ischaemic: 68; Haemorrhagic:7; unknown: 1 Site of lesion: Intracerebral haemorrhage:7 LACI:12 PACI:26 TACI:30 Unknown:1 ***Control group 1*** N: 19 (9 F, 10 M) Mean age, Y: 71.6 Time post-stroke, Mean (SD):0.98(0.51) Mo ***Experimental group 2*** N: 18 (7 F,11 M) Mean age, Y: 73.3 Time post-stroke, Mean (SD): 1.19(0.79) Mo ***Experimental group 3*** N:19 (11F, 8 M) Mean age, Y: 72.9 Time post-stroke, Mean (SD): 0.86(0.55) Mo ***Experimental group 4*** N:20 (11 F, 9 M) Mean age, Y: 72.5 Time post-stroke, Mean(SD):0.94(0.65) Mo	**Brief name:** mobilization and tactile sensation[330] **Sensory input (active and passive)**: Visual, auditory, verbal, non-verbal, thermal, environmental and auditory **Somatosensory tactile stimulation (active and passive):** touch/pressure **Proprioceptive training:** joint position, muscle position, skin position **Motor(passive):** - Massage - Soft-tissue stretch - Passive movements through anatomical range - Soft-tissue stretch: Passive movements through anatomical range- - Isolated/selective joint movement - Accessory movements - Placing hand on flat surface or edge/corner - Joint compression by weight-bearing through limb **Movement training(active):** coordinated movement of: - Reaching - Grasp and release - Fine finger activity **Facilitation provided by therapist for:** - Assisted mobilisation - Sensory feedback - Proprioceptive, visual and tactile feedback - Re-alignment of structure/body parts - Facilitation of muscle activity - Dynamic stabilisation	***Experimental groups:*** Group 2/3/4: varied doses of mobilisation and tactile stimulations (MTS) **Dosage experimental groups:** ***Group 2*** - Up to 30 min/session for 14 consecutive working days -Total dur Tx: 7 hrs - Actual total no. Tx, Mean (SD):12.3(1.3) - Actual total dur Tx, Mean(SD):5.40(0.82) hrs ***Group 3*** - Up to 1 hr/session for 14 consecutive working days - Total dur Tx : 14 hrs - Actual total no Tx sessions, Mean(SD):11.6(5.0)- -Actual total dur Tx , Mean(SD):8.70(3.39)hrs ***Group 4*** - Up to 2 hr/session for 4 days - Total dur Tx: 28 hrs -Actual total no. Tx sessions:22.2(7.5) -Actual total dur Tx, Mean (SD):15.36(4.47)hrs Adjunct exercise: **conventional physiotherapy** for all groups **Dosage Control group (**conventional physiotherapy): - 14 consecutive working days - Total no. Tx sessions: not reported - Total dur Tx: not reported	***Motor:*** Motricity Index (arm section) (MI); Action Research Arm Test (ARAT) **Between group difference:** *Corrected effect size Hedges g, [95% CI]:* ***Group 4 vs Group 1*** MI(arm): *0.262[-0.37,0.89] p=0.41 NS* ARAT: *0.207[-0.42, 0.84] p=0.51NS* ***Group 3 vs Group 1*** MI(arm):*0.261[-0.38, 0.90] p=0.42 NS* ARAT: *0.008[-0.63, 0.64] p=0.98 NS* ***Group 2 vs Group 1*** MI:*-0.115[-0.77, 0.54] p=0.73 NS* ARAT: *0.035[-0.62, 0.69 p=0.92] NS* ***Group 4 vs Group 3*** MI(arm)*:-0.066[-0.69,0.56] p=0.84 NS* ARAT: *0.182[-0.45,0.81] p=0.57 NS* ***Group 3 vs Group 2*** MI(arm):*0.276[-0.37,0.92] p=0.40 NS* ARAT:*-0.017[-0.66,0.63] p=0.96 NS* ***Group 4 vs Group 2*** MI(arm):*0.262[-0.38,0.90] p=0.42 NS* ARAT:*0.199[-0.44,0.84] p=0.54 NS* **Within group difference:** *mean [95% CI]* ***Group 4*** MI: *15.7[1.02,22.8] p<0.001 Sig diff* ***Group 3:*** MI:*17.0[0,27.8] p=0.007 Sig diff* ARAT:*6.6[0,13.4]* ***Group 2:*** MI: *10.2[0,22.1] p=0.01 Sig diff* ARAT:*6.8[0,9.7]* ***Group 1:*** MI: *12.4[0,16.4] p=0.001 Sig diff* ARAT: *6.5[0,11.4] p=0.024 Sig diff*

Ratanapat Chanubol et al. (2012)[319] Single-blind RCT Time post-stroke:<0.5 Mo Acute stroke Site of lesion: LACI: 26 PACI:4 TACI: 5 LACH:2 TACH:3 *Experimental group:* N: 20 (11 F, 9 M) Mean age, Y: 63.2 *Control group:* N: 16 (9 F,11 M) Mean age, Y: 60.0	**Brief name:** Cognitive sensory motor training therapy using Perfetti method **Integrated somatosensory-motor training (**joint position sense discrimination and movement training): - Passive to active movement of shoulder, elbow, wrist or finger to different positions - Passive movement of one joint at a time, followed by multijoint movements: - For joints with several planes of movement, training was conducted separately for each plane. - The participant reported their perception of the joint position after repositioning ***Progression of task difficulty****:* Proprioceptive training*:* Active joint position sense discrimination: perceptive tasks were individualized according to ability to discriminate (1) between 2-5 positions, and (2) between positions of specific joints in multijoint movements during complex tasks **Integrated somatosensory-motor training *(haptic object discrimination/recognition + active functional training):*** - Actively reaching the object and sensing its shape, position or size. (differentiation between 2-5 objects) - Gradual reduction of manual support until unsupported task completion	**Dosage experimental group:** - 30 min/ session/ 5x/ wk for 4 wks - Total no. Tx sessions: 20 - Total dur Tx: 10 hrs - Rest time: 15 min break if necessary *Adjunct exercise*: physiotherapy and swallowing therapy **Control group**: Conventional occupational therapy + physiotherapy and swallowing therapy	***Motor:*** ARAT, Box And Block ***Participation:*** Extended Barthel Index **Between group difference:** *Corrected effect size Hedges g* [95% CI] ARAT:*0.02[-0.60,0.64] p=0.95 NS* Box and block: *0.27[-0.35,0.90] p=0.38 NS* Extended Barthel Index: *-0.18[-0.81,0.44] p=0.56 NS* **Within group difference:** ***Experimental group:*** *raw mean difference (SD), Effect size* ARAT: *15.4(11.38), 0.88 Sig diff (p<0.001)* Box and block: 13.82(12.02), 0.83 *Sig diff* (p<0.001) Extended Barthel Index: 15.15(8.17), 1.66 *Sig diff* (p<0.001) ***Control group:*** raw mean difference (SD), *Effect size* ARAT: *11(10.39), 0.53 Sig diff (p<0.001)* Box and block: *8.25(10.42), 0.49 Sig diff (p<0.001)* Extended Barthel Index: *14.95(8.26), 1.78 Sig diff (p<0.001)*
Hunter et al. (2008)[322] Single-case experimental study ABA design (baseline-intervention-withdrawal phases) N:6 (2 F, 4M) Mean age, Y: 74.8 Time post-stroke, Mean(SD)[Range:2.07 (0.69)[1.26-3.33] Mo (< 3Mo) Subacute stroke Site of lesion: Right PACS / External capsule and lentiform nucleus:1 Left POCS/ upper pons and cerebral peduncle: 1	**Brief name:** mobilization and tactile sensation[330] See above description in Hunter et al. (2011)	**Dosage:** - 1 hr/session 5 days/wk for 6 wks - Total no. Tx sessions:30 - Total dur Tx :30 hrs *Adjunct exercise:* usual rehabilitation program focused on regaining general mobility and function	***Motor:*** MI(arm),ARAT **Within subject change:***% change* MI: 16-25%; Improvement in 2/6 participants ARAT: 7.0-29.8% in 6/6 participants; 17.5-29.8% clinically meaningful improvement in 3/6 participants

Right TACS/ middle cerebral artery :1 Right LACS/Ganglionic region: 1 Left OACS/frontoparietal region:1 Left PACS frontal/parietal lobe and posterior left lentiform nucleus, left middle cerebral artery territory:1			
Byl et al. (2008)[318] 3-arm pre-post non-RCT N=45 subjects (5 dropouts) Time post-stroke:>6 Mo Chronic stroke ***Experimental group 1:*** N:18 (6 F, 12 M) Mean age, Y: 63.2 Time post-stroke, Mean(SD):27.6(9.2) Mo ***Experimental group 2:*** N: 19 (8 F, 11 M) Mean age, Y: 62.6 Time post-stroke, Mean(SD): 27.6(20.4) Mo ***Experimental group 3:*** N:8 (3 F, 5 M) Mean age: Y: 61.1 Time post-stroke, Mean (SD): 28.8(25.2) Mo	**Brief name:** Learning-based sensorimotor training (LBSMT) **Tactile discrimination (active)**: matching tasks without vision (identifying/differentiating shapes, forms and textures) ***Progression of task difficulty****:* **-** proprioception, kinesthesia, vibration **Integrated somatosensory-motor training**: - Active graded movements e.g., force control of the hand **- Active haptic object discrimination/recognition:** Manipulation of objects with varying weights, shapes and surface textures **- Active functional training:** fine functional activities whilst focusing on their sensory aspects, mostly done with eyes closed, functional tasks **- Passive motor training:** mental practise of skilled arm movements prior to task performance; Use of mirror image of less affected hand to reinforce normal movements of the affected hand	***Experimental groups:*** Group 1: LBSMT + home program Group 2: LBSMT + walking Group 3: LBSMT increased dose + home program **Dosage experimental groups**: ***Group 1****:* - 1.5 hr/session for 1x/wk for 6-8 wks - Total no. Tx sessions:8 - Total dur Tx:12 hrs ***Group 2*****:** - 45 min/session for 3x/wk for 6-8 wks - Total no Tx sessions:17.7 - Total dur Tx:13.3 hrs ***Group 3:*** - 3 hrs/session for 4x/wk for 6-8 wks - Total no Tx sessions:24 - Total dur Tx:72 hrs ***Adjunct exercise:*** Walking: 35-45 min Home program:Patient and carer education	***Fine motor:***Digital reaction time test ***Gross motor:*** Combined Grip and Pinch strength ***Somatosensory:*** Sensory integration subtests and Praxis test (Kineasthesia, graphethesia) combined with Byl-Cheney-Boczai sensory discriminator Test ***Functional independence:***California functional evaluation test combined with subtests from Wolf Motor Function Test (item 8-16) **Between group difference:** *Mean, p value for mean % difference, Corrected effect size Hedges g* ***-Group 3 vs Group 1*** Digital reaction time test:*-96.6, p value not reported, -0.04971 NS* Grip pinch strength: *8.1, p value not reported, 0,0550 NS* Somatosensory:*-26.1, p value not reported, -0.71094 NS* Functional independence: *-380.3,p<0.018,0.0701 Sig diff* ***-Group 3 vs Group 2*** Digital reaction time test:*-146.6, p<0.016,* *-0.2753 Sig diff* Grip pinch strength: *6.4, p value not reported, 0.048831 NS* Somatosensory: *-28.2, p<0.002,-0.7044 Sig diff* Functional independence: *-85.3, p value not reported, 0.3112, NS* ***-Group 2 vs Group 1***

			Digital reaction time test: 50, p value not reported, 0.2256 NS Grip pinch strength: 1.7,p value not reported, 0.0061 NS Somatosensory: 2.1, p <0.043, -0.0065 *Sig Diff* Functional independence**:** -295, p value not reported, -0.2411 NS **Within group difference:** *% change Mean(SEM), p value, Corrected effect size* ***-Group 3*** Digital reaction time test: *-31.6(7.4), p<0.01), -0.4826 Sig diff* Grip pinch strength:*35.2(9.4), p<0.01, 0.2385 Sig diff* Somatosensory: -31.5(6.0), p<0.01,-1.0937 *Sig diff* Functional independence: *-55.5(4.1), p<0.0) -0.9754 Sig diff* ***-Group 2*** Digital reaction time test: *-6.3(6.2), p value not reported) , -0.1983 NS* Grip pinch strength: *26.5(15.6), (p<0.001),0.1881 Sig diff* Somatosensory:*-12.3(4.5), p<0.00),-0.366 Sig diff* Functional independence: *-40.8(5.5) p<0.0001, -1.297 Sig diff* ***-Group 1*** Digital reaction time test: *-8.6(1.8)), p<0.001, -0.4313 Sig diff* Grip pinch strength: *7.4(3.5), p value not reported, 0.1817 NS* Somatosensory:*8.9(7.8), p<0.0001, -0.3594 Sig diff* Functional independence: *-18.9(9.9), p value not reported, -1.0478 NS*
Diego et al. (2013)[321] Single-blind RCT Time post-stroke:>6 Mo Chronic stroke	**Brief Name:** Sensory stimulation and motor stimulation **Movement training (passive):**	**Dosage experimental group:** 60 min (30 min somatosensory stimulation training: + 30 min	***Motor:*** Fugl Meyer assessment (FMA); Motor Activity Log-Amount (MAL-AS); Motor Activity Log-How well (MAL-HW)

Experimental group: N:12 Mean age, Y: 61.9 Time post-stroke, Mean(SD):44.7 (24.5) Mo ***Control group:*** N:9 Mean age, Y:60.6 Time post-stroke, Mean(SD): 60.7 (58.2) Mo	- Specific movements of the hand to reduce muscle tone (pressure at metacarpophalangeal joints, passive mobilisation of thenar and hypothenar muscle groups and of interossei muscles) **Haptic object discrimination/recognition(active)**: - Holding objects of different sizes/shapes/weight and arranging them in order from smallest to biggest, consistency, weight or shape **Or Tactile discrimination (active)** - Patient must touch and name different texture with vision, then without vision **Integrated somatosensory and motor training (active haptic object discrimination/recognition + active functional training):** **- Reaching**: (1) Push objects placed on a table, (2) Touch object placed on a shelf at a different height **- Grasping**: (1) Grasp different fruits from a basket, (2) Take balls of different sizes from a box **- Handling**: (1) Open the lid of different containers, (2) Turn a box in the hand to read the labels at each side **- Supporting**: (1) Support with the hand to stand up from a chair, (2) Support with the upper limb when losing equilibrium **- Carrying**: (1) Carry a box in the hand, (2) Carry a shopping bag with the forearm - Facilitation of normal movements by therapist while avoiding compensations	functional training) /session,2x/wk for 8 wks - Total no. Tx sessions: 8 - Total dur Tx: 16 hrs *Adjunct exercise* (Functional activity training at home) - Passive tactile stimulation of hand with toothbrush - Mental imagination of activities of daily living practised - Practice of activities of daily living Dosage adjunct exercise: - 30 min: 1x/day for 8 wks - Total no. Tx sessions: 56 - Total dur Tx: 28 hrs **Control group:** Conventional rehabilitation according to Bobath concept	***Somatosensory:*** Tactile sensibility evaluation using Semmes-Weinstein monofilament (tactile discrimination); Proprioceptive sensibility (discrimination of motion, consistency discrimination, ***Participation and activity limitation:*** Stroke Impact Scale(SIS) **Between group difference:***Corrected effect size Hedges g, [95% CI]* FMA: *-0.357[-1.228, 0.514] p=0.41 NS* MAL-AS:*-0.838[-1.739, 0.063] p= 0.06 NS* MAL-HW:*-0.737[-1.629,0.156] p=0.1 NS* Tactile sensibility: *raw and mean values not reported* Proprioceptive sensibility: *raw and mean values not reported* SIS: *0.073[-0.791, 0.938] p=0.86 NS* **Within group difference:***mean difference (SD), Effect size* -Experimental group *FMA: 5*.1(2.55),0.31*Sig diff* p<0.05 MAL-AS: 0.27(0.75), 0.20: NS MAL-HW: 0.51(1.0.69),0.37*Sig diff* p<0.05 Tactile sensibility: *raw and mean values not reported. Sig diff p<0.05* Proprioceptive sensibility: *raw and mean values not reported. Sig diff p<0.05* SIS: 9.83(9.362),0.94 *Sig diffp<0.05* -Control group FMA: *3(2.55),0.11Sig diff p<0.05* MAL-AS: *0.13(0.75),0.002 NS* MAL-HW: *0.3(0.69),0.24 NS* Tactile sensibility: *raw and mean values not reported* Proprioceptive sensibility: *raw and mean values not reported* SIS: *0.2(9.36),0.006 NS*

Winter et al. (2013)[327] Single-case experimental study ABA design (baseline-intervention-withdrawal phases) N:8 (2 F and 6 M) Mean age, Y: 63.13 Time post-stroke, Mean(SD)[Range]: 30.13(13.16)[14-48]Mo Chronic stroke Stroke type: Ischaemic:3; Haemorrhagic: 1; Not available: 4 Site of lesion: PACS:1 TACS:1 Left cerebellar hemisphere, right basal ganglia, left external capsule: 1 Unknown:5	**Brief name:** mobilization and tactile sensation[330] See above description in Hunter et al. (2011)	**Dosage** - 60 min/day for 6 wks, excluding weekends- - Scheduled total dur Tx: 30 hrs -Range actual dur Tx/session:25-60 min - Mean dur Tx/session duration: 35.7-51.4 min - Actual total dur Tx: 12.50-21.46 hrs	***Motor:***MI(arm)**,** ARAT **Within subject change:***% change* ARAT: 1.7-42.1% in all participants; *14.0-42.1%; Clinically meaningful improvement in 4/8 participants* MI: 13.6-56.1%; Improvement in all participants
Song et al. (2013)[326] 2-groups pre-post non-randomized study Time post-stroke:3-12 Mo Subacute and chronic stroke *Sensorimotor deficit group:* N: 11 (7 F, 4 M) Mean age, Y:45.18 Time post-stroke, Mean(SD):10.00(2.57) Mo	**Brief name:** Somatosensory training **Motor training (active):** - Increase in range of motion between shoulder and trunk - Synchronized movement of the hands and shoulder complex during functional activities - Maintaining grip using cylindrical shaped objects and wooden sticks **Proprioception training (active and passive):** - Proprioceptive stimulation: activation of proprioception of the rotator cuff, deltoid, biceps, and triceps - Proprioceptive discrimination: movement of extrinsic muscles of 2nd to 5th fingers(active) **Somatosensory training (active and passive):** - Tactile stimulation + Tactile discrimination + Awareness of objects by applying therapeutic tools to the hands and palms with pressure, without causing any pain **Integrated somatosensory-motor (active haptic object discrimination + active functional training:** - Reaching and grasping of objects of various sizes and shapes ***Progression of task difficulty****:* practice with vision, then without vision	**Experimental and Control group:** Somatosensory training **Dosage**: - 40 min: 3 x/wk: 6 wks - Total no. Tx sessions: 18 - Total dur Tx: 12 hrs *Adjunct exercises experimental and control group:* Occupational therapy: 50 min: 5 x/wk: 6 wks Physical therapy: 60 min: 5 x/wk: 6 wks	***Motor:*** Functional reach test, Manual function test ***Participation:***Modified Barthel Index **Within group difference:***Mean, p value of mean difference, Effect size* ***-Sensorimotor deficit group*** Manual function test:*1.54, p<0.00, 0.1883 Sig diff* Functional reach test:*5.42, p<0.00, 1.3652 Sig diff* Modified Barthel Index: *11.18, p<0.00, 1.2060 Sig diff*
Smania et al. (2003)[325] Single-cases experimental study Multiple baseline and before-after follow-up design N:4 (2F,2M) Mean age, Y: 51.75	**Brief name**: Behavioural training **Somatosensory discrimination training(active and passive):** tactile discrimination tasks using sandpaper surfaces, different materials, and grating orientation with vision obscured: (1) guided passive tactile exploration provided by operator to avoid possible skin lesions; (2) Weight discrimination (active) by comparing the weight of an object with 3 other objects and matching to the one with the same weight;(3) Item Grouping(active) by separating several small objects (e.g., buttons, paper clips) into homogeneous group with vison obscured	***Dosage:*** - 50 min/session - Total no. Tx sessions: 30 - Total dur Tx: 25 hrs *Adjunct exercises:* - Home exercises: similar to treatment session;	***Motor:*** Motor sequences, Reaching and grasping, Paper sheet twisting, Thumb-index grip force control ***Sensory:*** Tactile discrimination, Joint position sense, Pressure sensation, Weight discrimination, Letters tactile recognition

Time post-stroke, Mean(SD)[Range]: 10(5.96) [5-20] Mo Sub-acute and chronic stroke Stroke type: Ischemic: 2; Haemorrhagic: 2 Site of lesion: Right parietal: 1 Left parietal: 1 Right Thalamus and internal capsule: 2	3 tactile object recognition tasks: (1) manipulation of target object and visually discriminate the target object among 3 objects, (2) manipulation of a group of small objects (rice, bolts, stones) and then visually discriminate among the 3 groups of objects, and (3) manipulation of 2 objects simultaneously with the affected and unaffected hand and reporting whether the 2 objects were the same or different **Proprioceptive training (active and passive):** - 3 joint position sense discrimination tasks: (1) Passive movement of wrist metacarpophalangeal joints, (2) Actively reproducing the indicated position indicated on the angular scale and (3) Reproducing a gesture with the affected hand while keeping the affected arm inside the box **Motor training (active):** 2 finger motor sequencing tasks: - Drumming of fingers - Playing a sequence of notes on a piano keyboard, with vision occluded **Integrated somatosensory-motor training (active haptic object discrimination/recognition + active grasp force control):** 4 grasping strength grading tasks:(1) letting the stick slide down while skipping 1 or more marks, (2) moving a partially filled plastic water bottle from one side of the table to the other without compressing the bottle, (3) picking up and moving objects of different dimensions and frailty with ice pliers without breaking the object, and (4) squeezing a tube containing gel with the affected hand to obtain strips of variable length, with vision obscured **Integrated somatosensory-motor (active haptic object discrimination/recognition + active functional training):** - Reaching and grasping of common objects of various dimensions with vision obscured **Functional training (active)**- without vision: (1) grasping several toothpicks and putting them into a box, (2) stacking up several checker pieces, (3) folding up a sheet of paper and fitting it into an envelope, (4) making a braid with 3 cords made of soft material, (5) hooking up a spring catch to a metal ring, (6) fitting the affected hand into a glove, and (7) picking up several playing cards that had been laid on the table and turning them over - 25 most challenging exercises chosen based on patient's specific impairment - Facilitation was provided for exercises patient was unable to carry out - Feedback was provided on performance: e.g., number of hits/errors, details about execution	- Dosage: - Daily:60 min/session; Total no. Txsessions:30 sessions - Total dur home exercises: 30 hrs	***Functional:*** Timed performance of activities of daily living(Timed ADL) **Within subject changes** Motor sequences: Improvement in 1/4 participants, *p=0.043,Sig Diff* Reaching and grasping: Improvement in 2/4 participants, *p=0.003-0.027,Sig diff* Paper sheet twisting: Improvement in 3/4 participants, *p=0.027-0.042*, *Sig diff* Thumb-index grip force control Improvement in 3/4 participants, *p=0.003-0.042,Sig diff* Tactile discrimination: Improvement in 1 /4 participants, *p=0.004,Sig diff* Joint position sense: Improvement in 3/4 participants, *p=0.000-0.001,Sig diff* Pressure sensation: Improvement in 3/4 participants, *p=0.003-0.006,Sig diff* Weight discrimination: Improvement in 2/4 participants, *p=0.000-0.041*, *Sig diff*, Letters tactile recognition: Improvement in 3/4 participants, *p=0.001-0.017*, *Sig diff* Timed ADL: Improvement in all 4/4 participants, *p=0.003- 0.013,Sig diff*

Molier et al. (2011)[324] Case reports Pre-post study design N: 5 (2F, 3 M) Mean age, Y: 54.44 Time post-stroke, Mean(SD[Range]: 35.4(10.91) [20-51] Mo Chronic stroke	**Brief name:** Active reaching tasks guided by position feedback **Integrated somatosensory-motor (joint position sense discriminationandactivefunctional training)** - Position feedback is provided during execution of 3 progressively difficult active reaching tasks as follows:1) Sliding the hand over the table; 2) Lifting and moving the hand above the table; 3) Lifting and moving the hand to a shelf - Position feedback is provided through resistance on shoulder and elbow joints using a robotic exoskeleton - No visual or auditory cues provided	**Dosage:** - 30 min/session; 3 times/wk for 6 wks - Total no. Tr sessions **:**18 - Total dur Tx: 9 hrs	***Motor:*** FMA-UL, MI,ARAT, Isometric strength, Circular Arm Movement (Workspace, Elevation plane, Elevation angle, Elbow excursion) FMA-UL:1.52-14.39%, Improvement in 4/5 participants MI: 8 to 13%, Improvement in 2/5 participants ARAT: 0.88 to 8.77%, Improvement in 4/5 participants Isometric strength: 5.4-16.5 Nm, Improvement in 3/5 participants Circular Arm Movement: -Workspace: 20.2-63.4%, Improvement in 3/5 participants -Elevation plane: 8.0-12.6%, Improvement in 3/5 participants -Elevation angle: 9.5-97%, Improvement in 5/5 participants -Elbow excursion: 9.9-52.2%, Improvement in 5/5 subjects improved
Dannenbaum et al. (1988)[320] Case report Pre-post study design N: 1(M) Time post-stroke: 18 Mo Chronic Stroke Site of lesion: left parietal	**Brief name:** Sensory rehabilitation of the hand with functional training **Somatosensory tactile stimulation (passive):** - Identification of finger being stimulated using electric stimulation to palmar distal surfaces of thumb, index and middle finger respectively **Somatosensory tactile discrimination (active):** - Localisation of touch pressure and identification of direction of movement by applying Velcro to the surfaces of the fingers **Integrated somatosensory-motor training: (active somatosensory tactile discrimination and active functional training):** Holding and manipulation skills of cutlery. ***Progression of difficulty*:** - Holding correct position using modified cutlery - Cutting with knife and picking up soft plasticine and firmer materials with fork - Holding a dowel in accurate position - Manipulation tasks by rolling a dowel covered with Velcro forward and backward in a controlled way across finger tips	***Dosage:*** - 15 min/session; 2x/wk for 52 wks - Total number of treatment sessions: 104 - Total duration of treatment: 26 hrs *Adjunct exercise:* - Home program: Daily repetition of stroking distal areas of the thumb, index and middle fingers with velcro	***Motor****:* Strength ***Sensory:*** Touch, pressure, proprioception discrimination ***Functional tests****:* Ability to eat with adapted cutlery, ability to remove objects from pocket At 9 months of intervention, participant was able to hold an adapted knife and fork; lack discriminatory skills At 13 months of intervention, participant is able to do the following: -Eat with adapted cutlery for 15 minutes -Dressing, washing and most activities of daily living -Remove wallet from pocket but not keys -Appreciation of pain, proprioception, moving touch: 100% accurate

						-Pressure of 70g forces on: -Thumb: 75% -Tip of Index: 62.5% -Point localisation: -Index: 75% -Thumb: 80%

CI: confidence intervals; Dur: duration ; F:Female; hr: hour; LACH: lacunar haemorrhage; LACI: lacunar infarction; LACS: lacunar stroke; L: Left; M: Male; Mo: Months; min: minute; N: Number of participants; No.: number; NS: not significant; PACI: partial anterior circulation infarction; PACS: partial anterior circulation stroke; POCS: posterior circulation stroke; R:Right; SD: standard deviation, Sig diff: significant difference; TACI: total anterior circulation infarction; TACH: total anterior circulation haemorrhage; TACS: total anterior circulation stroke; Tx: treatment; wk: week; Y: year

Table 3.4. Description of the training component categories

Training component	Description
Somatosensory tactile stimulation/discrimination	Retraining texture and pressure discrimination using active exploration by the affected hand through touch
Proprioceptive training	Proprioceptive discrimination such as joint position sense discrimination, limb positioning in space, hand configuration and/or proprioceptive stimulation such as activation of proprioceptors in muscles
Haptic object discrimination/recognition	Active exploration of objects by touch; involves integration of multiple somatosensory submodalities including: static/dynamic proprioception discrimination (finger positioning in space/hand configuration) and somatosensory tactile discrimination (size, shape, weight, texture, hardness, temperature)
Movement components/ whole movement training	Regaining movement execution of the affected upper limb, including training of movement components such as shoulder forward flexion, elbow extension and whole movements, such as combination of shoulder forward flexion with elbow extension during reaching
Functional training	Practicing activities of daily living that purposefully focus on either motor and/or somatosensory aspects of the task; sensorimotor function inherent, such as focusing on holding knife and fork during eating

Descriptions of the experimental interventions for the individual studies are summarized in Table 3.3. Five groups of intervention combinations were identified as follows: 1) tactile stimulation/discrimination and functional training[320]; 2) proprioception (joint position sense) training and movement components and whole movement training[319,324]; 3) tactile stimulation, proprioception stimulation/discrimination and movement training[322,323,327]; 4) tactile discrimination/proprioceptive stimulation, haptic object discrimination/recognition and functional training[321,331]; and 5) tactile stimulation/discrimination, proprioceptive discrimination, haptic object discrimination/recognition, movement components/whole movement and functional training[318,325,326].

The training components were combined in either a sequential or an integrated manner. S*equential* describes the serial combination of different components, for example, tactile discrimination followed by movement training. *Integrated* describes approaches where two or more components of training were incorporated purposefully or inherently within the same task. All studies, except Molier et al.[324] combined their training components predominantly in a sequential manner. Some integrated somatosensory and motor training was incorporated in seven studies[318-321,324-326], but involved at most two training tasks.

2) *Dosage parameters*

Duration of intervention

All studies reported the amount of time scheduled for therapy sessions and these ranged from 0.25 to 3 hours. Two studies[323,327] further reported the actual amount of therapy time received by participants which ranged from 41.0% to 77.1% of the scheduled therapy time. One study[321] reported the scheduled time to be spent on each component of training. The total duration of scheduled therapy time over the treatment period ranged from 7 to 72 hours, but only one study[318] scheduled more than 30 hours of therapy.

Frequency, total number of sessions and treatment period

All but one study[325] reported the frequency of treatment sessions which ranged from 1-4 sessions per week in five studies[318,320,321,324,326] or 5-7 sessions per week in four studies[319,322,323,327]. The total number of treatment sessions ranged from 8-30 sessions delivered over 2-8weeks in eight studies; one study delivered 104 sessions over 52 weeks[320], and another study delivered 30 sessions but did not report the treatment period[325].

3.4.5 Outcome measures

All studies assessed motor deficits and six studies used standardized outcome measures with good reliability and validity[319,321-324,327]. Five studies used the Action Research Arm Test (ARAT)[319,322-324,327] and four studies used the Motricity Index[322-324,327]. Three studies assessed isometric strength by grip and pinch[318], thumb index grip[325] or elbow extensor force[324]. One study used the Box and Block[319] and one study the Motor Activity Log[321].

Only four studies assessed somatosensory deficits[318,320,321,325], and only two studies[318,321] used standardized outcome measures with good reliability and validity. One study used the Semmes-Weinstein monofilament Tactile Discrimination Test[321] and the other study[318] used theByl-Cheney-Boczai discriminator test.

3.4.6 Efficacy of "combined somatosensory and motor training" interventions

The number of studies was small (n=10) and there was heterogeneity across studies with regards to study designs, participant characteristics, contents of interventions and outcome measures used, therefore the pooling of results in a meta-analysis was not possible. Consequently, the findings have been summarized in a narrative form. Given that the review included five papers from studies with low levels of evidence (case reports) and statistical power was limited in the RCTs, the results should be interpreted with caution. Only the study by Byl et al.[318] found significant improvements in a group of participants following a "combined somatosensory and motor training" intervention, and this was found only in the group that received 72 hours of scheduled therapy time. Significant improvements were not

found in any of the RCTs[319,321,323] or the pre-post study[326]. One single-case experimental study found improvements in all participants[327]. Two single-case experimental studies[322,325] and case reports[324] found improvements in some participants on some measures.

Tactile stimulation/discrimination training with functional training

Sequentially combining tactile stimulation, tactile discrimination training and integrated tactile stimulation/discrimination with functional training was evaluated in one participant with chronic stroke[320]. The participant improved in his ability to detect pressure of 70g forces, and in point localisation and in his appreciation of pain, proprioception, and moving touch accuracy (62-100% improvement).

Joint position sense training integrated with motor training

One RCT[319] found no significant differences between groups for the ARAT or the Box And Block test amongst people with acute stroke. In another study of five people with chronic stroke[324], some significant improvements were found in the Fugl Meyer Assessment Upper limb (FMA-UL), ARAT, circular arm movements (2-5 participants, 0.9-100%) and isometric strength (3 participants,5.4-16.5 Nm).

Tactile stimulation, proprioceptive stimulation/discrimination and functional training

There was no difference between groups for the ARAT or the Motricity Index in a sub-acute stroke population in an RCT[323]. In two single-case experimental studies, 50% of participants had clinically meaningful improvements post-intervention[322,327]. These improvements were observed in both chronic stroke participants (n=8) (ARAT: 14.0-42.1%; Motricity Index: 13.6-56.1%)[332] and acute stroke participants (n=6) (ARAT: 7.0-29.8%; Motricity Index: 16-25%)[322].

Tactile discrimination/proprioceptive stimulation training, haptic object discrimination/recognition and functional training

One RCT[321] found no significant differences between the intervention and control groups in the FMA and the Motor Activity Log.

Tactile stimulation/discrimination, proprioceptive stimulation/discrimination, haptic object discrimination/recognition, motor and functional training

In people with chronic stroke[318] (n=45), there was a significant difference in somatosensory discrimination ($p<0.002$, effect size: 0.70) and fine motor skills ($p<0.002$, effect size: 0.28) between the group receiving 72 hours of treatment and those receiving lower doses (12-13.3 hours). Results from the two lower-dose groups (12-13.3 hours) were inconsistent; one group (13.3 hours) improved in strength whereas the other group (12 hours) improved in sensory discrimination and fine motor skills[318]. One single-case design study (n=4)[325] reported improvements in functional tests in all participants. Among the motor outcome measures, improvements were found in paper sheet twisting, thumb-index grip force control tests, reaching and motor sequences (1-3 participants). Improvement in somatosensory measures were observed in joint position sense, pressure sensation, letters tactile recognition tests, weight discrimination and tactile discrimination (1-3 participants). Another pre-post non-RCT study that included people with acute and chronic stroke[326] found significant improvements in the manual function test [$p<0.01$, effect size: 0.19], functional reach test [$p<0.01$, effect size: 1.37], and modified Barthel Index [$p<0.01$, effect size: 1.21].

3.5 DISCUSSION

This review identified 10 papers where use of a combination of somatosensory and motor training was investigated in people with UL deficits after stroke. The interventions included combinations of tactile stimulation/discrimination, proprioceptive stimulation/discrimination, haptic object discrimination/recognition, movement components/whole movement and functional training. Overall there was a lack of positive evidence for the efficacy of the combined interventions in these studies. Reasons for these

limited effects are likely similar to those reported in other systematic reviews in stroke rehabilitation trials[62,63] and include reduced potential for improvement due to the severity of impairments post-stroke, the timing of rehabilitation for stroke survivors with increasing chronicity, a lack of responsiveness of outcome measures, and poor methodological rigour of study designs, as well as aspects of intervention content and dosage. This discussion will focus on the extent to which UL improvement could be influenced by how intervention components inter-relate, their interactions with characteristics of training, and the operationalisation of these interventions.

3.5.1 Training component combinations

A number of active training ingredients have been identified in the context of motor and perceptual learning literature and in the context of learning-based sensorimotor approaches to stroke rehabilitation[333]. There may be an advantage to incorporating 4-5 active training components[318] that simultaneously target deficits in somatosensory, motor, and UL function, and reinforce the integration of the somatosensory and motor networks required to improve task performance after stroke[334]. In the interventions reviewed, the training components consisted of a mixture of active ingredients that have potential to drive neural plasticity when delivered in sufficient dose to positively influence impairments and functional outcomes[47]. However, these interventions also included components likely to have limited efficacy in improving UL deficits and functions, such as passive stimulation.

The extent of therapy time devoted to passive forms of motor or somatosensory training may have compromised the quantity of active training. Active training approaches resulted in greater improvements in UL deficits and function[318]than passive training approaches[323]. Although a Cochrane systematic review on UL interventions post-stroke[332] reported some benefits of mobilisation, stretching and passive exercises[62], active movements of the UL[318] were found to be more beneficial as they produce greater cortical activation extending to multiple areas, such as the contralateral primary and secondary sensorimotor cortices, premotor cortex, supplementary motor area, basal ganglia and ipsilateral cerebellum, whereas passive movements, which activate the cortex a lesser extent, are

limited to the primary and secondary somatosensory cortices[335,336]. Despite the significant improvements observed by Byl et al.[318], less improvement was found in motor measures (effect size: 0.28) as compared to somatosensory measures (effect size: 0.70). It is suspected that the motor improvements were small because of the extent of passive movement training (mental practice and mirror therapy approach), despite active somatosensory (tactile discrimination and proprioceptive stimulation) and active functional training.

The lack of improvement reported in most studies could also indicate a need to incorporate more integrated (two or more components of training incorporated within the same task) rather than sequential somatosensory and motor training tasks to optimize the responses to the interventions[334]. Few studies tested interventions that included integrated tasks. Biological and behavioural evidence suggests that acquisition of sensorimotor skill is enhanced by training conditions involving complex tasks and in-depth processing[333,337,338]. Therefore, by combining somatosensory and motor training tasks in an integrated manner within the same tasks, the interventions may elicit greater activation in the somatosensory and motor cortices than if the somatosensory and motor tasks are combined sequentially.

Evaluation of the combinations of training components identified in this review was limited due to the poor reporting of which components of training were emphasized in the publications, although there is established evidence from related fields that both somatosensory[198,203,339] and motor training[340,341] are necessary for UL improvement because of their coupled interaction[34,35]. Except for two studies[321,325], it was not possible to determine whether there was differential emphasis on somatosensory or motor training components in the interventions due to inadequate reporting of the amount of practice, the number of tasks practiced for each training component, or the time allocated to each training component.

3.5.2 Augmented feedback

Another reason for insufficient improvements could be due to limited augmented feedback[318,320-323,326,327,330,342], as it is established that augmented feedback is an essential element to stimulate motor and somatosensory learning in stroke rehabilitation[157,213,333,343,344].

Also, less frequent feedback may be more effective[345] than high frequency or continuous feedback[324,325] as reduced frequency feedback could lead to more opportunities to learn from errors, which can increase information processing[346] and error correction capabilities[347]. Less frequent augmented feedback may better enhance error correction capabilities[345].

3.5.3 Dosage parameters

The results were promising in one study[318] that used more than double the dose (72 hours) of intervention of any other study and demonstrated consistency of significant improvement in the UL after stroke. These findings are in line with constraint-induced movement therapy delivered with similar dosage (60 hours)[348] and support evidence that greater overall treatment duration is associated with better recovery of UL impairments and function after stroke[208]. In addition, improvements were reported in some case studies with smaller doses (25-30 hours)[322,325,327]. This suggests that combined somatosensory and motor interventions have potential to improve aspects of both somatosensory and motor performance after stroke. It may be, however, that interventions need to substantially increase the dose of therapy being provided in order to identify the combinations of components and amount of training that are most beneficial.

The frequency and duration of treatment sessions could also influence outcomes. Results were inconsistent when the treatment was delivered at high frequency with short duration sessions or at relatively low frequency with long duration sessions, for the same treatment period[318]. It is acknowledged that the disparity could also be associated with low overall treatment dose (12-13.3 hours). Additionally, progress in optimizing therapy is limited

by insufficient reporting from the literature on how other parameters of dosage, such as the duration of treatment session, number of treatment sessions, frequency and spacing of treatments and overall treatment period parameters, influence UL recovery after stroke[45,62,63]. A Cochrane review is currently being undertaken to determine the effect of parameters of dosage on activity limitations after stroke[349]. Also, evaluation of the interventions was restricted by a lack of reporting on the number of repetitions in the interventions even though it is well-established that repetitions are critical in the neurobiology of learning by increasing synaptic efficacy[211]to enhance motor skill acquisition[350].

3.5.4 Varied tasks, grading complexity and progression of task difficulty

Progressing the task difficulty and complexity of training gradually, from specific somatosensory and motor impairment-oriented training to integrated somatosensory-motor training, followed by more complex functional training as done by Smania et al.[325] should be a promising approach to improve rehabilitation outcomes[351-354]. Maintaining an appropriate intensity to sufficiently challenge both somatosensory and motor functions is necessary to address the UL deficits, skill acquisition and transfer of learning improvement to facilitate task performance in activities of daily living. These factors influence neuroplastic mechanisms by incorporating the principles of learning-dependent plasticity such as specificity, salience, generalisation and transfer of learning that improve the efficacy of the UL intervention [338,350,355]. Additionally, limited improvements could be due to direct emphasis on functional training without first addressing somatosensory or motor impairments specifically[319], despite evidence of the contribution of the distinct improvements in both somatosensory[213]and motor[356,357] deficits to improve UL function.

3.5.5 Severity of deficits and timing of rehabilitation

More improvement was observed in participants with chronic stroke after 13-21 hours of intervention[327] than in participants with subacute stroke[322] after 30 hours of the same intervention. A larger dose of treatment in a sub-acute stroke population would have been expected to boost neuroplasticity to a greater extent than a smaller dose in a chronic stroke population. One possible explanation is that the sub-acute population[322] had more severe

motor deficits (ARAT: 0-11; Motricity Index: 4-11) than the chronic stroke participants (ARAT: 1-57; Motricity Index: 29-76). Therefore the intervention could be more effective in stroke participants with mild to moderate deficits than in people with severe deficits since initial severity of motor impairment is one of the most important predictive factors for UL recovery post-stroke[358]. An alternative hypothesis is that the ability to detect a treatment facilitated difference above spontaneous recovery in subacute stroke may require a larger treatment effect size. These findings suggest that 1) improvement in the chronic phase is possible and should be pursued, and 2) intervention contents and dosage should be titrated to the severity of deficits. Another reason for the poorer recovery in the sub-acute population[322] as compared to the chronic stroke population[327] could be the greater loss of somatosensation[359,360] and motor function[361-363] in the older sub-acute population[322].

3.5.6 Strengths and limitations

Three studies that sequentially evaluated the same intervention demonstrated the importance of a systematic developmental approach, in accordance with the MRC framework[54,364], addressing the modelling of the intervention[330], preliminary efficacy of treatment effects in those with different participant characteristics[322,327], dose optimality and superiority of the intervention[323]. The series of phased studies aimed to optimize the various active ingredients and improve their specificity with regards to deficits targeted, severity of impairments and timing of rehabilitation until the intervention is ready for a full evaluative RCT[54]. Fifty percent of studies included in this review consisted of moderate or low quality studies. Although exploratory trials have been prioritized in the developmental process of interventions, little attention has been paid to the modelling process prior to feasibility and pilot trials. Additionally, the value of small observational studies or single-case designs has often been under-rated for their poor external validity even though their designs provide opportunities to titrate active ingredients until the optimal content of an intervention is identified. This review was limited by the lack of RCTs and controlled studies on “combined somatosensory and motor training” interventions. The external generalisability of the findings was further limited by small sample sizes and low statistical power. Studies with low levels of evidence were included in part due to the small number of studies.

3.5.7 Implications for rehabilitation

Stroke

- "Combined somatosensory and motor training" interventions have potential but cannot be recommended to improve upper limb function after stroke in clinical practice due to insufficient evidence of their efficacy.
- Based on current evidence, it might be worth considering the use of integrated somatosensory-motor training approaches, besides traditional training approaches that combine somatosensory and motor training sequentially.
- Large doses of overall treatment duration (>30 hours) are suggested.

3.5.8 Future research

Complete reporting of the intervention contents (types and amounts of active ingredients) and the training dosage (number of repetitions, number of treatment sessions, scheduled and actual treatment duration, frequency and period) scheduled and whether that is delivered are encouraged as this could facilitate optimisation of the intervention by carefully mapping the contents and dosage of the intervention or by increasing the specificity of intervention for the deficits targeted, severity of deficits and chronicity of stroke. Also, it is critical to thoroughly consider the limitations of study designs, participant characteristics, intervention contents and outcome measures so as to avoid uninformative research and clinical waste. RCTs with sufficient statistical power are required to evaluate the efficacy of "combined somatosensory and motor training".

The design of a standardized treatment protocol could be informed by the following research questions:

1. Which specific somatosensory and motor active ingredients can be combined into training tasks for optimal improvement of UL deficits and functions post-stroke?

2. What are the optimal training dosage parameters of “combined somatosensory and motor training” interventions and expected UL functional recovery for people with acute, subacute and chronic stroke?

3. Is there a particular profile of participant characteristics that are more responsive to combined somatosensory and motor training?

Recommendations for training content for future trials aiming to investigate combined somatosensory and motor training could include: 1) Combinations of tactile and proprioceptive stimulation/discrimination, haptic object discrimination/recognition, movement components/whole movements and functional training components; 2) Delivery of predominantly active rather than passive training approaches; 3) Inclusion of training tasks emphasizing integration of both somatosensory and motor function; 4) Provision of augmented feedback on somatosensory and motor functions, including in the context of sensorimotor tasks and feedback should be delivered with reduced frequency; and 5) Inclusion of impairment-oriented training of somatosensory and motor deficits, together with integrated somatosensory-motor training, and task-oriented functional training.

3.6 CONCLUSION

The “combined somatosensory and motor training” interventions evaluated to date included combinations of tactile, proprioceptive stimulation/discrimination and haptic object discrimination/recognition, component and whole movement training, and functional task training. Relatively few “combined somatosensory and motor training” interventions are reported. Evidence of efficacy of these interventions to improve somatosensory and motor capacity and UL function is limited at present but has potential.

Appendix 3.1

Example of search terms:

1. (((cerebrovascular disorder*/ or exp basal ganglia/ or exp cerebrovascular disease*/ or exp brain isch?mia/ or exp carotid artery diseases/ or cerebrovascular accident/ or exp brain infarction/ or exp cerebrovascular trauma/ or exp hypoxia-isch?mia, brain/ or exp intracranial arterial disease*/ or intracranial arteriovenous malformation*/) and Thrombosis/) or exp intracranial h?morrhage*/ or vasospasm, intracranial/ or vertebral artery dissection/)
2. (stroke or poststroke or post-stroke or cerebrovasc* or brain vasc* or cerebral vasc* or cva* or apoplex* or SAH).tw.
3. ((brain* or cerebr* or cerebell* or intracran* or intracerebral) adj5 (isch?emi* or infarct* or thrombo* or emboli* or occlus*)).tw.
4. ((brain* or cerebr* or cerebell* or intracerebral or intracranial or subarachnoid) adj5 (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*)).tw.
5. hemiplegia/ or exp paresis/
6. (hemipleg* or hemipar* or paresis or paretic).tw.
7. 1 or 2 or 3 or 4 or 5 or 6
8. exp upper extremity/ or exp hand/ or exp hand joints/ or exp hand strength/ or exp arm/ or exp shoulder/ or exp elbow/ or exp forelimb/ or exp forearm/ or exp wrist/ or exp wrist joint/ or exp fingers/
9. ((upper adj3 limb*) or extremit*).tw.
10. (arm* or shoulder* or elbow* or forearm* or wrist* or finger*).tw.
11. reach to grasp.tw.
12. reaching.tw.
13. 8 or 9 or 10 or 11 or 13
14. rehabilitation/ or 'activities of daily living'/ or exercise therapy/ or occupational therapy/
15. physiotherapy/ or physical therapy/ or facilitation/ or treatment/ or intervention*/
16. 14 or 15
17. sensorimotor.tw.
18. sensory.tw.
19. sensation*.tw.
20. somatosensory.tw.
21. ((motor or movement* or task* or skill* or performance) adj5 (repetit* or repeat* or train* or re?train* or learn* or re?learn* or practic* or practis* or rehears* or rehers*)).tw.
22. ((recovery or regain) adj3 function*).tw.
23. ((((motor or movement or mov* or muscle* or muscu* or efferent* or control or co*ordinat* or skill* or timing or manual) adj task) or manipulat* or activ* or motor) adj planning).tw.
24. ((touch or tactile or texture or weight) adj3 discrimination*).tw.
25. ((two point*) adj3 discrimination*).tw.
26. ((touch or tactile) adj3 stimul*)
27. proprioception.tw.
28. (haptic* adj3 touch).tw.
29. ((surface* or material*) adj 3 detection*).tw.

30. 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29

31. 7 and 13 and 16 and 30

Appendix 3.2

Calculation of effect sizes

Study design	**Formulas for effect size**
Controlled trials: *Within-group difference*	$d = \frac{M_2 - M_1}{\sqrt{(SD_1^2 + SD_2^2)/2}}$,where d is the measure of the magnitude of effect size of the intervention of interest, M2 is the mean post-test score, M1 is the pre-test, and $\sqrt{(SD_1^2 + SD_{2)/2}^2}$ is the pooled standard deviation for the pre and post-test[365].
RCT: *Between-group difference*	$d = \frac{\bar{x}_1 - \bar{x}_2}{\sqrt{Sp}}$ $Sp = \sqrt{\frac{(n_1-1)SD_1^2 + (n_2-1)SD_2^2}{n_1+n_2-2}}$,where *d* is the measure of the magnitude of effect size of the group receiving the intervention of interest. $\bar{x}_1$ is the mean score of one group of study participants and $\bar{x}_2$. *d* is the mean score of a second group of participants. *Sp* is the pooled standard deviation for both groups of participants [366].
Non-RCTs: *Between-group difference*	$d_{corr} = d_E - d_C$, where d_E the measure of the magnitude of effect size of the experimental group, d_C is the measure of the magnitude of effect size of the comparison, d_{corr} is the difference between *Cohen d* of the experimental and comparison group in pre-post research designs[365].
Corrected Cohen d, Hedges g small sample size	$\text{Hedges's } gs = \text{Cohen\_s } ds \times (1 - 3/(4(n1 + n2)) - 9)$ where n_1 is the sample size for the experimental group and n_2 is the sample size for the comparison group[315]

Single case experimental designs and case reports: *Change within subject*	Raw mean difference = Post-test- Pre-test score Percentage change= $\left(\frac{Post-test-Pre-test}{Pre-test}\right) x100\%$

CHAPTER 4: COMBINED PHYSICAL AND SOMATOSENSORY TRAINING AFTER STROKE: DEVELOPMENT AND DESCRIPTION OF A NOVEL INTERVENTION TO IMPROVE UPPER LIMB FUNCTION

Preface

This chapter describes a new upper limb stroke rehabilitation intervention known as COMPoSE: "COMbined Physical and somatoSEnsory training" and addressing thesis aim 2 (i.e to describe the rationale and development of a combined somatosensory and motor training, designed to improve somatosensory and motor function in the upper limb after stroke) which was conducted to investigate Research question 2 (What are the essential features of a novel intervention combining somatosensory and motor training to improve upper limb function after stroke and what is the rationale for these features?).

The contents of this chapter are the final version of the article published in *Physiotherapy Research International* as: **Gopaul U**, van Vliet P, Callister R, Nilsson M & Carey L. COMbined Physical and somatoSEnsory training after stroke: Development and description of a novel intervention to improve upper limb function. *Physiotherapy Research International*. 2018;0(0):e1748., which has been published in final form athttps://doi.org/10.1002/pri.1748. This article may be used for non-commercial purposes in accordance with Wiley Terms and Conditions for Use of Self-Archived Versions. A copy of this article is included in Appendix 4.1.

Contribution statement

I was responsible for leading the development of all stages of the COMPoSE intervention. With the support of my supervisors, I selected the contents of the COMPoSE intervention with regards to the somatosensory parameters, motor parameters, selected tactile pressures, amount of practice, training duration, order of variables and varied practice and a standardised training matrix for delivery of COMPoSE while incorporating vision and without vision conditions. I also developed the objects with various physical and surface

properties used in the COMPoSE intervention, except for the TactArray device. I also developed the operationalisation of augmented feedback for selected grasp pressures using the TactArray device as well as operationalisation of somatosensory and motor feedback.

4.1 ABSTRACT

Title: COMbined Physical and somatoSEnsory training (COMPoSE) after stroke: Development and description of a novel intervention to improve upper limb function.

Background and Purpose: After stroke, reach-to-grasp (RTG) goal-directed movements are disrupted as a result of both residual motor and somatosensory impairments. This report describes the rationale and development of a new upper limb stroke rehabilitation intervention known as COMPoSE: "COMbined Physical and somatoSEnsory training", designed to improve somatosensory and motor deficits in the upper limb after stroke. A standardised training matrix has been developed to facilitate intervention delivery.

Methods: The COMPoSE intervention was developed through the following stages: 1) Definition and operationalisation of somatosensory and motor variables used in training sensation and movement after stroke; 2) Development of methods to give feedback to enhance skill acquisition; and 3) Combination of somatosensory and motor variables, and feedback, into a standardised training matrix. The reporting of the COMPoSE intervention adheres to the recommendations of the Template for Intervention Description and Replication (TIDieR) checklist to facilitate replication of the intervention in the future.

Results: The essential features of COMPoSE include: combined somatosensory-motor training variables (grasp pressure, distance, object size, crushability, surface texture and friction), feedback and calibration using a haptic device providing measures of grasp pressure, use of anticipation trials, and high dose repetitive task practice. Ten treatment sessions are delivered over 3 weeks, using a standardised matrix for treatment delivery.

Conclusion: COMPoSE is a new intervention that combines somatosensory and movement training, delivered *synchronously**,** within the same intervention and within the same task.*

Key words: Motor, Upper limb, Somatosensory, Stroke, Touch, Hand, Reach

COMbined Physical and somatoSEnsory training (COMPoSE) after stroke: Development and description of a novel intervention to improve upper limb function.

4.2 INTRODUCTION

4.2.1 Background

After stroke, reach-to-grasp (RTG) movements are disrupted as a result of residual motor and somatosensory impairments[154]. Compared to healthy adults, stroke survivors with motor impairment experience deficits, such as longer movement duration, slower peak velocity[158], earlier peak deceleration[158] and reduced movement smoothness[160] during the transport phase of RTG movements. Stroke survivors also suffer from impairments in grasp formation and release, such as inconsistent grasp apertures, which result from disruption in the coordination of muscle activity between finger flexors and extensors, as well as between proximal muscles involved in the hand transport phase of a RTG[162]. A lack of volitional control of finger and thumb extension further contributes to deficits in hand shaping during grasping and incorrect positioning of fingers for effective hand use[164].

Somatosensory function plays a critical role in controlled grasp and is tightly coupled with action. Impaired touch sensation after stroke makes it difficult to discriminate different physical properties of objects, such as texture, hardness and surface friction[21]. As a result, the fingers and the hand are limited in their ability to effectively coordinate grip and lift forces and to appropriately scale grip force for effective object handling, lifting and manipulation[156,166]. The selection of appropriate grip forces is largely determined by object properties, including weight, surface texture, slipperiness and shape, as well as the magnitude, direction and points of application of these grip forces on the objects[150]. As a consequence, people with somatosensory impairment rely extensively on vision to help gauge the force required in object grasping[166,171]. Effective grip force modulation is the result of a complex interplay of tactile sensory feedback signals provided by cutaneous mechanoreceptors found in the glabrous skin of the grasping fingers and modulated muscle activity in the hand and arm[20,139,146]. Proprioceptive and cutaneous information also play a

significant role in controlling finger span and hand shape during object handling[367]. Further, proprioceptive information is important for internal models of the body and peripersonal space[368], and is thus crucial in the planning, execution, correction and learning of goal-directed actions.

Significant correlation between motor and somatosensory impairment (tactile sensation and proprioception) has been found in the upper limb after stroke[36], suggesting that an underlying somatosensory impairment may limit performance of motor tasks[369]. In addition, controlled experimentation of the relative contribution of somatosensory and motor impairment to the fundamental pinch-grip lift-and-hold task identified that somatosensory impairment (in particular surface friction discrimination) has an additional and negative impact on timing and force adjustment during pinch grip[166]. Finally, functional arm use has been associated with improved somatosensory skills (tactile, proprioception and haptic object recognition) following sensory discrimination training; although the amount of change in arm use varied across survivors[294] .

Functional imaging studies in humans have demonstrated enhanced activation of the somatosensory cortex following motor training[340,341]. Similar studies also found that motor recovery is associated with reorganisation of somatosensory cortices after stroke[198,203,339-341]. For example, following tactile stimulation, increased activation responses were observed not only in the primary and secondary somatosensory cortices but also in the primary motor cortex and supplementary motor area[203]. This suggests that there may be benefits to synchronously coupling somatosensory training with motor training to enhance activation responses in the somatosensory and motor cortices.

Conditions of training and methods to enhance learning of somatosensory discriminations and controlled movement execution are also likely to be important. Additionally, augmented feedback is an important element to enhance motor learning and somatosensory re-training in upper limb stroke rehabilitation[157,213,343,344]. Similarly, the use of attention and a graded matrix of training tasks are important in skill based learning[333].

We therefore sought to develop an intervention combining somatosensory and motor functions**,** *within the same intervention and within the same task,* to improve upper limb function after stroke. The intervention uses principles of learning and conditions of training that have shown to be effective in task-specific motor training[370] and in training somatosensory discriminations[213]. Principles are applied to both motor and somatosensory components of the task and to the overall task, and are facilitated by specialised equipment such as the TactArray.

4.2.2 Objectives

The aim of this report is to describe the development and rationale for the essential features of this intervention, which we have named "COMbined Physical and somatoSEnsory training" (COMPoSE). In order to describe COMPoSE with sufficient detail and rigor to allow its application in a future randomised controlled trial, and in clinical practice should COMPoSE prove effective, we used the recommended Template for Intervention Description and Replication (TIDieR) checklist[371],an extension of the CONSORT 2010 statement[372]. The COMPoSE intervention is being tested in a Phase II study to determine the feasibility of delivery of the intervention and to monitor the responses of participants with stroke to the intervention to improve somatosensory and motor deficits and upper limb function after stroke.

4.3 METHODS

The development of the COMPoSE intervention was informed by a review of the literature and consensus was used to agree on the somatosensory and motor variables from the literature to be targeted in this combined intervention. The COMPoSE intervention was developed following three sequential stages:

1) Definition and operationalisation of somatosensory and motor variables used in training sensation and movement in the context of upper limb function after stroke.

COMPoSE is designed to improve reach and grasp, two fundamental actions needed for goal-directed use of the arm. Two motor and three somatosensory parameters were selected for training in the context of the reach and grasp task. Two motor parameters (object distance and object width) are combined with three somatosensory parameters (texture, friction and crushability) and three selected grasp pressures (preferred, minimum and maximum grasp pressure-the output). Each parameter has two variables. Object distance and object size were selected to vary as they impact the kinematics of the task[161,373]. Texture, friction and crushability were selected as they directly impact controlled grasp and manipulation of objects[166,213].Each combination is performed with and without vision.

2) Development of methods to give feedback to enhance skill acquisition

Principles of training and conditions of practice are primarily derived from approaches to task-specific training[370] and SENSe discrimination training[213,214,333]. These include augmented feedback enhanced by specially designed tasks, that are graded in relation to motor and somatosensory features. The mechanisms and rationales are discussed later.

3) Combination of somatosensory and motor variables, and feedback, into a standardised training matrix

A matrix approach was adopted consistent with that described for SENSe discrimination training[214,374,375]. Use of a matrix approach allows for graded progression within motor and somatosensory functions and across sensorimotor actions and tasks[374]. This approach aligns with neuroscience evidence that motor and somatosensory functions/attributes are distributed in interconnected networks with gradients of separation between them[292] and transfer may be facilitated with multimodal training[376].

The potential order of variables in the matrix was mapped using consensus based on a logical and pragmatic training approach consistent with the complex functional use of the upper limb and with regards to levels of difficulty of the somatosensory and motor components of reach and grasp. For example, integrated somatosensory and motor functions

and graded levels of difficulty were considered in relation to object size, distance, texture, crushability etc. Furthermore, the training of adaptive pressure is closely related to training of discrimination of properties of the object, such as crushability of the object[377], as well as for training for discrimination of surface properties, such as texture[378] and friction[146,150,165,379]. Training and grading of these attributes have been tested in the context of the SENSe intervention[213].

4.4 RESULTS

Description of the COMPoSE intervention using the TIDieR checklist

4.4.1 Item 1. Brief name

COMbined Physical and somatoSEnsory training (COMPoSE)

4.4.2 Item 2. Why: Rationale for the intervention

Motor and somatosensory functions are jointly integrated and tightly coupled in actions performed in everyday life[292]. However, in clinical practice, interventions directed at motor deficits have traditionally been separated from interventions directed at somatosensory deficits[62,63,297]. Moreover, treatment of somatosensory functions is often neglected[296]. By treating motor and somatosensory impairments separately, the potential beneficial effects of combining somatosensory training to further enhance sensorimotor function and action are not utilised. This notion could partially explain the relative lack of effectiveness or limited gains in upper limb functions from current interventions in stroke rehabilitation. A Cochrane review of systematic reviews (n=40 reviews; 503 RCTs; 18,078 participants) found moderate quality evidence for motor only interventions, such as constraint-induced movement therapy, mental practice, mirror therapy, virtual reality, and relatively high-dose repetitive task practice[62]. There was insufficient evidence to recommend upper limb interventions including task-specific training, robotics, Bobath approach, brain stimulation, and strength training[62]. Although another meta-analysis found significant improvements in upper limb motor function with motor interventions, such as robotics,

neuromuscular stimulation and constraint-induced movement therapy, the evidence indicates only small to moderate effects, except for constraint-induced movement therapy[63].

Studies reporting the efficacy of somatosensory interventions after stroke are currently limited. A Cochrane review[45] (n=13; without meta-analysis) found only preliminary evidence of efficacious sensory interventions after stroke, such as somatosensory discrimination training, thermal stimulation, and intermittent pneumatic compression. More recently, a meta-analysis of interventions for somatosensory function (n=12 RCTs) found significant positive summary effect sizes for somatosensory function and muscle tone following sensory retraining, but did not find significant summary effect sizes for motor function of the affected arm[63]. In summary, currently there is no high-quality evidence for any single sensory or motor upper limb intervention, except for constraint-induced movement therapy[45,62,63].

A few studies on upper limb interventions in stroke rehabilitation have attempted to train somatosensation and movement together[325,380]. Importantly, the somatosensory and motor interventions were delivered sequentially, not synchronously. These interventions resulted in no gain or only modest gains in functional independence, strength, somatosensory discrimination, and fine motor control[325,380]. Also, these studies had small sample sizes (n = 1-76) and low statistical power.

In order to more comprehensively address somatosensory and motor deficits, the potential exists to *combine* somatosensory and motor training and deliver them synchronously to improve upper limb function after stroke. We hypothesize that greater gains are likely with synchronous somatosensory and motor relearning and practice, on the basis that this would activate both the somatosensory and motor networks in the brain, as occurs in everyday skilled actions, than if somatosensory and movement interventions are delivered separately. In addition, stronger connections may be formed between the somatosensory cortex and the functionally-related motor cortex to boost neuroplasticity. No study has yet

investigated the effects of combining somatosensory and motor training and delivering it synchronously. This lead to the design of the COMPoSE intervention.

The COMPoSE intervention draws on the best available evidence for somatosensory and motor retraining of the upper limb, and systematically applies the principles of training and conditions of training to achieve combined sensorimotor training of the upper limb. The COMPoSE intervention was developed for use by people with residual somatosensory and motor deficits in their upper limb resulting from stroke. The aim is to retrain goal-directed use of the arm after stroke, with a focus on integration of RTG movements and discrimination of somatosensory features of objects important for controlled use of the arm in daily activities. It is derived from and extends existing neuroscience-based therapies focused on reach and grasp [381,382] and somatosensory discrimination training in the upper limb[213,214]. These therapies were selected as they have strong foundations in neuroscience and learning[337,374,382,383], are designed to help people who have experienced stroke regain skills in reach, grasp[384] and somatosensory discrimination[21,213], and have demonstrated statistically and clinically significant effectiveness in small randomised controlled trials[213,384]. These interventions have also been operationalised into clinical practice protocols[213,225,384].

4.4.3 Item 3. What: Materials used in the intervention

The materials used in the COMPoSE intervention include objects to be grasped and a haptic device to provide feedback. The objects vary in size diameter, surface texture, surface friction, and crushability. Two dimensions of a cylindrical object (salt shaker) are used. The smaller cylinder is 5 cm in diameter and 12.5 cm high; the larger cylinder measures 7.5 cm in diameter and is 12.5 cm high. The mass of both cylinders is adjusted to 160 g. Four versions of each cylinder are provided, with different surface properties to stimulate somatosensory cues involved in texture differentiation (texture and friction). For texture, felt material is used as a smooth surface on one cylinder, and sandpaper (100 grit) is used as a rough surface on a contrasting cylinder. For friction, rubber is used as the non-slippery surface on one cylinder, and polytetrafluoroethylene (Teflon) is used as the slippery surface on the contrasting

cylinder. Rubber and Teflon have different frictional properties (coefficients of friction, 0.35 and 0.96, respectively) while having similar macrostructures[166]. For crushability, soft and hard plastic cups are used because they replicate drinking cups used in real-life[214]. The cups measure 5.0 cm in diameter and are 9.2 cm high.

The TactArray pressure distribution system is a haptic device used for providing feedback on selected grasp pressures[385]. The TactArray pressure distribution system is a tactile data acquisition method devised by Pressure Profile Systems[385]. Two dimensions of TactArray cylinders are used, closely related to the size of the task objects. The TactArray cylinders are hard and covered with pressure sensor arrays (conformable TactArray T4500 SN1104; sensor SN5385,5438) constructed from a soft and flexible conductive cloth approximately 1 mm thick. Further details of the system will be elaborated in Item 4 below.

4.4.4 Item 4. What: Procedures, activities, and/or processes used in the intervention

4.4.4.1 Critical components of the COMPoSE intervention

The COMPoSE intervention has four critical components: 1) Matrix of specially designed somatosensory and motor tasks to permit progressive and systematic grading according to specific parameters (e.g. levels of difficulty progressing from easy to more difficult discriminations); 2) Performance of goal-directed somatosensory-motor tasks (reach-to-grasp and lift-and-hold)under two conditions of practice (i.e., with vision and without vision); 3) Targeted feedback about both motor and somatosensory performance; 4) Varied and intensive repetitive practice.

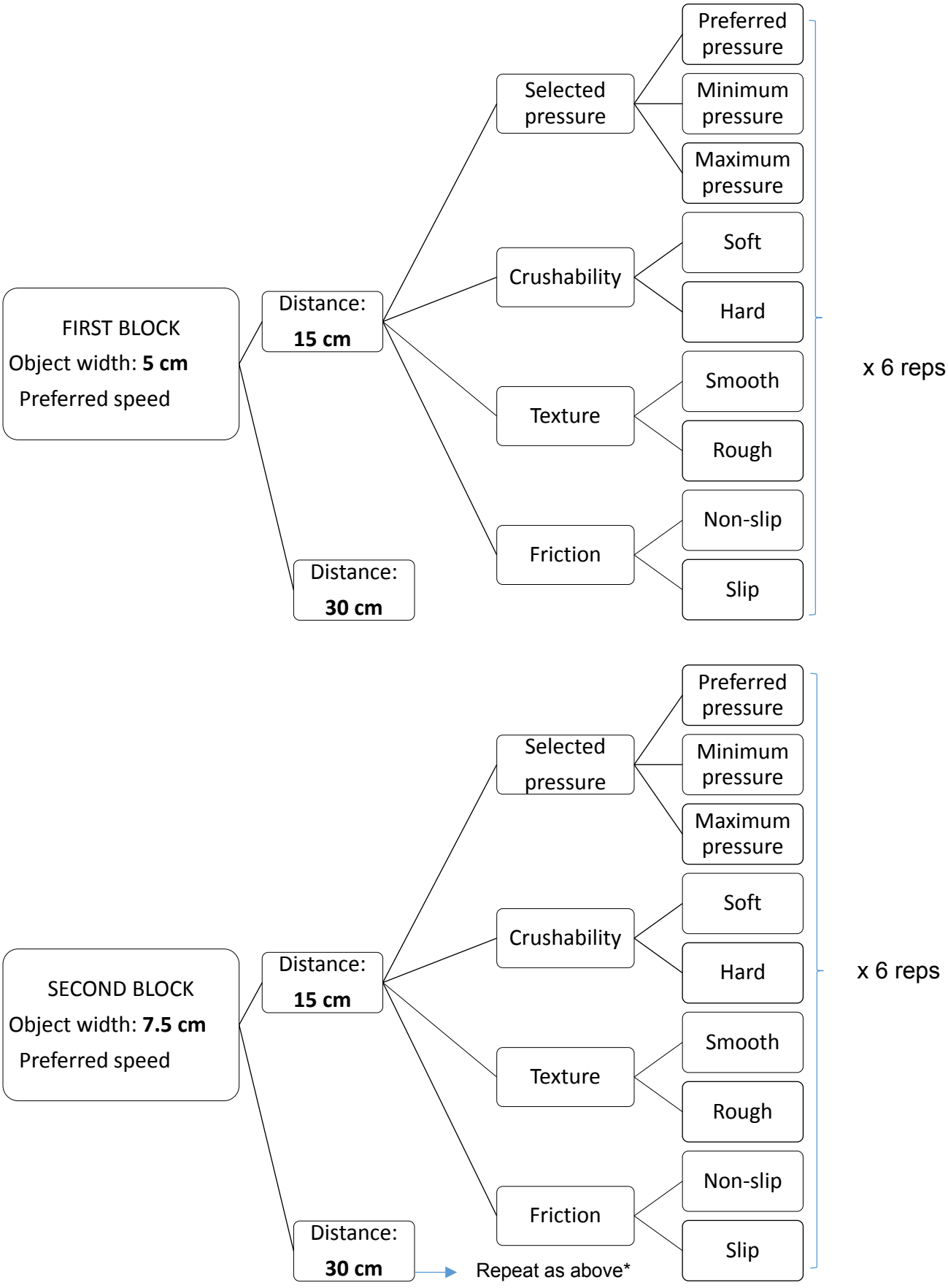
4.4.4.2 Matrix of specially designed training tasks with progressive and systematic grading of somatosensory-motor tasks according to specific parameters

4.4.4.2.1 Somatosensory and motor parameters of the COMPoSE intervention

There is a total of 36 combinations of somatosensory-motor tasks organised into a standardised training matrix (figure 4.1). Two motor parameters (object distance and object width) are combined with three somatosensory parameters (texture, friction and crushability)

and three selected grasp pressures (preferred, minimum and maximum grasp pressure) (figure 4.1). Each motor and somatosensory parameter has two variables. Motor parameter variables include object width (5 cm, 7.5 cm) and distance (15 cm, 30 cm). Somatosensory parameter variables include: surface texture (smooth, rough) and surface friction (slip, non-slip) and crushability (hard, soft). Object shape and weight (160 g) are kept constant throughout the intervention. All tasks are performed at preferred speed (figure 4.1).

The training is organised in two blocks within a matrix in a fixed order (figure 4.1). In the first block, object width (5 cm diameter cylinder) is kept constant, while object distance (15 cm, 30 cm) and all somatosensory parameters are varied. In the second block, object width (7.5 cm diameter cylinder) is kept constant, while object distance (15 cm, 30 cm) and all somatosensory parameters are varied. Additional somatosensory-motor variations are provided through selected grasp pressure training using preferred, minimum and maximum grasp pressure (figure 4.1).



Reps: Repetitions

Figure 4.1. COMPoSE Standardised training matrix

4.4.4.2.2 Graded levels of difficulty

Progressive difficulty for the motor and somatosensory variables is integrated within each somatosensory-motor combination and across the standardised training matrix[386]. Fitts' index of difficulty (ID)[118] is used to quantify the difficulty of the motor tasks, calculated from $\log_2\left(\frac{2\ X\ Object\ distance}{Object\ width}\right)$. For example, as object distance is doubled across the COMPoSE standardised matrix, the indices of difficulty are progressively increased. In the first block, training commences with easier tasks (e.g., smaller object width, closer object, non-slippery surface) followed by more difficult tasks (e.g., smaller object width, further object, slippery surface). In the second block, repetitions with the larger object width and increasing distances are practised to progress the level of difficulty for hand opening. The indexes of difficulty in COMPoSE are summarised in Table 4.1.

Table 4.1. Indices of difficulty in COMPoSE

Object parameters varied		**Parameters constant**	**Fitts'**
Width (cm)	*Distance (cm)*	*Speed*	**Index of difficulty**
5	15	preferred	< 2.585
5	30	preferred	<3.585
7.5	15	preferred	2
7.5	30	preferred	3

Fitts's Index of difficulty quantifies the difficulty of the movement task: as the ID increases, the difficulty of the movement increases[118]

4.4.4.3 Performance of goal-directed somatosensory-motor tasks (reach-to-grasp and lift-and-hold) under two conditions of practice (i.e., vision vs no vision)

4.4.4.3.1 Participant position

The participant sits in an upright position on a height-adjustable padded chair, the back against the backrest of the chair and feet flat on the floor. The elbow is flexed to 90 degrees, aligned with the shoulder. The wrist rests at the edge of the table with a loosely closed fist (thumb in opposition to other fingers). Trunk movements are not constrained throughout the trials but participants are reminded to minimise trunk movement.

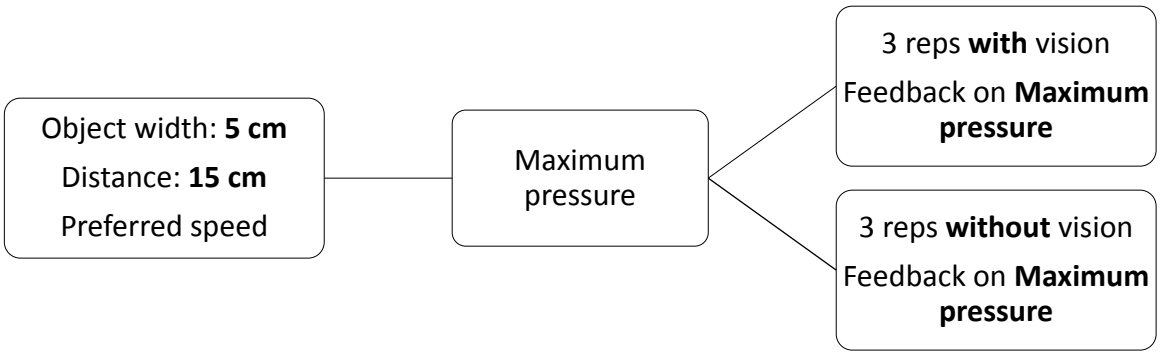
4.4.4.3.2 Performance of reach-to-grasp and lift-and-hold tasks

The somatosensory-motor task involves reach-to-grasp and lift-and-hold of the stationary cylindrical object. The participant reaches forward by flexing the shoulder and extending the elbow. The participant grasps the cylindrical object with a '5-digit multi-finger precision grasp'[133,140] and lifts it to a height of 2-5 cm for 5 seconds before lowering it back on the table. The 5 seconds is sufficient time for correct positioning of the fingers on the cylinder to ensure stable grasp and allows time for sensing and interpreting of tactile cues. The position of the fingers is not constrained on the target objects. Prior to starting the treatment trials, the task is first described to the participant, followed by two practice trials with the less affected hand for familiarisation with object size and weight. A rest of 10 minutes is given after completion of the first block or whenever the participant feels fatigued.

4.4.4.3.3 Conditions of practice: vision vs no vision

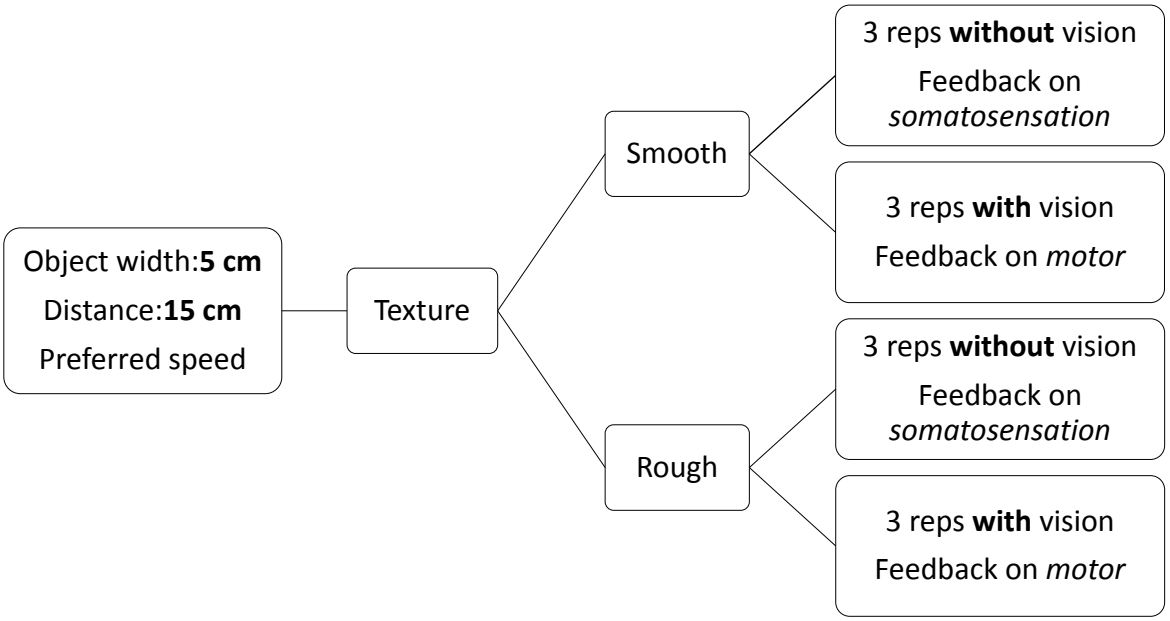
To maximise improvement in the stimulus discrimination being trained, attentive exploration of the stimuli is performed with vision and without vision[133,140,387,388]. These two conditions are standardised across the COMPoSE intervention. For *grasp pressure training*, the first three repetitions are performed *with vision* to facilitate use of visual feedback from the TactArray pressure measurement system and the last three repetitions are performed *without vision* to foster transfer of skill and to increase somatosensory demands of the task (figure 4.2a).

For training of *stimulus discrimination of each somatosensory-motor combination*, vision is occluded every time an object with a different surface property is presented for the first time. In contrast to the grasp pressure training, the first three repetitions are performed *without vision* for the somatosensory training part to allow participants to focus specifically on the somatic sensations[133,140,387,388]; otherwise vision may take over tactile and proprioceptive senses in some instances[171,389]. The last three repetitions are performed *with vision* for the motor training part since it is required to guide our motor actions in real time[390] (figure 4.2b).



Reps: Repetitions

Figure 4.2a: Conditions of practice and number of repetitions with or without vision: *Tactile pressure feedback task: Selected pressure - Maximum pressure variable*



Reps: Repetitions

Figure 4.2b: Conditions of practice and number of repetitions with or without vision: *Somatosensory-motor combination feedback task: Distance and Texture - Short distance parameter and texture*

4.4.4.4 Targeted feedback about both motor and somatosensory attributes of the task and performance

Intrinsic feedback processes are disrupted after stroke, so extrinsic feedback is important for people with stroke to learn a motor skill and improve movement efficiency and consistency of performance[344]. Therefore in COMPoSE, knowledge of results is provided about the outcome of the task, including movement errors and movement successes. Knowledge of performance is also provided in the form of verbal statements and are worded to facilitate an external focus of attention as this has been found to improve RTG performance[215]. The TactArray distributed pressure measurement system is used to give on-line sensorimotor feedback on tactile pressure relative to preferred, minimum and maximum grasp pressures. Somatosensory feedback is also provided on the sensory tactile parameters (crushability, texture and friction). Motor feedback is provided on kinematics of movement such total movement duration, total distance moved, start time of grasp aperture, peak aperture size. Feedback is provided on all trials[215] for grasp pressures, somatosensory and motor parameters of the task.

4.4.4.4.1 Tactile pressure feedback using TactArray distributed pressure measurement system

On-line tactile pressure feedback isprovided by the TactArray system. It consists of matching the pressure exerted by the affected hand to a standard reference (i.e. the pressure used by the less affected hand)[214,391]. The standard reference for tactile pressure feedback is determined by the measures of pressure exerted for 5 seconds during a 5-digit multifinger prehension with the less affected hand during 3 levels of grasp pressure: 1) preferred grasp; 2) minimal grasp, and 3) maximal grasp. A value and a graph (Chameleon TVR 2012 software) are displayed for each grasp pressure on a computer screen. The standard reference is determined prior to the start of each intervention session. To ensure calibration of the response with the affected hand, the pressure exerted by the affected hand is matched to that of the less affected hand for each level of grasp[225,391]. Knowledge of results is provided based on the value and graph display of the standard reference. Knowledge of performance concerns the opening/closure of hand and fingers to adjust the pressure exerted on the TactArray cylinder. Tactile feedback addresses specific grasp deficits, such as on correct finger

positioning on the object for optimal stability of object; development of appropriate grasp forces for safe grip; appropriate individual finger force production with respect to its contribution to grasp force during a 5-digit multifinger grasping; consistency in application of grasp forces; appropriate scaling of forces on the object (not pressing too much or too little to prevent slip or tilt); and timely release of object being held[392,393].

4.4.4.4.2 Somatosensory feedback on combined somatosensory-motor variables, with calibration of the altered sensation

Somatosensory feedback improves tactile discrimination[213]. Somatosensory feedback is provided on four main aspects of active exploration of the surface properties: 1) on the accuracy of response by allowing the client to see the correct response (e.g. smooth or rough object surface), the therapist telling the client what the actual texture is, or by exploration of the stimulus by the client with the other hand; 2) on the actual tactile sensation and critical difference of the somatosensory attribute being trained; 3) guidance on movements of the hand and exploratory finger movements that are most optimal to explore the tactile sensory attribute e.g. static contact, lateral motion, contour following; and 4) using calibration, which involves comparison of the tactile sensation felt by the affected hand with the less affected hand[213,225].

4.4.4.4.3 Motor feedback on movement performances, with calibration of motor response

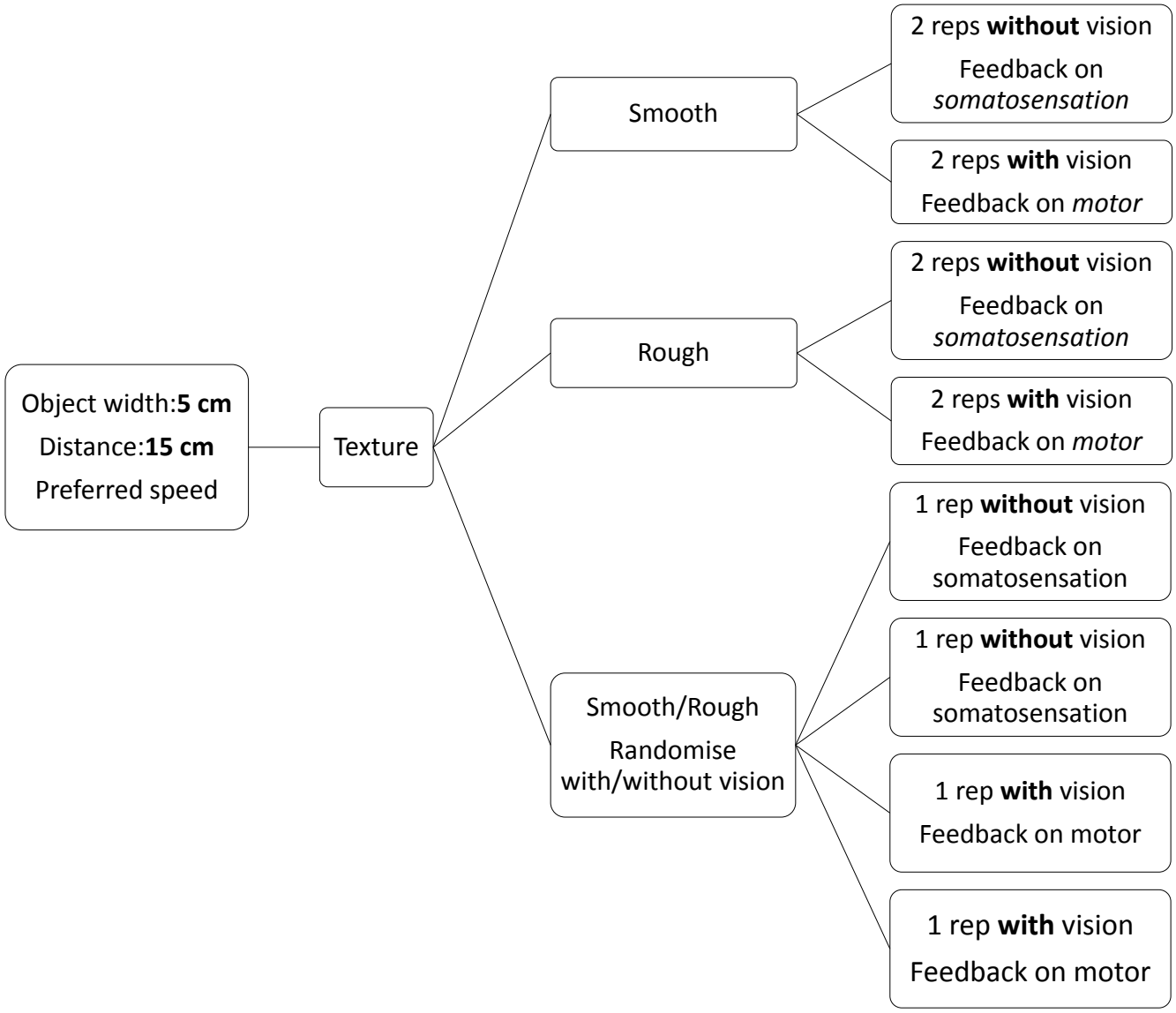
Motor feedback is essential to improve kinematic performances of RTG[215,394]. Motor feedback is provided using attentive exploration strategies applied to kinematic performances and is based on matching the kinematic measures of the affected upper limb to a standard reference (less affected upper limb). The standard reference for online motor feedback is determined prior to the start of each intervention session. To ensure calibration of the motor response, the kinematic measures of the affected hand are matched to those of the standard reference (less affected hand) during reaching and grasping.

To facilitate active learning, motor feedback is provided on movement duration of hand transport (using a stopwatch) during the first training block and on grasp aperture (qualitatively) during the second training block. Feedback on movement duration was chosen because it is a prominent kinematic variable associated with motor impairment and functional capacity[395]. Moreover, task parameters that emphasise speed positively influence reaching strategies with the more-affected upper-extremity[396]. Hence, encouraging the affected upper limb to perform RTG with the same movement duration as the less affected hand positively reinforces the affected arm to improve its preferred speed. Feedback on grasp aperture was chosen because the ability to actively extend the fingers and thumb post-stroke for grasping and releasing is a key criterion for participation in activities of daily living[397]. Therefore, increased grasp aperture as a result of improved digit extension is an important motor skill to enable effective object handling. Feedback also focuses on: speed of grasp formation; pre-shaping of hand and fingers; maximum grasp aperture as soon as reach starts; efficient closing of fingers in a single smooth movement.

4.4.4.5 Varied and intensive practice

Varied practice

Varied practice is integrated in COMPoSE training to reduce anticipation effects and make the intervention more challenging to enhance learning and to encourage the transfer of skill to the different tasks[398]. In the last five sessions, the two somatosensory variables within each somatosensory parameter are presented in a random order, e.g., for texture parameter, first the smooth texture is presented followed by the rough texture, then either the smooth or the rough variation (figure 4.3). This varied practice keeps the participant engaged in the task in order to promote active learning.



Reps: Repetitions

Figure 4.3. Varied practice for somatosensory-motor combinations: with or without vision e.g. short distance variable and texture

4.4.5 Item 5. Who provided: Description of the expertise, background, and training given to intervention provider

The COMPoSE intervention is expected to be delivered by one physiotherapist or occupational therapist, with expertise in neurorehabilitation and upskilling in the

COMPoSEapproach. For the Phase II study, the research therapist was upskilled in RTG training and SENSe therapy by the originators of those interventions.

4.4.6 Item 6. How: Mode of intervention delivery

The COMPoSE intervention is provided individually and face-to-face to participants.

4.4.7 Item 7. Where: Location of intervention delivery

The proof-of-concept COMPoSE study is being conducted in the motion analysis laboratory at the Hunter Medical Research Institute (Newcastle, Australia). It is anticipated that future delivery may be in a rehabilitation setting or specialist clinic. A quiet room is recommended to facilitate focused attention to the learning demands of the therapy.

4.4.8 Item 8. When and How Much

Intensive practice with a high number of repetitions is provided through repeated performance[62,209] of the *reach-to-grasp and lift-and-hold* task. Within a session the participant aims to complete 6 repetitions of each somatosensory-motor combination parameter within the training matrix. An example of the sequence and number of repetitions for combinations practiced throughout the matrix is illustrated in Table 4.2. The actual number of repetitions completed will vary with the capacity of the individual and where the individual lies in the learning continuum. For example, during early phases of learning the individual may be expected to take more time to integrate the feedback and thus the number of repetitions may be lower. Each session lasts approximately 1.5 hours (with rest) and participants are encouraged to perform up to 36 combinations of somatosensory-motor parameters within a session, each with 6 repetitions (216 repetitions in total). Ten training sessions are proposed to be delivered over 3 weeks at a frequency of 3-4 sessions per week, consistent with skill based learning approaches and current sensorimotor interventions[213].

Table 4.2. Examples of operationalisation of part of the training matrix

Object width/cm	**Object distance/cm**	**Selected grasp pressure**			**Crushability**		**Texture**		**Friction**		**Vision Yes/No**	**No. of reps**
		TactArray device			*Soft plastic cup*	*Hard plastic cup*	*Felt*	*Sand paper*	*Rubber*	*Teflon*		
5	15	Preferred									No	3
5	15	Preferred									Yes	3
5	15		Minimum								No	3
5	15		Minimum								Yes	3
5	30			Maximum							No	3
5	30			Maximum							Yes	3
5	30				Soft						No	3
5	30				Soft						Yes	3
5	30					Hard					No	3
5	30					Hard					Yes	3
7.5	15						Smooth				No	3
7.5	15						Smooth				Yes	3
7.5	15							Rough			No	3
7.5	15							Rough			Yes	3
7.5	30								Non-slip		No	3
7.5	30								Non-slip		Yes	3
7.5	30									Slip	No	3
7.5	30									Slip	Yes	3

No. of reps: Number of repetitions

4.4.9 Item 9. Tailoring: Individualising the intervention

The COMPoSE intervention is a structured therapy that is designed to address the somatosensory and motor challenges a stroke survivor may experience in the fundamental reach-to-grasp and lift-and-hold tasks required to perform a wide range of daily activities. All participants will receive the intervention in the same order as per the standardised matrix. This is to establish the framework for the key parameters selected and the levels of difficulty. Although the training is structured to cover the key parameters of training important to this task, the emphasis on somatosensory and/or motor feedback given for each somatosensory-motor combination task has scope to vary according to the needs of the individual. The intervention is also individualised based on rate of progression and the number of repetitions achieved within and across sessions. It is expected that the pace of progression through the learning tasks provided in the matrix will vary with severity of impairment and learning capacity. If the scheduled section of the training matrix is not completed in a particular session, the participant starts the next treatment session where the intervention was previously stopped so that the participant is exposed to all of the somatosensory-motor combinations.

4.5 DISCUSSION

Performance of complex tasks in everyday life requires successive and fast sensorimotor integration. However, strategies involving integrated somatosensory-motor retraining of the hand and arm have been poorly addressed by current stroke rehabilitation research. It could be argued that any manual task inherently involves the integration of both somatosensory and motor function. By combining and integrating several somatosensory and motor parameters within a task, and by frequently varying these parameters and the conditions of practice in the COMPoSE intervention, the sensory and motor pathways are continuously challenged to respond synchronously and more often to these changes. It is proposed that this integrated somatosensory-motor retraining approach could optimise processes that drive reorganisation of brain activation and neural connectivity to a greater extent leading to maximal functional improvement in the paretic upper limb compared to training somatosensory and motor function sequentially, which might be a suboptimal

approach to relearn functional movements. Therefore, in order to maximise improvement of functional movements such as reach-to-grasp after stroke, it is considered essential to address key sensory systems involved in this task[399]. It should be noted that even though the COMPoSE intervention does not directly target proprioceptive training, the latter is inherent in the reach and grasp aspects of the task and feedback is provided in part with the motor training. For example, the proprioceptive demands are increased under no vision conditions and feedback is provided with feedback on movement distance and grasp aperture.

The TIDieR checklist was a very valuable tool facilitating the reporting of essential information on the content of the COMPoSE intervention that could be useful for researchers and clinicians, even though items 10-12 in the TIDieR checklist, which pertain to an exploratory trial are not reported here.

Implications for practice

The COMPoSE intervention offers a learning based approach that involves processing of multisensory information from the tactile, proprioceptive and visual systems, which are simultaneously integrated with motor function.A novel aspect of this intervention involves using TactArray as a means of re-training sensorimotor function for scaling of grasp forces, which is crucial for dexterity. This could encourage skill transfer for adaptive control of grasp forces at the fingertips in response to surface feature detection and discrimination.Therefore, COMPoSE might be more effective in optimising functional improvement of upper limb after stroke compared to an intervention involving a single sensory approach.

The standardised training matrix further facilitates the delivery of the COMPoSE intervention as it explicitly and systematically incorporates all the combinations of somatosensory-motor parameters, conditions of practice, feedback delivery focused on somatosensory and motor aspects as well as adaptive pressure outputs. The matrix provides adequate standardisation so that the intervention could be replicated by clinicians and researchers.

4.6 CONCLUSION

A“COMbined Physical and somatoSEnsory training” (COMPoSE) intervention to improve upper limb function after stroke has been described and a standardised training matrix has been developed to facilitate intervention delivery. The COMPoSE intervention *combines* somatosensory and movement training, delivered *synchronously, within the same treatment and within the same task.*

Appendix 4.1

Gopaul U, van Vliet P, Callister R,Nilsson M, Carey L. COMbined Physical and somatoSEnsory training after stroke: Development and description of a novel intervention to improve upper limb function. *Physiother ResInt*. 2018;e1748.https://doi.org/10.1002/pri.1748

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RESEARCH ARTICLE

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COMbined Physical and somatoSEnsory training after stroke: Development and description of a novel intervention to improve upper limb function

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Abstract

Background and purpose: After stroke, reach-to-grasp goal-directed movements are disrupted as a result of both residual motor and somatosensory impairments. This report describes the rationale and development of a new upper limb stroke rehabilitation intervention known as COMPoSE: "COMbined Physical and somatoSEnsory training," designed to improve somatosensory and motor deficits in the upper limb after stroke. A standardized training matrix has been developed to facilitate intervention delivery.

Methods: The COMPoSE intervention was developed through the following stages: (a) Definition and operationalization of somatosensory and motor variables used in training sensation and movement after stroke; (b) development of methods to give feedback to enhance skill acquisition; and (c) Combination of somatosensory and motor variables, and feedback, into a standardized training matrix. The reporting of the COMPoSE intervention adheres to the recommendations of the Template for Intervention Description and Replication checklist to facilitate replication of the intervention in the future.

Results: The essential features of COMPoSE include combined somatosensory–motor training variables (grasp pressure, distance, object size, crushability, surface texture, and friction), feedback, and calibration using a haptic device providing measures of grasp pressure, use of anticipation trials, and high-dose repetitive task practice. Ten treatment sessions are delivered over 3 weeks, using a standardized matrix for treatment delivery.

Conclusion: COMPoSE is a new intervention that combines somatosensory and movement training, delivered *synchronously*, *within the same intervention*, and *within the same task*.

KEYWORDS

extrasensory, somatosensory-motor, stroke, upper limb

1 | INTRODUCTION

After stroke, reach-to-grasp (RTG) movements are disrupted as a result of residual motor and somatosensory impairments (Cirstea & Levin, 2000). Compared with healthy adults, stroke survivors with motor impairment experience deficits, such as longer movement duration, slower peak velocity (van Vliet & Sheridan, 2007), earlier peak deceleration (van Vliet & Sheridan, 2007), and reduced movement smoothness (Thielman, Dean, & Gentile, 2004) during the transport phase of RTG movements. Stroke survivors also suffer from impairments in grasp formation and release, such as inconsistent grasp apertures, which result from disruption in the coordination of muscle activity between finger flexors and extensors, as well as between proximal muscles involved in the hand transport phase of a RTG (Lang et al., 2005). A lack of volitional control of finger and thumb extension further contributes to deficits in hand shaping during grasping and incorrect positioning of fingers for effective hand use (Lang, DeJong, & Beebe, 2009).

Somatosensory function plays a critical role in controlled grasp and is tightly coupled with action. Impaired touch sensation after stroke makes it difficult to discriminate different physical properties of objects, such as texture, hardness, and surface friction (Carey & Matyas, 2011). As a result, the fingers and the hand are limited in their ability to effectively coordinate grip and lift forces and to appropriately scale grip force for effective object handling, lifting, and manipulation (Blennerhassett, Matyas, & Carey, 2007; Nowak et al., 2007). The selection of appropriate grip forces is largely determined by object properties, including weight, surface texture, slipperiness, and shape, as well as the magnitude, direction, and points of application of these grip forces on the objects (Flanagan & Johansson, 2002). As a consequence, people with somatosensory impairment rely extensively on vision to help gauge the force required in object grasping (Blennerhassett et al., 2007; Lederman, Thorne, & Jones, 1986). Effective grip force modulation is the result of a complex interplay of tactile sensory feedback signals provided by cutaneous mechanoreceptors found in the glabrous skin of the grasping fingers and modulated muscle activity in the hand and arm (Johansson & Westling, 1984, 1988; Kwakkel, Kollen, van der Grond, & Prevo, 2003). Proprioceptive and cutaneous information also play a significant role in controlling finger span and hand shape during object handling (Santello & Soechting, 1997). Further, proprioceptive information is important for internal models of the body and peripersonal space (Proske & Gandevia, 2012) and is thus crucial in the planning, execution, correction, and learning of goal-directed actions.

Significant correlation between motor and somatosensory impairment (tactile sensation and proprioception) has been found in the upper limb after stroke (Scalha, Miyasaki, Lima, & Borges, 2011), suggesting that an underlying somatosensory impairment may limit performance of motor tasks (Hunter & Crome, 2002). In addition, controlled experimentation of the relative contribution of somatosensory and motor impairment to the fundamental pinch-grip lift-and-hold task identified that somatosensory impairment (in particular surface friction discrimination) has an additional and negative impact on timing and force adjustment during pinch grip (Blennerhassett et al., 2007). Finally, functional arm use has been associated with improved somatosensory skills (tactile, proprioception, and haptic object recognition) following sensory discrimination training, although the amount of change in arm use varied across survivors (Turville, Carey, Matyas, & Blennerhassett, 2017).

Functional imaging studies in humans have demonstrated enhanced activation of the somatosensory cortex following motor training (Laible et al., 2012; Liu, Song, & Zhang, 2014). Similar studies also found that motor recovery is associated with reorganization of somatosensory cortices after stroke (Laible et al., 2012; Liu et al., 2014; Roiha et al., 2011; Rossini et al., 1998; Schaechter, Moore, Connell, Rosen, & Dijkhuizen, 2006). For example, following tactile stimulation, increased activation responses were observed not only in the primary and secondary somatosensory cortices but also in the primary motor cortex and supplementary motor area (Schaechter et al., 2006). This suggests that there may be benefits to synchronously coupling somatosensory training with motor training to enhance activation responses in the somatosensory and motor cortices.

Conditions of training and methods to enhance learning of somatosensory discriminations and controlled movement execution are also likely to be important. Additionally, augmented feedback is an important element to enhance motor learning and somatosensory retraining in upper limb stroke rehabilitation (Carey, 2012a; Carey, 2012b; Carey, Macdonell, & Matyas, 2011; Subramanian, Massie, Malcolm, & Levin, 2010; van Vliet & Wulf, 2006). Similarly, the use of attention and a graded matrix of training tasks are important in skill-based learning (Carey, Polatajko, Connor, & Baum, 2012).

We therefore sought to develop an intervention combining somatosensory and motor functions, *within the same intervention* and *within the same task*, to improve upper limb function after stroke. The intervention uses principles of learning and conditions of training that have shown to be effective in task-specific motor training (Hubbard, Parsons, Neilson, & Carey, 2009) and in training somatosensory discriminations (Carey et al., 2011). Principles are applied to both motor and somatosensory components of the task and to the overall task and are facilitated by specialized equipment such as the TactArray (PPS, 2014).

The aim of this report is to describe the development and rationale for the essential features of this intervention, which we have named COMbined Physical and somatoSEnsory training (COMPoSE). In order to describe COMPoSE with sufficient detail and rigour to allow its application in a future randomized controlled trial (RCT), and in clinical practice should COMPoSE prove effective, we used the recommended Template for Intervention Description and Replication (TIDieR) checklist (Hoffmann et al., 2014), an extension of the CONSORT 2010 statement (Schulz, Altman, & Moher, 2010). The COMPoSE intervention is being tested in a Phase II study to determine the feasibility of delivery of the intervention and to monitor the responses of participants with stroke to the intervention to improve somatosensory and motor deficits and upper limb function after stroke.

2 | METHODS

The development of the COMPoSE intervention was informed by a review of the literature, and consensus was used to agree on the

somatosensory and motor variables from the literature to be targeted in this combined intervention. The COMPoSE intervention was developed following three sequential stages:

1. Definition and operationalization of somatosensory and motor variables used in training sensation and movement in the context of upper limb function after stroke

COMPoSE is designed to improve reach and grasp, two fundamental actions needed for goal-directed use of the arm. Two motor and three somatosensory parameters were selected for training in the context of the reach and grasp task. Two motor parameters (object distance and object width) are combined with three somatosensory parameters (texture, friction, and crushability) and three selected grasp pressures (preferred, minimum, and maximum grasp pressure the output). Each parameter has two variables. Object distance and object size were selected to vary as they impact the kinematics of the task (Michaelsen, Magdalon, & Levin, 2009; van Vliet & Sheridan, 2009). Texture, friction, and crushability were selected as they directly impact controlled grasp and manipulation of objects (Blennerhassett et al., 2007; Carey et al., 2011). Each combination is performed with and without vision.

2. Development of methods to give feedback to enhance skill acquisition

Principles of training and conditions of practice are primarily derived from approaches to task-specific training (Hubbard et al., 2009) and SENSe discrimination training (Carey, 2011; Carey, 2012b; Carey et al., 2011). These include augmented feedback enhanced by specially designed tasks that are graded in relation to motor and somatosensory features. The mechanisms and rationales are discussed later.

3. Combination of somatosensory and motor variables, and feedback, into a standardized training matrix

A matrix approach was adopted consistent with that described for SENSe discrimination training (Carey, 2011; Carey, 2012b; Carey et al., 2011). Use of a matrix approach allows for graded progression within motor and somatosensory functions and across sensorimotor actions and tasks (Carey, 2012b). This approach aligns with neuroscience evidence that motor and somatosensory functions or attributes are distributed in interconnected networks with gradients of separation between them (Frey et al., 2011), and transfer may be facilitated with multimodal training (Olsson, Jonsson, & Nyberg, 2008).

The potential order of variables in the matrix was mapped using consensus based on a logical and pragmatic training approach consistent with the complex functional use of the upper limb and with regards to levels of difficulty of the somatosensory and motor components of reach and grasp. For example, integrated somatosensory and motor functions and graded levels of difficulty were considered in relation to object size, distance, texture, crushability, and so on. Furthermore, the training of adaptive pressure is closely related to training of discrimination of properties of the object, such as crushability of the object (Hermsdorfer, Li, Randerath, Goldenberg, & Eidenmuller, 2011), as well as for training for discrimination of surface properties, such as texture (Johansson, Hger, & Backstrom, 1992) and friction (Cadoret & Smith, 1996; Flanagan & Johansson, 2002; Johansson & Westling, 1984, 1988). Training and grading of these attributes have been tested in the context of the SENSe intervention (Carey et al., 2011).

3 | RESULTS

3.1 | Description of the COMPoSE intervention using the TIDieR checklist

Item 1. Brief name

COMbined Physical and somatoSEnsory training (COMPoSE)

Item 2. Why: Rationale for the intervention

Motor and somatosensory functions are jointly integrated and tightly coupled in actions performed in everyday life (Frey et al., 2011). However, in clinical practice, interventions directed at motor deficits have traditionally been separated from interventions directed at somatosensory deficits (Ackerley, Borich, Oddo, & Ionta, 2016; Pollock et al., 2014; Veerbeek et al., 2014). Moreover, treatment of somatosensory functions is often neglected (Kalra, 2010). By treating motor and somatosensory impairments separately, the potential beneficial effects of combining somatosensory training to further enhance sensorimotor function and action are not utilized. This notion could partially explain the relative lack of effectiveness or limited gains in upper limb functions from current interventions in stroke rehabilitation. A Cochrane review of systematic reviews (n = 40 reviews; 503 RCTs; 18,078 participants) found moderate quality evidence for motor only interventions, such as constraint-induced movement therapy, mental practice, mirror therapy, virtual reality, and relatively high-dose repetitive task practice (Pollock et al., 2014). There was insufficient evidence to recommend upper limb interventions including task-specific training, robotics, Bobath approach, brain stimulation, and strength training (Pollock et al., 2014). Although another meta-analysis found significant improvements in upper limb motor function with motor interventions, such as robotics, neuromuscular stimulation, and constraint-induced movement therapy, the evidence indicates only small to moderate effects, except for constraint-induced movement therapy (Veerbeek et al., 2014).

Studies reporting the efficacy of somatosensory interventions after stroke are currently limited. A Cochrane review (Doyle, Bennett, Fasoli, & McKenna, 2010; n = 13; without meta-analysis) found only preliminary evidence of efficacious sensory interventions after stroke, such as somatosensory discrimination training, thermal stimulation, and intermittent pneumatic compression. More recently, a meta-analysis of interventions for somatosensory function (n = 12 RCTs) found significant positive summary effect sizes for somatosensory function and muscle tone following sensory retraining but did not find significant summary effect sizes for motor function of the affected arm (Veerbeek et al., 2014). In summary, currently there is no high-quality evidence for any single sensory or motor upper limb intervention,

except for constraint-induced movement therapy (Doyle et al., 2010; Pollock et al., 2014; Veerbeek et al., 2014).

A few studies on upper limb interventions in stroke rehabilitation have attempted to train somatosensation and movement together (Byl et al., 2003; Smania, Montagnana, Faccioli, Fiaschi, & Aglioti, 2003). Importantly, the somatosensory and motor interventions were delivered sequentially, not synchronously. These interventions resulted in no gain or only modest gains in functional independence, strength, somatosensory discrimination, and fine motor control (Byl et al., 2003; Smania et al., 2003). Also, these studies had small sample sizes (n = 1–76) and low statistical power.

In order to more comprehensively address somatosensory and motor deficits, the potential exists to *combine* somatosensory and motor training and deliver them synchronously to improve upper limb function after stroke. We hypothesize that greater gains are likely with synchronous somatosensory and motor relearning and practice, on the basis that this would activate both the somatosensory and motor networks in the brain, as occurs in everyday skilled actions, than if somatosensory and movement interventions are delivered separately. In addition, stronger connections may be formed between the somatosensory cortex and the functionally related motor cortex to boost neuroplasticity. No study has yet investigated the effects of combining somatosensory and motor training and delivering it synchronously. This lead to the design of the COMPoSE intervention.

The COMPoSE intervention draws on the best available evidence for somatosensory and motor retraining of the upper limb and systematically applies the principles of training and conditions of training to achieve combined sensorimotor training of the upper limb. The COMPoSE intervention was developed for use by people with residual somatosensory and motor deficits in their upper limb resulting from stroke. The aim is to retrain goal-directed use of the arm after stroke, with a focus on integration of RTG movements and discrimination of somatosensory features of objects important for controlled use of the arm in daily activities. It is derived from and extends existing neuroscience-based therapies focused on reach and grasp (Cunningham, Turton, van Wijck, & van Vliet, 2016; van Vliet, Pelton, Hollands, Carey, & Wing, 2013) and somatosensory discrimination training in the upper limb (Carey, 2011; Carey et al., 2011). These therapies were selected as they have strong foundations in neuroscience and learning (Carey, 2012b; Cramer et al., 2011; Nudo, 2003; van Vliet et al., 2013); are designed to help people who have experienced stroke regain skills in reach, grasp (Turton et al., 2016), and somatosensory discrimination (Carey et al., 2011; Carey & Matyas, 2011); and have demonstrated statistically and clinically significant effectiveness in small RCTs (Carey et al., 2011; Turton et al., 2016). These interventions have also been operationalized into clinical practice protocols (Carey, 2012a; Carey et al., 2011; Turton et al., 2016).

Item 3. What: Materials used in the intervention

The materials used in the COMPoSE intervention include objects to be grasped and a haptic device to provide feedback. The objects vary in size diameter, surface texture, surface friction, and crushability. Two dimensions of a cylindrical object (salt shaker) are used. The smaller cylinder is 5 cm in diameter and 12.5 cm high; the larger cylinder measures 7.5 cm in diameter and is 12.5 cm high. The mass of both cylinders is adjusted to 160 g. Four versions of each cylinder are provided, with different surface properties to stimulate somatosensory cues involved in texture differentiation (texture and friction). For texture, felt material is used as a smooth surface on one cylinder, and sandpaper (100 grit) is used as a rough surface on a contrasting cylinder. For friction, rubber is used as the nonslippery surface on one cylinder, and polytetrafluoroethylene (Teflon) is used as the slippery surface on the contrasting cylinder. Rubber and Teflon have different frictional properties (coefficients of friction, 0.35 and 0.96, respectively) while having similar macrostructures (Blennerhassett et al., 2007). For crushability, soft and hard plastic cups are used because they replicate drinking cups used in real life (Carey, 2011). The cups measure 5.0 cm in diameter and are 9.2 cm high.

The TactArray pressure distribution system is a haptic device used for providing feedback on selected grasp pressures (Pressure Profile Systems) (PPS,2014). The TactArray pressure distribution system is a tactile data acquisition method devised by Pressure Profile Systems. Two dimensions of TactArray cylinders are used, closely related to the size of the task objects. The TactArray cylinders are hard and covered with pressure sensor arrays (conformable TactArray T4500 SN1104; sensor SN5385,5438) constructed from a soft and flexible conductive cloth approximately 1-mm thick. Further details of the system will be elaborated in Item 4 below.

Item 4. What: Procedures, activities, and/or processes used in the intervention

3.2 | Critical components of the COMPoSE intervention

The COMPoSE intervention has four critical components: (a) matrix of specially designed somatosensory and motor tasks to permit progressive and systematic grading according to specific parameters (e.g., levels of difficulty progressing from easy to more difficult discriminations), (b) performance of goal-directed somatosensory–motor tasks (RTG and lift-and-hold) under two conditions of practice (i.e., with vision and without vision), (c) targeted feedback about both motor and somatosensory performance, and (d) varied and intensive repetitive practice.

3.3 | Matrix of specially designed training tasks with progressive and systematic grading of somatosensory–motor tasks according to specific parameters

3.3.1 | Somatosensory and motor parameters of the COMPoSE intervention

There is a total of 36 combinations of somatosensory–motor tasks organized into a standardized training matrix (Figure 1). Two motor parameters (object distance and object width) are combined with three somatosensory parameters (texture, friction, and crushability) and three selected grasp pressures (preferred, minimum, and maximum grasp pressure; Figure 1). Each motor and somatosensory parameter has two variables. Motor parameter variables include object width

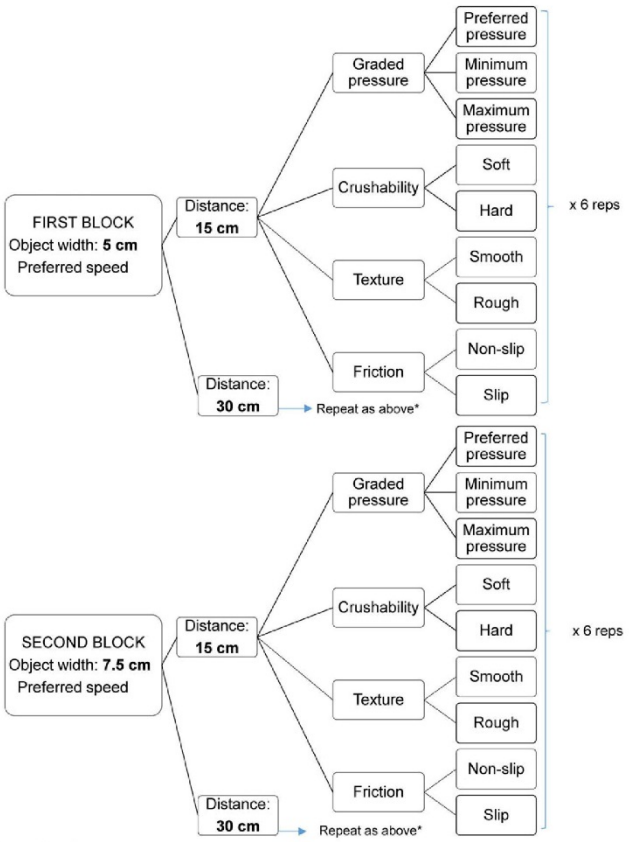


FIGURE 1 COMbined Physical and somatoSEnsory training standardized training matrix

Reps: Repetitions

(5 cm and 7.5 cm) and distance (15 cm and 30 cm). Somatosensory parameter variables include surface texture (smooth and rough) and surface friction (slip and nonslip) and crushability (hard and soft). Object shape and weight (160 g) are kept constant throughout the intervention. All tasks are performed at preferred speed (Figure 1).

The training is organized in two blocks within a matrix in a fixed order (Figure 1). In the first block, object width (5-cm diameter cylinder) is kept constant, whereas object distance (15 cm and 30 cm) and all somatosensory parameters are varied. In the second block, object width (7.5-cm diameter cylinder) is kept constant, whereas object distance (15 cm and 30 cm) and all somatosensory parameters are varied. Additional somatosensory–motor variations are provided through selected grasp pressure training using preferred, minimum, and maximum grasp pressure (Figure 1).

3.3.2 | Graded levels of difficulty

Progressive difficulty for the motor and somatosensory variables is integrated within each somatosensory–motor combination and across the standardized training matrix (Carey & Matyas, 2005). Fitts's index of difficulty (Fitts, 1954) is used to quantify the difficulty of the motor tasks, calculated from $\log_2\left(\frac{2\,X\,Object\ distance}{Object\ width}\right)$. For example, as object distance is doubled across the COMPoSE standardized matrix, the indices of difficulty are progressively increased. In the first block, training commences with easier tasks (e.g., smaller object width, closer object, and nonslippery surface) followed by more difficult tasks (e.g., smaller object width, further object, and slippery surface). In the second block, repetitions with the larger object width and increasing distances are practised to progress the level of difficulty for hand opening. The indexes of difficulty in COMPoSE are summarized in Table 1.

3.4 | Performance of goal-directed somatosensory–motor tasks (RTG and lift-and-hold) under two conditions of practice (i.e., vision vs. no vision)

3.4.1 | Participant position

The participant sits in an upright position on a height-adjustable padded chair, the back against the backrest of the chair, and feet flat on the floor. The elbow is flexed to 90°, aligned with the shoulder. The

TABLE 1 Indices of difficulty in COMPoSE

Object parameters varied		Parameters constant	Fitts's index of difficulty
Width (cm)	Distance (cm)	Speed	
5	15	Preferred	<2.585
5	30	Preferred	<3.585
7.5	15	Preferred	2
7.5	30	Preferred	3

Note. Fitts' index of difficulty quantifies the difficulty of the movement task: as the ID increases, the difficulty of the movement increases (Fitts, 1954). COMPoSE: COMbined Physical and somatoSEnsory training.

wrist rests at the edge of the table with a loosely closed fist (thumb in opposition to other fingers). Trunk movements are not constrained throughout the trials, but participants are reminded to minimize trunk movement.

3.4.2 | Performance of RTG and lift-and-hold tasks

The somatosensory–motor task involves RTG and lift-and-hold of the stationary cylindrical object. The participant reaches forward by flexing the shoulder and extending the elbow. The participant grasps the cylindrical object with a "five-digit multifinger precision grasp" (Napier, 1956; Zatsiorsky & Latash, 2008) and lifts it to a height of 2–5 cm for 5 s before lowering it back on the table. The 5 s is sufficient time for correct positioning of the fingers on the cylinder to ensure stable grasp and allows time for sensing and interpreting of tactile cues. The position of the fingers is not constrained on the target objects. Prior to starting the treatment trials, the task is first described to the participant, followed by two practice trials with the less affected hand for familiarization with object size and weight. A rest of 10 min is given after completion of the first block or whenever the participant feels fatigued.

3.4.3 | Conditions of practice: vision vs no vision

To maximize improvement in the stimulus discrimination being trained, attentive exploration of the stimuli is performed with vision and without vision (Carey, 1993; Carey, Matyas, & Oke, 1993; Napier, 1956; Zatsiorsky & Latash, 2008). These two conditions are standardized across the COMPoSE intervention. For *grasp pressure training*, the first three repetitions are performed *with vision* to facilitate the use of visual feedback from the TactArray pressure measurement system, and the last three repetitions are performed *without vision* to foster transfer of skill and to increase somatosensory demands of the task (see Figure 2a).

For training of *stimulus discrimination of each somatosensory–motor combination*, vision is occluded every time an object with a different surface property is presented for the first time. In contrast to the grasp pressure training, the first three repetitions are performed *without vision* for the somatosensory training part to allow participants to focus specifically on the somatic sensations (Carey, 1993; Carey et al., 1993; Napier, 1956; Zatsiorsky & Latash, 2008); otherwise, vision may take over tactile and proprioceptive senses in some instances (Clark, 1986; Lederman et al., 1986). The last three repetitions are performed *with vision* for the motor training part since it is required to guide our motor actions in real time (Goodale & Humphrey, 1998) (see Figure 2b).

3.5 | Targeted feedback about both motor and somatosensory attributes of the task and performance

Intrinsic feedback processes are disrupted after stroke, so extrinsic feedback is important for people with stroke to learn a motor skill and improve movement efficiency and consistency of performance (van Vliet & Wulf, 2006). Therefore in COMPoSE, knowledge of results is provided about the outcome of the task, including movement errors and movement successes. Knowledge of performance is also provided in the form of verbal statements and are worded to facilitate an external focus of attention as this has been found to improve RTG performance (Durham et al., 2014). The TactArray distributed pressure measurement system is used to give online sensorimotor feedback on tactile pressure relative to preferred, minimum, and maximum grasp pressures. Somatosensory feedback is also provided on the sensory tactile parameters (crushability, texture, and friction). Motor feedback is provided on kinematics of movement such total movement duration, total distance moved, start time of grasp aperture, and peak aperture size. Feedback is provided on all trials (Durham et al., 2014) for grasp pressures, somatosensory, and motor parameters of the task.

3.5.1 | Tactile pressure feedback using TactArray distributed pressure measurement system

On-line tactile pressure feedback is provided by the TactArray system. It consists of matching the pressure exerted by the affected hand to a standard reference (i.e. the pressure used by the less affected hand; Carey, 2011; Carey, Oke, & Matyas, 1997). The standard reference for tactile pressure feedback is determined by the measures of pressure exerted for 5 s during a five-digit multifinger prehension with the less affected hand during three levels of grasp pressure: (a) preferred grasp, (b) minimal grasp, and (c) maximal grasp. A value and a graph (Chameleon TVR 2012 software) are displayed for each grasp pressure on a computer screen. The standard reference is determined prior to the start of each intervention session. To ensure calibration of the response with the affected hand, the pressure exerted by the affected hand is matched to that of the less affected hand for each level of grasp (Carey, 2012a; Carey et al., 1997). Knowledge of results is provided based on the value and graph display of the standard reference. Knowledge of performance concerns the opening or closure of hand and fingers to adjust the pressure exerted on the TactArray cylinder. Tactile feedback addresses specific grasp deficits, such as on correct finger positioning on the object for optimal stability of object, development of appropriate grasp forces for safe grip, appropriate individual finger force production with respect to its contribution to grasp force during a five-digit multifinger grasping, consistency in application of grasp forces, appropriate scaling of forces on the object (not pressing too much or too little to prevent slip or tilt), and timely release of object being held (Hsu et al., 2012; Kurillo, Gregoric, Goljar, & Bajd, 2005).

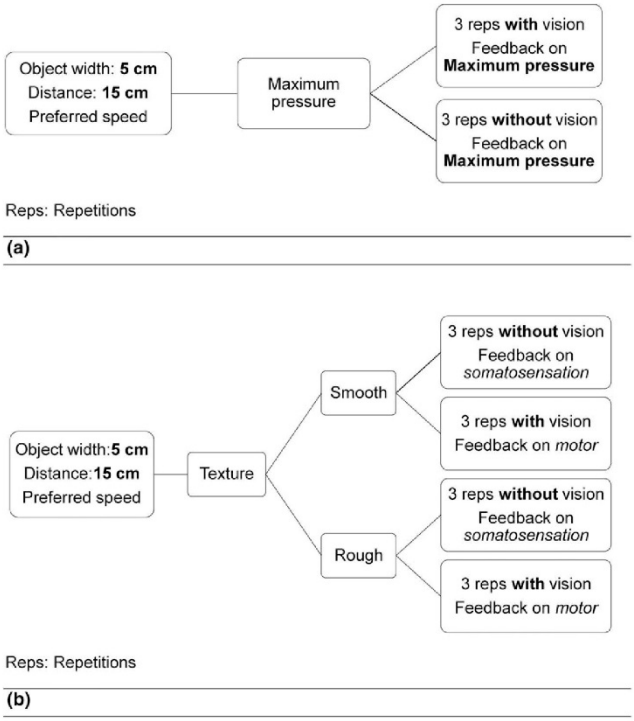


FIGURE 2 (a) Conditions of practice and number of repetitions with or without vision: Tactile pressure feedback task: Graded pressure–Maximum pressure variable. (b) Conditions of practice and number of repetitions with or without vision: Somatosensory–motor combination feedback task: Distance and Texture–Short distance parameter and texture

3.5.2 | Somatosensory feedback on combined somatosensory–motor variables, with calibration of the altered sensation

Somatosensory feedback improves tactile discrimination (Carey et al., 2011). Somatosensory feedback is provided on four main aspects of active exploration of the surface properties: (a) on the accuracy of response by allowing the client to see the correct response (e.g., smooth or rough object surface), the therapist telling the client what the actual texture is, or by exploration of the stimulus by the client with the other hand; (b) on the actual tactile sensation and critical difference of the somatosensory attribute being trained; (c) guidance on movements of the hand and exploratory finger movements that are most optimal to explore the tactile sensory attribute, for example, static contact, lateral motion, contour following; and (d) using calibration, which involves comparison of the tactile sensation felt by the affected hand with the less affected hand (Carey, 2012a; Carey et al., 2011).

3.5.3 | Motor feedback on movement performances, with calibration of motor response

Motor feedback is essential to improve kinematic performances of RTG (Cirstea & Levin, 2007; Durham et al., 2014). Motor feedback is provided using attentive exploration strategies applied to kinematic performances and is based on matching the kinematic measures of the affected upper limb to a standard reference (less affected upper limb). The standard reference for online motor feedback is determined prior to the start of each intervention session. To ensure calibration of the motor response, the kinematic measures of the affected hand are matched to those of the standard reference (less affected hand) during reaching and grasping.

To facilitate active learning, motor feedback is provided on movement duration of hand transport (using a stopwatch) during the first training block and on grasp aperture (qualitatively) during the second training block. Feedback on movement duration was chosen because it is a prominent kinematic variable associated with motor impairment and functional capacity (Li et al., 2015). Moreover, task parameters that emphasize speed positively influence reaching strategies with the more-affected upper extremity (Massie & Malcolm, 2012). Hence, encouraging the affected upper limb to perform RTG with the same movement duration as the less affected hand positively reinforces the affected arm to improve its preferred speed. Feedback on grasp aperture was chosen because the ability to actively extend the fingers and thumb post stroke for grasping and releasing is a key criterion for participation in activities of daily living (Wolf, Winstein, Miller, et al., 2006). Therefore, increased grasp aperture as a result of improved digit extension is an important motor skill to enable effective object handling. Feedback also focuses on speed of grasp formation, preshaping of hand and fingers, maximum grasp aperture as soon as reach starts, and efficient closing of fingers in a single smooth movement.

3.6 | Varied and intensive practice

3.6.1 | Varied practice

Varied practice is integrated in COMPoSE training to reduce anticipation effects and make the intervention more challenging to enhance learning and to encourage the transfer of skill to the different tasks (Krakauer, 2006). In the last five sessions, the two somatosensory variables within each somatosensory parameter are presented in a random order, for example, for texture parameter; first, the smooth texture is presented followed by the rough texture, then either the smooth or the rough variation (Figure 3). This varied practice keeps the participant engaged in the task in order to promote active learning.

Item 5. Who provided: Description of the expertise, background, and training given to intervention provider

The COMPoSE intervention is expected to be delivered by one physiotherapist or occupational therapist, with expertise in neurorehabilitation and upskilling in the COMPoSE approach. For the Phase II study, the research therapist was upskilled in RTG training and SENSe therapy by the originators of those interventions.

Item 6. How: Mode of intervention delivery

The COMPoSE intervention is provided individually and face-to-face to participants.

Item 7. Where: Location of intervention delivery

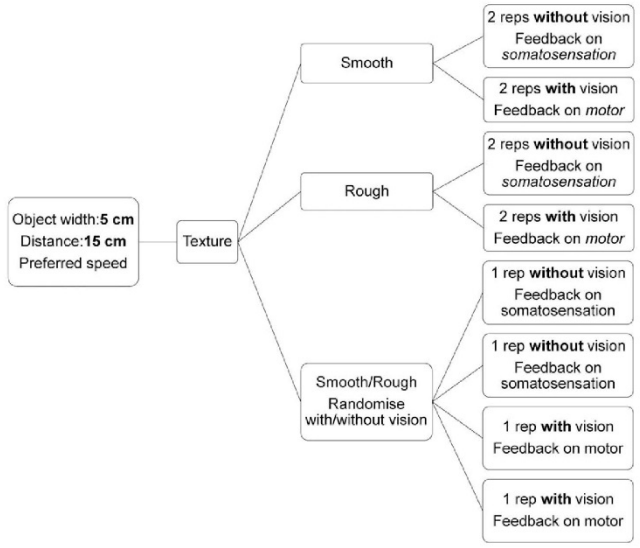
The proof-of-concept COMPoSE study is being conducted in the motion analysis laboratory at the Hunter Medical Research Institute (Newcastle, Australia). It is anticipated that future delivery may be in a rehabilitation setting or specialist clinic. A quiet room is recommended to facilitate focused attention to the learning demands of the therapy.

Item 8. When and how much

Intensive practice with a high number of repetitions is provided through repeated performance (Birkenmeier, Prager, & Lang, 2010; Pollock et al., 2014) of the *RTG and lift-and-hold* task. Within a session, the participant aims to complete six repetitions of each somatosensory–motor combination parameter within the training matrix. An example of the sequence and number of repetitions for combinations practised throughout the matrix is illustrated in Table 2. The actual number of repetitions completed will vary with the capacity of the individual and where the individual lies in the learning continuum. For example, during early phases of learning, the individual may be expected to take more time to integrate the feedback, and thus, the number of repetitions may be lower. Each session lasts approximately 1.5 hr (with rest), and participants are encouraged to perform up to 36 combinations of somatosensory–motor parameters within a session, each with six repetitions (216 repetitions in total). Ten training sessions are proposed to be delivered over 3 weeks at a frequency of 3–4 sessions per week, consistent with skill-based learning approaches and current sensorimotor interventions (Carey et al., 2011).

Item 9. Tailoring: Individualizing the intervention

The COMPoSE intervention is a structured therapy that is designed to address the somatosensory and motor challenges a stroke survivor may experience in the fundamental RTG and lift-and-hold



Reps: Repetitions

FIGURE 3 Varied practice for somatosensory–motor combinations: with or without vision, for example, short distance variable and texture

TABLE 2 Examples of operationalization of part of the training matrix

Object width (cm)	Object distance (cm)	Selected grasp pressure			Crushability		Texture		Friction			
		TactArray device			Soft plastic cup	Hard plastic cup	Felt	Sand paper	Rubber	Teflon	Vision Yes or No	No. of reps
5	15	Preferred									No	3
5	15	Preferred									Yes	3
5	15		Minimum								No	3
5	15		Minimum								Yes	3
5	30			Maximum							No	3
5	30			Maximum							Yes	3
5	30				Soft						No	3
5	30				Soft						Yes	3
5	30					Hard					No	3
5	30					Hard					Yes	3
7.5	15						Smooth				No	3
7.5	15						Smooth				Yes	3
7.5	15							Rough			No	3
7.5	15							Rough			Yes	3
7.5	30								Nonslip		No	3
7.5	30								Nonslip		Yes	3
7.5	30									Slip	No	3
7.5	30									Slip	Yes	3

Note. No. of reps: Number of repetitions.

tasks required to perform a wide range of daily activities. All participants will receive the intervention in the same order as per the standardized matrix. This is to establish the framework for the key parameters selected and the levels of difficulty. Although the training is structured to cover the key parameters of training important to this task, the emphasis on somatosensory and/or motor feedback given for each somatosensory–motor combination task has scope to vary according to the needs of the individual. The intervention is also individualized based on rate of progression and the number of repetitions achieved within and across sessions. It is expected that the pace of progression through the learning tasks provided in the matrix will vary with severity of impairment and learning capacity. If the scheduled section of the training matrix is not completed in a particular session, the participant starts the next treatment session where the intervention was previously stopped so that the participant is exposed to all of the somatosensory–motor combinations.

4 | DISCUSSION

Performance of complex tasks in everyday life requires successive and fast sensorimotor integration. However, strategies involving integrated somatosensory–motor retraining of the hand and arm have been poorly addressed by current stroke rehabilitation research. It could be argued that any manual task inherently involves the integration of both somatosensory and motor function. By combining and integrating several somatosensory and motor parameters within a task, and by frequently varying these parameters and the conditions of practice in the COMPoSE intervention, the sensory and motor pathways are continuously challenged to respond synchronously and more often to these changes. It is proposed that this integrated somatosensory–motor retraining approach could optimize processes that drive reorganization of brain activation and neural connectivity to a greater extent leading to maximal functional improvement in the paretic upper limb compared with training somatosensory and motor function sequentially, which might be a suboptimal approach to relearn functional movements. Therefore, in order to maximize improvement of functional movements such as RTG after stroke, it is considered essential to address key sensory systems involved in this task (Kato, Tanaka, Sugihara, & Shimizu, 2015). It should be noted that even though the COMPoSE intervention does not directly target proprioceptive training, the latter is inherent in the reach and grasp aspects of the task, and feedback is provided in part with the motor training. For example, the proprioceptive demands are increased under no vision conditions, and feedback is provided with feedback on movement distance and grasp aperture.

The TIDieR checklist was a very valuable tool facilitating the reporting of essential information on the content of the COMPoSE intervention that could be useful for researchers and clinicians, even though Items 10–12 in the TIDieR checklist, which pertain to an exploratory trial, are not reported here.

5 | IMPLICATIONS FOR PRACTICE

The COMPoSE intervention offers a learning-based approach that involves processing of multisensory information from the tactile, proprioceptive, and visual systems, which are simultaneously integrated with motor function. A novel aspect of this intervention involves using TactArray as a means of retraining sensorimotor function for scaling of grasp forces, which is crucial for dexterity. This could encourage skill transfer for adaptive control of grasp forces at the fingertips in

response to surface feature detection and discrimination. Therefore, COMPoSE might be more effective in optimizing functional improvement of upper limb after stroke compared with an intervention involving a single sensory approach.

The standardized training matrix further facilitates the delivery of the COMPoSE intervention as it explicitly and systematically incorporates all the combinations of somatosensory–motor parameters, conditions of practice, feedback delivery focused on somatosensory and motor aspects, and adaptive pressure outputs. The matrix provides adequate standardization so that the intervention could be replicated by clinicians and researchers.

6 | CONCLUSION

A COMPoSE intervention to improve upper limb function after stroke has been described, and a standardized training matrix has been developed to facilitate intervention delivery. The COMPoSE intervention *combines* somatosensory and movement training, delivered *synchronously*, *within the same treatment*, and *within the same task*.

CLINICAL TRIAL REGISTRY NUMBER

Australia New Zealand Clinical Trials Registry: ACTRN12615001222538.

CONFERENCE PRESENTATION

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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CHAPTER 5: THE COMBINED PHYSICAL AND SOMATOSENSORY TRAINING INTERVENTION TO IMPROVE UPPER LIMB RECOVERY AFTER STROKE: A FEASIBILITY STUDY

Preface

This chapter presents findings from a feasibility study to examine the feasibility of the COMPoSE training intervention and to gather preliminary data on the impact of the COMPoSE intervention, using a single-case experimental study design. This chapter addresses addressing thesis aim 3 (To evaluate the feasibility of the combined somatosensory and motor training intervention on improving upper limb recovery after stroke in a trial and gather preliminary data on the impact of the intervention) which was conducted to investigate Research question 3 (Is it feasible to conduct a trial of combined somatosensory and motor training intervention to improve upper limb recovery in people with chronic stroke?)

Contribution statement

I was responsible for leading all stages of conducting this clinical trial. I was the liaison and contact person for all aspects of this study. With the support of my supervisors, I carried out the steps described below to conduct the COMPoSE trial.

Acquisition of funding

I was the lead investigator on two funding applications that partly funded the COMPoSE trial:

- Research equipment grant ($4,990) from the School of Health Sciences, University of Newcastle.
- Research support grant ($5,637) from the Priority Research Centre for Stroke and Brain Injury, Hunter Medical Research Institute.
- Clinical Research Design & Statistics Support Grant (AUD$2500) from the Priority Research Centre for Stroke and Brain Injury, Hunter Medical Research Institute.

Ethics approval

For the COMPoSE trial, I was responsible for drafting, submitting and obtaining ethical approval from the Hunter New England Human Research Ethics Committee (HNEHREC Reference No: 13/12/11/4.02) and with the University of NewcastleHuman Research Ethics Committee (HREC Reference No: H-2015-0052). This involved developing the study protocol, completing all paperwork for site-specific approvals, completing all administrative procedures for application for ethics and approval, designing recruitment materials and preparing information statements and consent forms.

Participant recruitment

I was responsible for the identification and recruitment of people with stroke for the Compose trial. I developed all recruitment materials such as flyers, posters and e-posters for web-media. I also attended service-user groups and meetings as well as stroke support groups to promote the study and for recruitment of participants. I conducted all screening assessments, analysed the data and determined eligibility for participation in this study.

Conduct of the COMPOSE trial

With the guidance of my supervisors, I developed the overall trial protocol. I was responsible for the overall conduct of the COMPoSE trial. I coordinated all scheduling of appointments for the treatment and assessments sessions. I delivered the COMPoSE intervention training for all treatment sessions. A physiotherapist was recruited to carry out all outcome assessments.

Data collection and management

I selected all outcome measures used in the Compose trial in consultation with my supervisors. I also developed the assessment procedure of maximal tactile pressures using

the TactArray device. Before the start of the Compose trial, I developed assessment protocol to facilitate the administration of all outcome measures. I provided comprehensive training to the main outcome assessor for all outcome measures and the other assessors who assisted this process. I was responsible for entering all data on data processing spreadsheets. With the assistance of Professor Derek Laver, we developed a customised MATLAB script to process the data from the TactArray device. I was responsible for the offline processing of all data from the TactArray.

Data analysis

With the collaboration of my supervisors and the HMRI Clinical Research Design and Statistical Services, we devised a data analysis plan to suit the needs of the COMPoSE trial. I carried out all individual data analyses. Support was provided by the HMRI Clinical Research Design and Statistical Services for group data analyses.

5.1 ABSTRACT

Title: The COMbined Physical and somatoSEnsory training intervention to improve upper limb recovery after stroke: A feasibility study

Background/Aim: The COMbined Physical and somatoSEnsory (COMPoSE) program, is a novel, complex intervention combining training of somatosensory and motor variables synchronously within the same tasks to improve upper limb recovery after stroke. The feasibility of the COMPoSE intervention was examined and preliminary data were gathered on the impact of COMPoSE, using a single-case experimental study design.

Methods: Five chronic stroke survivors (62-89 years) completed the COMPoSE intervention trial (10 sessions of 90 minutes per session over 3 weeks). The outcomes from this feasibility trial included: 1) feasibility of the recruitment of participants; 2) review of the intervention protocol and feasibility of the study design; 3) acceptability of the intervention and trial; 4) appropriateness of data collection procedures; 5) resources required; and 6) preliminary impact on participants using laboratory measures (maximal tactile pressures) and clinical motor and somatosensory measures.

Results: The combination of somatosensory and motor variables synchronously, within the same tasks was feasible. The delivery of the COMPoSE intervention according to the standardised training matrix was feasible, however modifications to allow more specific tailoring to participant deficits is recommended. All participants attended 90-100% of intervention sessions. Amount of practice ranged from 108-360 repetitions/session across all intervention sessions and across all participants. The scheduled training duration ranged from 90 to 120 minutes per intervention session, with 90 minutes of actual training. Data collection (14 outcome measures, 14 timepoints) was time and labour intensive. There was a trend for improvement (12.0-62.5%) for measures of maximal tactile pressures in four participants between baseline and post-intervention. All participants were satisfied with the COMPoSE intervention and would recommend it.

Conclusion: The COMPoSE intervention was feasible to deliver. The contents of the COMPoSE intervention and its dosage parameters need to be adjusted, prior to subsequent trials in order to maximise somatosensory and motor improvements in the upper limb after stroke.

The COMbined Physical and somatoSEnsory training intervention to improve upper limb recovery after stroke: A feasibility study

5.2 INTRODUCTION

5.2.1 Background

Somatosensory and motor signals are highly integrated and tightly coupled to coordinate the performance of tasks performed in everyday life[292]. People with stroke experience both somatosensory and motor losses[154], which disrupt their capacity for coordinated movements of the upper limb and somatosensory awareness, resulting in deficits in reach-to-grasp (RTG) and object manipulation[158,162]. As reported in Chapter 3, therapeutic interventions for the upper limb after stroke have typically combined somatosensation and motor function sequentially rather than synchronously (Chapter 3).

The COMbined Physical and SomatoSEnsory (COMPoSE) intervention was devised to train somatosensory and motor upper limb function synchronously[400]. This approach is promising theoretically because of the contribution of tactile somatosensory information in enhancing sensorimotor function to improve motor function after stroke[213,370]. It is proposed that COMPoSE may improve upper limb recovery by optimising processes that boost reorganisation of brain activation and neural connectivity due to synchronous recruitment of both somatosensory and motor systems. Based on the MRC (UK) framework[54], a feasibility study of the COMPoSE intervention was conducted, which is reported in this chapter.

5.2.2 Objectives

The objectives of this feasibility study were 3-fold:

1) To provide a description of the COMPoSE feasibility study in terms of:
    a) the participant population to be targeted
    b) the study design
    c) the intervention protocol
    d) the laboratory and clinical assessment tools to be used
2) To investigate the conduct of the trial in terms of:

a) the feasibility of the recruitment of participants and their characteristics

b) the review of the intervention protocol and the feasibility of the study design

c) the acceptability of the trial and the intervention to participants

d) the appropriateness of the data collection procedures

e) the resources required to conduct the trial

3) To conduct a preliminary evaluation of the impact of the COMPoSE intervention on the somatosensory and motor measures assessed.

While objective 1 relates to the description of the COMPoSE feasibility study, the objectives 2 and 3 are aligned with the MRC (UK) framework[54] to assist in the evaluation of the feasibility of delivery of the COMPOSE intervention and conduct of the COMPoSE trial.

5.3 METHODS

5.3.1 Objective 1

5.3.1.1 Participants

Participants with upper limb movement and/or somatosensory deficits were targeted for this study, irrespective of their time post-stroke. Participant identification, screening and recruitment were planned to last 12 months to achieve a target sample size of 16 stroke survivors. Recruitment targeted stroke survivors currently receiving therapy at Hunter New England health district hospitals.

Eligibility criteria

Stroke participants were eligible based on selection criteria summarised in Table 5.1. The severity of motor impairment of the affected arm was categorised as substantial if the Motor Activity Log (MAL) score was <2.5 for the how well (HW) or the amount scale (AS)[348,401]. The severity of somatosensory impairment of the affected arm was defined according to the standardised deficit range score of the Tactile Discrimination Test (TDT) as follows: mild (0 to -33.33), moderate (-33.33 to -66.67) and severe (<-66.67)[391].

Table 5.1. Selection criteria for stroke participants

Inclusion criteria

1. confirmed diagnosis of stroke
2. adults aged 18 years or older
3. sufficient voluntary muscle contraction in the affected upper limb to reach forward
4. sufficient ability to generate the beginning of prehension to grasp a 3.5 cm wide object
5. one or both of the following:
    a. stroke-related upper limb movement deficit defined as being unable to pick up a 6mm ball bearing from the table top between index finger and thumb, and place it on a shelf 37 cm above table (item from Action Research Arm Test) OR
    b. somatosensory impairment in the upper limb identified by the Tactile Discrimination Test and Fabric Matching Test
6. no obvious motor dyspraxia as assessed by ability to imitate a reaching movement with the less affected upper limb
7. able, prior to stroke, to use the paretic upper limb to lift a cup and drink from it
8. able to follow a 1-stage command, i.e., sufficient cognitive ability to follow instructions during the this trial

Exclusion criteria

1. history of central nervous system dysfunction other than stroke
2. upper limb deficits resulting from non-stroke pathology
3. any peripheral neuropathy in the upper limb
4. moderate to severe receptive aphasia (<7 on 'receptive skills' of Sheffield Screening Test for Acquired Language Disorders[402]).

5.3.1.2 Ethics approval

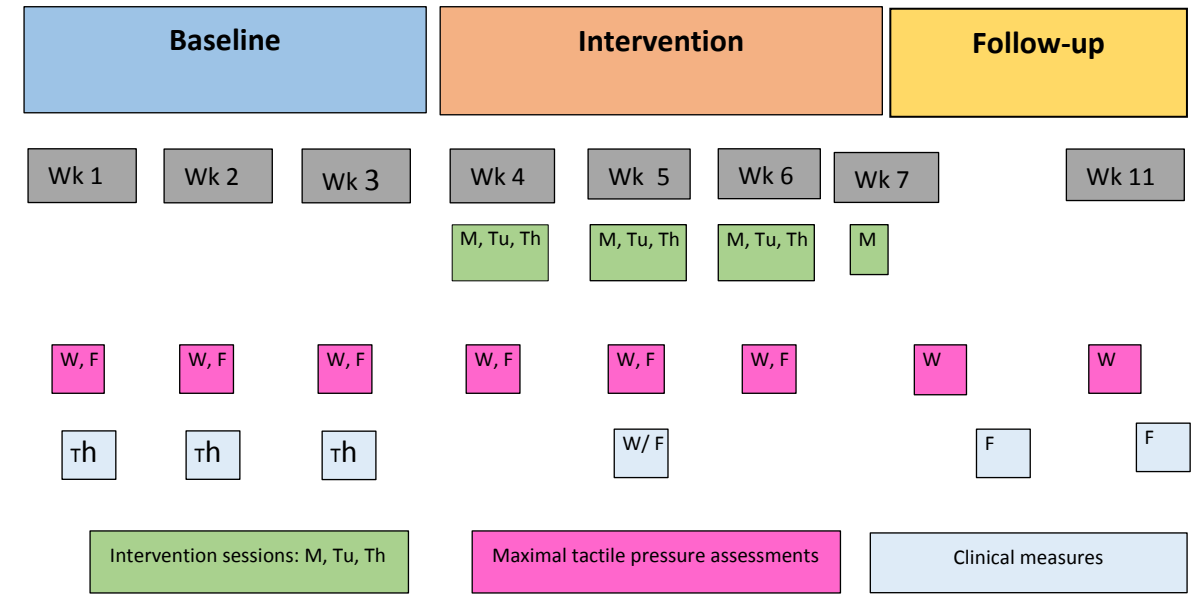
All participants provided written informed consent, according to the Declaration of Helsinki[403]. The study was approved by the Hunter New England Human Research Ethics Committee (Reference No: 13/12/11/4.02) and registered with the University of NewcastleHuman Research Ethics Committee (Reference No: H-2015-0052).

5.3.1.3 Study design

Single-case experimental designs are characterised by repeated measures over time from the baseline to the intervention phase. The study used a single-case experimental design with three phases: baseline (3 weeks), intervention (3 weeks) and follow-up (4 weeks)[404,405] as shown in figure 5.1. Assessments were conducted multiple times during the baseline and intervention phases, during Week 7 (post-intervention) and Week 10 (end of follow-up) to determine the individual responses over time to the COMPoSE intervention amongst people with chronic stroke[66]. Repeated assessments during the baseline phase were designed to

determine the stability of the pre-intervention measures and to allow a basis for determining changes due to the intervention[66,67]. The initial baseline phase also acts as a control such that data recorded across the baseline can be compared with any change in the intervention phase[65,66]. Repeated assessments during the intervention phase were to determine the rate and extent of any improvements in these measures. Measures of maximal tactile pressure were performed twice weekly during the baseline and intervention phases. The clinical measures were performed once a week in the baseline phase and once at mid-intervention. All outcome measures were assessed once immediately after the intervention phase[406] and once at follow-up 1 month later. A gap of one month was chosen to match the duration of the intervention phase. Ten sessions of the COMPoSE intervention training were scheduled over the intervention phase. The design of this single-case study adhered to the standard of quality indicators proposed by Horner et al (2005) such as the description of participants, settings, variables, baseline, internal and external[407].

This study was registered with the Australian New Zealand Clinical Trials Registry ACTRN12615001222538.The reporting of this paper adheres to key items of the CONSORT 2010 checklist[408] relevant to small exploratory studies and to the single-case reporting guideline in behavioural interventions (SCRIBE) 2016 Checklist[409].



Wk: Week; M: Monday, T: Tuesday; W: Wednesday; Th: Thursday; F: Friday

Figure 5.1. Timing of outcome measures

5.3.1.4 Setting

The COMPoSE assessments and training were conducted in the Movement Laboratory at the Hunter Medical Research Institute (Australia).

5.3.1.5 COMPoSE intervention protocol

A detailed description of and rationale for the COMPoSE intervention has been presented in Chapter 4[400].A key aspect of the COMPoSE intervention was that it uses high-dose, repetitive tasks that combine somatosensory-motor training of the affected upper limb. All the tasks required reach-to-grasp and object manipulation. A number of variables were manipulated to vary the somatosensory information to be processed and the motor performance required. These were grasp pressures (preferred, minimal and, maximal); object distance (15 and 30 cm); object diameter (5 and 7.5 cm); object crushability (crushable and non-crushable); surface texture (smooth and rough); and surface friction (slippery and non-slippery) in a systematic and standardised training matrix, with each unique combination of variables performed 6 times (3 with vision; 3 without vision) (Chapter 4). The tasks were performed using a number of cylindrical task objects. Scaling of grasp pressure training was performed using two diameters of TactArray cylinders (small: 5cm and large: 7.5 cm) (figure 5.2) and trials of minimum, maximum and preferred tactile pressures. Other cylinders with their surfaces covered with various materials (figure 5.3) were used to vary object size, crushability, surface texture and friction (Chapter 4). The target number of repetitions in the complete training matrix was 216 repetitions. Feedback on tactile pressures was provided using the TactArray device; other forms of feedback were provided for the other stimuli. Graded tasks and varied practice were also incorporated in the COMPoSE intervention (Appendix 5.1).

Ten treatment sessions of 90 min scheduled training duration were planned over a period of three weeks (figure 5.1), using the standardised matrix for treatment delivery (Chapter 4)[400]. Participants were requested not to participate in any other exercise training or therapy regime for the upper limbs during the course of the study. Participants were informed that usual lower limb activity levels could be maintained.

Figure 5.2. TactArray cylinder devices (from left to right: 5 cm and 7.5 cm diameter)

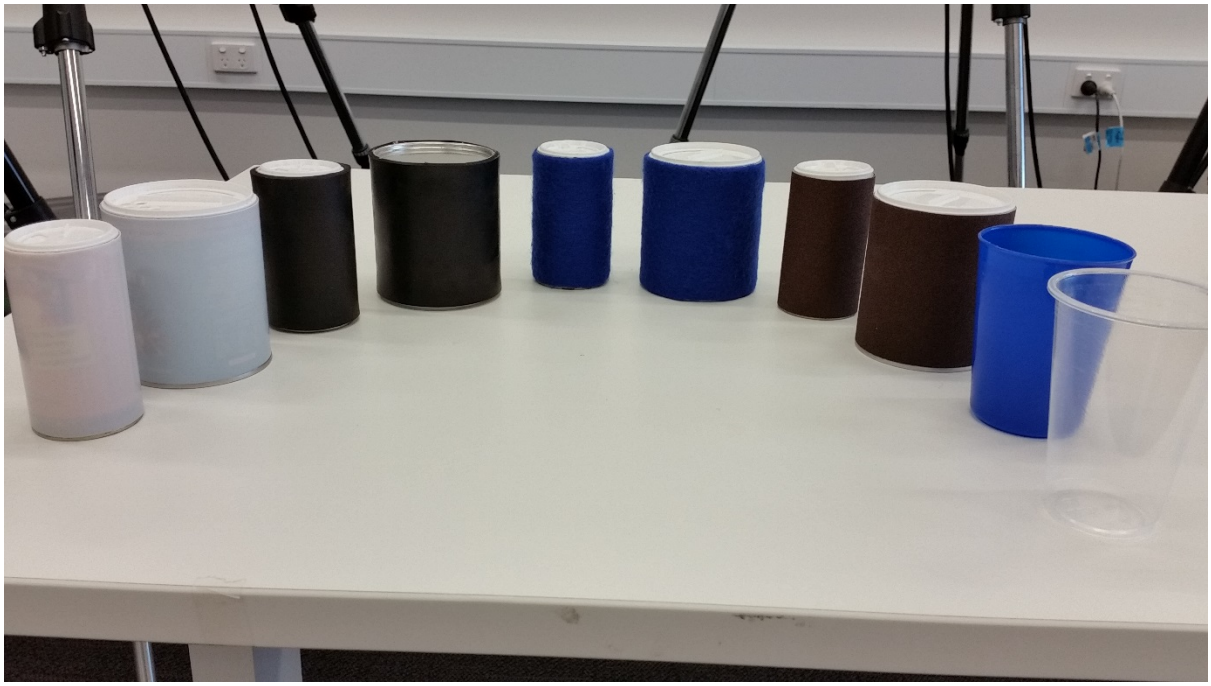


Figure 5.3. Cylinders covered with materials used in COMPoSE.

From left to right, the materials used were teflon, rubber, felt, sandpaper, hard and soft plastic cup

5.3.1.6 Laboratory and clinical assessments

A range of assessments were conducted using both novel laboratory and established clinical measures to quantitatively evaluate upper limb somatosensory and motor impairments, performance and functions, with respect to International Classification of Functioning, Disability and Health (ICF) domains (Table 5.2). The inclusion of multiple outcome measures allowed testing of the appropriateness of these outcome measures before conducting future trials[410].

Table 5.2. Outcome measures used in the COMPoSE trial

Instrument	Assessment type: measurement domain	ICF domain
Laboratory measures		
Maximal tactile pressure and forces	Performance: somatosensory-motor	Body functions and structures
Clinical measures		
Wolf Motor Function Test (WMFT)[411]	Performance: motor	Activity
Grip strength (Jamar dynamometer)[232,412]	Performance: motor	Body functions and structures
Motor Activity Log (MAL)[413,414]	Participant reported: motor	Activity and participation
Box and Block Test (BBT)[415,416]	Observer: motor	Activity
Modified Tardieu Scale (MTS)[417]	Performance: motor	Body functions and structures
Tactile Discrimination Test (TDT)[391]	Performance: somatosensory	Body functions and structures
Fabric Matching Test (FMT)[391]	Performance: somatosensory	Body functions and structures
Wrist Position Sense Test (WPST)[387,418]	Performance: somatosensory	Body functions and structures
Functional Tactile Object Recognition Test (FTORT)[419]	Performance: somatosensory	Body functions and structures
Stroke Impact Scale (SIS)[420]	Participant reported: health status	Activity and participation
Fatigue Assessment Scale (FAS)[421]	Participant reported: fatigue in daily life	Activity and participation
Stanford Fatigue Visual Analogue Scale (SFVAS)[422]	Participant reported: mental and physical fatigue*	Activity and participation
Pain Visual Analogue Scale (PVAS)[423]	Participant reported: pain*	Activity and participation

*Also measured pre and post treatment sessions and pre and post outcome assessment sessions
SFVAS: fatigue(VAS4–10); no/minimal fatigue (VAS: 0–3)[424] ; FAS: fatigue ≥24[425].

Laboratory assessment of maximal tactile pressures

Tactile pressures reflect the complex integration of tactile somatosensory feedback and motor ability to grasp and hold an object because they require the detection and interpretation of the tactile cues on the object surface, coupled with muscle contraction by the fingers[20,146,379]. Maximal tactile pressures were measured using TactArray sensors[426] placed on a cylinder to create a testing device (figure 5.2) . This sensor-based technology was developed by Pressure Profile System, Inc[385], however the measurement procedures for maximal tactile pressures were specifically developed by the study team to align with the tasks incorporated in the COMPoSE intervention (Chapter 6). The feasibility of using the TactArray sensors on a cylinder as an evaluation tool in people after stroke was previously shown in two case reports by Gopaul et al.[426]. Measures of maximal tactile pressures during a sustained grasp task using the TactArray device (sustained contraction over 8s, average of three trials) have been shown to be reliable in people with stroke (Chapter 6).

Procedure for measuring maximal tactile pressures and forces

The TactArray cylinder (adjusted mass 160g) was placed 15 cm from the hand start position. Participants were instructed to reach at a preferred speed[168], grasp, lift the TactArray cylinder to a height of 2-5cm above the table, hold for 7s, then place the object back on the table (grasp release over 1 s)[427] using a 5-digit multi-finger prehension grasp[428]. Participants were also instructed to pick up the object with the distal pads of the fingers without involving the proximal phalanxes or the palm of the hand[428]. Finger positions were not restricted to specific locations, thus allowing for measurement of the participant's natural grasp performance. Movement started upon an auditory cue. Measures of 'normal' pressures, i.e., perpendicular to the surface of the TactArray device with which the finger is in contact,were obtained using this pressure device.

Measures of maximal tactile pressures were repeated three times for each hand. Rest (1-2 min) was provided between each measurement trial to minimise fatigue[429,430]. The measurements were carried out under two conditions: with vision and without vision[171]. Maximal tactile pressures of the affected hand were reported for both conditions. Unsuccessful lifts, defined as trials in which participants either stopped the task early or failed

to complete the task as instructed, were discarded and the participant was asked to repeat the trial. TactArray data were pre-processed and filtered offline to reduce noise using customised MatLab software (R2015b), prior to data analysis.

Clinical outcome measures

Five **clinical motor measures** were used. The Wolf Motor Function Test (WMFT) evaluated the motor ability of the upper limbs during 15 timed function-based tasks and 2 strength-based tasks[411]. It has excellent test-retest reliability (r=0.95)[431] and inter-rater reliability (ICC=0.99)[431]. Maximum voluntary grip strength with the Jamar dynamometer was used as a conventional measure of muscle strength in the upper limb post-stroke[232,412]. This test demonstrated excellent test-retest reliability (ICC>0.86)[252,432], intra rater reliability (ICC > 0.086-0.95)[252] amongst people with stroke. The Motor Activity Log (MAL) evaluated the quality (how well) and the quantity (how much) of movements of the impaired upper limb in 30 activities of daily living[413,414]. The MAL has demonstrated high test-retest reliability (r>0.91) and internal consistency (alpha 0.88-0.91) in stroke participants[414]. The Box and Block Test (BBT) was used to assess gross manual dexterity[415,416]. Excellent test-retest reliability (0.93-0.98) have been established in both affected and less affected hand with adequate concurrent validity with the MAL (-0.37to 0.52) and stroke impact scale (0.52-0.59)[433]. The Modified Tardieu Scale (MTS) quantified spasticity by measuring a muscle's response to passive stretch applied at low and fast velocities[417]. The modified Tardieu scale has excellent test-retest reliability (ICC 0.76-0.87), inter/intra-rater reliability (ICC 0.66-0.89) in measuring elbow flexor spasticity[434].

Four **clinical somatosensory measures** were used. The Tactile Discrimination Test (TDT)[391] and the Fabric Matching Test (FMT)[37,435] evaluated touch discriminations in the affected hand. The TDT has high reliability (r=0.92) with good discriminative properties for evaluation. The Wrist Position Sense Test (WPST) evaluated proprioception, quantifying the participant's ability to determine wrist position after an imposed movement involving flexion-extension and ulnar-radial deviation[37,418]. The WPST has high reliability (r = 0.88 and 0.92) amongst people with stroke[418,436]. The Functional Tactile Recognition Test (FTORT) assessed the ability to match everyday objects having selected sensory attributes such as crushability,

texture, shape, weight, size and temperature and functional movements through the sense of touch[419].

The Stroke Impact Scale (version 3.0) (SIS) evaluated the health status measure covering eight domains of stroke outcomes including strength, hand function, activities of daily living, mobility, communication, emotion, memory and thinking, andparticipation[420]. The SIS has e**xcellent** interrater reliability for the hand function domain (ICC = 0.82) and a**dequate** interrater reliability for strength (ICC = 0.61), ADL/IADL (ICC = 0.74). The SIS has adequate to excellent construct validity between the hand function (*r* = 0.52), strength (*r* = 0.52), and ADL/IADL (*r* = 0.74)[437].

The Fatigue Assessment Scale (FAS) is a 10-item self-rated scale and was used to evaluate physical and mental symptoms of chronic post-stroke fatigue[421]. The FAS has good test-retest reliability (ICC=0.77 to 0.94) [421].

Perception of fatigue and pain were also measured to monitor tolerability of the assessment and intervention sessions (Objective 3; Appendix 5.3). The Stanford Fatigue Visual Analogue Scale (SFVAS), which is a single-item scale with a rating of 1 (no fatigue) to 10 (severe fatigue), was used to assess the presence and extent of mental and physical fatigue[209]. Although the reliability and validity of the SFVAS has not been published, this scale has been used by recent studies [209] because of its clinical relevance and usefulness and the good psychometric properties of a single-item measure [438,439].

The pain visual analogue scale (PVAS) is a single-item scale ranging from 0 (no pain) to 10 (excruciating pain) which is widely used due to its simplicity[438-440] and excellent reliability ($r=0.94$, $p< 0.001$) [441]. The SFVAS and the PVAS were measured before and immediately after each assessment and intervention session (Appendix 5.3).

No treatment was provided on days when outcome measures were assessed. The assessor was trained in assessment of outcome measures and was different from the person delivering the intervention.

5.3.2 Objective 2

The feasibility of the COMPoSE trial was evaluated using the recommendations for evaluating the feasibility of behavioural intervention studies by Orsmond and Cohn (2015)[410]. These guiding questions[410] complement the Structured Assessment of Feasibility (SAFE) scale and checklist[442] by providing an in-depth evaluation of the: 1) feasibility of the recruitment of participants; 2) appropriateness of data collection procedures; and 3) resources required to carry out the trial (Appendix 5.2 Objectives 2a-c). Additionally, the feasibility of the intervention protocol and study design were evaluated, as well as the acceptability of the intervention and trial.

5.3.2.1 Review of the intervention protocol and feasibility of the study design

The contents of the COMPoSE intervention were evaluated by the author of this thesis, using guiding questions adapted from the TREND checklist (Item 4), which is part of a 22-item checklist designed to standardise the evaluation of non-randomised controlled trials[443]. The COMPoSE intervention was evaluated against the descriptors of item 4 of the TREND checklist which focuses on the content of the intervention and how it was administered (Appendix 5.2 Objective 1). The types and dosage of active ingredients of the COMPoSE intervention that were proposed to induce change in the targeted somatosensory, motor and functional deficits of the upper limb post-stroke were specified and measured. The SAFE scale and guidelines were used to assess the practical considerations for conduct of the intervention[442] (Appendix 1 Objective 1)**.** The SAFE scale, initially designed to evaluate the feasibility of interventions in mental health services, comprises of 16 items rated on a Likert scale focusing on barriers and enablers of the intervention per se and to a lesser extent the operational aspects of the trial[442].

A manual of procedures was developed to support the fidelity[444] of the COMPoSE intervention by the treating therapist (Appendix 5.1). This included preparatory procedures and the protocol for the intervention delivery[445-447]. The protocol included the standardised COMPoSE training matrix, operationalisation of feedback delivery on somatosensory and motor performance (including statements for knowledge of performance and knowledge of results), and standardised instructions for participants during treatment delivery[213,215,220,343].

Measures of fidelity were recorded in each session using checklists to monitor intervention delivery[448]. These included: number of intervention sessions attended, the combinations of somatosensory-motor training variables practiced, the number of somatosensory-motor training combinations practiced, the amount of practice (number of repetitions), scheduled training duration, i.e., time taken to complete the intervention session (including rest time) (number of minutes), and actual training duration i.e., duration of active practice in one intervention session (number of minutes) (Appendix 5.3).

Adherence to the overall treatment was expressed as a percentage of treatment sessions attended (number of treatment sessions attended divided by the planned number of possible treatment sessions).

Evaluation of participant engagement was based on self-reports of perceived difficulty and extent of engagement, and was assessed at the end of the intervention period (week 7) (Appendix 5.4 part 1). Measures of participant engagement were also assessed by the external view of the treating therapist at the end of each intervention session using a Likert scale and included: the effort with which the training was performed, the frequency at which instructions and advice were followed, receptiveness to changes in the training, extent of participant engagement and the extent of frustration (Appendix 5.4 parts 2 and 3).

5.3.2.2 Acceptability of the intervention and trial to the participants

The acceptability of the COMPoSE intervention was evaluated through the participants' perceptions of the contents of the COMPoSE intervention, its delivery and

perceived impact, using a patient feedback form (18 items, including 4 open-ended questions), adapted from Buschfort et al.[449] and Gerber et al.[450] (Appendix 5.5).

5.3.3 Objective 3

The preliminary impact of the COMPoSE intervention on somatosensory and motor functions in the upper limb was evaluated in accordance with guidelines by Orsmond and Cohn (2015)[410] (Appendix 5.2 Objective 3). Although the aim was not to test effectiveness, this evaluation was used to indicate whether the COMPoSE intervention was likely to be beneficial for upper limb recovery after stroke.

5.3.4 Data analysis

Raw scores of outcome measures were represented graphically for each timepoint for each participant. To evaluate changes in the time-series data of a single-case experimental design, at least five data points are recommended to detect stability or trends in the data[407]. Therefore, changes in measures of maximal tactile pressures were explored using non-regression methods to evaluate changes in each individual participant[451] and regression methods for changes across the group[452]. Descriptive statistics such as means, standard deviations, and medians were used to evaluate changes in clinical measures in each participant and across the group.

For each individual participant, visual analyses of the time-series data of maximal tactile pressures were performed to assess the baseline stability, identify variability within any phase (fluctuation of scores) and the magnitude of changes between baseline and intervention phases[407,453]. A quantitative summary of the difference within and between the baseline and intervention phases were calculated using change in trend (direction of best-fitting line in which series of outcome scores progresses within a phase), change in slope (as the average change between consecutive measurements) and change in level (as a mean difference, once change in slope is taken into account)[454]. Trend is estimated only for the baseline phase to avoid any confusion between the trend and potential intervention effects in the intervention phase[455]. The stability criterion for the baseline phase was satisfied if: 1)

there was an absence of a trend (almost flat) or slope (close to zero) in the data when analysed visually[456-458], and 2) at least 80% of the data fall within a 15% range of the mean of all data points[459]. The net change in level was the mean difference between the baseline and intervention phase[454].

For group analyses, linear mixed models were fitted to the measures of maximal tactile pressures for the baseline, intervention and post-intervention phases. The models were specified to account for the dependency between measurements within each individual. Segmented regression models were used to measure the slope over the baseline and intervention assessments. All regression analyses were performed in R version 3.4.1 (2017-06-30). Improvements were considered clinically meaningful if the changes were greater than the variation in maximal tactile pressures when performed under with vision (4.32 units; CI:3.15-7.10) and without vision conditions (4.52 units; CI:3.30-7.44) (Chapter 6).

For clinical measures, the three repeated measures during the baseline phase were insufficient for a time series analysis. Therefore, the stability of the baseline was evaluated against two criteria: 1) absence of trend (almost flat) in raw scores across the three baseline timepoints when analysed visually; and 2) a variation of <5% was considered as an indication of stability during the baseline phase aligned with recommendations for reproducibility studies[283,284].

For all outcome measures, the percentage change index[458] was also used to report changes in the preliminary impact of the COMPoSE intervention on each individual participant between the baseline and post-intervention phase, the post-intervention and follow-up phase and the baseline and follow-up phase. Percentage change index facilitated the interpretation of changes across phases of the trial and also facilitated the comparison of magnitudes of changes within and between participants. An improvement of 10% or more on an outcome measure was considered clinically meaningful [460,461]. A reduction of less than 5% was used as a threshold to identify any deterioration in performance[462].

5.4 RESULTS

5.4.1 Objective 1 and 2: Recruitment of participants

5.4.1.1 Recruitment of participants

The recruitment process lasted 24 months (2014-2016) with a final lower than expected number of participants (n=5). Due to low referral numbers from the Hunter New England hospitals, recruitment was extended to reach people with stroke who had been discharged from regular therapy and through routes such as the Hunter Medical Research Institute volunteer register, private physiotherapy/occupational therapy practices, stroke support meetings and groups, stroke recovery association of NSW websites (figure 5.4). Amongst the potential participants identified through the different recruitment routes, 82% (n=36) were screened. Of these potential participants, 61% (n=22) met the inclusion criteria. In turn, 27% (n=6) of these potential participants were enrolled in the study. One participant subsequently dropped out during the baseline phase due to a hip fracture. The main reason for declining participation in the COMPoSE trial was inability to commit to the assessment and intervention sessions schedule (figure 5.4).

description of, and rationale for, the COMPoSE feasibility study in terms of:

a) the participant population to be targeted

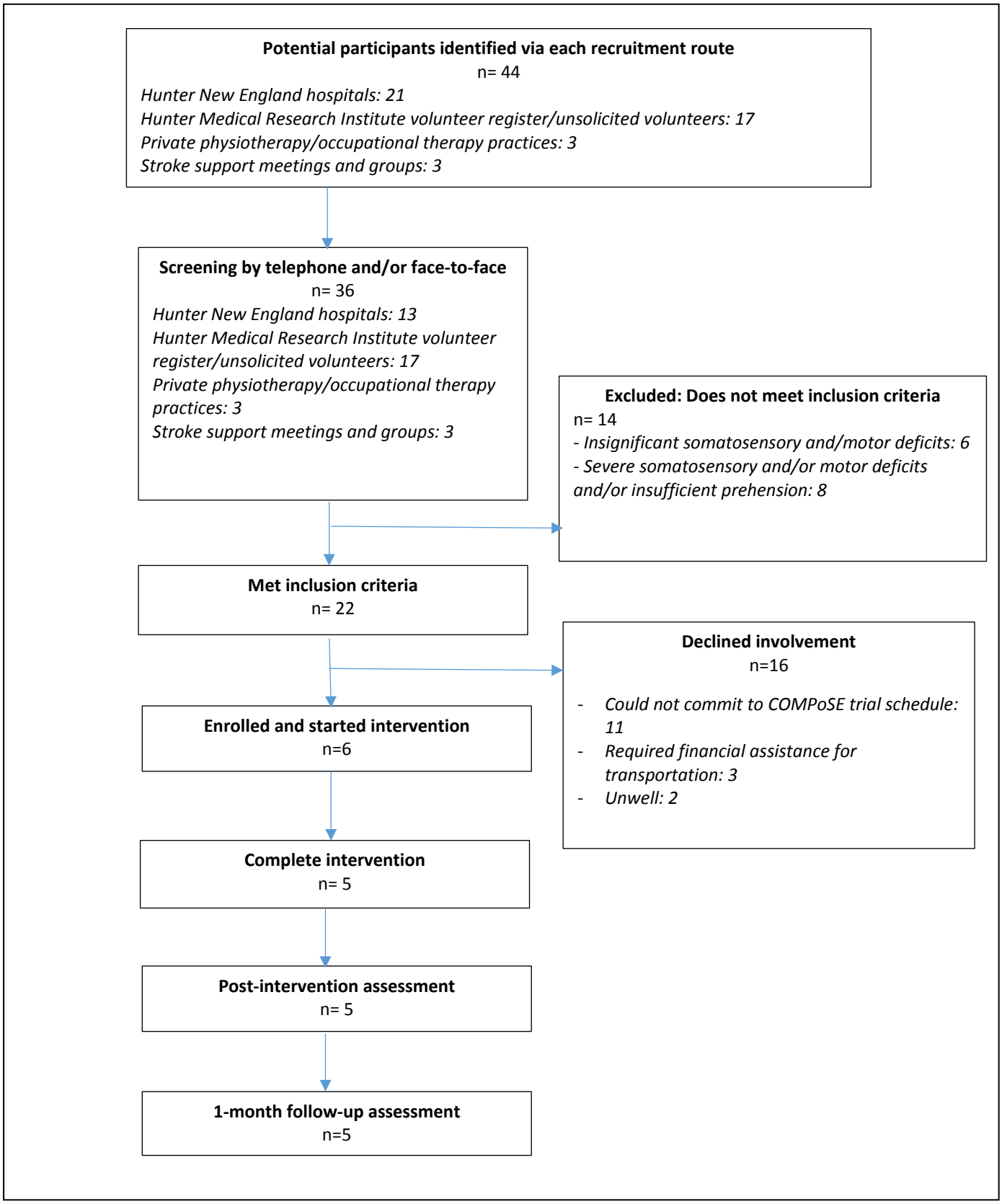


Figure 5.4. Recruitment, participation and assessment

5.4.1.2 Participant characteristics

Five participants (4 males and 1 female) completed the COMPoSE trial. At baseline, their mean age was 70.7 years (range: 60.9 -88.6 years) and their mean time since stroke was 82 months (range: 17-192 months). Tables 3 and 4 summarise the demographic data and characteristics of the participants based on standard objective performance-based neuropsychological tests including the Montreal Cognitive Assessment (general indicator of cognitive performance)[463,464], the Star Cancellation Test (neglect)[465,466], the Rey-Osterrieth Complex Figure Test (copy condition)[467], Trail Making Tests A and B (visual sustained attention)[468], the Story Recall Test (memory)[469], and the Sheffield Screening Test For Acquired Language Disorders (Language and screening tests)[470]. Regular therapy had long been discontinued for all included participants.

Table 5.3. Demographic data of participants

ID	Gender (M/F)	Age (Y)	Hand dominance (R/L)	Time since stroke(Mo)	Hemiparetic side (R/L)	Type of stroke	Lesion side (R/L)	Lesion location
1	M	88.6	L	17	L	Unknown	R	Unknown
2	M	64.4	L	66	L	Unknown	L	Unknown
3	M	60.9	R	124	R	Ischaemic	L	L MCA
4	M	63.7	R	192	R	Ischaemic	R+L	L occipital lobe
5	F	75.7	R	11	R	Haemorrhagic	L	L parietal lobe

M: male; F: female; Y: year R: right; L: left;; Mo: month; MCA: middle cerebral artery

Table 5.4. Participants' characteristics at beginning of training

ID	MOCA	SCT	TM A	TM B	SST	RCFT	SR	MAL-AS	MAL-HW	TDT
1	17	50	116.0	466.0	6	26	8.5	1.3	1.0	-114.4
2	27	56	44.86	72.0	9	32	8.5	2.3	1.5	-42.9
3	25	56	23.9	110.3	9	30	41	1.8	1.7	-1.2
4	23	56	64.23	114.8	8	33	29	4.7	4.6	-17.9
5	29	56	35.0	148.0	9	27	17	3.7	3.3	-95.9

MOCA: Montreal Cognitive Assessment[463,464]; SCT: Star Cancellation Test[465,466]; TM A and B: Trail Making Test[468]; SST: Sheffield Screening Test For Acquired Language Disorders[470]; RFCT: Rey-Osterrieth complex Figure Test (copy condition)[467]; SR: Story Recall Test[469]; MAL-AS: Motor Activity Log-Amount Scale; MAL-HW: Motor Activity Log-How Well; R: right; TDT: Tactile Discrimination Test

5.4.2 Objective 2: Feasibility of conduct of the COMPoSE intervention trial

5.4.2.1 Review of the intervention protocol and feasibility of study design

It was feasible within the COMPoSE intervention to address somatosensory and motor function altogether by using an impairment-oriented training approach with a functional task to improve the somatosensory, motor and functional deficits of the upper limb post-stroke. It was possible to use selected pressures (preferred, minimum, maximum) to retrain control of finger forces during a sustained grasp by using the online display of the pressure-time curves provided by the TactArray software. Also, the online display of tactile pressure values made it feasible to use the performance values of the 'less affected' hand as the standard reference. This allowed objective and realistic goal-setting for training of force control of the affected hand during delivery of the COMPoSE intervention. Calibration with the less affected hand also enabled individualisation of the selected grasp pressures with regards to each participant. Additionally, it was observed that the graded difference in the physical characteristics of the object properties between the two variables of the somatosensory parameters was relatively large, e.g., there was a large difference in texture between felt and the 100-grit sandpaper. It was possible to give personalised feedback face to face to each participant by one therapist in the COMPoSE intervention.

5.4.2.2 Measures of fidelity

The range of combinations practiced, repetitions performed, varied practice, scheduled training duration and actual training duration are summarised in Table 5.5. Repetitive practice of the target number of somatosensory-motor combinations (36 combinations per session) and the target amount of practice (216 repetitions per session) were feasible to some extent. The targeted amount of varied practice across the standardised training matrix in the last five treatment sessions (48 varied repetitions per session; 11.1% of total targeted repetitions of complete intervention) was also partly feasible. Three participants (ID2, ID3 and ID5) practiced all combinations in one treatment session. Another participant (ID4) practiced between 22 and 60 combinations in six treatment sessions. One participant did not achieve the target number of combinations in any session (range: 15-23 combinations). Though it was not expected for the participants to achieve these at the start

of the intervention, a general trend of increase in the number of somatosensory-motor combinations practiced and the number of repetitions performed was observed across all treatment sessions. The number of combinations ranged between 15 and60 (42-165% target combinations). The minimum number of repetitions ranged from 90-162 (41.7-75% target repetitions) and the maximum number of repetitions ranged from 116-360 (50.0-166.7% target repetitions) across all treatment sessions across all participants. The amount of varied practice in four participants (ID1, ID2, ID3 and ID5) ranged from 24-48 repetitions per session (50-100% target varied practice). One participant (ID4) achieved 48-96 varied repetitions per session (100-200% target varied practice).

It was not feasible to effectively deliver the intervention during a *scheduled* training duration of 90 minutes, due to the number of movement trials required and the delivery of high frequency feedback, as well as the need to incorporate rest. It was feasible to deliver the intervention in a *scheduled* training session of up to 120 minutes.Consequently, the *actual* training duration, i.e., actual amount of therapy time was set at 90 minutes (10 sessions= 15 hours) and was adequate to deliver the intervention. Rest time was additionally provided (range: 5-30 minutes per session). The frequency of the intervention sessions (3x per week for 3 weeks) was feasible and one session was delivered in the 4th week to complete the intervention.

Table 5.5. Range of combinations practiced, repetitions performed, scheduled training duration and actual training duration

Participant ID	No. of combinations	% Combinations achieved	No. of repetitions	% Repetitions achieved	No. of varied repetitions	% varied repetitions achieved	Scheduled training duration/min*	Actual training duration/min
1	15-23	42-64	90-135	41.7-62.5	24-36	50-75	100-135	90-115
2	18-28.5	50-100	108-216	50.0-100	24-36	50-75	105-120	90-110
3	21-36	58-100	126-216	58.3-100	36-48	75-100	90-120	90
4	22-60	51-167	152-360	70.4-166.7	48-96	100-200	90-109	85-95
5	7.7-36	21.4-100	108-216	50.0-100.0	28-48	58.3-100	90-120	90

***including break time**

5.4.2.3 Participant's adherence

All participants completed the study, except for one who withdrew during the baseline phase due to a hip fracture following a fall. Four participants completed all ten treatment sessions and one participant completed nine sessions.

5.4.2.4 Participants' engagement

Two participants (ID1 and ID4) reported difficulty in learning and performing the combined somatosensory and motor tasks with the TactArray device and the other objects with varying surface properties. Another two participants (ID3 and ID5) reported that learning was easy but task performance was difficult. One participant (ID2) reported that learning and task performance were both easy. One participant (ID5) reported trying not to rely on the sound heard when exploring the different surface properties, for example the grinding noise from rubbing sandpaper. The measures of self-engagement across the intervention are summarised in Table 5.6. The participants' engagement assessed by the treating therapist is summarised in Table 5.7.

Table 5.6. Measures of participants' engagement across the intervention: self-report perceptions of difficulty and extent of engagement

Difficulty level	**Number of participants**
Learning and Performance both difficult	2
Learning and Performance both easy	1
Learning easy, performance difficult	2
Learning difficult, performance easy	0
Difficulty attributed to lack of ability	3
Difficulty attributed to equipment	0
Did you use a strategy to perform the task? Yes/No	Yes: 1(participant tried not to use sound during task performance with eyes closed)/ No: 4
Were you engaged in the task or bored? Yes/No	Engaged: Yes: 5

Table 5.7. Measures of participants' engagement assessed by the treating therapist

ID	Participant's engagement	Intervention session									
		1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
1	Effort*	5	5	5	5	5	5	5	4	4	5
	Frequency#	3	2	4	3	5	3	2	4	4	5
	Receptiveness	5	5	5	5	5	5	5	5	5	5
	Engagement	Very frequently	Very frequently	Always	Always	Always	Occasionally	Very frequently	Always	Always	Always
	Frustration	Rarely	Very frequently	Occasionally	very rarely	Occasionally	Occasionally	Occasionally	Occasionally	Occasionally	Never
2	Effort*	5	5	5	5	5	5	5	5	5	5
	Frequency#	5	5	5	5	5	5	5	5	5	5
	Receptiveness	5	5	5	5	5	5	5	5	5	5
	Engagement	Always	Always	Always	Always	Always	Always	Always	Always	Always	Always
	Frustration	Never	Never	Never	very rarely	Never	Never	Never	Never	Never	Never
3	Effort*	5	5	5	5	5	5	5	5	5	5
	Frequency#	5	5	5	5	5	5	5	5	5	5
	Receptiveness	5	5	5	5	5	5	5	5	5	5
	Engagement	Always	Always	Always	Always	Always	Always	Always	Always	Always	Always
	Frustration	very rarely	Never	very rarely	Never	Rarely	Rarely	Occasionally	Rarely	Rarely	Always
4	Effort*	5	5	5	5	5	Absent	5	5	5	5
	Frequency#	3	3	5	5	5	Absent	5	5	5	5
	Receptiveness	5	5	5	5	5	absent	5	5	5	5
	Engagement	Very frequently	Always	Always	Very frequently	Always	absent	Always	Always	Always	Always
	Participant frustration	Never	Never	Never	Never	Never	absent	Never	Never	Never	Never
5	Effort*	5	5	5	5	5	5	5	5	5	5
	Frequency#	5	5	5	5	5	5	5	5	5	5
	Receptiveness	5	4	5	5	5	5	5	5	5	5
	Engagement	Very frequently	Always	Always	Always	Always	Always	Always	Always	Always	Always
	Frustration	Occasionally	Very frequently	Occasionally	Occasionally	Occasionally	Occasionally	Occasionally	Occasionally	Rarely	Always

* Effort with which exercise completed; # Frequency at which instructions were followed

5.4.2.5 Participants' tolerability and adverse effects of the COMPoSE intervention

There was an increase in pain in the upper limb (VAS score 0 to 1) for two participants (ID2 and ID3) in up to three intervention sessions. One participant (ID1) had substantial fatigue (SFVAS range: 4-8) before 80% of the intervention sessions, followed by an increase in fatigue (SFVAS range: 1-3) at the end of 60% of the intervention sessions. Another participant (ID4) had fatigue prior to treatment delivery in 30% of the intervention sessions, with an increase (SFVAS score 2) at the end of 20% of the intervention sessions. The remaining participants (ID2, ID3 and ID5) had no or minimal fatigue (SFVAS range: 0-2) at the beginning of the intervention sessions but there was an increase in perception of fatigue (SFVAS range: 1-3) at the end of the sessions for these participants. All participants attended the complete duration of each the session. The participants found the duration of each intervention session tolerable (range score: 5-7) and feasible. The changes in perception of fatigue and pain before and after the intervention have been summarised in Tables 5.8 and 5.9.

Table 5.8. Perception of fatigue before and after intervention session

Participant ID		**Intervention session**									
		1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
1	Before	2	4	3	4	6	4	8	5	5	4
	After	4	4	6	5	7	2	9	6	6	4
2	Before	0	0	0	0	0	0	0	0	0	1
	After	0	3	3	3	2	0	0	3	3	0
3	Before	2	0	0	0	1	0	1	0	0	0
	After	2	2	2	3	3	2	3	3	0	2
4	Before	2	3	2	1	1	absent	5	4	4	1
	After	2	3	2	1	1	absent	3	6	6	1
5	Before	2	3	2	2	1	2	1	1	1	1
	After	3	4	3	2	1	2	1	1	2	1

Table 5.9. Pain before and after intervention session

Participant ID		Intervention session									
		1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
1	Before	0	0	0	0	0	0	0	0	0	0
	After	0	0	0	0	0	0	0	0	0	0
2	Before	0	0	0	0	0	0	0	0	0	0
	After	0	0	0	1	0	0	0	0	1	1
3	Before	0	0	0	0	0	0	0	0	0	0
	After	0	0	0	0	0	1	0	0	0	0
4	Before	0	1	0	0	0	absent	0	0	0	0
	After	0	1	0	0	0	absent	0	0	0	0
5	Before	0	0	0	0	0	0	0	0	0	0
	After	0	0	0	0	0	0	0	0	0	0

5.4.2.6 Acceptability of intervention and trial to participants

The participants' perceptions of the COMPoSE intervention have been summarised in Table 5.10. All participants reported that they were satisfied (range score out of 10: 6-10) with the intervention and that they enjoyed the training which increased their motivation. All participants reported that the instructions were sufficient, and not difficult to understand. All participants said that they tried to improve their performance and scores. Two participants (ID2 and ID4) responded that they did not feel frustrated during the training while three participants (ID1, ID3 and ID5) reported some frustration. All participants reported that the tasks in COMPoSE were meaningful and related to their daily activities. One participant (ID1) reported cutting food more independently and improved in tasks such as picking up a glass of water. Another participant (ID5) reported doing more ironing, gardening and cross-stitching with the affected upper limb. Four participants (ID1, ID2, ID4, ID5) reported increased confidence while performing daily tasks. All participants reported enjoying using the TactArray device. Four participants (ID1, ID2, ID3, ID4) thought that the COMPoSE intervention could help improve somatosensory and motor functions of their affected upper limbs. One participant (ID5), who was unsure about the impact of COMPoSE, reported that she "*found some of the days difficult towards the end where it was daily, it was difficult to push self to make it in. However, found this probably useful as it's good to push yourself sometimes, might help with recovery".* All participants reported that they would recommend this training to other stroke survivors with upper limb deficits.

Table 5.10. Measures of participants' perceptions of the COMPoSE Intervention

Questions	Yes, absolutely	Yes	Do Not Know	No	Not at all
1. How content were you with the intervention?	2	3			
2. Did you enjoy the training? Did you enjoy the training with the devices?	4	1			
3. Did the training increase your motivation?	4	1			
4. Were the instructions sufficient?	4	1			
5. Did you find the instructions difficult to understand?		3		1	1
6. Were you frustrated whilst you were doing the training?		3		1	1
7. Do you think that this kind of training may enhance the somatosensory and motor functions of your upper limb?	4		1		
8. Did you try to improve your performance and scores? Did you use a strategy to do this?	3	1		1	
9. Would you recommend this combined somatosensory and motor training to other stroke survivors with upper limb deficits?	5				

5.4.2.7 Appropriateness of data collection procedures

Participants attended a separate testing session where neuropsychological tests were conducted, prior to the baseline assessments. There was a total of 14 assessment sessions scheduled across the COMPoSE trial. Due to the large battery of somatosensory and motor measures, the clinical measures were completed on a separate day (2 hours) from the laboratory-based measures (2 hours) during the baseline phase. During the intervention phase, evaluation of maximal tactile pressures and clinical measures were completed during the same assessment sessions in order to adhere to the scheduled treatment sessions (figure 5.1). Consequently, the assessment session lasted up to 4 hours, including rest time.

Three participants attended all assessment sessions. Two participants missed one assessment session of maximal tactile pressures during the baseline phase (ID1) and during the intervention phase (ID1 and ID4) because they were unwell for reasons unrelated to this trial. The missed assessment sessions were not re-scheduled due to unavailability of the participants at other times.

During the assessments conducted over the baseline, there was an increase in perception of fatigue (SFVAS score range: 1-6) across all participants. There was an increase in perception of fatigue (SFVAS range score: 2-5) in three participants (ID1, ID2 and ID3) in 16.7-50.0% of the assessment sessions during the intervention phase, at post-intervention and at follow-up. Two participants (ID4 and ID5) had little or no change in perception of fatigue (SFVAS score range: 0-1) during assessments conducted during the intervention phase, at post-intervention and follow-up. The changes in perception of fatigue before and after the assessment sessions are summarised in Table 5.11.

Table 5.11. Perception of fatigue before and after the assessment sessions

ID		Baseline assessment sessions						Intervention assessment sessions						Post-Int	Follow-up
		B1	B2	B3	B4	B5	B6	Ax1	Ax2	Ax3	Ax4	Ax5	Ax6		
1	Before	0	3	0	4	0	0	0	0	5	0	0	absent	0	0
	After	4	5	3	5	6	2	0	5	7	5	0	absent	4	5
2	Before	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	After	3	3	3	3	3	0	0	3	0	0	0	0	0	0
3	Before	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	After	4	2	2	1	2	2	0	2	2	0	0	0	2	2
4	Before	2	3	3	4	absent	3	2	1	2	4	4	absent	2	0
	After	6	7	6	5	absent	4	1	1	1	4	4.5	absent	3	1
5	Before	0	1	1	4	1	3	4	1	4	2	1	2	3	1
	After	2	3	3	4	2	5	4	1	4	2	1	2	3	2

B1;Baseline assessment 1; B2:Baseline assessment 2; B3: Baseline assessment 3; B4: Baseline assessment 4; B5: Baseline assessment 6; Ax1: Intervention assessment 1; Ax2; Intervention assessment 2; Ax3; Intervention assessment 3; Ax4: Intervention assessment 4; Ax5: Intervention assessment 5; Ax6: Intervention assessment 6; Post-Int: Post-intervention

5.4.2.8 Evaluation of resources required to conduct the COMPoSE trial

This research was not funded by any specific grants from external funding agencies; the university and HMRI provided supported for the time, space and equipment to conduct the study. Lack of funding limited the recruitment of participants requiring financial assistance with transport to attend the sessions. The assessments were conducted by one main assessor who was a qualified therapist with limited experience in the outcome measures used. For a small number of outcome measures, assistance was provided by a qualified therapist with extensive research and clinical experience and two graduate physiotherapy students with limited experience. All assessors were trained in conducting the outcome measures on healthy individuals but did not have any practice of the tests administration and scoring on people with stroke, prior to the start of the trial.

The materials, equipment and softwares and any assistance with their use such as the TactArray software for the intervention training and outcome measures were readily available. Given that all equipment and materials used were commercially available, any malfunction could be resolved. No issues were encountered with their use during the trial.

5.4.3 Objective 3: Preliminary impact of intervention on participants

Changes between phases were based on mean values for measures of maximal tactile pressures and median values for clinical measures[471].

Table 5.12 presents the raw scores of maximum tactile pressures for each participant in the affected hand with vision and without vision at each assessment timepoint across the baseline, intervention, post-intervention and follow-up phases. Table 5.13 presents the change in slope and level in the affected hand with vision and without vision across baseline and intervention phases. Table 5.14 presents the raw scores for changes in clinical measures for each participant in the affected hand at each assessment timepoint across the baseline, intervention, post-intervention and follow-up phases. Table 5.15 presents the group scores for changes in clinical measures. The findings on each participant are then summarised.

The time series plots of measures of maximal tactile pressures for all participants (ID1-ID5) across the baseline, intervention, post-intervention and follow-up are illustrated in figures 5.5 A and B. Figures 5.6-5.15 illustrate the plots of clinical measures, for all participants (ID1-ID5) across the baseline, intervention, post-intervention and follow-up. Figure 5.16 illustrates the mean slope of measures of maximal tactile pressures of the affected hand with and without vision across group.

Table 5.12. Maximum tactile pressures (kPa) at each assessment timepoint

ID		Baseline assessment sessions						Intervention assessment sessions						Post-Int	Follow-up
		B1	B2	B3	B4	B5	B6	Ax1	Ax2	Ax3	Ax4	Ax5	Ax6		
1	Vision	21.6	17.6	27.6	29.2	26.2	26.2	32.2	40.1	22.5	30.9	absent	35.0	40.2	36.0
	No vision	20.3	18.7	26.9	24.8	27.6	26.2	33.7	38.6	33.7	24.6	absent	33.7	36.2	39.2
2	Vision	29.7	32.3	31.6	26.1	34.5	28.9	38.8	35.4	34.0	36.2	37.8	37.6	35.8	38.7
	No vision	23.3	35.8	31.6	29.6	31.6	24.6	37.2	34.7	37.4	37.4	38.4	43.5	38.1	37.7
3	Vision	23.9	24.4	31.6	30.6	30.0	33.5	31.4	33.6	29.3	33.2	29.6	30.6	31.4	29.6
	No vision	25.6	26.2	28.3	26.7	26.5	32.8	30.4	31.2	31.0	28.0	30.7	29.7	31.0	35.4
4	Vision	48.2	41.1	42.9	45.9	46.3	absent	75.9	53.9	51.7	45.9	50.3	absent	45.9	48.7
	No vision	46.7	46.2	36.1	45.9	51.5	absent	52.5	51.4	50.1	45.7	47.6	absent	46.0	49.8
5	Vision	35.0	42.2	40.7	37.8	43.7	37.7	43.0	40.6	44.5	39.6	50.3	43.3	45.3	47.0
	No vision	39.3	37.6	38.7	37.8	45.0	37.7	42.7	40.6	44.0	39.9	48.4	42.2	47.8	51.7

B1;Baseline assessment 1; B2:Baseline assessment 2; B3: Baseline assessment 3; B4: Baseline assessment 4; B5: Baseline assessment 6; Ax1: Intervention assessment 1; Ax2; Intervention assessment 2; Ax3; Intervention assessment 3; Ax4: Intervention assessment 4; Ax5: Intervention assessment 5; Ax6: Intervention assessment 6; Post-Int: Post-intervention

Table 5.13. Change in slope and level across baseline and intervention phases

ID	Conditions	Baseline		Intervention		Δ between baseline and intervention			
		level*(kPa)	slope	level*(kPa)	slope	Δ in level intervention vs baseline phase*	% Δ post-int vs baseline*	% Δ post-int vs follow-up	% Δ follow-up vs baseline*
1	Vision	24.7	1.4	31.4	-0.4	6.7	62.5	-10.4	27.1
	No vision	24.1	1.6	32.8	-1.4	8.8	50.5	8.2	36.4
2	Vision	30.5	-0.1	36.6	0.1	6.1	17.4	7.9	20.0
	No vision	29.4	-0.2	38.1	1.2	8.7	29.4	-1.1	29.4
3	Vision	29.0	1.8	31.3	-0.3	2.3	8.4	-5.9	7.8
	No vision	27.7	1.0	30.2	-0.2	2.5	12.0	14.4	9.0
4	Vision	44.9	0.1	55.6	-5.9	10.6	2.1	6.2	23.7
	No vision	45.3	0.9	49.4	-1.6	4.2	1.5	8.2	9.2
5	Vision	39.5	0.4	43.6	0.7	4.1	14.8	3.7	10.3
	No vision	39.4	0.4	43.0	0.5	3.6	21.4	8.3	9.2

** based on mean value; Δ: change*
Post-int:post-intervention

Table 5.14. Raw clinical measure scores at each assessment timepoint

Outcome measures	ID	Assessment timepoints					
		Baseline 1	**Baseline 4**	**Baseline 6**	**Mid-Int**	**Post-Int**	**Follow-up**
WMFT score	**1**	55.0	58.0	59.0	59.0	65.0	62.0
	2	56.0	65.0	60.0	59.0	66.0	63.0
	3	46.0	42.0	42.0	42.0	44.0	43.0
	4	67.0	75.0	80.0	72.0	78.0	79.0
	5	66.0	69.0	65.0	71.0	74.0	75.0
	Mean	58.0	61.8	61.2	60.6	65.4	64.4
	SD	8.7	12.7	13.6	12.1	13.1	14.1
WMFT time/s	**1**	102.2	184.9	113.1	153.6	125.2	136.9
	2	62.9	60.0	58.1	75.1	63.7	59.0
	3	233.7	248.9	330.3	430.1	430.4	446.9
	4	82.7	55.9	28.7	40.4	36.2	33.3
	5	81.8	66.7	75.8	44.2	41.5	44.3
	Mean	112.6	123.3	121.2	148.7	139.4	144.1
	SD	69.1	88.5	120.8	163.8	166.4	174.1
BBT	**1**	16.3	21.0	23.0	23.0	21.0	23.7
	2	29.0	31.0	30.0	30.7	31.0	29.7
	3	22.0	19.0	22.3	23.3	23.7	22.3
	4	51.0	51.3	52.7	56.0	55.7	54.7
	5	33.4	34.3	36.3	37.0	39.0	37.7
	Mean	30.3	31.3	32.9	34.0	34.1	33.6
	SD	13.3	12.9	12.5	13.6	14.0	13.2
MAL-AS	**1**	1.3	0.6	1.4	0.9	0.9	1.7
	2	2.4	2.3	1.3	1.4	2.7	2.8
	3	1.8	1.8	1.8	2.6	2.2	1.5
	4	4.8	4.4	4.7	4.5	4.5	4.8
	5	3.6	4.1	3.7	3.8	4.1	3.7
	Mean	2.8	2.6	2.6	2.7	2.9	2.9
	SD	1.4	1.6	1.5	1.5	1.5	1.4
MAL-HW	**1**	1.0	0.5	1.7	1.0	1.0	1.5
	2	2.2	1.5	1.3	1.2	2.8	2.6
	3	1.7	2.0	1.7	2.4	2.2	1.6
	4	4.6	4.2	4.6	4.5	4.6	4.8
	5	3.3	3.8	3.3	3.4	3.6	3.6
	Mean	2.6	2.4	2.5	2.5	2.9	2.8
	SD	1.4	1.6	1.4	1.5	1.4	1.4
Grip strength/Kg	**1**	16.7	20.7	18.6	18.1	18.2	16.2
	2	25.3	28.9	29.7	35.6	35.0	33.4
	3	18.8	19.4	18.0	17.9	17.3	19.8
	4	27.8	33.9	35.1	36.8	34.9	35.2
	5	16.0	15.3	14.1	16.2	20.7	16.0
	Mean	20.9	23.6	23.1	24.9	25.2	24.1
	SD	5.3	7.6	8.9	10.3	9.0	9.5
MTS-elbow V1:V2:V3	**1**	1:1:2	1:1:2	1:1:1	1:1:1	1:1:2	0:0:1
	2	0:0:0	0:0:0	0:0:0	0:0:0	0:0:0	0:0:0
	3	1:1:2	1:1:1	1:1:2	1:1:2	1:1:2	1:1:2
	4	0:0:0	0:0:0	0:0:0	0:0:0	0:0:0	0:0:0
	5	0:0:0	0:0:0	0:0:0	0:0:0	0:0:0	0:0:0
	Mean	0.4:0.4:0.8	0.4:0.4:0.6	0.4:0.4:0.6	0.4:0.4:0.6	0.4:0.4:0.8	0.4:0.4:0.6
	SD	0.5:0.5:1.1	0.5:0.5:0.9	0.5:0.5:0.9	0.5:0.5:0.9	0.5:0.5:1.1	0.4:0.4:0.9
MTS-wrist V1:V2:V3	**1**	1:1:2	1:2:2	1:1:2	0:1:1	1:1:0	0:0:0
	2	0:0:0	0:0:0	0:0:0	0:0:0	0:0:0	0:0:0
	3	1:1:3	1:1:3	1:1:1	1:1:3	1:1:2	1:1:2
	4	0:0:0	0:0:0	0:0:0	0:0:0	0:0:0	0:0:0

	5	0:0:0	0:0:0	0:0:0	0:0:0	0:0:0	0:0:0
	Mean	0.4:0.4:1	0.4:0.6:1	0.4:0.4:1	0.2:0.4:0.4	0.4:0.4:0.4	0.2:0.2:0.4
	SD	0.5:0.5:1.4	0.5:0.9:1.4	0.5:0.5:1.4	0.4:0.5:0.5	0.5:0.5:0.9	0.4:0.4:0.9
MTS-fingers V1:V2:V3	**1**	0:0:0	1:1:1	0:0:0	1:1:1	0:0:0	0:0:0
	2	0:0:0	0:0:0	0:0:0	0:0:0	0:0:0	0:0:0
	3	0:0:0	0:0:0	0:0:0	0:0:0	0:0:0	0:0:0
	4	0:0:0	0:0:0	0:0:0	0:0:0	0:0:0	0:0:0
	5	0:0:0	0:0:0	0:0:0	0:0:0	0:0:0	0:0:0
	Mean	0:0:0	0.2:0.2:0.2	0:0:0	0.2:0.2:0.2	0:0:2	0:0:0
	SD	0:0:0	0.4:0.4:0.4	0:0:0	0.4:0.4:0.4	0:0:4	0:0:0
WPST mean error/° [*]	**1**	21.0	16.9	16.4	18.1	19.1	19.4
	2	9.6	6.6	11.2	5.9	9.4	18.2
	3	20.4	9.6	11.45	7.5	8.0	10.8
	4	17.5	11.3	12.5	16.7	20.1	20.6
	5	25.5	18.9	17.0	15.1	19.1	22.7
	Mean	18.8	12.6	13.7	12.6	15.1	18.3
	SD	5.9	5.13	2.8	5.6	5.9	4.5
TDT/%[**]	**1**	-14.8	2.3	-3.5	-20.0	-35.5	4.8
	2	36.4	26.0	36.9	45.7	48.3	69.5
	3	57.6	59.7	65.3	52.4	89.7	89.7
	4	54.5	50.3	2.2	45.7	28.6	50.9
	5	25.5	6.9	6.4	4.3	42.6	56.0
	Mean	20.9	23.6	23.1	24.9	25.2	24.1
	SD	29.2	25.5	29.1	31.9	45.4	31.4
FMT[#]	**1**	-0.2	-0.3	-0.1	-0.3	-0.1	-0.6
	2	1.1	1.6	2.3	1.9	2.1	2.0
	3	1.6	1.7	2.6	2.0	1.7	1.8
	4	1.4	2.0	2.1	1.5	1.8	1.6
	5	0.5	0.8	1.1	0.3	-0.3	1.9
	Mean	0.9	1.2	1.6	1.1	1.0	1.4
	SD	0.7	0.9	1.1	1.0	1.2	1.1
FTORT[##]	**1**	0.0	0.0	0.0	0.0	0.0	0.0
	2	37.0	41.0	39.0	40.0	41.0	42.0
	3	37.0	41.0	40.0	40.0	42.0	41.0
	4	41.0	38.0	41.0	38.0	41.0	41.0
	5	20.0	14.0	18.0	10.0	18.0	23.0
	Mean	27.0	26.8	27.6	25.6	28.4	29.4
	SD	17.1	18.8	18.1	19.2	18.8	18.3
SIS-strength	**1**	50.0	45.0	30.0	45.0	30.0	30.0
	2	60.0	60.0	60.0	70.0	80.0	60.0
	3	70.0	75.0	70.0	60.0	75.0	60.0
	4	55.0	65.0	60.0	70.0	60.0	70.0
	5	70.0	70.0	70.0	80.0	80.0	80.0
	Mean	61.0	63.0	58.0	65.0	65.0	60.0
	SD	8.9	11.5	16.4	13.2	21.2	18.7
SIS-ADL	**1**	44.0	44.0	34.0	42.0	46.0	34.0
	2	68.0	64.0	68.0	74.0	78.0	78.0
	3	70.0	78.0	76.0	74.0	70.0	62.0
	4	78.0	80.0	80.0	80.0	78.0	80.0
	5	54.0	46.0	52.0	56.0	48.0	56.0
	Mean	62.8	62.4	62.0	65.2	64.0	62.0
	SD	13.6	17.1	19.0	15.8	15.9	18.7
SIS-hand	**1**	13.3	11.1	8.9	8.9	8.9	15.6
	2	8.9	22.2	15.6	28.9	37.8	31.1
	3	13.3	17.8	31.1	15.6	24.4	20.0
	4	42.2	44.4	40.0	44.4	44.4	44.4
	5	22.2	15.6	15.6	22.2	28.9	24.4
	Mean	20.0	22.2	22.2	24.0	28.9	27.1
	SD	13.3	13.1	12.9	13.6	13.6	11.3

SIS-participation	**1**	25.0	32.5	27.5	40.0	52.5	45.0
	2	45.0	62.5	35.0	50.0	65.0	57.5
	3	80.0	55.0	75.0	80.0	65.0	57.5
	4	42.5	65.0	65.0	60.0	80.0	75.0
	5	42.5	35.0	47.5	47.5	40.0	55.0
	Mean	47.0	50.0	50.0	55.5	60.5	58.0
	SD	20.1	15.3	19.9	15.5	15.0	10.8
SIS-Stroke recovery	**1**	10.3	11.0	10.0	10.0	32.0	80.0
	2	70.0	70.0	70.0	70.0	80.0	80.0
	3	70.0	70.0	70.0	70.0	70.0	70.0
	4	75.0	85.0	90.0	95.0	95.0	85.0
	5	80.0	70.0	80.0	80.0	80.0	80.0
	Mean	61.1	61.2	64.0	65.0	71.4	79.0
	SD	28.7	28.8	31.3	32.4	23.8	5.5
FAS	**1**	23.0	24.0	24.0	23.0	25.0	20.0
	2	26	28	28	22	20	23
	3	24	22	27	28	23	28
	4	17	22	24	24	29	21
	5	25	23	27	25	24	24
	Mean	23.0	23.8	26.0	24.4	24.2	23.2
	SD	3.5	2.5	1.9	2.3	3.3	3.1

WMFT: Wolf Motor Function Test; BBT: Box and Block test; MAL-AS: Motor Activity Log-Amount Scale; MAL-HW; Motor Activity Log-How Well; Kg: Kilogram; Modified Tardieu Scale: MTS; WPST: Wrist Position Sense Test; Tactile Discrimination Test; FMT: Fabric Matching Test; FTORT: Functional Tactile Recognition Test; SIS: Stroke Impact Scale; FAS: Fatigue Assessment Scale; Int: intervention
SD: Standard deviation; * mean error; ** corrected area under curve; # Fisher scores; ## sum

Table 5.15. Changes in clinical measures scores across group

Clinical measures	% Δ Post-int vs baseline: median(95% CI)	% Δ Follow-up vs Post-int: median(95% CI)	% Δ follow vs baseline: median(95% CI)
WMFT score	10.0(6.5,13.5)	-2.3(-4.9,0.3)	5.3(1.6,9.0)
WMFT time/s	6.1(-34.8,47.1))	3.9(-3.2,10.9)	-1.7(-45.7,42.3)
BBT	7.6(3.0,12.2)	-3.4(-10.0,3.2)	6.6(1.5,11.6)
MAL-AS	10.0(-9.5,29.5)	5.2(-36.5,46.9)	10.0(-9.5,29.5)
MAL-HW	10.0(-23.9,43.9)	-1.7(-27.6,24.3)	8.2(-24.2,40.5)
Grip strength/Kg	3.0(-12.7,18.8)	-4.6(-16.7,7.5)	4.6(-4.4,13.6)
WPST Mean error/°*	1.1(-28.0,30.1)	18.8(-14.4,52.1)	20.1(-14.2,54.4)
TDT % **	50.3(-315.1,415.7)	31.6(-32.8,95.9)	50.3(-259.6,360.2)
FMT#	-7.4(-62.6,47.9)	-4.4(-351.0,342.1)	21.7(-51.9,95.4)
FTORT##	0.0(-2.4,2.4)	0.0(-11.0,11.0)	2.5(-7.8,12.8)
SIS - strength	7.1(3.0,14.3)	0.0(2.1,14.8)	0.0(2.6,18.3)
SIS – ADL	-2.5(1.2,5.9)	0.0(2.3,16.5)	0.0(2.0,14.3)
SIS – hand	37.5(-19.6,94.6)	-15.4(-50.4,19.7)	40.0(6.6,73.4)
SIS – participation	23.1(-13.9,60.0)	-11.5(-30.7,7.6)	27.8(0.3,55.2)
SIS - Stroke Recovery/100	11.8(-69.1,92.6)	0.0(-60.0,60.0)	0.0(-265.4,265.4)
FAS	-0.2(-19.1,18.8)	-2.2(-20.9,16.6)	-5.3(-17.5,6.9)

WMFT: Wolf Motor Function Test; BBT: Box and Block test; MAL-AS: Motor Activity Log-Amount Scale; MAL-HW; Motor Activity Log-How Well; Kg: Kilogram; WPST: Wrist Position Sense Test; TDT: Tactile Discrimination Test; FMT: Fabric Matching Test; FTORT: Functional Tactile Recognition Test; SIS: Stroke Impact Scale; FAS: Fatigue Assessment Scale; int: intervention; CI: Confidence interval;
Δ: change; * mean error; ** corrected area under curve; # Fisher scores; ## sum

5.4.3.1 Individual participant analyses

Participant 1

This participant had substantial motor and severe somatosensory tactile deficits at baseline. Baseline was not stable for maximal tactile pressures with vision (change in slope: 1.4; 66.7% data within 15% of mean) or without vision conditions (change in slope: 1.6; 66.7% data within 15% of mean). Baseline was stable for the MTS (elbow: V1, V2), FTORT and FAS.

There was a net increase in level of maximal tactile pressures from baseline to the intervention phase for vision and without vision conditions (change in level range: 6.7-8.8). At post-intervention, there was improvement in maximal tactile pressure with vision (62.5%) and without vision conditions (50.6%) compared to baseline. Improvements were also observed in the WMFT score (12.1%), WPST (12.7%), MTS (fingers: V3), SIS-participation (90.9%) and SIS-stroke recovery (21.8%). Little or no change was observed in the BBT (0%), MAL-HW (0%), grip strength (-2.0%), MTS (elbow: V1, V2, V3; wrist: V1, V2; fingers: V1, V2, V3) (0%), FTORT (0%) and FAS (4.2%). The participant's performance deteriorated in the WMFT time (10.7%), MAL-AS (31.0%), TDT (926.6%), FMT (-32.9%), SIS-strength (33.3%) and SIS-hand (20.0%).

From post-intervention to follow-up at 1 month, deteriorations were observed in maximal tactile pressures with vision (10.4%) with little or no improvement in the without vision condition (8.2%). Improvements were observed in the BBT (12.7%), MAL-AS (93.3%), MAL-HW (52.0%), MTS (elbow: V1, V2, V3; wrist: V1, V2) (50-100%), SIS-hand (75.0%), TDT (-113.6%), FMT (321.0%), SIS-stroke recovery (48.0%) and FAS (20.0%). Little or no change was observed in the WMFT score (-4.6%), WMFT time (9.3%), WPST (1.6%), MTS (wrist: V3; fingers: V1, V2) (0%), FTORT (0%) and SIS-strength (0%). There was loss of improvement in grip strength (11.1%) and SIS-participation (14.3%).

From baseline to 1-month follow-up, improvements were observed in the maximal tactile pressures with and without vision (range: 27.1-36.4%). Improvements were also

observed in the WMFT score (6.9%), BBT (12.7%), MAL-AS (33.3%), MAL-HW (52.0%), MTS (elbow: V1, V2, V3; wrist: V1, V2, V3) (50-100%), WPST (14.5%), TDT (-240.0%), FMT (176.5%), SIS-hand (40.0%), SIS-participation (63.6%), SIS-stroke recovery (69.8%) and FAS (16.7%). Little or no change was observed in the FTORT (0.0%) and MTS (fingers: V1, V2, V3) (0%). Deteriorations were observed in WMFT time (21.0%), grip strength (12.9%) and SIS-strength (33.3%).

Participant 2

This participant had substantial motor deficits with moderate somatosensory tactile loss at baseline. Baseline was stable for maximal tactile pressure with vision (change in slope: -0.1; 100% within 15% of mean) but not stable without vision (change in slope range: -0.2; 50% data within 15% of mean). Baseline was stable for WMFT time, MTS (elbow: V1, V2, V3; wrist: V1, V2, V3; fingers: V1, V2, V3), SIS-Strength, and SIS-stroke recovery.

There was a net increase in level of maximal tactile pressures from baseline to the intervention phase for vision and without vision conditions (change in level range: 6.1-8.7). At post-intervention, improvements were found in maximal tactile pressures for vision and without vision conditions compared to baseline (17.4-29.4%). Improvements were found in WMFT score (10.0%), MAL-AS (17.0%), MAL-HW: 92.5%), grip strength (21.2%), TDT (32.7%), FMT (27.4%), SIS-strength (33.3%), SIS-hand (142.9%), SIS-participation (44.4%), SIS-stroke recovery (10.0%) and FAS (16.0%). Little or no change was observed after the intervention in the BBT (3.3%), MTS (elbow: V1, V2, V3; wrist: V1, V2, V3; fingers: V1, V2, V3) (0%), WPST (-2.1%) and FTORT (5.1%). Some deterioration was observed in the WMFT time (6.1%).

From post intervention to 1-month follow-up, little or no change was found in maximal tactile pressures for vision and without vision conditions (-1.1-7.9%). There were improvements in the WPST (94.1%) and TDT (43.9%). There was little or no change in the WMFT Score (-4.5%), WMFT time (-7.4%), BBT (-4.3%), MAL-AS (5.2%), grip strength (-4.6%), MTS (elbow: V1, V2, V3; wrist: V1, V2, V3; fingers: V1, V2, V3), FMT (-4.4%), FTORT (2.4%) and

SIS-Stroke recovery (0%). There was loss of improvement observed in MAL-HW (7.4%), SIS-strength (25.0%), SIS-hand (-17.6%), SIS-participation (-11.5%) and FAS (15.0%).

From baseline to 1-month follow-up, improvements were found in maximal tactile pressures for vision and without vision conditions (20.0-29.4%). The participant improved in the MAL-AS (23.0%), MAL-HW (78.2%), grip strength (15.7%), MTS (elbow: V1, V2, V3; wrist: V1, V2, V3; fingers: V1, V2, V3), WPST (90.1%), TDT (91.0%), FMT (21.7%), SIS-hand (100%), SIS-participation (27.8%), SIS-stroke recovery (10.0%) and FAS (17.9%). Little or no change was observed in the WMFT score (5.0%), WMFT time (-1.7%), BBT (-1.1%), FTORT (7.7%) and SIS-stroke recovery (0%). No deterioration was observed in any outcome measures.

Participant 3

At baseline, this participant had substantial motor deficits with mild somatosensory tactile loss. Baseline was not stable for maximal tactile pressure with vision (change in slope: 1.8; 50.0% data within 15% of mean) but stable without vision (change in slope: 1.0; 83.3% data within 15% of mean). Baseline was stable for maximal tactile pressures without vision, the MAL-AS, MTS (elbow: V1, V2, V3; wrist: V1, V2, V3; fingers: V1, V2, V3), FMT and the SIS-stroke recovery score.

There was a net increase in level of maximal tactile pressures from baseline to the intervention phase for vision and without vision conditions (change in level range: 2.3-8.7). At post-intervention, improvements were found in maximal tactile pressures without vision (12.0%) but not with vision (8.4%) compared to baseline. Improvements were found in the MAL-AS (26.0%), MAL-HW (25.4%), MTS (elbow: V3) (33.0%), TDT (50.3%) and SIS-hand (37.5%). There was no change in the WMFT score (4.8%), BBT (7.6%), MTS (elbow: V1, V2, V3; wrist: V1, V2; fingers: V1, V2, V3), FMT (2.9%), FTORT (5.0%), SIS-Strength (7.1%), SIS-stroke recovery (0%) and FAS (-4.2%). The participant deteriorated in the WMFT score (72.9%), grip strength (-8.0%), WPST (-30.1%) and SIS-participation (-13.3%).

From post-intervention to 1-month follow-up, some deteriorations were found in maximal tactile pressures for vision (-5.9%) and improvements in without vision conditions (14.4%). Improvements were found in the grip strength (14.3%), MTS (fingers: V3) (100%) and WPST (34.4%). There was little or no change in the WMFT score (-2.3%), WMFT time (3.9%), BBT (-5.8%), MTS (elbow: V1, V2, V3; wrist: V1, V2, V3; fingers: V1, V2), TDT (0%), FMT (6.6%), FTORT (-2.4%) and SIS-stroke recovery (0%). Some deterioration was observed in the MAL-AS (-31.4%), MAL-HW (28.1%), SIS-strength (20.0%), SIS-hand (18.2%), SIS-participation (11.5%) and FAS (21.7%).

From baseline to 1-month follow-up, little or no change was found in maximal tactile pressures for vision and without vision conditions (range: 7.8-9.0%). There were improvements in MTS (elbow: V3) (33.0%), TDT (50.3%) and SIS-hand (12.5%). Little or no change was found in the WMFT score (2.4%), BBT (1.4%), grip strength (5.2%), MTS (elbow: V1, V2, V3; wrist: V1, V2, V3; fingers: V1, V2), FMT (9.7%), FTORT (2.5%) and SIS-stroke recovery (0%). The participant deteriorated in the WMFT time (79.5%), MAL-AS (13.6%), MAL-HW (9.8%), WPST (6.1%), SIS-strength (-14.3%), SIS-participation (-23.3%) and FAS (16.7%).

Participant 4

This participant had mild motor deficit with mild somatosensory tactile deficits at baseline. Baseline was stable for maximal tactile pressure with vision (change in slope: 0.1; 100% data within 15% of mean) and without vision (change in slope: 0.9; 80.0% data within 15% of mean). Baseline was stable for BBT and MTS (elbow: V1, V2, V3; wrist: V1, V2, V3; fingers: V1, V2, V3).

There was a net increase in level of maximal tactile pressures from baseline to the intervention phase with vision and without vision (change in level range: 4.2-10.7). At post-

intervention, little or no improvement was found in maximal tactile pressures for vision and without vision conditions compared to baseline (1.5-2.1%). The participant improved in the WMFT time (35.2%), WPST (60.4%), SIS-participation (23.1%) and SIS-stroke recovery (10.0%). There was little or no changes in the WMFT score (4.0%), BBT (8.5%), MAL-AS (-3.6%), MAL-HW (0.7%), MTS (elbow: V1, V2, V3; wrist: V1, V2, V3; fingers: V1, V2, V3) (0%), FTORT (0%), SIS-strength (0.0%) and SIS-hand (5.3%). There were deteriorations in the TDT (-43.1%), FMT (7.4%), and in the FAS scale (31.8%).

From post-intervention to follow-up, little or no change was observed in maximal tactile pressures for vision and without vision (6.2-8.2%). Improvements were observed in the TDT (77.7%), SIS-strength (16.7%) and FAS (27.6%). Little or no change was found in the WMFT score (-1.3%), WMFT time (-8.0%), BBT (-1.8%), MAL-AS (6.0%), MAL-HW (4.3%), grip strength (0.8%), MTS (elbow: V1, V2, V3; wrist: V1, V2, V3; fingers: V1, V2, V3) (0%), WPST (2.7%), FTORT (0%) and SIS-hand (0%). Some deterioration was found in the FMT (11.3%), SIS-participation (-6.3%) and SIS-stroke recovery (-10.0%).

From baseline to 1-month follow-up, improvements were observed in maximal tactile pressures for vision (23.7%) with little or no change without vision (9.2%). Improvements were observed in the WMFT time (40.5%), WPST (64.8%), SIS-strength (16.7%) and SIS-participation (15.4%). Little or no change was found in the WMFT score (5.3%), BBT (6.6%), MAL-AS (2.1%), MAL-HW (5.0%), grip strength (3.9%), MTS (elbow: V1, V2, V3; wrist: V1, V2, V3; fingers: V1, V2, V3) (0%), TDT (1.0%), FTORT (0%), SIS-hand (5.3%), SIS-stroke recovery (0.0%) and FAS (-4.5%). Deteriorations were found in the FMT (17.8%).

Participant 5

This participant had mild motor deficits with severe somatosensory tactile deficits at baseline. Baseline was stable for maximal tactile pressure with vision (change in slope: 0.4; 100% data within 15% of mean) and without vision (change slope: 0.4; 100% data within 15%

of mean). Baseline was stable for the BBT, MTS (elbow: V1, V2, V3; wrist: V1, V2, V3; fingers: V1, V2, V3) and SIS-strength.

There was a net increase in level of maximal tactile pressures from baseline to the intervention phase for vision and without vision conditions (change in level: 3.6-4.1). At post-intervention, improvements were observed in maximal tactile pressures for vision and without vision conditions (14.8-21.4%) compared to baseline. Improvements were also noted in the WMFT score (12.1%), WMFT time (45.2%), BBT (13.7%), MAL-AS (10.0%), MAL-HW (10.0%), grip strength (35.6%), MTS (elbow: V1, V2, V3; wrist: V1, V2, V3; fingers: V1, V2, V3) (0%), TDT (517.2%), SIS-strength (14.3%) and SIS-hand (85.7%). Little or no change was found in the WPST (1.1%), FTORT (0.0%), SIS-stroke recovery (0.0%), FAS (0.0%) and some deterioration in the FMT (-135.0%) and SIS-participation (-5.9%).

From post-intervention to follow-up, little or no change was observed in maximal tactile pressures for vision and without vision conditions (3.7-8.3%). Further improvements were found in the WPST (19.2%), TDT (31.6%), FTORT (27.8%) and SIS-participation (37.5%). Little or no change was observed in the WMFT Score (1.4%), WMFT time (6.7%), BBT (-3.4%), MAL-HW (-1.7%), MTS (elbow: V1, V2, V3; wrist: V1, V2, V3; fingers: V1, V2, V3) (0%), SIS-strength (0.0%), SIS-stroke recovery (0.0%) and FAS (0.0%).Some deteriorations were found in the MAL-AS (-9.8), grip strength (22.9%), FMT (-754.0%), and SIS-hand (-15.4%).

From baseline to follow-up, little or no change was observed in maximal tactile pressures with vision (10.3%) and some improvements were found in the without vision condition (9.2%). The participant improved in the WMFT score (13.6%), WMFT time (-41.5%), MTS (elbow: V1, V2, V3; wrist: V1, V2, V3; fingers: V1, V2, V3) (0%), WPST (20.4%), TDT (712.0%), FMT (128.6%), FTORT (27.8%), SIS-strength (14.3%), SIS-hand (57.1%) and SIS-participation (29.4%). There was little or no change in the BBT (9.8%), MAL-AS (-0.8%), MAL-HW (8.2%), grip strength (4.6%), SIS-stroke recovery (0.0%) and FAS (0.0%). No deterioration was found in any outcome measures.

Summary of individual responses

All participants improved in 3-8 outcome measures with four participants (ID1, ID2, ID3, ID5) showing improvement in at least maximal tactile pressures and at least one somatosensory and one motor clinical measure at post-intervention. All participants showed improvements on a similar number of somatosensory and motor measures, except for one participant (ID5) who improved in a larger number of motor measures (n=5) compared to somatosensory measures (n=1). Motor improvements were most commonly found in the WMFT (ID1, ID2, ID4 and ID5) and the MAL (ID2, ID3 and ID5). Similarly, somatosensory improvements were most commonly found in the TDT (ID2, ID3 and ID5) and the WPST (ID1 and ID4).

5.4.3.2 Group analyses

Residuals from the linear mixed model analysis showed that the first assessment from one participant (ID 5) in the intervention assessments (Ax1) was an outlier. Although this data point is plotted in the figures, it was not included in the modelling. Results of the segmented regression analyses across the group found that compared to baseline, the maximal tactile pressures were estimated to be higher during the intervention phases (8.02 units; 95%CI: 3.95, 12.08) with vision and without vision conditions, indicating clinically meaningful changes. There was no difference in maximal grasp pressures between the vision and no vision conditions (figure 5.16).

Across the group, improvements were observed in the WMFT score, WMFT time, BBT, MAL-AS, MAL-HW, grip strength, WPST, TDT, SIS-strength, SIS-hand, SIS-participation and SIS-stroke recovery at post-intervention (range: 3.0-50.3%) compared to baseline. No changes were observed in FTORT (0%). Deteriorations were observed in FMT, SIS-ADL and FAS at post-intervention as compared to baseline (0.2- 7.4%).

From post-intervention to follow-up, improvements were observed in WMFT time, MAL-AS, WPST and TDT (range: 3.9-31.6%). Deteriorations were found in WMFT score, BBT,

MAL-HW, grip strength, FMT, SIS-hand, SIS-participation and FAS (range: 1.7-15.4%). No changes were observed in FTORT, SIS-ADL and SIS-Stroke recovery (0%).

From baseline to follow-up, improvements were found in WMFT score, BBT, MAL-AS, MAL-HW, grip strength, WPST, TDT, FMT, FTORT, SIS-hand and SIS-participation (range: 2.5-50.3%). Deteriorations were observed in WMFT time and FAS (1.7-5.3%). No changes were found in SIS-strength, SIS-ADL and SIS-stroke recover (0%).

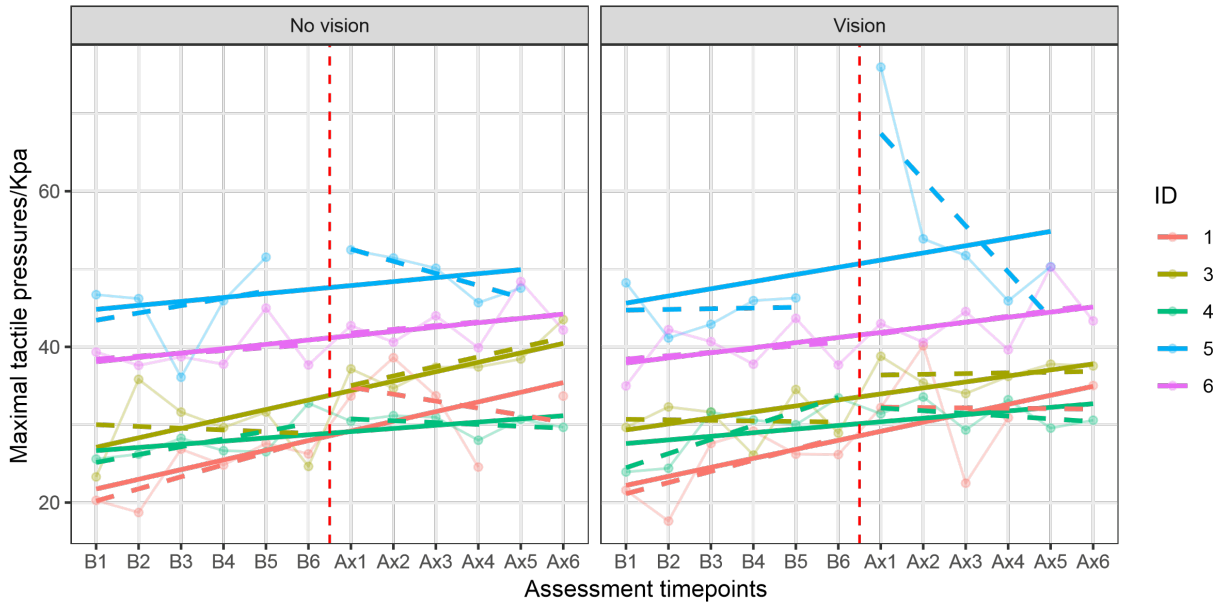


Figure 5.5. Measures of maximal tactile pressures of affected with and without vision for all participants (ID1-ID5)

Note: Dashed red vertical distinguishes between baseline and intervention assessments. The solid lines represent the mean slope between assessments for each participant.

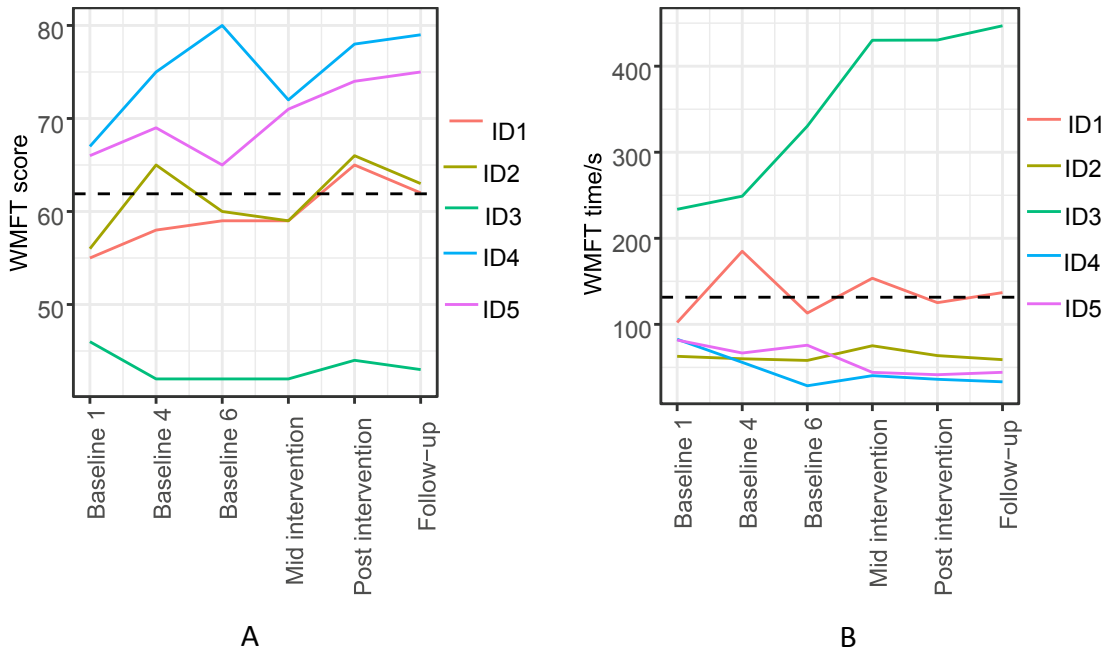


Figure 5.6 A. WMFT scores; B. WMFT time for all participants (ID1-ID5).

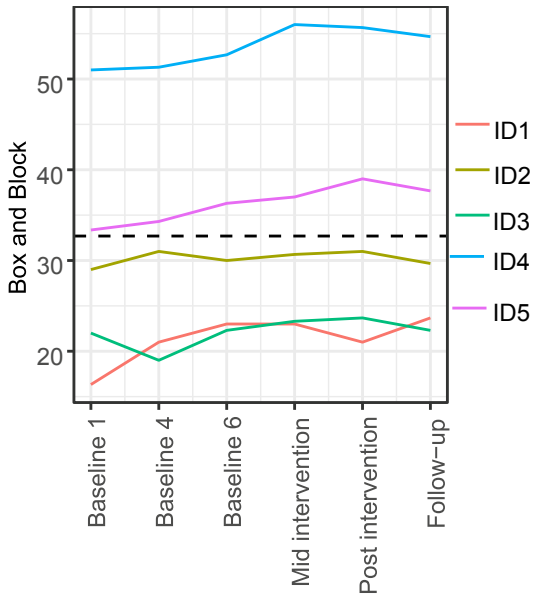


Figure 5.7. Box and Block scores for all participants (ID1-ID5).

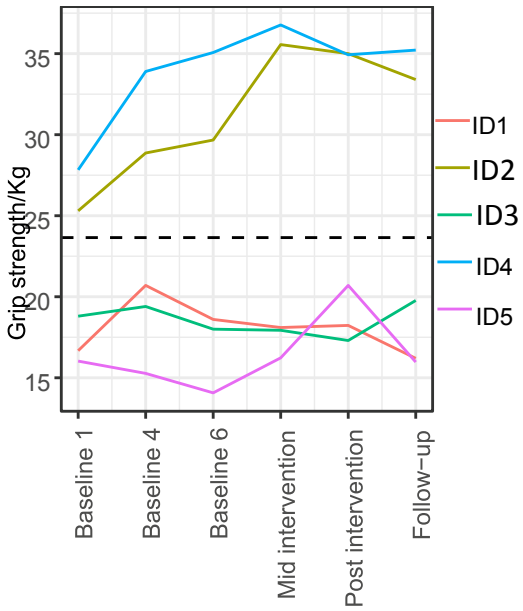


Figure 5.8. Grip strength for all participants (ID1-ID5).

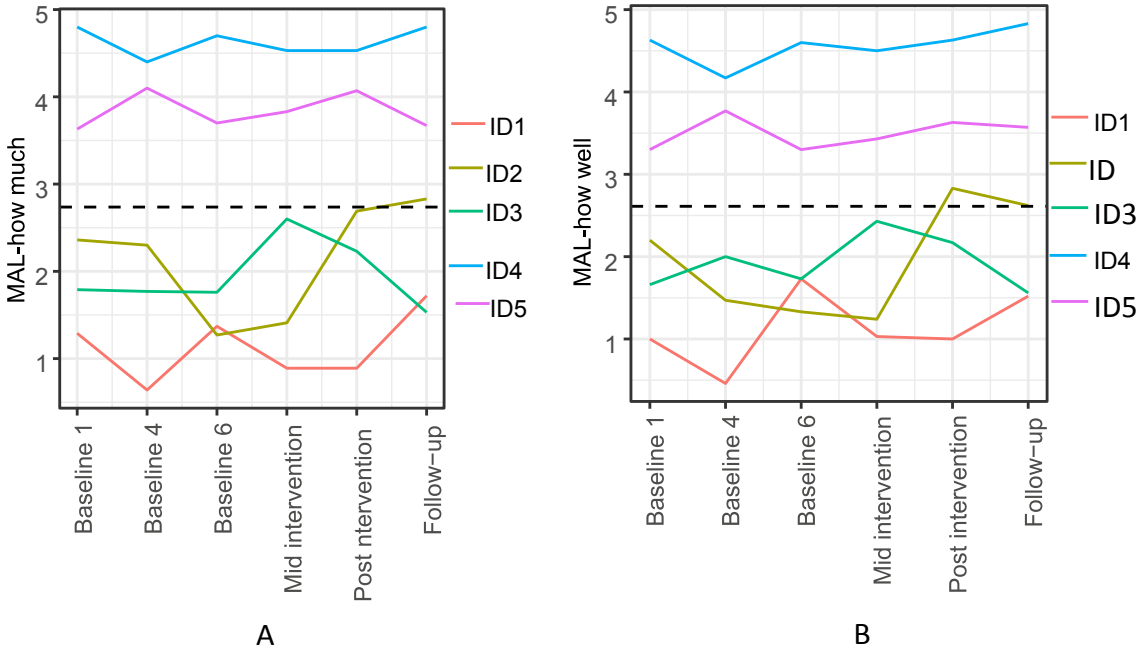


Figure 5.9 A: MAL-how much score; B: how well for all participants (ID1-ID5).

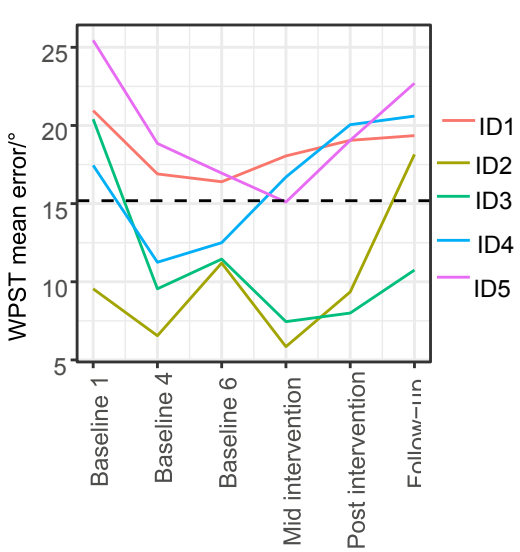


Figure 5.10. WPST score for all participants (ID1-ID5).

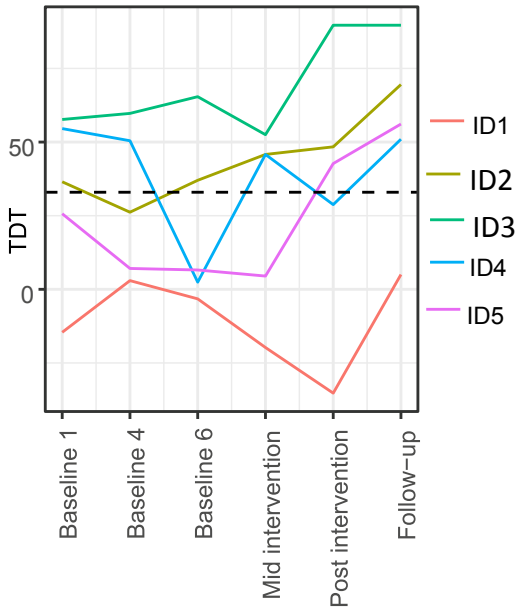


Figure 5.11. TDT score for all participants (ID1-ID5).

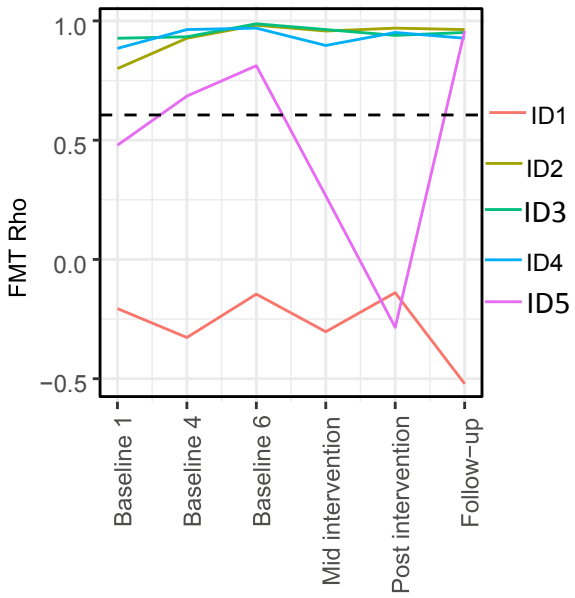


Figure 5.12. FMT score for all participants (ID1-ID5).

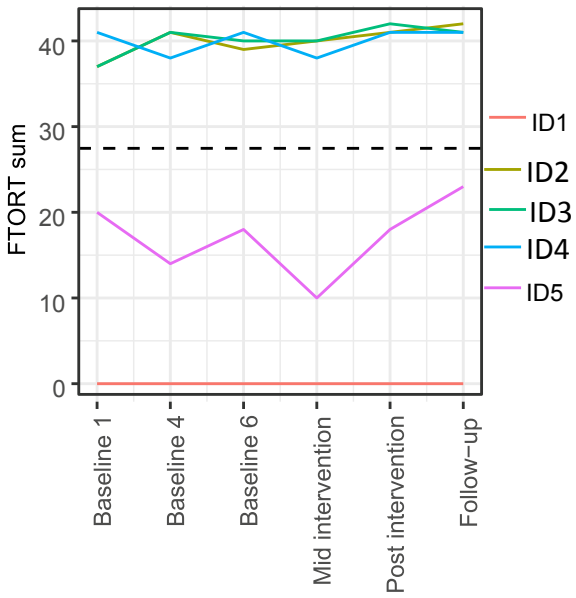
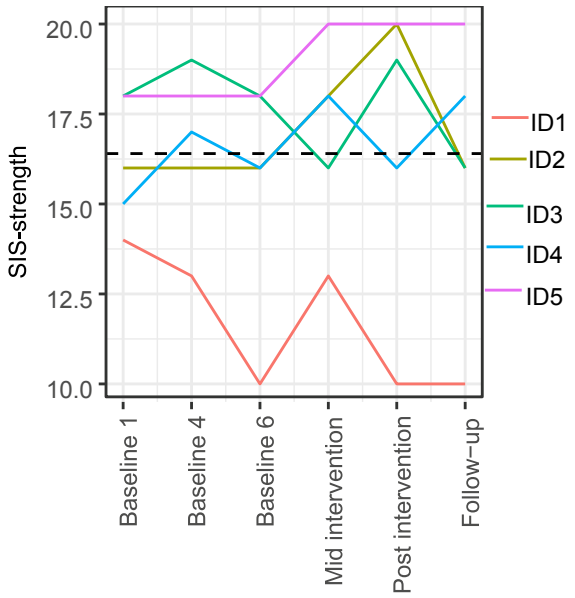
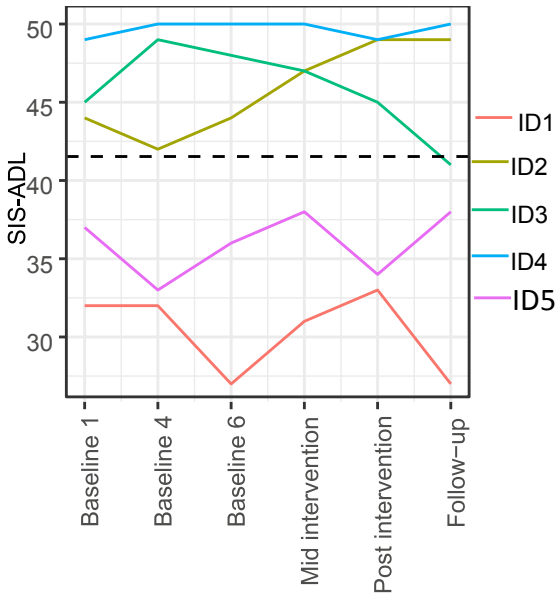


Figure 5.13. FTORT score for all participants (ID1-ID5).



A



B

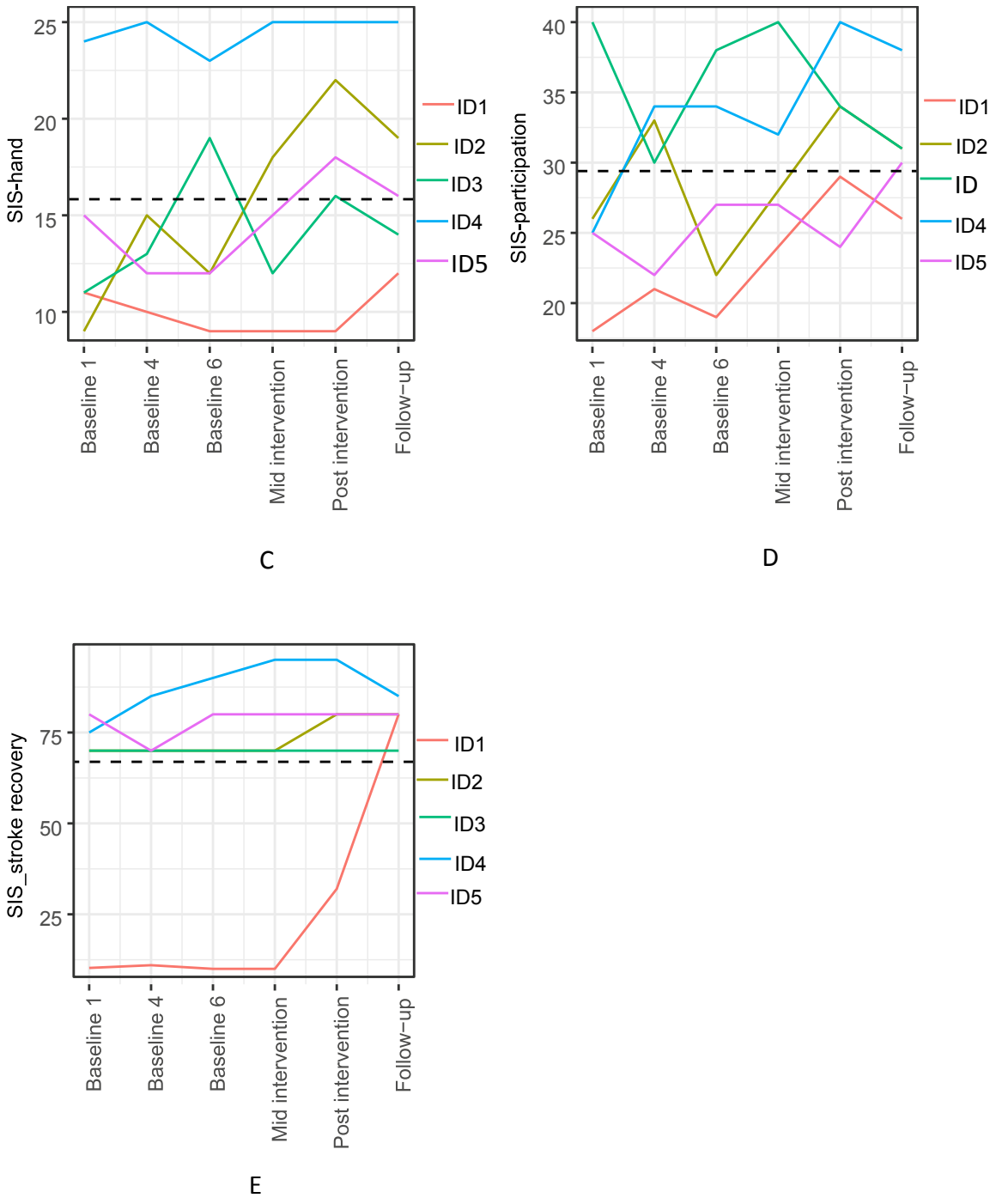


Figure 5.14 A: SIS-strength score; B: SIS-ADL score; C: SIS-hand score; D: SIS-participation score and E: SIS-stroke recovery for all participants (ID1-ID5).

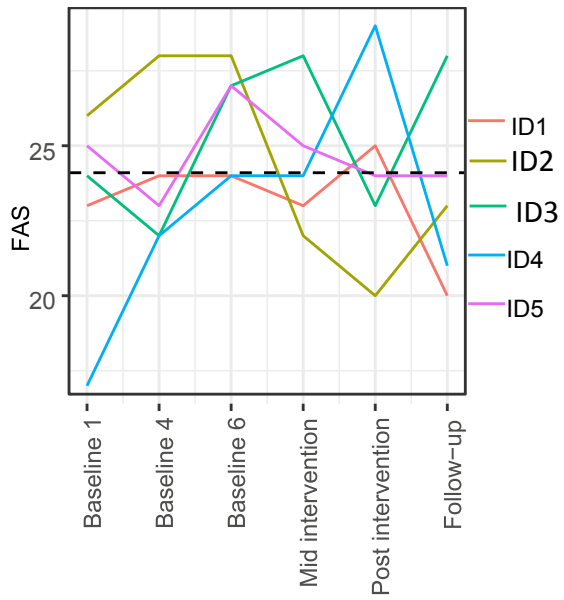


Figure 5.15. FAS score for all participants (ID1-ID5).

Note: The dashed line in figure 5.6-5.15 represents the mean of the group.

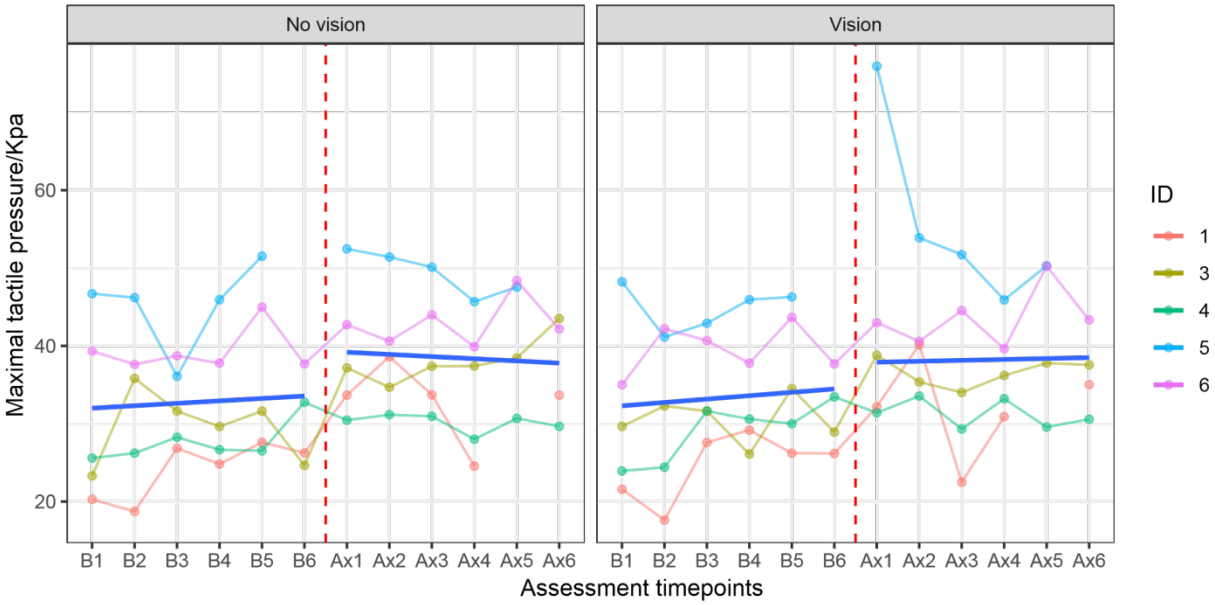


Figure 5.16. Mean slope of measures of maximal tactile pressures of affected with and without vision across group

Note: Dashed red vertical distinguishes between baseline and intervention assessments. Blue solid line measure the mean slope between assessments.

5.5 DISCUSSION

This study investigated the feasibility of the COMPoSE intervention and trial and gathered data on the preliminary impact of the COMPoSE intervention to improve upper limb recovery after stroke. Five participants with chronic stroke were evaluated. Training with the combination of somatosensory and motor variables synchronously, within the same tasks was feasible. The delivery of the COMPoSE intervention according to the standardised training matrix was feasible but modifications to allow more specific tailoring to participant deficits is recommended. The target amount of practice per session was feasible to some extent. All participants were satisfied with the COMPoSE intervention. The overall data collection procedure in the COMPoSe trial was time and labour intensive, and a burden on participants. Some improvements were observed in laboratory measures of maximal tactile pressures and clinical somatosensory and motor measures following the COMPoSE intervention.

5.5.1 Recruitment of participants

The eligibility criteria of a trial are a critical determinant in evaluating intervention effects. In this study, broad eligibility criteria were applied to explore participant characteristics who might benefit the most from COMPoSE. Consequently, participants enrolled in this study had diverse types of somatosensory and/or motor deficits with varied severity at baseline.

Adequate recruitment for stroke trials is a common challenge in stroke rehabilitation trials[472,473]. While it was expected that the broad eligibility criteria would facilitate the recruitment of participants with stroke, the target sample size of 16 participants could not be achieved within the scope of this PhD even though the COMPoSE intervention was of interest to potential participants. Challenges with participant recruitment are common and has been found to be unpredictable with less than 50% of trials achieving their target number of participants within the time period estimated for completion of the trial[474-477]. Low recruitment rates were attributed to problems associated with the eligibility criteria of participants[478], trial-specific design and the recruitment site and staff. Issues related to

recruitment sites and staff in the COMPoSE intervention could have been caused by: 1) a lack of engaged therapists in the hospital departments to identify potential participants for this study; 2) heavy workload of therapists onsite which compromised time for identification of potential participants; 3) multiple clinical trials concurrently recruiting participants with stroke from similar recruitment sites; 4) withdrawal of consent for recruitment of participants from one major hospital due to other research projects concurrently recruiting participants such that their patients with stroke were being sought for too many trials at the same time. To address this issue, recruitment routes were extended to referral by private hospitals, rehabilitation clinicians, promotion of the study in service-user groups and meetings, stroke support groups, advertisement in the stroke research networks newsletter, private rehabilitation practices but this did not substantially improve the enrolment rate of participants.

Another reason for low enrolment rate was that participants were required to have sufficient grasp aperture to facilitate exploration of the objects used in COMPoSE. Additionally, it was identified that participants were required to have sufficient control to open and close their fingers without assistance to enable measurements with the TactArray, even though this was not originally a criterion for eligibility. Having sufficient prehension implies that the participants were fairly well-recovered[164,479] such that the trial was limited to people with mild or moderate deficits with grasping. Therefore, people with stroke who were likely to benefit from this intervention were excluded due to a lack of ability to control finger opening and closing and grasp release for measurement with the TactArray device, despite having significant motor and somatosensory deficits. For those who require assistance in finger opening and closure, maximal tactile pressures can be evaluated by selectively using measures of the plateau phase (5s) of the sustained grasp as suggested in Chapter 6 or by excluding the data during the time frame where assistance is being provided as recommended in Chapter 7.

Recruitment issues that were specific to the COMPoSE trial were also identified. Firstly, the high number of visits due to the repeated measures, inherent in a single-case

experimental design[480] combined with the intervention sessions imposed a heavy time burden which made people with stroke less likely to participate in this trial. If the COMPoSE trial was delivered over a longer period of time, the repeated assessments would have been spread over a longer period, thus reducing the requirement for multiple visits per week, especially during the baseline phase. It is anticipated that when the COMPoSE intervention is ready to be evaluated in a randomised controlled study, the time burden of assessments will be significantly less due to the less frequent and smaller number of assessment timepoints, as compared to single-case experimental studies. Secondly, there was limited financial assistance to support transportation to and from the sessions which led to further exclusion of potential participants.

Based on the findings from the COMPoSE intervention, the following strategies are proposed when devising a detailed participant recruitment strategy tailored for the trial design:1) to include people with severe deficits with grasping after stroke; 2) restricting the number of visits whilst considering the need of the study design; 3) extending the duration of recruitment by a fixed length of time or keep the recruitment ongoing until the target sample size is achieved; 4) making provision for costs of attendance; 5) motivating clinicians on-site by frequent communication or by providing a professional/financial incentive.

5.5.2 Contents of the COMPoSE intervention protocol

The COMPoSE intervention provided a novel means of combining somatosensory and motor training synchronously. The evaluation of the content of the COMPoSE intervention protocol indicated that the combination of active ingredients such as somatosensory-motor tasks, control of finger forces, feedback, high volume repetitions, graded tasks and varied practice were appropriate as they could directly improve upper limb deficits[45,62]. Upper limb interventions post-stroke generally focus on improving function without necessarily addressing impairments[481,482]. Thus, by targeting somatosensory and motor deficits in a functional context, COMPoSE addresses an important gap in developing restorative approaches to improve upper limb rehabilitation post-stroke.

5.5.2.1 Specificity of training

The somatosensory-motor components of the COMPoSE intervention were designed to address a wide range of participants' characteristics to inform the appropriate selection of somatosensory-motor variables for specificity of training. The frequent and stepwise progression across the 36 somatosensory-motor combinations offered multiple and frequent opportunities to challenge the integration of sensorimotor function by encouraging active cognitive processing to enhance learning[400]. Though the choices of somatosensory and motor variables specifically targeted somatosensory and motor deficits affecting reach-to-grasp, all the combinations were not necessarily required by all participants due to the heterogeneity in types of somatosensory and motor deficits across participants. This could be because the inclusion criteria in this study were assessed with the ARAT, TDT and FMT, which are limited to gross motor deficits and touch discrimination deficits assessed using surface types that were not necessarily included in the COMPoSE intervention. Ideally, the choice of somatosensory and motor variables should have constructs specific to the deficits of the participants. Therefore, for some participants, COMPoSE could be delivered in part only, with the intervention contents individualised to match specific somatosensory-motor variables according to targeted deficits.

5.5.2.2 Review of feedback delivery

Feedback delivery is recommended in stroke rehabilitation[62,63,483] to address the impaired use of implicit information during task performance after stroke[221]. In the COMPoSE intervention, it was feasible to use both augmented and intrinsic feedback for the calibration of somatosensory and motor responses during task performance. Augmented feedback was provided according to the 'value-error estimation' principle, combined with knowledge of results and knowledge of performance[484], through external attentional focus using verbal statements from the therapist[216]. Intrinsic feedback in COMPoSE was emphasised through self-evaluation of performance by the participant by identification of errors and aspects of somatosensory and motor performances that were correct, in addition to guided feedback from the therapist. Augmented feedback has been traditionally limited to improve motor

learning[157] and has been incorporated in established interventions such as task-specific training[384] and constrained-induced movement therapy[401]. Few studies have explored the use of intrinsic feedback on tactile information obtained during task performance to improve somatosensory function[157,213,343,388,435], with little application of intrinsic feedback to improve motor function. Therefore, the COMPoSE intervention proposed feedback delivery applicable for both somatosensory and motor learning.

In the COMPoSE intervention, knowledge of results emphasised the patient's cognitive ability to self-evaluate his performance for more self-directed problem solving[485] to enhance somatosensory-motor learning, in addition to making necessary adjustments following feedback from the therapist. In COMPoSE, explicit information is integrated using internal focus feedback, which is in turn used to enhance implicit processes when external focus feedback is provided[215,222]. However, because feedback was delivered in a continuous schedule in 100% of the trials by the therapist, it could be argued that the extent of learning may have been limited due to reduced error correction opportunities by the patient[347]. Nevertheless, the self-evaluation part the feedback kept the participant engaged by maintaining a learning challenge due to the cognitive demand of the tasks in the COMPoSE intervention.

In the COMPoSE intervention, kinematic feedback provided quantitatively using a stopwatch to measure duration of hand transport and qualitatively for grasp aperture were limited by difficulties in providing accurate, discrete and quantifiable movement parameters. Real-time feedback can facilitate the reacquisition of the compromised movements. So far, virtual reality-based interventions after stroke have successfully integrated the use of real-time feedback to improve upper limb motor performance[486]. However, the application of real-time feedback remains scarce in other upper limb rehabilitation interventions that deliver augmented feedback such as constrained induced movement therapy[401] and task-specific training[384]. This could be improved by the use of real-time kinematic devices to allow feedback delivery on movement characteristics such as the velocity, acceleration, and grasp aperture which influence motor learning and execution[226].

Provision of real-time feedback on selected tactile pressures using the TactArray was useful to retrain the control of finger forces. Modulation and scaling of selected tactile pressures in the COMPoSE intervention focused on finger control necessary to perform functional tasks such as buttoning a shirt[163,487,488]. For instance, a stroke survivor having good grip strength but poor control of finger forces could learn to control finger forces to reduce the excessive force when lifting and holding an object by applying less pressure so as to reduce the safety margin between the actual finger forces and also to reduce the minimum force required to prevent object slipping[427]. Retraining of control of finger forces during grasping has been poorly addressed so far in stroke rehabilitation, even though it is skill necessary for successful object manipulation in everyday life[318,325]. Some training modalities involving sensor-based hand rehabilitation robotics were found to be valuable in providing real-time feedback on force after stroke, although there is no comprehensive review discussing strategies for retraining of control of finger forces[489].

5.5.2.3 Amount of practice and impact on somatosensory and motor learning

In this study, even though the target number of repetitions was achieved in few treatment sessions, the COMPoSE intervention prioritised maintaining a balance between delivering a relatively high number of repetitions, tailored to the severity of deficits, and providing adequate exposure to the somatosensory-motor variables while allowing sufficient time for feedback to be delivered in a conducive way to enhance the learning-dependent mechanisms. Traditionally, motor training has prioritised high volume repetitions as a key active ingredient to induce cortical reorganisation[211] in order to improve motor learning[212] and motor functions[62]. On the other hand, somatosensory retraining strategies have focused on duration of exposure to the stimuli to improve somatosensory functions[213]. Although, high volume repetitions are feasible for people with stroke[209], the optimal dose of practice for upper limb recovery after stroke has not yet been established[349]. While dosage has commonly been defined in terms of duration of intervention or amount of practice, other important parameters such as progressions in level of task difficulty and their complex interactions with mechanisms of learning have been poorly addressed[47].

It can further be argued that the large amount of practice delivered in COMPoSE is beneficial when accompanied by good task performances or when guided feedback is provided to correct errors, similar to task-specific training approaches[490]. While findings from the measures of fidelity showed that the amount of practice varied across intervention sessions, feedback was delivered on each trial as planned. Thus, the COMPoSE intervention emphasised that high volume repetitions ought not be encouraged to the detriment of exposure to stimuli or feedback delivery which could result in poor compensatory strategies during task performance leading to maladaptive neuroplasticity[491]. Additionally, this study indicated that care should be taken in delivering high volume repetitions combined with high frequency feedback while progressing across the COMPoSE intervention, so that the increase in physical and cognitive demand is systematic but not overwhelming to prevent fatigability which is related to an objective decline in performance[492].

5.5.2.4 Use of visual conditions in somatosensory-motor training approaches

Deficits in somatosensation are often compensated by vision to guide motor task performance[166,171], which highlights the importance of varying visual conditions during upper limb interventions. Improvements in somatosensory and motor functions in the upper limb could be influenced by modulation of visual feedback after stroke[493,494]. For instance, in COMPoSE, practicing the selected tactile pressures with and without vision could be a viable option for retraining of finger force control as shown by the clinically meaningful improvements in maximal tactile pressures in with and without vision conditions. Another study on stroke survivors also found improvements in force control of the hand after performing maximal voluntary contractions in a gripping task under graded visual feedback conditions[495]. These improvements were associated with increased activity in the visuomotor networks, cerebellum and ipsilateral primary motor cortex which are areas often targeted in stroke rehabilitation[495]. Likewise, several studies have demonstrated that manipulation of visual feedback during robotics[496-498] and virtual reality-based interventions[494] could improve also motor function by reducing motor errors and motor variability post-stroke[499]. Similar, improvements in somatosensory function were also reported after calibration of perceived stimuli using active exploration with and without vision during texture discrimination

training[213,214]. These findings reinforced the impact of somatosensory and motor relearning approaches with varying visual conditions in the COMPoSE intervention.

5.5.2.5 Use of the less affected hand for calibration

Retraining of the affected upper limb based on calibration of somatosensory and motor function with the less affected hand could be a sub-optimal approach due to ipsilesional somatosensory[500] and motor deficits[501]. For example, using the values of selected tactile pressures of the 'less affected' upper limb as a target in COMPoSE could be suboptimal where the affected hand preserved better control of grasp forces than the less affected hand post-stroke. This has been demonstrated in a study comparing impairments according to hand-dominance post-stroke that reported that there were less impairments in grip strength if the dominant hand was affected hand than in the non-dominant less affected hand[502]. However, this approach is not necessarily a limitation in this intervention because training of finger force control at submaximal efforts are useful since they are more difficult to achieve due to the higher levels of motor control required to scale forces during muscle contractions[503].

5.5.2.6 Observed limitations of the COMPoSE intervention protocol

The COMPoSE intervention could have presented insufficient challenge to stimulate learning due to the large difference between graded tasks that failed to maintain the right intensity level limiting opportunities for learning, despite the high number of repetitions. To address this, varied practice was incorporated to additionally stimulate learning, but its effect could have been masked by three factors. Firstly, the varied practice did not necessarily increase task difficulty because the object properties remained easily identifiable due to the large difference between the variables in the graded tasks. Secondly, the target amount of varied practice could be sub-optimal since it constituted a small portion of the overall target number of repetitions. Thirdly, failure to achieve the target amount of varied practice further reduced the effect of varied practice.

The standardised order of the training matrix could have also contributed to limiting the extent of learning, though it facilitated treatment delivery. A lack of randomisation in the order of presentation of the variables could have limited the progression in task difficulty, thus possibly contributing to a learning effect. The COMPoSE trial therefore further reinforced that high dose repetitions alone might not necessarily translate into better outcomes[47] since repetitions alone do not necessarily reflect the amount of effort required in performing the task (intensity of training) and the quality of task performance[211]. It is also established that changes in cortical activity and improvement in skill acquisition result from repetition of continuously challenging tasks but not from repetition of previously learnt or overlearned movements[504-506]. Another limitation of COMPoSE was that the reaching component was unidirectional which limited opportunities for proprioceptive retraining, even though reaching and grasping without vision incorporated some proprioceptive stimulation.

It is acknowledged that the COMPoSE intervention focused on the practice of reach-to-grasp, lift and hold which is a meaningful skill required in everyday life and did not incorporate other essential task-specific skills required to perform activities in everyday life such as object manipulation. Thus, the combination of impairment-oriented training with a reaching-and grasping task addressed only part of the needs of upper limb rehabilitation. COMPoSE could therefore be a valuable step-wise progression from impairment-focused training, prior to functional training interventions with real-life tasks.

5.5.2.7 Suggestions to make the COMPoSE intervention more challenging

To further optimise the COMPoSE intervention, the tasks could be progressively made more challenging by: 1) using somatosensory or motor parameters with a smaller difference between the two variables could be used such as 80 and 100 grit sandpaper instead of felt and sand paper or small and large objects of 1cm difference in diameter; 2) randomising the order of presentation of the somatosensory-motor combinations; 3) introducing varied practice earlier in the intervention and in larger doses; 4) incorporating proprioceptive training by making the reaching component of COMPoSE multi-directional in the horizontal plane to improve limb position sensation and improve motor learning[507]; 5) introducing objects with varying shapes (shape discrimination) to assist proprioceptive training of finger

positioning which is essential for object manipulation[130,131]; 6) incorporating weight discrimination to improve scaling of fingertip forces with regards to object weight[168] and; 7) using real-life objects with varying size, shapes, surface texture, surface slipperiness as a progression of task difficulty.

Facilitators and barriers to clinical implementation are worth considering during the early stages of the development of an intervention[508]. The detailed reporting of the key contents of the COMPoSE intervention and delivery protocol helps increase its implementation fidelity, especially when the intervention needs to be adapted to the participants' needs[509]. Another study investigating the constraint-induced movement therapy emphasised the importance in explicitly characterising intervention protocols to enhance its use in a research and clinical context[510].One barrier to implementing COMPoSE in a clinical context could be the time intensive nature of the intervention. For instance, the duration of each session of the COMPoSE intervention (up to 2 hours) and the face-to-face treatment delivery could be limited by time constraints causing therapists to see less patients or be taken away from other administrative duties. Time pressure due to insufficient staff and competing responsibilities of staff has been consistently reported as a key barrier to implementation of stroke rehabilitation[508,511]. It is noteworthy that the provision of personalised feedback in COMPoSE is feasible in the clinical context. Therefore, if COMPoSE is to be implemented, adequate therapy time would need to be committed within the caseload seen by the therapist for which sufficient support from organisational management is critical[508].

5.5.2.8 Participants' engagement

Participants' engagement level is a key determinant in maximising the benefits of a rehabilitation intervention[512,513]. The COMPoSE trial found that all participants reported that they were engaged during the intervention sessions. Similar observations were reported by the therapist delivering the intervention. The importance of active participants' engagement in the therapy sessions of the COMPoSE intervention is consistent with findings that active engagement promotes neural plasticity in motor learning[514]. However, it is acknowledged that there could be potential bias in the therapist's perception of the participants'

engagement in the COMPoSE trial. More sophisticated methods using electroencephalography could be explored to assess cognitive engagement of patients with stroke in therapy sessions[515].

5.5.2.9 Tolerability and acceptability of the COMPoSE intervention

The COMPoSE intervention resulted in tolerable levels of fatigue and was feasible in people with stroke. Despite the general increase in perception of fatigue (SFVA) across all intervention sessions, there was a high adherence rate to the intervention sessions. This could imply that the participants' tolerability to fatigue due to intensive practice may have improved. Fatigue was minimised in the intervention sessions by individualising the amount of practice of each participant to avoid excessive high-volume repetitions which might not be tolerable by stroke survivors causing worsening of motor function[516,517]. Additionally, the scheduled training duration of each intervention session was at most 2 hours to minimise fatigue because lengthy daily sessions could contribute to elevated perception of fatigue and fatigability. This could in turn adversely affect motor training by reducing the neural activation required for beneficial neuroplastic changes that influence motor improvements[518]. It could also be argued that the participants were motivated to complete the intervention and found the COMPoSE intervention satisfactory despite the burden of fatigue because they became more aware of their potential to recover as reported by one participant (ID5) who thought it was beneficial to push oneself even when fatigued. Though it was not the aim of this feasibility study, it is acknowledged that a qualitative interview could have further explored the acceptability of the COMPoSE intervention by the participants.

5.5.2.10 Participants' experience of task performance

The participants persevered to complete the intervention sessions despite feelings of frustration. Participants who had the most severe deficits (ID1, ID3 and ID5) could have felt frustrated due to difficulties experienced in task performance, even when learning felt easy (ID3 and ID5). It was therefore critical to ensure that during delivery of COMPoSE, the instructions and feedback provided were sufficient and easy to understand to facilitate

successful task performance in order to motivate them to continue to practice, even when the tasks felt challenging.

5.5.3 Data collection procedures and outcome measures

5.5.3.1 Selection of outcome measures

The selection of outcome measures was challenging because the COMPoSE intervention addressed both somatosensory and motor impairments and there is currently no single outcome measure that could appropriately evaluate the various clinical aspects of interest. A systematic literature review found that the use of upper limb measures in stroke rehabilitation trials were frequently limited to motor outcomes such as the MAL and WMFT. Additionally, very few studies (0.6%) included sensory measures[248]. These gaps were addressed in the COMPoSE trial as multiple outcome measures were used to comprehensively assess the different types of somatosensory, motor and functional impairments and to allow capturing of the participants' individual impairments. It is acknowledged that the COMPoSE trial could not consider the recommendations of the Stroke Recovery and Rehabilitation Roundtable consensus[519] as the latter was published after the conduct of the trial. However, it is noteworthy that the Stroke Recovery and Rehabilitation Roundtable consensus were limited to the ARAT and Fugl Meyer for upper limb motor assessments, without addressing sensory measures [519].

Clinical measures with good validity and reliability were used for motor assessments [37,213,252,391,414,418,421,431,433,434,437-439,441,520,521] and somatosensory assessments[213] in the COMPoSE trial. Furthermore, measures of activity and participation were important to determine if the intervention could result in changes in the daily life of people with stroke in the long-term, though significant improvement might not necessarily occur within the short duration of the COMPoSE trial. All measures were completed with no unusable or missing data.

A recent consensus on the use of outcome measures for upper limb trials after stroke[519] encouraged the use of kinetic measures using force sensors to objectively measure

and quantify impairments after stroke. These measures could also help to distinguish between restitution of impairments and behavioural compensatory strategies[519]. In line with these recommendations, maximal tactile pressures were assessed using the TactArray pressure distribution system in the COMPoSE trial. This laboratory-based measure constituted a novel means of evaluating the integrated somatosensory-motor function during scaling of grip forces and offered the advantage of directly evaluating the construct trained within the COMPoSE intervention. The study reported in Chapter 6 found that measures of maximal tactile pressures using the TactArray device have good reliability in people with chronic stroke. It is acknowledged that because the selected pressure measures were similar to the training of selected pressures and performed repeatedly during the trial (14 timepoints), there could have been a learning effect which could have confounded the impact of the COMPoSE intervention.

5.5.3.2 Impact of responsiveness of outcome measures

A lack of responsiveness of the outcome measures could limit the detection of small improvements across the intervention and post-intervention phases. For example, some improvements were observed across all participants in the WMFT score (range: 4-12.1%). However, even though the established effect size of WMFT score is large (standardised response mean: 1.30; confidence interval: 1.03, 1.67)[522], its responsiveness is limited due to relatively large values for minimal detectable change for the WMFT score (38.6%)[523]. Similarly, the minimal detectable change for the BBT is relatively large (18%)[524]. The minimal clinically meaningful changes for measurement of grip strength assessed with the Jamar dynamometer are also relatively large (5-6.2 kg)[525]. Changes of these proportions were less unlikely within the short time frame of the COMPoSE intervention trial. For future trials, it is suggested to use 3-D motion analysis measures which are more sensitive to small changes in motor function for more objective monitoring on intervention effects[519].

Responsiveness of outcome measures could be further limited amongst stroke survivors with severe deficits resulting in a lack of change at post-intervention. For instance, one participant (ID3) with substantial motor deficits did not show much change in the BBT across the intervention phase, at post-intervention or follow-up (range: -5.8-7.6%). This lack

of change could be because the BBT has better responsiveness in mild to moderate stroke as compared to severe deficits due to a floor effect[526]. Similarly, the same participant (ID3) had a small change in WMFT score (range: 42-44) but worsened considerably in the WMFT time (range: 330.3-430.4s). However, this observation would not have been evident if the WMFT time was reported as a maximum of 120s, regardless of the amount of time taken to complete the tasks[411]. This suggests that the WMFT has low responsiveness for people with severe motor deficits after stroke due to a floor effect[527]. The variations in responsiveness of outcome measures indicated a need to selectively choose tests with sufficient responsiveness to the severity of deficits for better monitoring of participant responses to improve individualisation of rehabilitation interventions.

5.5.3.3 Burden of data collection procedures

The combination of burden of large number of outcome measures, and high frequency of assessment sessions in the COMPoSE trial imposed lengthy assessment sessions during the baseline phase (2 hours) and intervention phase (up to 4 hours). This was time intensive and laborious for the participants and may have contributed to the increase in fatigue (SFVAS) in the baseline phase (all participants), intervention phase, post-intervention and at follow-up (ID1, ID2, ID3). Therefore, it was likely that fatigue could have confounded their performance during testing leading to poorer outcomes. For instance, the fluctuations in SIS-participation scores could result from fatigue. This is supported by a qualitative study (n=19) on stroke survivors' views of post-stroke fatigue reporting the debilitating influence of fatigue upon daily occupational performance, social participation and return to work[528]. Alternatively, the variability in fatigue across participants in the baseline phase could be due to fluctuations in fatigue being so prevalent in chronic stroke[529] or that the participants had differential ability to rate their fatigue consistently. This therefore highlighted that the overall burden of outcome measures should be carefully considered with regards to the time and effort placed on participants and on those who administer the outcome measures to minimise the extent of confounding factors on the results. Measures with good responsiveness are likely to reduce the number of outcome measures required to detect changes following the intervention[519]. Consequently, this could reduce the length of assessment sessions and minimise the risks of confounding the results due to fatigue.

One limitation of this study was that people with stroke and public involvement were not considered in the design of the COMPoSE trial. The experiential expertise on challenges faced by stroke survivors combined with the expertise of researchers and clinicians could improve the study design and the conduct of the trial[530]. Therefore, it is likely that issues related to the data collection procedures might have been identified if there were patient and public involvement during the design of the trial.

5.5.3.4 Appropriateness of outcome measures

Laboratory measures such as kinematic and kinetic measures are recommended for more robust evaluation of changes in impairments, in addition to the use of clinical measures with high reliability[519]. The COMPoSE trial evaluated maximal tactile pressures in people with mild, moderate and severe somatosensory and motor deficits as well as mild and moderate deficits in grasp control. Findings from the reliability study indicated that maximal tactile pressures were reliably measured by the TactArray device (Chapter 6). For individuals with mild to moderate motor deficits, measures such as the BBT, the WMFT, and the MAL could be appropriate. For instance, the BBT has the strongest clinical utility amongst upper-limb measurement tools for stroke[531], though a more recent consensus recommended the Action research arm test (ARAT) and the Fugl-Meyer assessment (FMA-motor) for upper limb trials after stroke[519]. Additionally, the BBT requires only one-two minutes to complete[415,416]and is therefore less time consuming than the ARAT[532] or the WMFT[411]. The BBT also requires grasping action, which was a construct trained in the COMPoSE intervention unlike the tasks in the Fugl-Meyer assessment and some items of the ARAT which do not require the participant to make a grip (gross movement section). However, it is worth noting that the BBT has excellent construct validity with the FMA[533] and excellent concurrent validity with the ARAT[526].

For somatosensory assessments, the TDT and FTORT were most appropriate in people with mild to moderate motor deficits the COMPoSE trial. To date, there has been no recommendations for somatosensory assessments of the upper limb after stroke[519], even

though the TDT, FMT, WPST and the FTORT have good discriminative test properties with high reliability (r = 0.85 to 0.92) as well as age-adjusted normative standards[213] . It should be pointed out that this lack of consensus could have resulted from the somatosensory assessments failing to meet a strict list of 19 desirable criteria[519], despite having good psychometric properties.

For people with substantial motor deficits, the MAL is recommended. No somatosensory measure evaluating touch discrimination could be recommended for people with severe tactile deficits. Additionally, the SIS is recommended for people with varying severity of deficits. These findings indicated that measures with high responsiveness are necessary i.e., outcome measures which are sensitive to small changes over time. Additionally, outcome measures that are sensitive to severity of deficits are necessary[235,534] with little or no ceiling effect in people with mild deficits who are already high functioning; similarly, little or no floor effect in people with moderate to severe deficits. Given the limitations of existing outcome measures and practical constraints such as time, ease of test administration and construct targeted, it is suggested that stroke rehabilitation trials evaluate interventions in homogeneous groups of participants i.e., those having similar type and severity of deficits and then accordingly select the most responsive outcome measures.

5.5.4 Preliminary impact of the intervention on participants

Assessment of outcome measures provided indications of pre-intervention baseline performance and allowed identification of variations in performance. The findings regarding the participants' responses should be interpreted with caution given the limitations of this study with regards to the small sample size and the lack of responsiveness of outcome measures, amongst other factors.

5.5.4.1 Impact of lack of stability of baseline measures

The lack of stability in the maximal tactile pressures and the clinical measures in the baseline phase in some participants indicated a threat to the internal validity of this study and

therefore limited the interpretations of intervention impact of COMPoSE[456]. A baseline of three weeks was chosen because it was anticipated that people with chronic stroke (>6 months) who had long discontinued regular therapy would be stable due to the low possibility of spontaneous recover and therefore most likely to be constant in the baseline measures[327]. However, the positive trend observed in the baseline phase of maximal tactile pressures during vision (ID1 and ID3) and without vision conditions (ID1, ID2 and ID3) suggested that the three weeks were too short to ensure a stable baseline. Similar fluctuations were observed in the Action Research Arm Test and the Mobility Index in some participants of a single-case study (n=6) evaluating combined mobilisation and tactile stimulation, even though a 4-weeks baseline phase was used[322]. This could happen because the participants might be overcoming the effect of long-standing functional deconditioning[535] or of learned non-use of the upper limb affected by stroke[491]. Additionally, people with chronic deficits post-stroke could improve, worsen or fluctuate over short periods of time[536], resulting into variations in the short baseline phase. This could be corrected by introducing the intervention phase only after the participant has achieved a stable baseline in at least 8 of 10 tests[325]or any measure ought to be repeated periodically for several weeks until limited variability is found[453]. This representative baseline phase could then serve as an appropriate comparison for the intervention and post-intervention phases. Another alternative could be delivery of a conventional intervention for six sessions or more until the participants reach a plateau by the conventional treatment as a 'phase-in' to the new intervention[537].

The variations during repeated assessments of the clinical measures across the baseline phase could result from large measurement errors. For instance, grip strength measurements were not stable across the baseline for all participants (range variation:-17.9-11.3%). This could be because grip strength measurements with the Jamar dynamometer have shown large variations in the standard error of measurement (4-20%) between two consecutive sessions (at least 10 days apart)[244]. Therefore, any change within 20% of the standard error of measurement was not reliable which could explain the fluctuations in measures. However, compared to the clinical measures, less variations were observed in measures of maximal tactile pressures across the baseline. So, this supports their use as an appropriate choice of measure because the TactArray pressure sensors have high sensitivity,

low accuracy error and low repeatability error such that the measures of tactile pressures were less affected by measurement errors[385,538].

Another reason for the variations in the baseline could be that the responsiveness of the outcome measures was limited in people with severe impairments. For example, two participants with the most severe somatosensory deficits (ID1 and ID5) showed large fluctuations (-165.5-7.5%) in the TDT and FMT. It is possible that these large variations were a consequence of random errors resulting from a lack of responsiveness of the TDT and FMT for people with very severe tactile deficits post-stroke rather than because of a change in performance or biological variations. Although the TDT and FMT have good reliability, the responsiveness of these tests have not been evaluated and interpreted with regards to baseline severity of tactile somatosensory deficits which limited the interpretation of the fluctuations[213,391,539].

5.5.4.2 Impact of the COMPoSE intervention

A preliminary beneficial impact of combining somatosensory and motor variables synchronously was observed to some extent in the COMPoSE trial but not consistently across all outcome measures or participants. For instance, improvements in maximal tactile pressures were observed in all participants except one (ID4) with vision (14.8-62.5) and without vision (12.0-50.5%) at post-intervention. One participant (ID5) had an important improvement (13.7%) in the BBT while small improvements (range: 3.3-8.5%) were observed in three participants (ID2, ID3, ID4). Similar inconsistencies were observed in the TDT with improvements (32.7-517.2%) observed in three participants (ID2, ID3, ID5) but deteriorations (43.1-929.6%) in two participants (ID1 and ID4). These findings were consistent to some extent with other studies including a 3-arm nonrandomised controlled trial (72 hours therapy)[318] and one single-case study (25-30 hours therapy)[325]delivering integrated somatosensory-motor tasks that also found some improvements in somatosensory and motor measures. These results reinforce the importance of integrated somatosensory-motor tasks to improve both somatosensory and motor performance. Neuroimaging studies using MRI have further supported this argument by demonstrating the role of tactile stimulation in

promoting motor recovery in animal studies[193] and in people with stroke[203]. Additionally, increased activation responses in the sensorimotor control area, the secondary somatosensory cortex and the supplementary motor area were observed following tactile stimulation in stroke survivors[203].

The mixed impact of COMPoSE resulting in improvement in some measures and deteriorations in others suggests that an overall duration of 15 hours of therapy might be insufficient. This argument is supported by another RCT delivering combined somatosensory and motor training with integrated training (16 hours therapy) which showed a lack of improvement in outcome measures with the intervention compared to the control, though significant improvements were found within the experimental group in the Fugl-Meyer assessment, MAL-HW and tactile sensibility[321]. These findings suggest that there could be potential impacts of the COMPoSE intervention if delivered in a larger dose to improve somatosensory, motor and functional deficits of the upper limb.

The findings from this study suggest that COMPoSE could be beneficial to people with mild to severe somatosensory and motor deficits after stroke. It is also possible that the COMPoSE intervention had limited benefits in people with minor impairments. For instance, one participant (ID4) who presented with mild impairment at baseline (WMFT score; 75; MAL-AS: 4.7; MAL-HW: 4.6; TDT: -17.9) was possibly too well-recovered to be suited to this intervention, which limited the possibility of improvements. These observations suggest the need to include participants with more specific inclusion criteria with regards to severity of deficits to better guide upper limb rehabilitation needs after stroke. Laboratory measures such as 3-D motion analysis and tactile pressures could also be used to set cut-off scores for the severity of deficits in selection criteria.

5.5.4.3 Possible reasons for the varying impact of the COMPoSE intervention

The lack of consistent improvement in all participants across the measures from the intervention phase to follow-up could be because the extent of improvement might be associated with the severity of deficits at baseline. For example, the participant with

substantial motor and moderate somatosensory deficits (ID2) improved in a larger number of somatosensory and motor outcomes (WMFT score, MAL, grip strength, TDT and FMT, SIS-strength, SIS-hand and FAS) than another participant (ID1) with more severe somatosensory and motor deficits (WMFT score, WPST, SIS-participation, SIS-Stroke recovery) at post-intervention, implying that participants with milder deficits may recover to a larger extent than those with more severe deficits with this intervention[540]. Similar findings were observed in a single case study (n=4) delivering integrated somatosensory-motor tasks where one participant with worse deficits in measures such as tactile discrimination, reaching and grasping, motor sequencing did not improve or improved to a lesser extent (4-9 outcome measures) than the other participants with less severe deficits (7-9 outcome measures)[325]. These observations align with neuroimaging studies using TMS and MRI that showed that initial severity of upper limb impairment is the most important predictor of outcomes in the long-term[183]. For instance, CST-lesion load was found to be a significant predictor of motor deficit when evaluated amongst people with chronic stroke who presented with moderate to severe motor impairments in the acute phase[541]. The proportional recovery rule also demonstrated that stroke survivors with a fractional asymmetry of the corticomotor tract > 0.25, are likely to have poor improvements of the upper limb function, low functional potential and poor recovery of upper limb function[179]. Since somatosensory deficits are typically present with motor deficits, it is therefore suggested to use TMS and MRI neuroimaging to evaluate the integrity of the corticospinal tract to improve the predictability of recovery with regards initial severity of deficits.

It is also possible that the severity of motor deficits is more likely to influence the extent of recovery than the severity of somatosensory deficits. The findings of this study showed that one participant (ID5) with mild motor but severe somatosensory deficits (ID5) improved in a larger number of somatosensory and motor measures (WMFT score, WMFT time, BBT, MAL AS, MAL HW, grip strength, TDT, SIS-strength and SIS-hand) than another participant (ID2) with substantial motor but moderate somatosensory deficits (WMFT score, MAL AS, MAL HW, grip strength, TDT, FMT, SIS-strength, SIS-hand, SIS-participation, SIS-stroke recovery and FAS. In turn, this participant (ID2) improved in more outcome measures than another participant (ID3) having mild somatosensory deficits (MAL AS, MAL HW, TDT,

SIS-strength). However, based on the WMFT time, it was obvious that ID3 had more severe deficits in timed motor functional tasks as compared to ID2 such that ID2 was expected to recovery to a greater extent than ID3. Such variations remain unexplained due to limited predictability of recovery of upper limb impairment and function when using clinical measures in people with severe upper limb deficits. A recent study found that paresis in the upper limb has a strong masking effect on tactile somatosensory deficits regarding activity participation after stroke[542] such that motor deficits could be a better predictor of upper limb recovery than somatosensory deficits. Likewise, a systematic review and another study using neuroimaging that have demonstrated that severity of paresis is the best predictor of motor deficits and function[543,544]. Compared to severity of motor deficits, the severity of somatosensory deficits has been poorly investigated as a predictor of recovery. In fact, recovery in somatosensory function is often associated with motor recovery[545]. This finding was also observed in COMPoSE amongst three participants with moderate to severe deficits in somatosensory function (ID1, ID2 and ID5) improved in the TDT and in a majority of motor outcomes at post-intervention. Variations in motor or somatosensory recovery could therefore be explored using MRI biomarkers to help in re-mapping training-related cortical changes and advance understanding about changes in clinical measures are encouraged[546]. MRI studies could help to better understand of the theory underpinning the COMPoSE intervention by determining the underlying mechanisms by which interactions between contents of the intervention influence outcomes[55].

Variations in the outcome measures could also be due to inter-rater variability in administration and rating of the tests. In the COMPoSE trial, assessments by multiple assessors, some of whom lacked familiarity and testing experience, could have contributed to the variations in the results. The assessors could have been improving their assessment skills over the course of the trial which could have introduced variability in the administration of the tests. The lack of opportunity to practice the conduct of the outcome measures on people with stroke was due to the delayed involvement of the main assessor, despite attempts for timely recruitment of assessors for the COMPoSE trial. Although for a small number of outcome measures, the involvement of additional assessors to substitute the main assessor during periods of sick leave was not anticipated early in the trial which in turn limited the

opportunity for training. To our best knowledge, no study has investigated the impact of experience in outcome assessment with regards to the amount and type of training required in post-stroke rehabilitation. One means to reduce variance in test administration is through standardised training and a certification protocol[547]. A study is currently underway to standardise the assessment of sensory loss and therefore reduce inter-rater variability in stroke trials[548].

The lack of improvement as a result of the COMPoSE intervention could also be due to limited potential of recovery post-stroke due to the worsening effects of ageing and severity of fatigue on somatosensory and motor deficits after stroke. For instance, participant ID1 was significantly older than participant ID5 (by 25 years) such that there could be significant somatosensory losses due to ageing. Both participants (ID1 and ID5) had similar severity of somatosensory deficits (range TDT: -95.9- -114.4%) but ID1 improved on a smaller number of outcome measures (n=3) compared to participant ID5 (n=8). In fact, using somatosensory evoked-potential mapping and electric source localisation, a strong decline in tactile performances were found with ageing with an expansion of hand representation of 40% in the primary somatosensory cortex to compensate for age-related changes in normal older adults (60-85 years)[549]. Similarly, motor performance of complex tasks involving fine and gross motor skills also decline in older adults[539]. Participant ID1 also had significant cognitive deficits (MOCA 17) as compared to participant ID5 (MOCA 29) which could have limited his performance on the outcome measures. This argument is supported by a systematic review (six studies) that found a moderately strong association (r= 0.48) between executive function and arm motor recovery amongst people with cognitive deficits after stroke[550]. Additionally, performance on complex tasks requiring attention or problem-solving have been found to decline progressively with age[551]. It could therefore be suggested that the COMPoSE intervention might be more beneficial to stroke survivors with mild or moderate cognitive impairment, but not necessarily for those with severe cognitive losses. It was also observed that ID1 had worse perception of fatigue (range SFVAS: 2-9) than ID5 (range SFVAS: 1-4) during the intervention sessions which could have limited motor recovery.

The overall lack of improvement in the upper limb could also result from substantial learnt non-use of the affected upper extremity[552]. Four participants had limited use of the affected arm (MAL-AS range: 1.3-3.7) prior to the COMPoSE intervention. Consequently, this could have reduced the potential recovery because inhibitory effects of the non-lesioned hemisphere onto the lesioned hemisphere could have impeded the cortical re-organisation in the lesioned hemisphere limiting the extent of short-term training-induced improvement of the upper limb[553].

The COMPoSE trial indicated that the extent of change in participants depends on multiple factors. Therefore, it is suggested that any improvement following an intervention is interpreted with regards to the characteristics of people with stroke (type and severity of deficit targeted), the construct being trained in the intervention, expected effect size of improvement related to intervention dosage and possible generalisation of relearned abilities to untrained somatosensory-motor tasks. Additionally, the strength of reliability of the measures and their responsiveness should also be considered when interpreting the extent of recovery. Other factors such as ageing, severity of mental and physical fatigue and severity of cognitive impairment also warrant careful consideration in gauging expected recovery.

Additional considerations

It could also be argued that the small improvements in some outcome measures could have resulted from placebo effects resulting from the psychological benefits of receiving a rehabilitation intervention and not necessarily by the COMPoSE intervention contents or training dosage. This argument is reinforced by the participants being satisfied with the COMPoSE intervention even though some of their clinical measures did not consistently reflect meaningful changes after the intervention.

5.5.5 Strengths and limitations

This study illustrated the value of single-case experimental studies in exploring the impact on individual participants to a novel intervention at various timepoints as well as informing the development of trials of complex interventions. This trial of the COMPoSE

intervention provided valuable insights into how unexpected variabilities in findings could result from operational flaws of the trial and not necessarily from poor validity of the theory underpinning the COMPoSE intervention[554]. Consequently, the impact of the COMPoSE intervention could not be appropriately interpreted. However, this study was useful to monitor incremental changes over a short time period, prior to planning larger studies.

This trial had a number of limitations such as the short time frame and dosage of the intervention, small sample size, the lack of responsiveness of outcome measures and too short duration baseline phase that have been addressed in the previous sections. Additionally, it is acknowledged that this type of study design with repeated measures across baseline and intervention phases and lengthy assessment sessions involves substantial costs, though a formal cost-analysis was not conducted.

5.5.6 Implications for rehabilitation

The COMPoSE intervention offers potential benefits to improve upper limb recovery after stroke, if delivered at the appropriate dosage. The standardised training matrix could be adapted such that only part of the training can be delivered. Consequently, the choice of somatosensory-motor combinations could be adjusted to specifically target somatosensory, motor or finger force control deficits. The amount of practice of each combination could be delivered with regards to severity of somatosensory and motor deficits respectively.

5.5.7 Recommendations for future trial

The contents of the COMPoSE intervention and its dosage parameters (amount of practice, frequency of treatment, duration of treatment session, overall treatment duration) need to be adjusted, prior to subsequent trials in order to maximise somatosensory and motor improvements in the upper limb after stroke.

This thesis evaluated the feasibility of the conduct of the COMPoSE intervention and trial. To further optimise the COMPoSE intervention and trial, a series of pilot studies might be required according to the MRC (UK) framework[54]. Therefore, it is suggested that a series

of single-case studies are conducted to evaluate the preliminary responses of people with stroke in which different aspects of the intervention can be systematically explored[452]. For example, the preliminary effects of the COMPoSE matrix tailored to target specific somatosensory and motor deficits and severity of deficits with lengthier overall treatment duration could be evaluated. This continuum of the development process along with a systematic manipulation of treatment parameters and replication of effects of within and across trials could lead to a more promising COMPoSE intervention in the future. This process could help increase the efficiency of the COMPoSE intervention delivery so as to inform the design of a randomised controlled trial.

5.6 CONCLUSION

The COMPoSE intervention was feasible to deliver. The COMPoSE trial was useful in identifying specific ingredients of the contents and delivery of the COMPoSE intervention and operational aspects of its trial that need to be revised in order to optimise its effects on somatosensory, motor and functional deficits of the upper limb after stroke. The preliminary positive outcomes on some measures indicated that the COMPoSE intervention could be useful in improving somatosensory and motor deficits in chronic stroke.

Appendix 5.1

Manual of procedure for COMPoSE intervention

1. **Prior to participant arrival**

a. Participant scheduling

- Arrange potential timeframes for intervention trials.
- Ring participants and organise for timeframes for intervention.
- Organise taxi vouchers or gift vouchers.

b. Room setup

1. Desk of 110cm in height and height adjustable chair

c. TactArray Equipment setup

1. Turn on computer
2. Log on
3. Connect TactArray monitor to computer tower via micro-USB cable.
4. Connect small TactArray cylinder to TactArray monitor via large screw in cable.
5. Connect Webcam via USB to computer tower.
6. Double click on Chameleon TVR 2012 icon on desktop.
7. In pop-up window select:
   - For small (3.5cm diameter) TactArray cylinder choose "Newcastle CTA 27x16 5mm x 5mm".
   - For Large (7.5cm diameter) TactArray cylinder choose "Newcastle_CTA_ 16x32_5mmx6mm".
   - Press "OPEN".
8. To start using webcam click on "Data Acquisition" drop down menu
   - Click "Configure Data Acquisition".
   - Under "Video source" select "Logitech Webcam Pro 9000" in drop down menu.
   - Put a check in "Record synchronised video.
   - Press ok.

9. Change the units of pressure, force, area and distance.

   - Press ‘units’ under ‘data analysis’ on RHS of screen and change the following to:

   -Pressure -Kpa

   - Force - N

   - Area - sq mm

   - Distance - mm

   Press ok.

10. Increase “Recording buffer” (length of time the buffer will record for before rewriting):

    - Click on Data Acquisition at top of screen.
    - Select “Configure data logging” in drop down menu.
    - Increase “Circular buffer size” to desired time e.g. 10 minutes.

11. On graph- change values on LHS to “0.00” on the bottom and “0.22” on the top.

12. Edit the type of pressure displayed on the graph:

    - Double click on box to the RHS of the graph that says (double click to edit traces).
    - Check the boxes that say ‘average pressure’, ‘maximum pressure’ and ‘minimum pressure’.

13. Increase the size of blue pressure mapping area-

    - Click the magnify button above it (second icon from the right hand side).
    - To move the blue pressure mapping area press the cross 4th icon from the right hand side.

14. Put coloured tape around edge of the sensors to make sure the participant doesn’t press outside of the sensors.
15. Place the cardboard cylinder inside of the small TactArray.
16. Adjust the small TactArrays weight to 160g by placing the required amount of weight in the cardboard cylinder, using zinc-plated washers (2 small, 1 medium, 1 large).
17. Press the ‘Tare’ button on the right hand side of the screen to reset the sensors to zero and reduce noise in the data.

2. Participant Arrival

i. Meet participant at taxi point (HMRI visitor entrance)
ii. Pay for Taxi with voucher and obtain a receipt
iii. Take participant to wash and dry their hands
iv. Direct participant to Motion Room, 4th floor, HMRI building
v. Participant seated at desk set up in room
vi. Participant to sign consent form
vii. Fill in case report form
viii. Participant should remove jewellery (rings, bracelets, watches etc.)
ix. Participant should roll up sleeve on arm to be tested
x. Participant to complete preliminary assessments following first test

3. Participant preparation for Intervention

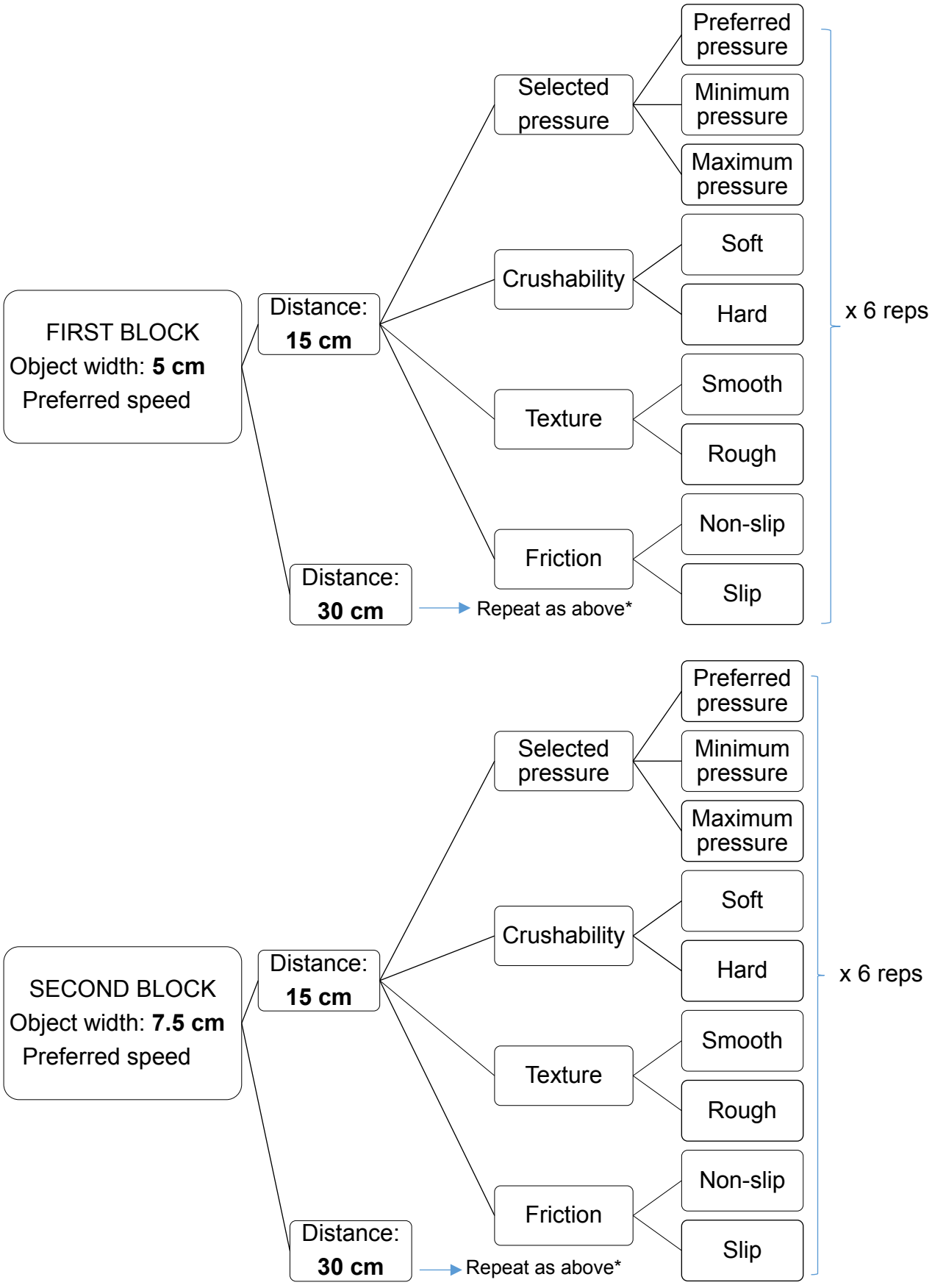
i. Direct participant to wash hands with soap and tap water
ii. Participants need to thoroughly dry hands with paper towel and air-dry for 15 minutes
iii. Participant sits at testing desk on height adjustable chair
iv. Participantsits in upright position with:
v. Waist touching the edge of the table in front
vi. Back against the backrest of the chair
vii. Feet flat on floor
viii. Elbow flexed to 90 degrees, aligned with shoulder
ix. Forearm and hand to be kept parallel to the floor in mid-prone position
x. Wrist rested at edge of table
xi. Participant is asked to maintain same initial hand position (loosely clenched fist with thumb in opposition to other fingers) prior to each reach-to –grasp lift
xii. Participant position's to be checked so that arm can reach object easily
xiii. Participants affected hand that is not being tested first, will rest on their lap
xiv. NOTE: height of chair will be adjusted for participants with limited elbow extension
xv. Explain Experiment: This set of exercises aims at improving arm and hand movement and sensation. We shall first do some measurements with your good arm. We will use these measurements to set up goals for your affected hand.

xvi. Explain the task to the participant: You will be required to pick up this object and lift it to about 2-5 cm. Hold it for 5 s and put it back on the table. (Therapist demonstrates task). I will gradually introduce you to objects with different surfaces and textures to perform the same task. Have you got any questions? Are you ready to start?

xvii. Before starting the treatment, record measures of pain on modified McGill pain questionnaire and Stanford fatigue visual analogue scale.

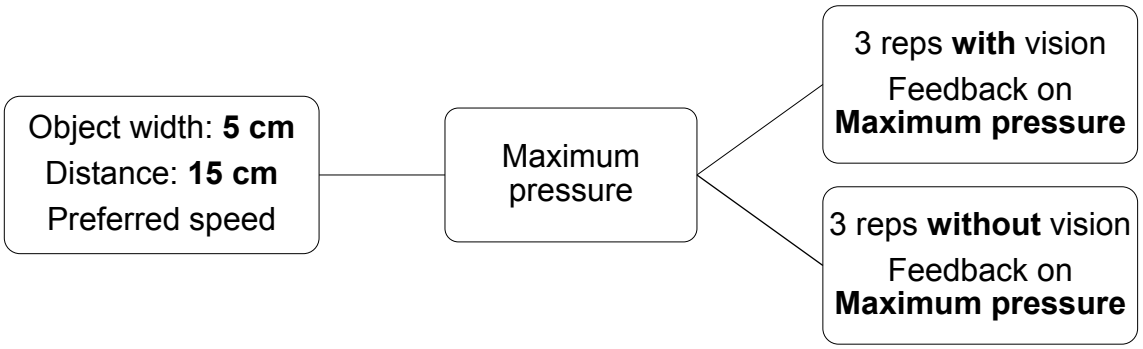
xviii. After the treatment, record measures of pain on modified McGill pain questionnaire and Stanford fatigue visual analogue scale. Also, administer on Feasibility.

4. Protocol for the COMPoSE intervention-Standardised training matrix



Reps: Repetitions

Figure 1: Standardised training matrix



Reps: Repetitions

Figure 2a: Conditions of practice and number of repetitions with or without vision: *Tactile pressure feedback task: Selected pressure - Maximum pressure variable*

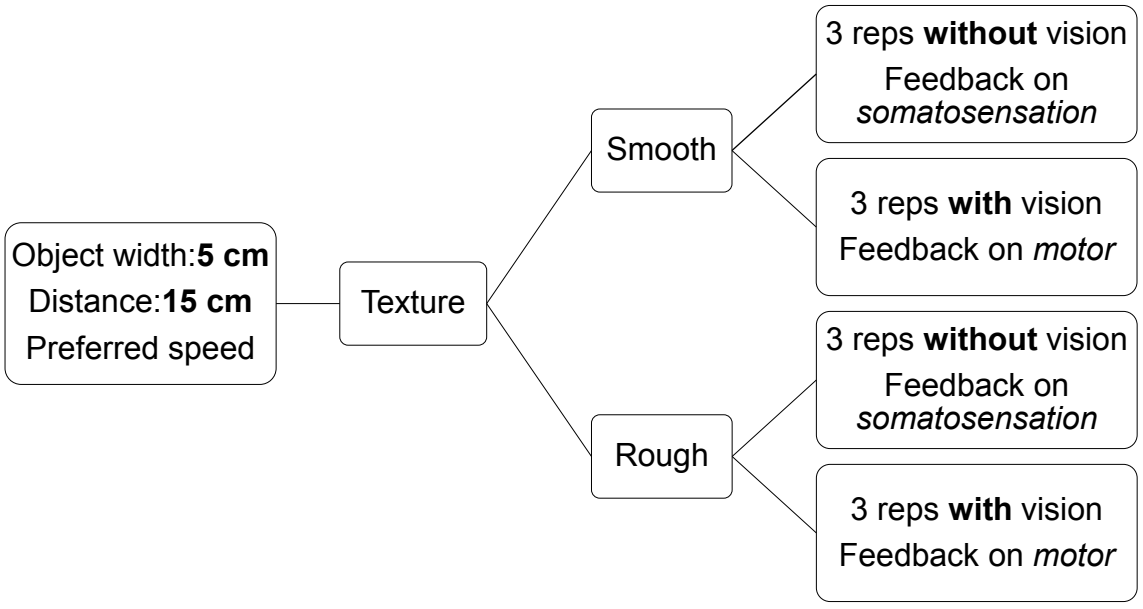
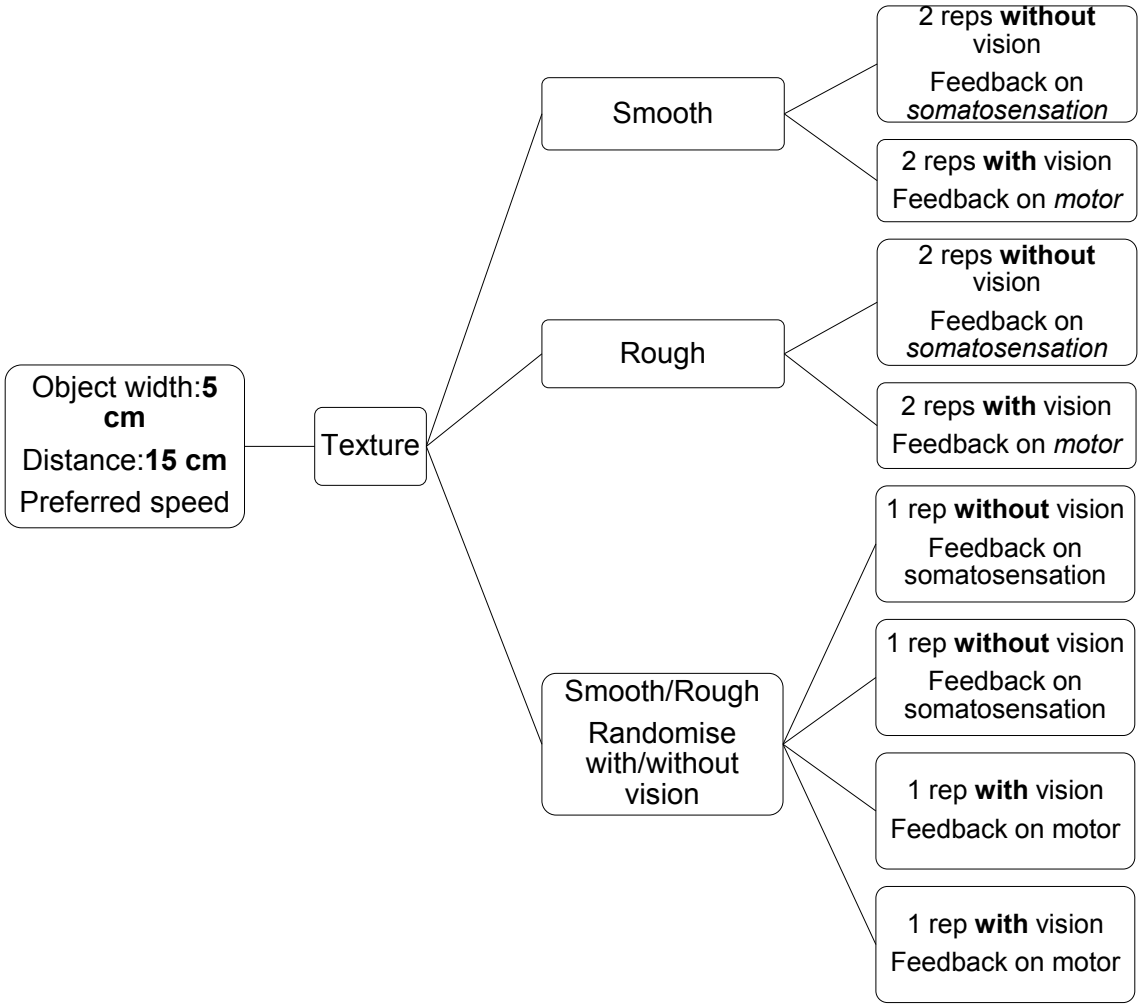


Figure 2b: Conditions of practice and number of repetitions with or without vision: *Somatosensory-motor combination feedback task: Distance and Texture - Short distance parameter and texture*



Reps: Repetitions

Figure 3. Varied practice for somatosensory-motor combinations: with or without vision e.g. short distance variable and texture

5. Therapist guideline for delivery of COMPoSE intervention

- Each sensorimotor combination is practiced 6 times in all. The repetitions are performed in 2 conditions: with vision and without vision.
    - For selected pressure using TactArray cylinder, the first 3 repetitions are performed *with vision* and the last 3 repetitions are performed *without vision* (figure 4). When the other objects are introduced, the repetitions are performed *without vision* for sensory stimulation and *with vision* for motor stimulation.
    - For a specific sensory attribute, the first variation is presented, followed by the second variation, then either the first or second variation is randomly presented. This will ensure that the participant is engaged in the task in order to promote active learning. For the first and second variation respectively, within a specific sensory attribute, 2 repetitions will be performed without vision, followed by 2 repetitions with vision. Then, either the first or the second variation will be practised once with vision and once without vision. It should be noted that the order of randomisation between the 2 variations will be chosen by the therapist. An example of a combination of short distance variable and texture is illustrated below.

6. Instructions for training procedure for selected grasp pressures and forces

i. Preferred grasp

a. Small TactArray cylinder will be introduced
b. Instructions: “Reach to grasp the cylinder using only your fingertips. Lift it about 2-5 cm above the table, hold for 5 s and put it down. Bring your wrist back to the edge of the table. It should look like this” (Therapist demonstrates).
c. Demonstrate task: RTG with preferred grasp
d. Allow 2 practice trials with good hand with preferred grasp
e. Take 3 measurements with good hand for preferred grasp; Allow 1 min rest between each measurement
f. Perform 6 repetitions with affected hand: 3 with vision and 3 without vision

ii. Minimum grasp

a. Demonstrate task: RTG with minimum grasp
b. Instructions: “Reach to grasp the cylinder using only your fingertips. Lift it about 2-5 cm above the table. Hold it as lightly as you can without dropping it. Hold for 5 s and put it down. Bring your wrist back to the edge of the table.”
c. Allow 2 practice trials with good hand with minimum grasp
d. Take 3 measurements with good hand for minimum grasp; Allow 1 min rest between each measurement
e. Perform 6 repetitions with affected hand: 3 with vision and 3 without vision

iii. Maximum grasp

a. Demonstrate task: RTG with maximum grasp
b. Instructions: “Reach to grasp the cylinder using only your fingertips. Lift it about 2-5 cm above the table. Hold it as strongly as you can. Hold for 5 s and put it down. Bring your wrist back to the edge of the table.”
c. Allow 2 practice trials with good hand with maximum grasp
d. Take 3 measurements with good hand for maximum grasp; Allow 1 min rest between each measurement
e. Perform 6 repetitions with affected hand: 3 with vision and 3 without vision

7. <u>Instructions for training procedure with other cylinders</u>

i. Instructions for patient: Pick up the cylinder at a comfortable speed. Lift it about 4 cm above the table, hold for 5 s and put it down. Bring your wrist back to the edge of the table.
ii. Therapist demonstrates task
iii. Each object will be introduced one at a time (as per standardised matrix).
iv. Allow exploration for 2-3 min
v. Allow 2 practice trials with good hand
vi. Perform repetitions for each sensorimotor combinations with affected hand in above mentioned conditions (with and without vision) and provide feedback accordingly.

vii. Introduce next object as per standardised matrix

8. Feedback

a. Operationalisation of feedback

1. Tactile pressure feedback with TactArray

- Provide 1 Knowledge of performance and 1 Knowledge of result

2. Feedback on somatosensory variables

Somtosensory feedback is provided on 4 main aspects (1) on the accuracy of response by allowing the client to see the correct response (e.g. smooth or rough), the therapist telling the client what the actual texture is or by exploration of the stimulus by the client with the other hand; (2) on the actual sensation and critical difference of the sensory attribute being trained; (3) giving guidance on movements of the hand and exploratory finger that are most optimal to explore the sensory attribute e.g. static contact, lateral motion, contour following; and (4) using calibration which involves comparison of the sensation felt by the affected hand with the less affected hand[374].

3. Kinematic feedback with stopwatch and ruler

- Motor feedback will be given on movement duration for distance variables (15cm and 30cm) and maximum grasp aperture for width variables (5cm and 7.5 cm)
- Provide 1 Knowledge of performance and 1 Knowledge of result

4. *Motor feedback on the following*:

- Movements of body parts using external focus of attention of Trunk, Shoulder flexion, external rotation and adduction, elbow extension, wrist extension, finger extension, thumb abduction, thumb opposition
- For grasp, additional feedback will be provided on any of the following:
    - For grasp formation:
        - speed of grasp formation;
        - pre-shaping of hand and fingers;
        - maximum grasp aperture as soon as reach starts;
        - ability to efficiently close fingers in a single smooth movement;

- correct finger positioning on object for optimal stability of object and development of appropriate grip forces for safe grip;

- For grasp release:
  - timely release of object being held
- For grip scaling of forces
  - Even distribution of force in all digits when holding object; consistency in application of grip forces;
  - Appropriate scaling of forces on the object (not pressing too much or too little to prevent slip or tilt;

Operationalisation of feedback for selected grasp pressures and forces using TactArray

	Preferred/Minimum/Maximum
Accuracy	• The pressure you applied on the cylinder with your good hand was …….. (Therapist shows the the line on the screen). Try to reproduce the same pressure with your affected hand. On the graph, try to make wave reach here (Therapist points out on computer screen). • To reduce/increase pressure for preferred grasp: Press less/more OR Put/ Apply less/more force on the object OR Put less/more pressure on the object
Sensory attribute: Critical difference	**Actual pressure sensation:** • What does the pressure from your finger pads feel like on the object? • What do you feel in your hand and fingers when grasping the object with ***preferred/minimum/maximum*** pressure? • Is it easy or difficult to grasp (between your fingers)? • Did the pressure feel the same (or as light or strong) as with the good hand? **Actual difference:** • What do you think helps you to know that this is your preferred/minimum/maximum pressure on the object? • In what way is it different from applying a ***preferred/ minimum/maximum*** pressure?
Method of exploration	• Do your fingers feel different when you press/squeeze more? Or if you press/squeeze less? • Can you observe any changes in the movement or position of your fingers on the object?
Calibration **With/without vision**	• Feel the object with your good hand • Now, feel the object with your affected hand. Imagine what it should feel like (as with your good hand) • Using your affected hand, try to put the same amount of pressure on the object as with your good hand. Feel the right amount of pressure.

Operationalisation of somatosensory feedback

	Crushability (hard and Soft)	Texture (Smooth or rough)	Friction (Slip or non slip)
Accuracy Ask same questions when new sensory attribute is introduced	• Do you know what object this is? • Are you able to crush it? • Is it easy or hard to crush/squeeze? • What type of material this is?	• What does the surface texture of this object feel like? • Is it smooth or rough to touch? • What type of surface texture this is?	• What does the surface texture of this object feel like? • Is it easy or difficult to grip the object with the fingers? • Is the object surface slippery or not slippery? • What type of surface texture this is?
Sensory attribute: Critical difference Ask same questions when new sensory attribute is introduced	• **Actual sensation:** - What do you notice about the crushability of this object? What does the object feel like? - Is it easy or hard to crush/squeeze? • **Actual difference:** - What do you think helps you to know that this object is hard or soft? - **When soft cup is introduced:** Does it feel same or different from previous object? What helps you to know that this object is different?	• **Actual sensation:** - What do you notice about this texture? - Can you feel the fine abrasion? - Does the surface feel smooth or rough? • **Actual difference:** - What do you think helps you to know that this object is smooth or rough? - **When rough surface is introduced:** Does it feel same or different from the previous surface texture? What helps you to know that this surface texture is different?	• **Actual sensation:** - What do you notice about the extent of slip in this material? - Is it easy to grip with the fingers? - Can you feel how slippery the surface is? • **Actual difference:** - What do you think helps you to know that this object is slippery or not? - **When slippery surface is introduced:** What do you think helps you to know that this object is different?
Method of exploration Ask same questions when new sensory attribute is introduced	• Does it different if you squeeze more? Or if you squeeze less? • Can you observe any changes in the object? Is there any change in the shape? What does it look like now? • **When soft cup is introduced:** Does this feel the same or different from the previous surface?	• Does it feel different if you rub your finger on the surface of the object: vertically (up and down) and laterally (right to left)? • **When rough surface is introduced:** Does this feel the same or different from the previous surface?What helps you pick up the difference?	• Does it feel different if you rub your finger on the surface of the object: vertically (up and down) and laterally (right to left)? • **When slippery surface is introduced:** What helps you pick up the difference?

Calibration **With/without vision** Ask same questions when new sensory attribute is introduced	• Feel the object with your good hand • Now, feel the object with your affected hand. Imagine what it should feel like (as with your good hand) • Using your affected hand, try to put the same amount of pressure on the object as with your good hand. Feel the right amount of pressure. • **When soft cup is introduced:** Feel the right amount of pressure. Know what it feels like being confident in holding the cup without crushing it	• Feel the object with your good hand • Now, feel the object with your affected hand. Imagine what it should feel like (as with your good hand) • Using your affected hand, try to put the same amount of pressure on the object as with your good hand • **When rough surface is introduced:** Can you feel the roughness? Can you feel the little slips that you need to feel the roughness?	• Feel the object with your good hand. Can you feel a bit of resistance to the slip. Notice that the object does not go through the fingers so quickly. • Now, feel the object with your affected hand. Imagine the micro-slip felt with your good hand. Imagine what it should feel like (as with your good hand). Notice the little amount of pressure that you need to apply on the surface to prevent it from slipping. • Using your affected hand, try to put the same amount of pressure on the object as with your good hand • **When slippery surface is introduced:** Feel the right amount of pressure you need to apply on the surface to prevent it from slipping. Know what it feels like being confident in holding the cup without it slipping away

Discrimination of sensory attributes and the differences: crushable/ hard; smooth/rough; slip/non-slip

Name/ID:

Surfaces	**Discriminate if surfaces are same or different**	**Identify surfaces**	**Comments** **e.g. method of exploration, clients words for critical difference, confidence with judgements**
Crushable			
Hard			
Smooth			
Rough			
Slip			
Non-slip			

Operationalisation of kinematic feedback

	Distance variables (15 cm and 30 cm)	**Grasp variables (grasp formation and releasing; grip scaling of forces)**	
	Movement duration	**Grip formation—e.g. positioning, opening and closing the fingers and thumb around the smaller object**	**Grasp release of a larger object opening the hand and controlled release of the larger object (if patient cannot grasp larger object, use smaller object)**
Accuracy Ask same questions when new sensory attribute is introduced	• How slow or fast does the time taken for this task feel like? • Was the movement slow or as fast as the good hand? • You took X seconds to reach the cup (with the affected hand) OR You took longer to reach the cup (with the affected hand): Move faster	• What do you feel in your fingers when grasping the object? • What does the size of the object feel like when opening to grasp the object? • Is it a small or large object? What helps you know that it is smaller or larger? • You opened your hand to (X cm) OR You opened less than with your good hand: Open wider • You closed your fingers around the object but not all at the same time. Close all fingers at the same time.	• What do you feel in your fingers when releasing the object? • What makes it easy or difficult to release the object? • You opened your hand to (X cm) OR You opened less than with your good hand: Open wider • You opened your fingers from the object but not all at the same time. Open all fingers at the same time.
Sensory attribute: Critical difference Ask same questions when new sensory attribute is introduced	• **Actual sensation of movement:** - What do you notice about the time to reach the object? - Is it quick or slow to reach? • **Actual difference:** - What do you think helps you to know that this object is close or far? - **When object is placed at further distance:** Is the object in a different position? What	• **Actual sensation of movement**: - What do you feel in your hand and fingers when opening to grasp the object? - Is it easy or difficult to grasp (between your fingers)? - Can you feel how wide you open (your hand or fingers)? • **Actual difference:**	• **Actual sensation of movement** : - What do you feel in your hand and fingers when opening to release the object? - Is it easy or difficult to release the object? - Can you feel how wide you open (your hand or fingers) to release the object? • **Actual difference:** - What helps you to know that this object is small or big?

	helps you to know that this object is at a different position? Is it closer or further away?	- What helps you to know that this object is small or big? • **When a larger object is introduced:** Is the size of the object the same or different? What helps you to know that the size of this object is different? Is it a small or large object? What helps you know that it is smaller or larger? - You opened your	• **When a larger object is introduced:** Is the size of the object the same or different? What helps you to know that the size of this object is different? Is it a small or large object? What helps you know that it is smaller or larger? - You opened your
Method of exploration Ask same questions when new sensory attribute is introduced	• Does your arm feel different when you straighten out (your arm) more? Or if you straighten out less? Does your arm feel different when you reach for the object further away? • Can you observe any changes in the movement of your arm and hand? • **When object is placed at further distance:** Does your arm feel different when the object is further away?	• How does your hand and fingers feel when you open to grasp the object? Does your hand feel different when you open your hand more? Or when you open less? Does your hand feel different when you grasp the larger object? • **When a larger object is introduced:** What helps you pick up the difference?	• How does your hand and fingers feel when you open to grasp the object? Does your hand feel different when you open your hand more? Or when you open less? Does your hand feel different when you grasp the larger object? • **When a larger object is introduced:** What helps you pick up the difference?
Calibration With/without vision Ask same questions when new sensory attribute is introduced	• Reach the object with your good hand • Now, reach the object with your affected hand. Imagine what it should feel like (as with your good hand) • Using your affected hand, reach for the object in the same amount of time as with your good hand	• Feel what happens in your hand and fingers when you grasp the object with your good hand • Now, feel what happens in your hand and fingers when you grasp the object with your affected hand. Imagine what it should feel like (as with your good hand) • Using your affected hand, open (your fingers) to the same extent as with your good hand	• Feel what happens in your hand and fingers when you grasp the object with your good hand • Now, feel what happens in your hand and fingers when you grasp the object with your affected hand. Imagine what it should feel like (as with your good hand) • Using your affected hand, open (your fingers) to the same extent as with your good hand

Discrimination of motor attributes and the differences:

Name/ID:

Motor parameters	Discriminate if surfaces are same or different	Identify surfaces	Comments e.g. method of exploration, clients words for critical difference, confidence with judgements
Distance-15 cm (Feedback on movement duration)			
Distance-30 cm (Feedback on movement duration)			
Width-5 cm (Feedback on grasp formation)			
Width-7.5 cm (Feedback on grasp release)			

Operation of motor feedback

Body part (desired movement)	**Knowledge of performance: External focus statements**
Trunk	• *This time you need to keep close to the chair behind as you reach (demo)* • *Keep close to the backrest of the chair as you reach towards the object*
Shoulder F	• *This time as you reach forwards think about being higher off the table top* • *As you reach forwards, keep a distance/space from the table top*
Shoulder ER and adduction	• *Do you see the tape I have just placed on the table? Try to follow it while reaching for the object* • *Reach forward towards the object along the tape* • *Follow the tape as you reach for the object*
Elbow E	• *This time try and reach closer/nearer to the object* • *Straighten more*
Wrist E	• *With this straw I have taped on, can you ensure you keep close to it as you approach the jar. (bendy straw on dorsum of hand, taped to wrist – and straw bent to required amount of wrist extension)*
Finger (E) (amount)	• *To grasp well you need to curl around the object more (demo with jar)* • *To grasp well you need to curl closely around the object (demo with jar)*
Thumb abd during transport	• *This time open wider/more as you move nearer to the object*
Thumb Abd at object	• *This time try to open as wide as you can to encompass the jar (Demo with object)*
Thumb (opposition)	• *Next time try and get the two stickers to touch (sticker on the jar and sticker on pad of thumb)*
Grasp (amount)	• *This time try and encompass the jar fully to make it more secure*

	• *To hold the object securely, bend closely around the object*
Speed	• *This time move faster/quicker/more rapidly towards the object* • *You will need to generate force more rapidly as you move towards the object*
Stationary hold for 5 s	• *Hold the object off the table until I tell you to stop* • *This time keep the jar higher off the table as you move*
Grip for transport	*Hold/Grasp/Grip the object securely while reaching*

Appendix 5.2.

Feasibility assessment of the COMPoSE intervention and trial

Objective 1: Feasibility of the COMPoSE intervention development and delivery	Reported? ✓
1. *Intervention goals* a. Do the intended goals of the intervention match the prioritised goals of upper limb rehabilitation after stroke?	✓
2. *Complexity of intervention* a. Is the COMPoSE intervention complex? b. What is the underlying mechanism of action? c. How many separate components constitute the intervention?	✓
3. *Active ingredients of intervention* a. What are the active ingredients of the COMPoSE intervention? b. Did the active ingredients included effectively interact to positively influence upper limb outcome measures? c. How did these compare with key ingredients in other upper limb training interventions that were found to be effective (e.g. task specific, CIMT) after stroke?	✓
4. *Was the choice of somatosensory and motor variables in the COMPoSE intervention appropriate?* a. Which somatosensory and motor variables were combined? b. How many combinations of somatosensory and motor variables were included? c. What upper limb deficits after stroke were being specifically targeted? d. Were the combinations of somatosensory and motor variables sufficiently challenging to stimulate learning?	✓
5. *Feedback* a. What type of feedback was provided? b. How was feedback delivered for somatosensory, motor and grasp pressure variables? c. Was the type, amount, timing, and nature and quantity of feedback appropriate?	✓
6. *Varied practice* a. Was varied practice sufficiently challenging to stimulate learning?	✓
7. *Dosage* a. Amount of practice i. How many repetitions were targeted in one session? ii. How demanding was it to achieve the target amount of practice? iii. How many repetitions were achieved per session? iv. Was the amount of practice sufficient? b. Duration of intervention i. How do the dosage parameters (scheduled duration of treatment session, actual duration of treatment session, number of treatment sessions, frequency, treatment period) compare with upper limb interventions effective stroke rehabilitation- e.g CIMT or task specific training or somatosensory retraining?	✓

ii. How demanding or difficult was it for the participant to receive the intervention at the intended frequency, intensity, and duration of treatment session, overall treatment duration?

iii. Was the dosage feasible to be delivered in a clinical setting?

8. *Adherence rates to intervention attendance and engagement* ✓

a. Does the intervention require the participants to be engaged during treatment delivery?

b. How many participants completed the intervention sessions?

c. To what extent were the intervention sessions completed?

d. What is the level of safety and burdensomeness of the frequency, intensity, and duration of the intervention?

9. *Suitability of the standardisation procedure for the intervention delivery* ✓

a. Standardised training matrix
   i. Did the matrix facilitate treatment delivery?
   ii. Was the order of combinations of variables appropriate?
   iii. What were the limitations of the standardised matrix?
b. Intervention delivery manual
   What are the contents of the intervention manual?

10. *Appropriateness of treatment delivery method* ✓

a. How is individual and face to face treatment delivery beneficial to participants in this intervention?
b. Is individual and face to face treatment delivery appropriate and feasible in clinical context?

11. *Support and supervision by therapist* ✓

a. What is the treating therapist required to do prior to treatment and during delivery treatment?
b. Does the treating therapist require training to deliver the intervention?
c. Do the therapist improve over the course of the trial? Can variations in skill levels across therapist affect the delivery of the intervention and/or outcomes?
d. Can the therapist individualise the intervention contents and amount of practice for each participant?
e. Does the intervention require additional human resources?

12. *Additional material resources* ✓

a. Which equipment or material resources are required to deliver the intervention?
b. What are the cost implications?
c.Can the equipment be easily repaired/ replaced in case of damage?

13. *Adverse events associated with the intervention* ✓

a. What adverse events might be anticipated?
b. Are the effects of the intervention permanent or can the intervention be stopped at any point within any harmful effects?

Objective 2. Feasibility of operational aspects of the COMPoSE intervention trial

Objective 2a. Evaluation of Recruitment Capability and Resulting Sample Characteristics

1. *Recruitment rates*

   a. How many participants were contacted?

   b. How many participants were assessed for eligibility?

   c. How many participants were excluded for not meeting the inclusion criteria?

   d. What are the refusal rates for participation?

   e. How many participants enter the study at a time?

   f. How long does it take to recruit enough participants into the study?

2. *Obstacles to recruitment*

   a. How were participants recruited?

   b. What were barriers for participant identification from recruitment sites?

   c. What are the reasons for participant refusal or ineligibility?

   d. What were the most effective means of recruitment?

3. *Feasibility and suitability of eligibility criteria*

   a. Are criteria clear and sufficient or too inclusive or restrictive?

   b. Is it obvious who meets and who does not meet the eligibility requirements?

4. Relevance of the intervention to the intended population

   a. Do study participants show evidence of need for the intervention?

   b. Are the characteristics of the study participants consistent with the range of expected characteristics as informed by the research literature?

Objective 2b. Evaluation and Refinement of Data Collection Procedures and Outcome Measures

1. Feasibility and suitability of data collection procedures

   a. Do participants understand the questions and other data collection procedures?

   b. Do they respond with missing or unusable data?

2. Feasibility and suitability of amount of data collection

   a. Were the data collections operationalised?

   b. Do the participants have the capacity to complete the data collection procedures?

   c. Does the overall data collection plan involve a reasonable amount of time or does it create a burden for the participants?

d. Was the timing of data collection appropriate?

3. Consistency of outcome measures with the intended population

a. Can outcomes be assessed objectively and reliably?

b. Do planned outcome measures appear to be reliable, valid, sensitive and trustworthy for the targeted population for this specific intervention?

c. Do the assessments capture individual participants' needs and measure their responsiveness to these needs?

c. Are internal consistency indicators of measures with the recruited sample congruent with expectations based on prior studies reported in the research literature?

d. Which outcome measures are the most suitable?

e. Does a suitable outcome measure need to be developed?

4. *Adherence rates to data collection*

a. How many participants completed data collections?

b. What is the level of burdensomeness of the frequency, intensity, and duration of the data collection procedures?

5. Change on the most likely suitable outcome measures

a. What is the expected degree of change (i.e., responsiveness) of the participants?

b. What are the estimates of the intervention effect and the variance of that effect across the planned sample?

Objective 2c. Evaluation of Acceptability and Suitability of Intervention and Study Procedures to participants

1. Retention and follow-up rates

a. What are the retention and follow-up rates as the participants move through the study and intervention?

2. *Adherence rates to intervention attendance, and engagement*

a. Does the intervention fit with the daily life activities of study participants?

b. Does the intervention involve a reasonable amount of time or does it create a burden for the participants?

c. Do the participants have enough time and capacity to complete the intervention?

d. To what extent is the intervention acceptable and appealing to participants?

Objective 2d. Evaluation of Resources and Ability to Manage and Implement the Study and Intervention

1. *Research capacity*

a. Does the research team have the administrative capacity, expertise, skills, space and time to conduct the study and intervention?

2. *Equipment sufficiency to conduct the study and intervention, including collection, management, and analysis of data*

   a. Is equipment for outcome measures available when needed?

   b. What is involved in training personal to carry out outcome assessments?

3. *Ability to deal with broken, lost, or stolen equipment and materials*

   a. Are there backup plans for obtaining needed equipment and materials?

4. *Software for capture and data processing*

   a. What software is available for conducting the research?

Objective 3: Preliminary Evaluation of Participant Responses to Intervention

1. *Likelihood of success of intervention*

   a. Is the intervention likely to be effective (i.e. evidence based and expected to produce positive outcomes)?

   b. Does examination of the data at the participant level suggest that changes in key outcome variables occurred?

   c. Are the changes of the outcome variable (s) in the expected direction?

   d. Do the estimates of effects show promise of being successful with the intended population?

2. Participant feedback

   a. Do participants or relevant others provide qualitative feedback that may be indicative of the likelihood that the intervention will be successful?

3. If the quantitative and/or qualitative data suggest that the intervention is not promising:

   a. Are the data collection procedures and outcome measures appropriate for the population and study?

   b. Are the outcome measures and intervention theoretically aligned?

   c. Is there evidence that the intervention does not produce change in the desired outcomes?

   d. Is there evidence that the intervention was not implemented in the intended manner?

   e. Have too many adaptations been made in the intervention process to adequately assess the participants' responses to the intervention?

   f. Are the findings congruent with the proposed theoretical model for the intervention?

4. Safety of the procedures in the intervention

   a. Are there any unexpected adverse events?

Appendix 5.3

Measures of fidelity

Participant ID:

Session no:

Date:

Standard reference measures of selected tactile pressures

Selected tactile pressures	Grip 1	Grip 2	Grip 3	Mean of 3 trials
Preferred				
Minimum				
Maximum				

Standard reference measures of kinematic measures

Kinematic measures		Measures (Mean of 3 trials)	
Distance/Width (cm)	15/5	Movement duration/s	
Distance/Width (cm)	30/5	Movement duration/s	
Distance/Width (cm)	15/5	Peak aperture/cm	
Distance/Width (cm)	30/7.5	Peak aperture/cm	

Measures of feasibility	
Number of repetitions achieved:	
Time taken to complete intervention (including breaks):	
Number of times break was required:	
Total break time:	
At which combined sensorimotor variable session started:	
At which combined sensorimotor variable session ended:	

Somatosensory-motor training combinations practiced and sequence of practice

	Width 5cm							
	Distance 15cm				Distance 30cm			
	TactArray	Crushability	Texture	Friction	TactArray	Crushability	Texture	Friction
No of Repetitions								

	Width 7.5cm							
	Distance 15cm				Distance 30cm			
	TactArray	Crushability	Texture	Friction	TactArray	Crushability	Texture	Friction
No of Repetitions								

Measures of tolerability and side effects of the intervention

	Before intervention	**After intervention**
Pain in upper limb on VAS (0-10)		
Fatigue on VAS (0-10)		

Appendix 5.4

Participant's engagement

Part 1. Measures of self-report engagement: perceptions of difficulty, reports of engagement

1. Self-report of perceived difficulty with tasks	**Tick as appropriate**
Learning and performance both difficult	
Learning and performance both easy	
Learning easy, performance difficult	
Learning difficult, performance easy	
Difficulty attributed to lack of ability	
Difficulty attributed to equipment	
Did you use a strategy to perform the task?	
2. Were you engaged in the task or bored?	

Adapted from Gerber et al. (2014)[450]

Part 2. Measures of participant's engagement assessed by treating therapist

1. Circle the number that best indicates the effort with which this participant completed the training during today's appointment:	1 2 3 4 5 minimum effort maximum effort
2. During today's appointment, how frequently did this participant follow your instructions and advice?	1 2 3 4 5 Never Always
3. How receptive was this participant to changes in the rehabilitation program during today's appointment?	1 2 3 4 5 Very unreceptive Very receptive
4. Was the participant engaged?	Always Very Frequently Occasionally Rarely Very Rarely Never
5. Was the participant frustrated?	Always Very Frequently Occasionally Rarely Very Rarely Never

Part 3. Measures of participant's engagement: perceived difficulty and extent of engagement assessed by treating therapist

1. Perceived difficulty with tasks	**Tick as appropriate**
Learning and performance both difficult	
Learning and performance both easy	
Learning easy, performance difficult	
Learning difficult, performance easy	
Difficulty attributed to lack of ability	
Difficulty attributed to equipment	
Did you use a strategy to perform the task?	
2. Were you engaged in the task or bored?	
Adapted from Gerber et al. (2014)[450]	

Appendix 5.5

Participants' acceptability of the COMPoSE intervention

Measures of participants' perceptions of the COMPOSE intervention

Participants' perceptions	Circle as appropriate				
1. How content were you with the intervention?	excellent	good	no change	bad	very bad
2. Did you enjoy the training? Did you enjoy the training with the devices?	yes absolutely	yes	do not know	no	Not at all
3. Did the training increase your motivation?	yes absolutely	yes	do not know	no	Not at all
4. Were the instructions sufficient?	yes absolutely	yes	do not know	no	Not at all
5. Did you find the instructions difficult to understand?	yes absolutely	yes	do not know	no	Not at all
6. Did you find the tasks difficult to perform?	yes absolutely	yes	do not know	no	Not at all
7. Were you frustrated whilst you were doing the training?	yes absolutely	yes	do not know	no	Not at all
8. Do you think that this kind of training may enhance the sensory and motor functions of your upper limb?	yes absolutely	yes	do not know	no	Not at all
9. Did you try to improve your scores? Did you use a strategy to do this?	yes absolutely	yes	do not know	no	Not at all
10. Would you recommend this combined sensory and motor training?	yes absolutely	yes	do not know	no	Not at all
Adapted from Buschfort et al.(2010)[449]					

11. How would you rate the duration of each intervention session (1.5 hours)?

Too short Tolerable Too long

1 2 3 4 5 6 7 8 9 10

12. Do you rate the tasks in this intervention as meaningful and related to your daily activities?

Yes No

Why?

_____

_____

13. Has completing this program increased you participation and independence in daily activities? If so, which activities?

_____

_____

14. What is your overall experience rating of this program with 1 being not satisified and 10 being extremely satisfied?

Not satisfied Very satisfied

1 2 3 4 5 6 7 8 9 10

Why?

_____

_____

15. Are there any changes that could have been made to improve your experience?

_____

_____

CHAPTER 6: RELIABILITY OF MAXIMAL TACTILE PRESSURES AND FORCES OF A SUSTAINED GRASP TASK USING A TACTARRAY DEVICE IN HEALTHY PEOPLE AND IN PEOPLE WITH STROKE

Preface

This chapter presents findings from a study investigating the reliability of maximal tactile pressures and forces of a sustained grasp task using the TactArray device in healthy people and in people with stroke. This chapter addresses thesis aim 4 (to assess the test-retest reliability of maximal tactile pressures and forces using a TactArray device and determine which measures of maximal tactile pressures or forces are most reliable in both healthy people and those with stroke) which was conducted to investigate research question 3 (Are measures of tactile pressures or forces of a sustained grasp task using the TactArray device reliable amongst healthy people and stroke survivors?). This study was conducted in parallel with the conduct of the COMPoSE trial (Chapter 5). Findings from this reliability study contributed to the development of an outcome measure targeting maximal tactile pressures, which was a key component evaluated in the COMPoSE trial (Chapter 5). It was also Important that the TactArray device provided reliable feedback of grasp pressure to participants during the intervention sessions.

Contribution statement

I was responsible for leading all the stages of conducting this clinical trial. I was the liaison and contact person for all aspects of this study. With the support of my supervisors, I carried out the steps described below to conduct the COMPoSE trial.

Ethics approval

For the reliability study on the TactArray device, I was responsible for drafting, submitting and obtaining ethical approval from the Human Research Ethics Committee of theUniversity of Newcastle, Australia (Reference No: H-2015-0052)and the Hunter New

England Human Research Health Committee (Reference No: 13/12/11/4.02). This involved developing the study protocol, completing all paperwork for site-specific approvals, designing recruitment materials and preparing information statements and consent forms.

Participant recruitment

I was responsible for the identification and recruitment of people with stroke for the study. I developed all recruitment materials such as flyers and posters. I also attended service-user groups and meetings as well as stroke support groups to promote the study for recruitment of participants. I also liaised with the HMRI healthy volunteers and Stroke Volunteer Registry for recruitment of participants. I conducted all screening assessments, analysed the data and determined eligibility for participation in this study.

Conduct of reliability study

I was responsible for the overall conduct of the reliability study. With the guidance of my supervisors, I developed the overall assessment protocol using the TactArray device. The TactArray device had been custom-made by Pressure Profile Systems (Los Angeles, USA). I coordinated all scheduling of appointments. I conducted all screening assessments and all outcome measures, including measures with the TactArray device.

Data collection and management

I selected all outcome measures used in this study in consultation with my supervisors. I also developed the assessment procedure of maximal tactile pressures using the TactArray device, including the selection of the grasp tasks. Before the start of the study, I developed standardised assessment protocol to conduct measures with the TactArray device. With the assistance of Professor Derek Laver, we developed a customised MATLAB script to process the data from the TactArray device. I selected and created a list of all the variables required to create the commands in the MATLAB script. Together with Professor Laver, we decided and tested the conditions and parameters to apply to the data processing in MATLAB.

Professor Laver wrote the commands in MATLAB and I carried out testing of all the versions of the MATLAB script up to the final program. I was responsible for data cleaning and the offline processing of all data from the TactArray. I conducted all data analysis to determine the reliability of the measures of maximal tactile pressures. Statistical support was partly provided by Associate Professor Thomas Matyas in evaluating the interaction effects using analysis of variance.

6.1 ABSTRACT

Title: Reliability of maximal tactile pressures and forces of a sustained grasp task using a TactArray device in healthy people and in people with stroke

Background: Instantaneous peak grip strength is widely used to characterise muscle weakness after stroke. Sustained grasp is essential for functional tasks in daily life. Sensor-based devices can record pressure or force over time during grasping and therefore offer a more comprehensive approach to quantifying grip strength during sustained contractions. The reliability of grip strength using the TactArray device has not been investigated.

Objective: To investigate the reliability of maximal tactile pressures and forces of a sustained grasp task using the TactArray device in healthy people and in people with stroke.

Methods: Healthy participants (n=18) and participants with stroke (n=11) performed three trials of sustained maximal grasp over 8 seconds. Both hands were tested in within-day (two sessions, one hour apart) and between-day (two sessions, one week apart) sessions, with vision and without vision. Measures of maximal tactile pressures and forces were measured for the complete grasp duration (8s) and for the plateau phase (5s). Measures of maximal tactile pressures and forces were reported using the highest value among the three repetitions, the mean of two repetitions, and the mean of three repetitions. Reliability was determined using changes in mean, coefficients of variation and intraclass correlation coefficients (ICCs).

Results: In healthy individuals, changes in mean were very good (range: -0.09-3.11%), coefficients of variation acceptable (range: 9.85-12.95%) and ICCs were good (range: 0.59-0.84) for maximal tactile pressures using highest value among the three repetitions and the mean of three repetitions for the complete grasp duration (8s) and for the plateau phase (5s) in the dominant hand with and without vision for within-day and between-day sessions. In the non-dominant hand, changes in mean were very good to good (range: -1.48-6.22%) and coefficients of variation were good to acceptable (range: 8.08-12.82%) and ICCs very good to

good (range: 0.89-0.92) without vision for within-day and between-day sessions. In people with stroke, changes in mean were good (range: -2.02- -7.18%), coefficients of variation were good to acceptable (range: 9.52-14.72%) and ICCs very good (range: 0.90-0.97) for maximal tactile pressures using Pres(8s)avg3 in the affected hand with and without vision for within-day sessions and without vision for between-day sessions. In the less affected hand, changes in mean were very good (range: 0.00-5.04%), coefficients of variations were acceptable (range: 11.73-15.92%) and ICCs were good to very good (range: 0.88-0.93) for maximal tactile pressures using Pres(5s)avg3 and Pres(8s)avg3 in between-day session with and without vision.

Conclusion: The TactArray device demonstrates satisfactory reliability for measures of maximal tactile pressures during a sustained grasp for within-day and between-day testing sessions using an average of three trials with or without vision in healthy people and those with stroke.

Reliability of maximal tactile pressures and forces of a sustained grasp task using a TactArray device in healthy people and in people with stroke

6.2 INTRODUCTION

6.2.1 Background

Loss of grip strength in the upper limb is one of the most common impairments after stroke that significantly affects the ability to use the arm and hand in daily functional activities[23,555,556]. Strength deficits in the paretic hand, such as weakness of finger and wrist flexors and extensors[557-559], contribute significantly to motor impairments in moderate to severe stroke[555]. Therefore, grip strength is widely used to characterise muscle weakness after stroke[232,233].

Grip dynamometry is a standard method of measuring grip strength which is quantified by the amount of force that the hand can exert on a dynamometer[234]. Maximal muscular contractions standardise grip strength measurements as they provide consistent maximal effort due to the relatively simple motor control required for maximal recruitment and firing frequency of motor units[560]. Maximal grip strength measurement has been shown to have good reliability after stroke (ICC>0.86) and such measurements have been shown to have associations with upper limb functional deficits[252].

Amongst grip dynamometers, the Jamar hand dynamometer is the most widely used[237-241]. The Jamar dynamometer has good test-retest reliability in healthy adults (ICC 0.82)[243] and in people with stroke (ICC 0.80-0.89)[244], and is accepted as the gold standard[242]. However, the Jamar dynamometer lacks responsiveness to respond to changes in people with severe loss of grip strength post-stroke[246]. Also, by curling the fingers around the instrument, the contribution of forces from the fingerpads are small during a power grip, as most of the gripping force is provided by the extrinsic muscles of the hand with little contribution from the intrinsic muscles [561,562]. However, during grasping and lifting tasks in activities of daily life, objects are commonly handled between the finger pads[133] using the intrinsic muscles. This suggests a need for measures with enhanced responsiveness, assessed using a functional

grasp that involves the use of the fingerpads for a more functional evaluation of grip strength deficits and recovery in the upper limb after stroke.

Sensor-based technologies using thin, flexible force sensors, such as the Tekscan grip pressure mapping system (South Boston, MA, USA)[265] and the TactArray pressure distribution system (Pressure Profile System)[274], have been used to acquire data about the pressure applied by the hand on object surfaces. As each sensor is electrically isolated, contact areas can be measured and both tactile pressures and forces can be evaluated in relation to time curve profiles. These sensor systems offer a novel means of quantifying deficits in grip strength[563,564].Tekscan uses piezoresistive tactile sensor matrices which have low noise in the measurements[272,273] but were found to be susceptible to breakdown as the polyester layers become detached after numerous tests[565]. One advantage of the TactArray is that is uses capacitive sensor arrays, which have excellent tactile sensitivity[566], and therefore have potential for detecting small changes in tactile pressures or forces[275] in stroke trials. TactArray has been used to evaluate the control of voluntary grasp forces in healthy people and those with moderate to severe stroke[567]. The feasibility of using a TactArray device to evaluate grasp forces after stroke has been evaluated in two case reports[426]. To the best of our knowledge, no study has investigated the reliability of a TactArray device to evaluate grip strength in healthy people or those with stroke.

Test-retest reliability can be assessed using a number of different statistical methods[283,284]. Assessments of intraclass correlation coefficients (ICCs) are common, but assessments of change in the mean, systematic error, and typical error of measurement are also required to provide a comprehensive evaluation of the reliability of an assessment tool[283,284]. There are also other factors that need to be considered in the context of handgrip assessment, particularly after stroke, such as the number of trials performed and included in the statistical analysis, whether both the dominant and non-dominant hand or affected and less-affected hand are assessed, if sustained force is being assessed, the duration of the contractions, and whether the tests are performed with or without vision. These issues are summarised below.

The number of trials used to evaluate the reliability of maximal isometric grip strength in symptomatic and asymptomatic populations varies considerably, from using the maximum value obtained from multiple trials or the mean of two or three trials[236,241-243,568-570]. There is no consensus on the number of trials to be included, particularly during estimation of reliability of sustained grasp[571-573].

Evaluating grip strength in both hands[236,241] could be useful to characterise deficits post-stroke. In healthy people, a comparison of maximal grip force between hands may show no differences[252]. However, in people with stroke a significant reduction in maximal grip force was observed in the affected hand compared to the less affected hand[252,574]and to the dominant hand in healthy people[574]. Forces produced by fingers of the affected hand are reported to be 36% less than those of the less affected hand in people with stroke[488]. Deficits in grip strength were also observed in the less affected hand post-stroke compared to healthy individuals[575]. It is noteworthy that these deficits post-stroke were those that corresponded to comparisons of the right or left side, but not to hand dominance of people with stroke. In contrast, studies investigating grip deficits with regards to hand dominance reported no significant differences between the less affected hand after stroke and the dominant[574] or non-dominant[252]hand in healthy people. Given that ipsilesional grip strength deficits could limit the ability to compensate for functional impairment of the affected upper limb, further studies are required to investigate the grip strength deficits bilaterally after stroke and with regards to healthy people. Determining whether the reliability of handgrip measurements differ between hands may be important for the interpretation of studies comparing the values obtained from different hands.

Studies measuring maximal grip strength have typically used the instantaneous peak force obtained during an isometric contraction up to 3 seconds in duration to evaluate muscle weakness of the paretic hands after stroke[236,255,576]. This type of grip force profile may not be truly representative of the grip strength required for more sustained everyday tasks. Hence, investigating sustained grip strength may provide information on the time course of grip force from point of contact, during the plateau phase holding until grasp release[195,572] so as to

better understand functional impairments after stroke. One study in people with mild paresis after stroke (n=61) found a positive relationship between activity limitation related to muscle weakness and maximal grip strength when maximal strength was sustained for more than 3 seconds[256] but not for a contraction lasting less than 3 seconds[256]. Amongst healthy people, sustained maximal isometric contractions for 6 and 10 seconds showed good reliability in both the dominant and non-dominant hands (ICC 0.83-0.96)[572].

The visual conditions under which grip strength is assessed may influence the values obtained and the reliability of these measures. Reducing visual cues increases the reliance on tactile somatosensory information at the fingerpads for motor output[171]. In healthy individuals, the absence of visual feedback resulted in a decrease in force production during sustained maximum voluntary contractions even when participants tried to maintain the same magnitude of grip force[577-579]. In stroke survivors, variations in maximal voluntary contractions in a grip task have been reported when evaluated under different visual feedback conditions[495]. When vision was occluded, fluctuations were observed in people with stroke, with more irregular or discontinuous force output in those with marked deficits in grip control whereas a uniform pattern of grip force was maintained during a pinch-lift task in healthy people[167]. This suggests that it is important to determine the reliability of grip strength measurements with and without vision.

6.2.2 Objectives

The primary objectives of this study were to:

1) assess the test-retest reliability of maximal tactile pressures and forces of a sustained grasp task using a TactArray device and determine which measures of maximal tactile pressures or forces are most reliable in both healthy people and those with stroke;

2) determine whether the duration over which sustained grip data are measured influences the reliability of the TactArray device pressure and force measures;

The secondary objectives were to:

1) determine whether there are differences in maximal tactile measures between hands in healthy people and people with stroke;

2) determine whether there are differences in maximal tactile measures between vision and no vision conditions.

3) compare the values of maximal tactile measures of the affected hand in people with stroke and the nondominant hand in healthy people using the most reliable TactArray device measure.

6.3 METHODS

6.3.1 Design

A repeated measures design was used to evaluate the reliability of measures of maximal tactile pressures and forces using a TactArray device[580]. The participants were tested on two occasions on the same day, one hour apart to evaluate the reliability of within-day sessions. A third test [283] was performed one week later to evaluate the reliability of between-day sessions. Durations of one hour[283,571] and one week[231] were chosen between the consecutive sessions to limit any biological variations. All measures were performed by one assessor. The reporting of this reliability study adhered to the guidelines and checklist for Reporting Reliability and Agreement Studies (GRRAS)[580].

6.3.2 Participants

6.3.2.1 Healthy participants

Healthy participants were recruited through flyers and posters displayed at the Hunter Medical Research Institute. The healthy participants were included if they had no neuro-muscular, orthopaedic, rheumatic or other conditions preventing normal reach-to-grasp movements. They were screened over the phone to determine initial eligibility, prior to attending the assessment sessions. The standardised clinical measures performed on healthy participants included the Box and Block test (BBT)[415,416] and grip strength (Jamar dynamometer)[232,412].

6.3.2.2 Participants with stroke

Stroke survivors were recruited through hospitals, the Hunter Medical Research Institute research register and stroke support meetings. Stroke survivors were included if they: 1) had a confirmed diagnosis of stroke; 2) were adults aged 18 years or older; 3) had sufficient voluntary muscle contraction in the paretic upper limb to reach forward; and 4) had sufficient ability to generate the beginning of prehension to grasp a 3.5 cm wide object. Stroke survivors were excluded if they: 1) had a prior history of central nervous system dysfunction other than stroke; 2) had upper limb deficits resulting from non-stroke pathology; 3) had any peripheral neuropathy in the upper limb; 4) had moderate to severe receptive aphasia (<7 on 'receptive skills' of Sheffield Screening Test for Acquired Language Disorders[402]; and 5) if they were receiving therapy for the upper limb at the time of the study. The participants with stroke were screened over the phone to determine initial eligibility. Those who passed the phone screening attended a pre-clinical visit involving a physical test of the ability to hold the TactArray device with the affected hand without any assistance to determine final eligibility.

The characteristics of the participants with stroke were based on the following standard clinical measures: the Wolf Motor Function Test (WMFT)[411], Action Research Arm Test (ARAT)[532], Fugl-Meyer-upper limb scale, Box and Block Test (BBT)[415,416], grip strength (Jamar dynamometer)[232,412], pulp-to-pulp pinch strength (B & L Engineering)[581], Modified Tardieu Scale (MTS)[417], Tactile Discrimination Test (TDT)[391], Stroke Impact Scale (SIS)[420], the Motor Activity Log (MAL)[413,414], and a pain visual analogue scale (PVAS)[423]. Standard objective performance-based neuropsychological tests were also performed: the Montreal Cognitive Assessment (general indicator of cognitive performance)[463,464], the Star Cancellation Test (neglect)[465,466], and the Rey-Osterrieth Complex Figure Test (copy condition)[467].The clinical and neuropsychological measures were performed at the end of the 2nd assessment session.

All participants provided written informed consent for the study, according to the Declaration of Helsinki[582]. The Human Research Ethics Committee of the University of

Newcastle, Australia (Reference No: H-2015-0052) and the Hunter New England Human Research Health Committee (No: 13/12/11/4.02), approved the study.

6.3.3 Data collection with TactArray device

6.3.3.1 Description of TactArray device

The TactArray pressure distribution system is a commercially available sensor which was used to custom-build a haptic device. This TactArray device consisted of conformable pressure sensor arrays wrapped around a cylindrical object (5cm diameter; 12cm height; mass: 100g) (TactArray model T4500, Pressure Profile Systems; Los Angeles, CA, USA)[385]. The cylindrical shape and size of the Tactarray device facilitated a functional grasp. The TactArray sensors can detect pressures as low as 10 Pascal with low accuracy error (<=2%) and low repeatability error (0.35%)[538]. The TactArray device was made up of 432 individual pressure sensing units (5mm x 5mm) (figure 6.1). The sensed data were transferred to a computer using the accompanying Chameleon Visualization and Data Acquisition TVR Software via a signal conditioning unit through a USB port[538]. The data was then saved in ASCII-delimited format to facilitate export of data for processing and analysis. The sampling rate of the device ranged from 7-10 KHz (element to element). The datalog rate was 23.81 Hz[385].To avoid measurement errors, the pressure sensors were reset to zero before each data acquisition[583].

Figure 6.1. TactArray cylinder device

6.3.3.2 Procedure for assessing maximal tactile pressures

The TactArray cylinder was placed on a table surface directly aligned with the hand start position, with the wrist in a neutral position[584]. Participants were instructed to reach, grasp, and lift the TactArray cylinder to a height of 2-5cm, then hold and squeeze as hard as they could over an 8-second period [427] using a 5-digit multi-finger prehension grasp[428], then place the object back on the table. A 5-digit multi-finger prehension grasp[428] involved picking up the object with the distal pads of the fingers without involving the palm of the hand [428] to maximise consistency of measurements across participants. When grasping the object, punctual contact without friction between the fingerpads and the object was used, where the applied pressure is always normal, i.e., perpendicular to the contact surface[585]. Finger positions were not restricted to specific locations, thus allowing for measurement of the participant's natural grasp performance.

The assessor first demonstrated the task, followed by one practice trial with each hand by the participants to try the finger positions on the TactArray device using a sub-maximal practice. Standardised instructions were read to each participant: "We will repeat this task three times. Are you ready? Pick up the cylinder and press as hard as you can - two, three, four, five, six, seven, put it down, relax." Participants were blinded from their results during the assessment. There was no verbal or other encouragement during the maximal grasp task execution.

Maximal tactile pressures/forces were assessed bilaterally with three repeated measures for each hand[252]. The trials were recorded in sequences of three trials to optimise time for data saving and processing. Ten to fifteen seconds rest were provided between each measurement trial to minimise fatigue[429]. The measurements were carried out in two conditions: with vision and without vision[171]. In both visual conditions, the pre-contact phase of reaching and grasping the TactArray cylinder was carefully performed to ensure appropriate targeting (i.e., correct positioning of the fingertips during grasping)[122] and avoiding collision (i.e., ensuring that the fingers did not knock the cylinder over during reaching or grasping)[586]. During the trials with vision, the screen displaying the online recording and display of the pressure-time curve was turned away from the participants to

avoid any possible influence[587] as visual feedback could increase maximal force[588] by up to 3%[588]. One to two minutes rest was provided between the measurements for each condition[429,430,576].

In the first testing session, measures were first performed with the dominant hand in healthy participants and the less affected hand in people with stroke. The order of the handed testing was randomised across the other 2 testing sessions. Testing was performed with vision first for each hand. Testing was performed with alternating hands for each condition.

Unsuccessful trials were discarded and these were defined as trials in which participants: 1) failed to grasp the cylinder; 2) were unable to achieve a stable grasp; 3) knocked over the cylinder; 4) let go of the cylinder prior to the verbal 'put it down' command; or 5) stopped the task[589]. The online display of pressure-time curves was visually checked for sub-maximal effort after each trial, characterised by a rapid initial increase that gradually drops over the last few seconds of the grasp[590]. Trials with clear submaximal effort or outliers were discarded. Trials were also discarded if the participant reported reduced sincerity of effort[503].

6.3.3.3 Data processing

6.3.3.3.1 Processing of TactArray data using Matlab

The pressure (kPa) on each active sensor was collected and pre-processed offline to reduce noise using customised MatLab script (R2015b). The MatLab script was tailored to process data for the sequence of three repeated trials at the same time. Baseline readings for each sensor were determined at the beginning of each sensor recording and subtracted from each sensor reading. Data were only taken from sensors that were deemed as active during some point in the recording; i.e., sensors having a non-zero value[591]. The criterion for sensor activity was more than 10 consecutive sensor readings above a threshold of 3 x root mean square noise on baseline (typically 0.004% of all sensors). Residual drift in baseline during the recording was determined from the time course of total pressure summed over all active sensors and was subtracted using interpolation. Baseline drift was typically less than 0.10% of maximum total pressure. Grasp intervals were defined by periods where total pressure exceeded a threshold of 1/3 of maximum total pressure. Visual inspections of all plots of maximal tactile pressures were also carried out before inclusion in data analysis to avoid erroneous selection of outcomes. The details of the data processing procedure using the customised MatLab script are shown in Appendix 6.1.

6.3.3.3.2 Extraction of measurement variables: total normal pressure and total normal force

It was anticipated that the contact area between the finger pads and the TactArray cylinder could vary within individuals across trials. Therefore, since average pressure is the ratio of normal force to contact area, both pressure and force distributions on the TactArray cylinder could also vary according to the contact area across trials. For instance, a larger finger pad contact area could reduce the average pressure for a given normal force[592]. Therefore, it was essential to also explore the reliability of maximal tactile forces, in addition to maximal tactile pressures. In order to achieve this, the measures of maximal tactile pressures were converted to provide a distribution of tactile forces[567].

From the processed sensor data of each trial, average values were derived for each second throughout the duration of grasps for the following: 1) total number of active sensors, 2) the total pressure, 3) total contact area, and 4) total force.

The total normal pressure was calculated over each one second interval of each grasp by summing these pressures on all active sensors (pressure x number of active sensors) sampled at 0.04 second intervals. The total normal force was then calculated by summing the normal forces on all active sensors on the TactArray surface cylinder (pressure x number of active sensors x sensor size)[563,564,593]. The total contact area between the finger pads and the TactArray sensors was determined by multiplying the sensor size (5mm^2) by the number of active sensors[564,593]. Running averages were performed to obtain the total normal pressure and the total normal force.

6.3.3.3.3 Determining maximal grasp measures

For each trial, maximal tactile pressures and forces were calculated across: 1) the complete duration of the grasp over 8s (from finger contact to finger release), and 2) over the middle 5s of the stationary hold or plateau phase of the grasp[594]. The plateau phase was adjusted to start two seconds after the auditory cue to accommodate for finger contact, time to overcome pre-load forces, and after changes in acceleration during lifting had ceased)[427].

Maximal tactile pressures and forces were reported using: 1) the highest value among the three repetitions; 2) the mean of two repetitions[429,573,595] having the least variation; and 3) the mean of the three repetitions[429]. Table 6.1 provides a summary of the maximal tactile pressures and forces values used in this study.

Table 6.1. Summary of maximal grasp measures and abbreviations

Variables	Grasp phase	Number of trials	Definitions of maximal grasp measures	Abbreviations
Pressure	8s	Highest value	Highest value of average pressure amongst the three repetitions over complete grasp duration of 8s	Pres(8s)max
		Mean of two trials	Average pressure of the mean of two repetitions having least variation within 10% variation over complete grasp duration of 8s	Pres(8s)avg2
		Mean of three trials	Average pressure of the mean of three repetitions over complete grasp duration of 8s	Pres(8s)avg3
	5s	Highest value	Highest value of average pressure amongst the three repetitions over plateau phase of 5s	Pres(5s)max
		Mean of two trials	Average pressure of the mean of two repetitions having least variation within 10% variation over plateau phase of 5s	Pres(5s)avg2
		Mean of three trials	Average pressure of the mean of three repetitions over plateau phase of 5s	Pres(5s)avg3
Force	8s	Highest value	Highest value of average force amongst the three repetitions over complete grasp duration of 8s	Force(8s)max
		Mean of two trials	Average force of the mean of two repetitions having least variation within 10% variation over complete grasp duration of 8s	Force(8s)avg2
		Mean of three trials	Average force of the mean of three repetitions over complete grasp duration of 8s	Force(8s)avg3
	5s	Highest value	Highest value of average force amongst the 3 repetitions over plateau phase of 5s	Force(5s)max
		Mean of two trials	Average force of the mean of two repetitions having least variation within 10% variation over plateau phase of 5s	Force(5s)avg2
		Mean of three trials	Average force of the mean of three repetitions over plateau phase of 5s	Force(5s)avg3

6.3.4 Data analysis

All data were entered into Microsoft Excel (Microsoft Office Professional plus 2013) for data management and then exported into the appropriate analysis programs. Analyses were performed using Microsoft Excel 2013 and the Statistical Package for the Social Sciences version 24 (SPSS Inc., Chicago, IL). Descriptive statistics including means and standard deviations were calculated.

6.3.4.1 Test–retest reliability analysis

The test–retest reliability of maximal tactile pressures and forces were estimated separately for each pair of consecutive sessions (within-day and between-day) using a consecutive pairwise analysis spreadsheet[596]. Mean raw scores were reported for each testing session. Because tests for normality for small sample sizes (<30 participants) have poor statistical power[597-599], measures of reliability were calculated based on the log transformed data to reduce bias arising from non-uniformity error[283,285]. The log-transformation also enabled changes in mean and expression of typical error into percentage values to facilitate interpretation of the variations[284,596]. Precision was maintained by multiplying the natural logarithm by 100[596]. To evaluate the test-retest reliability, the percentage change in mean scores, systematic error, typical error and intraclass correlation coefficients (ICCs) with 90% confidence intervals were calculated for each estimate of maximal tactile pressures and forces as recommended by Hopkins[283,600]. The assessment of reliability using the Bland – Altman limits of agreement have been shown to be inappropriate for evaluating reliability since the values of the limits of agreement depend on the sample size, unlike the typical error [283]. It is noteworthy that the approach to reliability analysis by Hopkins[283,600] has been widely acknowledged and adopted (up to 3511 citations).

6.3.4.2 Indices of reliability

Percentage change in mean scores between consecutive sessions assessed group reproducibility[283,601]. Values <5 % mean change were interpreted as very good, <10% were

good and >10% were unsatisfactory [278].If the confidence interval did not overlap zero, there was a statistically significant change between the means of the two consecutive sessions[284,601,602].

Systematic errors were evaluated by examining the slope and the intercept of the regression line through the test-retest scores from a scatterplot of the scores and by calculating the average difference (AVdiff) between the test and retest scores[245]. If the Avdiff was not 0, a student's t test was conducted on the log-transformed data to determine the significance of the difference. A non-significant difference ($p<0.05$) would indicate only a small systematic error[245].

Typical error assessed within-subject reproducibility, expressed as coefficient of variation (%CV) according to the formula: $\mathrm{CV} = 100(\mathrm{e}^{\mathrm{s}} - 1)$, where $\text{typical error(s) in each trial} = \mathrm{s}_{\mathrm{diff}/\sqrt{2}}$and s_{diff} is the standard deviation of difference scores between trials[283,284]. Values <5 % were desirable, <10% were good, <15% were acceptable and >15% were unsatisfactory[278,281,573]. The presence of heteroscedasticity, i.e., variation of typical error among participants with different values[283] was determined by visual inspection of a scatterplot of change score against the average of the two consecutive sessions for each participant[284]. The smallest detectable change, which is the smallest difference between two independent measures due to a true change or a change that exceeds measurement errors was also calculated[283,284,596].

The ICCs were based on a two-way analysis of variance (ANOVA), absolute agreement, single rater (ICC 2,1)[283,596]. Guidelines by Portney and Watkins were used to interpret ICCs as follows: very good reliability (>0.9), good reliability (>0.75) and unsatisfactory (<0.5)[278].

6.3.4.3 Analysis of variance

To evaluate the difference between vision and no vision conditions in each hand and the difference between both hands, with and without vision using the most reliable maximal tactile measure, analysis of variance (ANOVA) models were fitted to the data for the repeated measurements. Since test performance could be influenced by visual conditions, the hand side used, and the repetition of testing sessions, a 2 (VISION) X 2 (SIDE) X 3 (SESSION) ANOVA for repeated measures was carried out on all three factors to quantify the main effects and interactions of these variables. Independent factor one (with vision and without vision) was called VISION; independent factor two (dominant versus non-dominant hand in healthy participants or affected versus less-affected hand in people with stroke) was called SIDE. Independent factor three (testing session 1 versus testing session 2 versus testing session 3) was called SESSION. A p-value < 0.05 was statistically significant.

To assess if there was a significant difference between groups (healthy participants versus participants with stroke) in hand side and vision effects, a 2 (GROUPS) x 2 (SIDE) x 2 (VISION) ANOVA with repeated measures was carried out on the last two factors while the Groups factor was an independent group variable. The more affected side in the group with stroke was aligned with the non-dominant side in the healthy group.

6.4 RESULTS

6.4.1 Participants characteristics

This study included 18 healthy participants and 11 participants with stroke. The dominant hand was defined as the one used for writing or the hand predominantly used when performing a task[603]. Tables 6.2 and 6.3 summarise the demographic data and characteristics for healthy participants (mean age: 62.2 (9.9) years) and participants with stroke (mean age: 64.1 ± 9.0 years). None of the participants with stroke reported pain (pain visual analogue scale). Tables 6.4 and 6.5 summarise the scores on the clinical measures for the affected and less affected upper limb in people with stroke.

Table 6.2. Demographic data and characteristics of healthy participants

ID	Gender (M/F)	Age (Y)	Hand dominance (R/L)	Grip strength/Kg[#] (Dom/NonDom)	Box and block* (Dom/NonDom)
21C	F	62.3	R	25.7/24.7	62/58
22C	F	62.1	R	20.0/18.0	70/71
23C	F	44.8	R	24.3/27.3	50/52
24C	F	70.2	R	24.7/24.0	58/61
25C	F	56.6	R	21.7/18.3	47/46
26C	F	54.7	R	16.7/16.0	53/54
27C	F	69.7	R	22.7/19.0	59/68
28C	M	60.3	R	42.7/41.3	59/56
29C	F	60.8	R	20.0/13.3	77/75
30C	F	71.7	R	18.0/15.3	66/66
31C	M	66.6	L	40.3/32.3	50/49
32C	M	80.3	R	29.3/28.7	54/54
33C	M	76.1	R	30.7/30.7	64/63
34C	F	72.7	R	21.3/21.3	52/46
35C	F	71.0	R	23.0/21.3	64/60
36C	M	89.3	R	29.3/30.0	61/62
37C	M	68.7	R	36.0/34.0	71/70
38C	F	65.7	R	21.0/19.3	68/66

F: female; M: male; Y:years; R: right; L:left; Dom: Dominant hand; NonDom: Non-dominant hand;
[#] Jamar dynamometer; * Mean of three trials

Table 6.3. Demographic data and characteristics of participants with stroke

ID	Gender (M/F)	Age (Y)	Hand dominance (R/L)	Paretic side (R/L)	Time since stroke (Mo)	Type of stroke (Isch/Haem)	MOCA	SCT	RFCT	MTS Elbow V1:V2:V3	MTS Wrist V1:V2:V3	MTS Fingers V1:V2:V3
A1S	M	66.2	R	L	79	Haem	23	53	34.5	0:0:0	0:0:0	0:0:0
B2S	M	66.6	R	L	43	Isch	25	54	31	0:0:0	0:0:0	0:0:0
C3S	M	59.3	R	L	224	Haem	23	53	18.5	0:0:0	0:1:1	0:0:1
D4S	F	68.4	R	L	40	Isch	24	53	33	0:0:0	0:0:1	0:0:0
E5S	F	77.0	R	R	24	Haem	23	53	33	0:0:0	0:0:0	0:0:0
F6S	M	63.7	R	R	137	Isch	30	54	34	0:1:2	0:0:0	0:0:0
G7S	F	46.3	R	R	47	Isch	28	54	36	0:0:0	0:0:0	0:0:0
H8S	M	64.9	L	R	185	Isch	24	54	35	0:0:0	0:0:0	0:0:0
I9S	M	70.4	R	R	76	Isch	25	54	36	0:0:0	0:0:0	0:0:0
J10S	M	50.6	R	L	124	Isch	23	54	35	1:1:2	0:0:0	0:0:0
K11S	F	71.4	R	R	79	Isch	16	54	32	0:0:0	0:0:0	0:0:0

M: male; F; female; Y: years; R: right; L: left; Mo: month; Isch: Ischaemia; Haem: Haemorrhagic; MOCA: Montreal Cognitive Assessment (maximum score:30); SCT: Star cancellation test (maximum score:54); RFCT: Rey figure copy test (maximum score:36) ; MTS: Modified Tardieu Scale

Table 6.4. Clinical measures of the affected upper limb of participants with stroke

ID	WMFT Score	WMFT Time/s	ARAT	BBT*	Grip strength#	Pinch strength*	FMA Total motor score	FMA Total sensory score	TDT Deficit range score	SIS Strength	SIS Memory	SIS Emotion	SIS Communication	SISA DL	SIS Mobility	SIS Hand function	SIS Participation	SIS Stroke recovery	MAL How much	MAL How well
A1S	63	50.5	41	34.0	30.0	10.0	66	12	-5.8	20	34.3	55.6	22.9	56	51.1	24	30	50	1.1	1.3
B2S	78	38.9	56	37.3	32.0	9.3	66	11	-11.4	60	45.7	42.2	68.6	62	77.8	36	45	60	1.6	1.8
C3S	41	168.0	30	15.3	18.7	7.3	44	9	-198	40	57.1	53.3	77.1	32	31.1	4	57.5	40	0.7	0.4
D4S	72	42.1	50	28.3	9.3	4.7	62	12	-83.8	40	60.0	60.0	71.4	74	57.8	56	52.5	80	1.8	1.7
E5S	76	43.9	51	36.7	17.3	8.0	66	12	-57.8	75	62.9	68.9	65.7	40	75.6	40	67.5	80	3.5	3.2
F6S	38	92.2	20	16.7	16.7	6.7	42	12	-10.4	55	77.1	55.6	68.6	64	57.8	40	75	70	2.2	2.2
G7S	80	38.7	56	45.3	29.7	9.3	66	12	74.8	50	57.1	66.7	54.3	48	57.8	52	60	75	4.7	4.1
H8S	80	33.5	56	52.7	27.7	9.0	65	12	-12.3	55	71.4	64.4	71.4	76	77.8	76	57.5	80	4.5	4.7
I9S	80	39.3	57	37.3	17.7	7.3	64	12	71.8	20	74.3	60.0	62.9	68	57.8	28	65	60	5.0	3.2
J10S	57	55.1	56	45.0	26.0	5.7	61	12	-4.9	15	65.7	53.3	60.0	6	73.3	56	62.5	60	1.8	2.0
K11S	79	40.2	57	46.0	18.0	6.0	66	12	-81.9	35	2.9	28.9	20.0	72	55.6	56	42.5	80	3.9	4.3

WMFT: Wolf Motor Function Test; ARAT: Action Research Arm Test; BBT: Box and Block Test; FMA-UL: Fugl-Meyer upper limb; TDT: Tactile Discrimination Test; SIS: Stroke Impact Scale; MAL-AS: Motor Activity Log-Amount Scale; MAL-HW: Motor Activity Log-How Well;[#] *Mean of three trials using Jamar dynamometer;* [*] *Mean of three trials using* B & L Engineering pinch grip *dynamometer*

Table 6.5. Clinical measures of less affected upper limb of participants with stroke

ID	BBT*	Grip strength[#]	Pinch strength[*]
A1S	51.8	39.7	8.4
B2S	50.1	38.3	8.0
C3S	48.9	26.3	7.9
D4S	49.8	14.7	7.8
E5S	50.0	26.0	7.9
F6S	47.7	20.0	7.7
G7S	53.2	33.3	7.6
H8S	53.8	30.0	7.3
I9S	53.0	16.7	6.3
J10S	50.5	36.7	5.5
K11S	46.0	15.3	5.0

BBT: Box and Block test;[#] Mean of three trials using Jamar dynamometer;[*]Mean of three trials using B & L Engineering pinch grip dynamometer

6.4.2 Results of primary objectives

6.4.2.1 Reliability of values of maximal tactile pressures/forces in healthy participants

The results for the test-retest reliability of measures of maximal tactile pressures and forces in healthy participants are summarised in Tables 6.6-6.13. A summary of the evaluation of measures of maximal tactile pressures and forces against the reliability criteria are summarised in Tables 6.14-6.15.

For values of maximal tactile pressure in the dominant hand with vision, the reliability criterion for within-day and between-day sessions for changes in mean were very good, coefficients of variation were good to acceptable and ICCs were very good to good using Pres(8s)max, Pres(8s)avg3, Pres(5s)max and Pres(5s)avg3. Without vision, changes in means were very good, coefficients of variation were acceptable, but ICCs were unsatisfactory for within-day and between-day sessions for all measures of maximal tactile pressures.

For measures of maximal tactile force in the dominant hand, changes in mean were very good, coefficients of variation were acceptable and ICCs were good without vision using Force(8s)max, Force(5s)max and Force(5s)avg3 for within-day sessions. With vision, the changes in mean were good to very good but coefficients of variation, and/or ICCs were unsatisfactory using Force(8s)avg2, Force(8s)avg3, Force(5s)avg2 and Force(5s)avg3 for within-day and between-day sessions.

For measures of maximal tactile pressure in the non-dominant hand without vision, the reliability criterion for within-day and between-day sessions for changes in mean and coefficients of variation were acceptable to good, and for ICCs were good to very good using all measures of maximal tactile pressure. With vision, changes in mean were good, coefficients of variation were acceptable to good, and ICCs were good to very good for within-day sessions using all measures of maximal tactile pressure. For between-day sessions, changes in mean were good to very good but coefficients of variation and ICCs were unsatisfactory using all measures of maximal tactile pressure.

For measures of maximal tactile force in the non-dominant hand without vision, the reliability criterion for within-day sessions for changes in mean were very good, coefficients of variation were acceptable and ICCs were good using Force(5s)max. For between-day sessions with and without vision, changes in mean were good to very good but coefficients of variations and ICCs were unsatisfactory for all measures of maximal tactile force.

The changes in mean were smaller in between-day sessions as compared to within-day and between-day sessions, with the confidence intervals overlapping zero in conditions, except with the nondominant hand without vision using Pres(8s)max, Pres(8s)avg3 and Pres(5s)max and Pres(5s)avg3.

Table 6.6. Measures of reliability in the dominant hand of healthy participants with vision during complete grasp duration (8s)

		Session 1	Session 2	Session 3	Mean 3 sessions		Change in mean (%)	90% CI	CV (%)	90% CI	Smallest effect (%)*	90% CI	ICC	90% CI
Pressure/kPa														
Pres(8s)max	Mean	37.63	36.58	36.90	37.04	Session 2-1	-2.82	-8.34, 3.03	10.61	8.24, 15.16	4.11	2.65, 5.20	0.82	0.63, 0.92
	SD	8.60	8.21	6.75	7.90	Session 3-2	1.75	-4.28, 8.15	11.10	8.61, 15.88	3.60	2.38, 4.51	0.76	0.53, 0.89
Pres(8s)avg2	Mean	34.76	34.25	34.77	34.59	Session 2-1	-1.73	-7.57, 4.48	11.15	8.65, 15.95	3.89	2.49, 4.92	0.79	0.57, 0.90
	SD	7.50	7.82	6.42	7.27	Session 3-2	2.24	-1.81, 6.46	7.23	5.63, 10.26	4.03	2.90, 4.91	0.90	0.79, 0.96
Pres(8s)avg3	Mean	35.08	34.27	34.65	34.67	Session 2-1	-2.65	-8.44, 3.51	11.15	8.66, 15.96	4.14	2.60, 5.26	0.81	0.61, 0.91
	SD	7.93	8.08	6.52	7.54	Session 3-2	2.03	-3.38, 7.75	9.85	7.65, 14.06	3.99	2.66, 4.99	0.83	0.65, 0.92
Force/N														
Force(8s)max	Mean	52.80	49.94	48.19	50.31	Session 2-1	-4.09	-12.56, 5.21	17.30	13.35, 25.04	5.19	2.58, 6.91	0.74	0.49, 0.88
	SD	17.45	13.06	13.92	14.93	Session 3-2	-3.57	-11.74, 5.35	16.49	12.73-23.83	4.62	2.25-6.18	0.71	0.45, 0.86
Force(8s)avg2	Mean	48.82	45.98	46.05	46.95	Session 2-1	-3.88	-14.07, 7.52	21.32	16.38-31.07	5.20	1.95, 7.15	0.66	0.36, 0.83
	SD	17.45	12.54	12.50	14.35	Session 3-2	0.71	-8.47, 10.82	17.93	13.82-25.97	4.40	1.82, 5.98	0.66	0.36, 0.83
Force(8s)avg3	Mean	48.93	45.11	44.34	46.13	Session 2-1	-6.19	-14.57, 3.01	17.51	13.50, 25.35	5.49	2.79, 7.30	0.76	0.52, 0.88
	SD	17.17	12.14	12.50	14.13	Session 3-2	-1.40	-9.77, 7.74	16.52	12.76, 23.88	4.68	2.29, 6.24	0.71	0.45, 0.86

*:smallest effect from pure SD; CI: Confidence interval: CV: Coefficient of variation; SD: standard deviation

Table 6.7. Measures of reliability in the dominant hand of healthy participants without vision during complete grasp duration (8s)

		Session 1	Session 2	Session 3	Mean 3 sessions		Change in mean (%)	90% CI	CV (%)	90% CI	Smallest effect (%)*	90% CI	ICC	90% CI
Pressure/kPa														
Pres(8s)max	Mean	35.65	36.70	36.61	36.32	Session 2-1	3.11	-3.42, 10.09	11.95	9.27, 17.13	3.00	2.13, 3.67	0.66	0.36, 0.83
	SD	7.18	6.76	6.49	6.82	Session 3-2	-0.09	-6.40, 6.65	11.91	9.23, 17.06	2.79	2.19, 3.28	0.62	0.31, 0.82
Pres(8s)avg2	Mean	34.01	34.62	33.77	34.13	Session 2-1	2.65	-3.80, 9.54	11.85	9.19, 16.97	2.76	2.22, 3.21	0.62	0.31, 0.81
	SD	7.17	5.16	6.64	6.38	Session 3-2	-3.11	-9.91, 4.21	13.38	10.36, 19.22	2.40	2.00, 3.91	0.50	0.13, 0.74
Pres(8s)avg3	Mean	33.25	34.10	33.63	33.66	Session 2-1	2.89	-3.45, 9.65	11.59	8.99, 16.60	2.94	2.21, 3.53	0.66	0.37, 0.84
	SD	6.76	5.89	6.49	6.39	Session 3-2	-1.62	-8.23, 5.47	12.75	9.88, 18.30	2.75	1.98, 3.36	0.59	0.26, 0.79
Force/N														
Force(8s)max	Mean	50.46	51.15	47.23	49.61	Session 2-1	1.84	-5.78, 10.08	14.35	11.10, 20.66	5.40	3.06, 7.03	0.81	0.62, 0.91
	SD	14.88	14.90	14.99	14.92	Session 3-2	-8.28	-16.44, 0.67	17.42	13.44, 25.21	5.05	2.46, 6.75	0.73	0.47, 0.87
Force(8s)avg2	Mean	48.38	46.02	42.31	45.57	Session 2-1	-4.45	-13.36, 5.38	18.40	14.18, 26.68	5.17	2.42, 6.95	0.71	0.45, 0.86
	SD	14.72	14.23	10.47	13.27	Session 3-2	-6.83	-15.60, 2.85	18.59	14.33, 26.97	4.22	1.52, 5.82	0.62	0.31, 0.81
Force(8s)avg3	Mean	46.45	46.23	41.57	44.75	Session 2-1	0.21	-7.71, 8.81	15.26	11.79, 22.00	5.06	2.73, 6.65	0.77	0.55, 0.89
	SD	13.29	12.95	11.18	12.51	Session 3-2	-10.06	-17.65, -1.77	16.42	12.68, 23.72	4.54	2.20, 6.07	0.71	0.44, 0.86

*:smallest effect from pure SD; CI: Confidence interval: CV: Coefficient of variation; SD: standard deviation

Table 6.8. Measures of reliability in the dominant hand of healthy participants with vision during the plateau phase (5s)

		Session 1	Session 2	Session 3	Mean 3 sessions		Change in mean (%)	90% CI	CV (%)	90% CI	Smallest effect (%)*	90% CI	ICC	90% CI
Pressure/kPa														
Pres(5s)max	Mean	46.09	44.66	45.18	45.31	Session 2-1	-3.02	-8.93, 3.27	11.44	8.88, 16.38	4.08	2.54, 5.20	0.79	0.59, 0.90
	SD	10.70	9.81	8.18	9.62	Session 3-2	1.99	-3.79, 8.11	10.58	8.21, 15.12	3.68	2.47, 4.59	0.78	0.57, 0.90
Pres(5s)avg2	Mean	42.55	41.81	42.64	42.34	Session 2-1	-2.11	-8.64, 4.89	12.64	9.80, 18.14	3.86	2.29, 4.97	0.74	0.49, 0.88
	SD	9.32	9.72	7.86	9.00	Session 3-2	2.94	-2.13, 8.27	9.10	7.07, 12.97	3.93	2.71, 4.87	0.85	0.68, 0.93
Pres(5s)avg3	Mean	42.88	41.99	42.23	42.36	Session 2-1	-2.49	-8.59, 4.02	11.78	9.14, 16.88	4.24	2.59, 5.43	0.80	0.59, 0.91
	SD	9.88	10.08	8.02	9.37	Session 3-2	1.63	-3.84, 7.41	10.00	7.77, 14.28	4.13	2.71, 5.19	0.84	0.66, 0.92
Force/N														
Force(5s)max	Mean	65.12	61.50	58.97	61.86	Session 2-1	-4.35	-12.70, 4.81	17.07	13.17, 24.69	5.35	2.73, 7.09	0.75	0.52, 0.88
	SD	21.29	16.11	16.73	18.19	Session 3-2	-3.96	-12.49, 5.41	17.40	13.42, 25.19	4.59	2.09, 6.19	0.69	0.41, 0.85
Force(5s)avg2	Mean	58.93	56.79	56.72	57.48	Session 2-1	-2.26	-12.38, 9.04	20.76	15.96, 30.22	5.32	2.17, 7.26	0.68	0.39, 0.84
	SD	20.50	15.96	16.47	17.76	Session 3-2	0.29	-8.57, 10.00	17.29	13.33, 25.78	4.89	2.35, 6.55	0.72	0.45, 0.86
Force(5s)avg3	Mean	59.87	55.49	54.20	56.52	Session 2-1	-5.93	-14.43, 3.43	17.76	13.70, 25.73	5.60	2.85, 7.45	0.76	0.52, 0.89
	SD	20.99	15.21	15.40	17.41	Session 3-2	-1.82	-10.08, 7.21	16.38	12.65, 23.66	4.87	2.45, 6.47	0.73	0.48, 0.87

*:smallest effect from pure SD; CI: Confidence interval: CV: Coefficient of variation; SD: standard deviation

Table 6.9. Measures of reliability in the dominant hand of healthy participants without vision during the plateau phase (5s)

		Session 1	Session 2	Session 3	Mean 3 sessions		Change in mean (%)	90% CI	CV(%)	90% CI	Smallest effect (%)*	90% CI	ICC	90% CI
Pressure/kPa														
Pres(5s)max	Mean	44.01	44.16	44.57	44.25	Session 2-1	0.43	-5.65, 6.90	11.37	8.82, 16.27	3.11	2.24, 3.79	0.69	0.42, 0.85
	SD	8.89	8.26	8.20	8.46	Session 3-2	1.04	-5.30, 7.81	11.83	9.17, 16.95	2.95	2.16, 3.57	0.65	0.35, 0.83
Pres(5s)avg2	Mean	42.29	41.44	40.43	41.39	Session 2-1	-1.20	-7.35, 5.34	11.70	9.08, 16.76	2.99	2.18, 3.63	0.66	0.37, 0.84
	SD	9.23	6.55	7.89	7.97	Session 3-2	-3.02	-9.54, 3.97	12.75	9.88, 18.30	2.74	1.99, 3.33	0.58	0.25, 0.79
Pres(5s)avg3	Mean	40.94	41.17	41.06	41.06	Session 2-1	0.95	-5.15, 7.43	11.34	8.80, 16.22	3.03	2.25, 3.65	0.68	0.40, 0.85
	SD	8.56	7.14	8.03	7.93	Session 3-2	-0.56	-6.82, 6.13	11.87	9.21, 17.01	2.95	2.15, 3.58	0.65	0.35, 0.83
Force/N														
Force(5s)max	Mean	62.33	62.06	57.63	60.67	Session 2-1	0.41	-6.26, 7.56	12.60	9.76, 18.07	5.50	3.29, 7.09	0.85	0.69, 0.93
	SD	18.66	17.42	18.81	18.31	Session 3-2	-8.16	-15.75, 0.11	16.03	12.38, 23.15	5.18	2.73, 6.83	0.76	0.53, 0.89
Force(5s)avg2	Mean	58.79	56.02	50.97	55.26	Session 2-1	-4.39	-13.31, 5.45	18.40	14.18, 26.68	5.15	2.40, 6.93	0.71	0.45, 0.86
	SD	17.90	17.04	13.50	16.26	Session 3-2	-8.29	-16.69, 0.95	18.02	13.89, 26.10	4.67	2.05, 6.31	0.68	0.40, 0.85
Force(5s)avg3	Mean	57.30	55.98	51.69	54.99	Session 2-1	-1.44	-8.97, 6.72	14.69	11.36, 21.16	5.17	2.87, 6.76	0.79	0.58, 0.90
	SD	16.65	15.40	15.83	15.97	Session 3-2	-8.51	-16.12, -0.22	16.14	12.46, 23.30	4.94	2.54, 6.55	0.75	0.50, 0.88

*:smallest effect from pure SD; CI: Confidence interval: CV: Coefficient of variation; SD: standard deviation

Table 6.10. Measures of reliability in the nondominant hand of healthy participants with vision during complete grasp duration (8s)

		Session 1	Session 2	Session 3	Mean 3 sessions		Change in mean (%)	90% CI	CV (%)	90% CI	Smallest effect (%)*	90% CI	ICC	90% CI
Pressure/kPa														
Pres(8s)max	Mean	34.14	36.05	38.15	36.11	Session 2-1	5.77	0.15, 11.72	9.89	7.68, 14.12	4.50	2.91, 5.69	0.86	0.71, 0.94
	SD	7.74	7.86	8.13	7.91	Session 3-2	6.08	-4.21, 17.46	19.22	14.80, 27.91	2.97	-1.12, 4.39	0.43	0.05, 0.70
						Session 3-2[#]	1.09	-4.98, 7.55	10.90	8.40, 15.79	4.07	2.52, 5.19	0.81	0.60, 0.91
Pres(8s)avg2	Mean	32.07	34.02	34.96	33.68	Session 2-1	6.39	0.11, 13.08	11.08	8.60, 15.85	4.77	2.96, 6.09	0.85	0.69, 0.93
	SD	7.70	7.98	8.71	8.14	Session 3-2	2.56	-7.62, 13.86	19.75	15.20, 28.71	3.50	-0.74, 5.05	0.50	0.14, 0.75
						Session 3-2[#]	-2.57	-8.24, 3.66	10.72	8.26, 15.53	4.5	2.78, 5.74	0.84	0.67, 0.93
Pres(8s)avg3	Mean	32.08	33.77	35.46	33.77	Session 2-1	5.43	-0.30, 11.50	10.12	7.86, 14.45	4.97	3.15, 6.32	0.88	0.74, 0.94
	SD	7.71	8.05	8.14	7.97	Session 3-2	5.41	-5.01, 16.96	19.65	15.12-28.55	3.41	-0.84, 4.93	0.49	0.12, 0.74
						Session 3-2[#]	0.32	-5.73, 6.75	10.94	8.43, 15.85	4.43	2.72, 5.66	0.83	0.65, 0.92
Force/N														
Force(8s)max	Mean	45.86	46.49	47.38	46.57	Session 2-1	1.98	-7.26, 12.14	17.79	13.72, 25.77	5.98	3.13, 7.91	0.78	0.56, 0.90
	SD	14.65	14.71	15.23	14.86	Session 3-2	2.07	-8.78, 14.21	21.38	16.43, 31.17	5.05	1.77, 6.97	0.64	0.34, 0.83
Force(8s)avg2	Mean	40.84	43.22	43.61	42.56	Session 2-1	6.82	-5.18, 20.35	22.83	17.52, 33.37	6.31	2.77, 8.56	0.71	0.45, 0.86
	SD	14.62	14.86	15.76	15.09	Session 3-2	0.54	-10.02, 12.34	21.09	16.21, 30.72	6.12	2.85, 8.24	0.73	0.48, 0.87
Force(8s)avg3	Mean	41.55	42.24	43.01	42.27	Session 2-1	2.75	-6.97, 13.47	18.68	14.39, 27.09	6.14	3.16, 8.15	0.77	0.55, 0.89
	SD	14.13	13.71	13.48	13.77	Session 3-2	2.21	-7.91, 13.44	19.70	15.16, 28.63	5.28	2.31, 7.15	0.70	0.42, 0.85

[#]:outlier removed; *:smallest effect from pure SD; CI: Confidence interval: CV: Coefficient of variation; SD: standard deviation

Table 6.11. Measures of reliability in the nondominant hand of healthy participants without vision during complete grasp duration (8s)

		Session 1	Session 2	Session 3	Mean 3 sessions		Change in mean (%)	90% CI	CV (%)	90% CI	Smallest effect (%)*	90% CI	ICC	90% CI
Pressure/kPa														
Pres(8s)max	Mean	33.63	35.56	34.68	34.62	Session 2-1	6.22	0.98, 11.73	9.12	7.09, 13.00	4.71	3.07, 5.93	0.89	0.76, 0.95
	SD	8.09	7.73	8.33	8.05	Session 3-2	-2.94	-9.50, 4.09	12.82	9.93, 18.40	4.39	2.57, 5.68	0.78	0.56, 0.90
Pres(8s)avg2	Mean	31.73	33.03	32.48	32.41	Session 2-1	3.87	-3.64, 11.97	13.82	10.69, 19.87	4.64	2.61, 6.05	0.78	0.55, 0.89
	SD	7.72	8.00	7.20	7.65	Session 3-2	-1.07	-6.54, 4.72	10.31	8.00-, 4.72	4.80	3.04, 6.10	0.87	0.72, 0.94
Pres(8s)avg3	Mean	31.41	33.10	32.46	32.32	Session 2-1	5.53	0.51, 10.80	8.77	6.82, 12.49	4.86	3.18, 6.12	0.90	0.79, 0.96
	SD	7.43	7.57	7.36	7.45	Session 3-2	-1.80	-7.55, 4.31	10.96	8.51, 15.68	4.56	2.85, 5.81	0.84	0.67, 0.93
Force/N														
Force(8s)max	Mean	46.25	43.26	45.26	44.92	Session 2-1	-5.62	-13.13, 2.55	15.38	11.89, 22.18	6.07	3.44, 7.92	0.83	0.65, 0.92
	SD	15.31	13.74	16.43	15.20	Session 3-2	3.33	-6.99, 14.80	19.90	15.31, 28.93	5.59	2.55, 7.53	0.72	0.45, 0.86
Force(8s)avg2	Mean	41.96	38.73	40.76	40.48	Session 2-1	-6.53	-16.10, 4.14	20.48	15.75, 29.80	5.65	2.52, 7.64	0.71	0.44, 0.86
	SD	14.20	12.55	13.42	13.41	Session 3-2	5.00	-4.38, 15.31	17.52	13.51, 25.36	5.35	2.68, 7.12	0.75	0.50, 0.88
Force(8s)avg3	Mean	41.60	39.20	41.01	40.60	Session 2-1	-4.89	-12.79, 3.72	16.12	12.45, 23.28	5.89	3.24, 7.72	0.81	0.61, 0.91
	SD	13.70	12.56	14.09	13.47	Session 3-2	3.74	-5.41, 13.77	17.25	13.31, 24.97	5.62	2.92, 7.45	0.77	0.54, 0.89

*:smallest effect from pure SD; CI: Confidence interval: CV: Coefficient of variation; SD: standard deviation

Table 6.12. Measures of reliability in the nondominant hand of healthy participants with vision during the plateau phase (5s)

		Session 1	Session 2	Session 3	Mean 3 sessions		Change in mean (%)	90% CI	CV (%)	90% CI	Smallest effect(%)*	90% CI	ICC	90% CI
Pressure/kPa														
Pres(5s)max	Mean	41.55	43.82	46.28	43.88	Session 2-1	5.82	0.35, 11.58	9.58	7.45, 13.67	4.73	3.05, 5.97	0.88	0.74, 0.94
	SD	9.92	9.71	10.49	10.04	Session 3-2	5.75	-5.16, 17.91	20.66	15.88, 30.08	2.87	-1.61, 4.41	0.38	-0.01, 0.67
						Session 3-2[#]	0.21	-5.56, 6.33	10.41	8.03, 15.08	4.20	2.64, 5.34	0.83	0.65, 0.92
Pres(5s)avg2	Mean	39.45	41.37	42.30	41.04	Session 2-1	5.51	-1.53, 13.06	12.66	9.81, 18.16	5.18	3.07, 6.68	0.84	0.66, 0.92
	SD	10.58	10.46	10.56	10.53	Session 3-2	2.39	-8.02, 13.98	20.32	15.63, 29.56	3.72	-0.66, 5.35	0.52	0.16, 0.76
						Session 3-2[#]	-2.81	-8.57, 3.32	10.74	8.28, 15.56	4.76	2.93, 6.09	0.86	0.69, 0.93
Pres(5s)avg3	Mean	39.22	41.25	43.21	41.23	Session 2-1	5.68	-0.19, 11.89	10.36	8.04, 14.79	5.25	3.30, 6.69	0.89	0.76, 0.95
	SD	10.20	10.15	10.35	10.23	Session 3-2	5.16	-5.81, 17.42	20.93	16.09, 30.49	3.38	-1.32, 5.01	0.46	0.08, 0.72
						Session 3-2[#]	-0.36	-6.30, 5.96	10.81	8.34, 15.67	4.57	2.81, 5.85	0.84	0.67, 0.93
Force/N														
Force(5s)max	Mean	56.46	56.91	57.25	56.88	Session 2-1	1.89	-7.41, 12.11	17.94	13.83, 25.98	6.13	3.23, 8.10	0.79	0.57, 0.90
	SD	18.73	18.17	18.44	18.45	Session 3-2	0.67	-9.82, 12.38	20.89	16.06, 30.43	5.10	1.93, 7.01	0.66	0.36, 0.83
Force(5s)avg2	Mean	51.20	53.34	53.32	52.62	Session 2-1	6.50	-5.52, 20.05	22.95	17.60, 33.54	6.45	2.88, 8.73	0.72	0.46, 0.87
	SD	19.64	18.02	19.47	19.06	Session 3-2	-0.95	-12.14, 11.65	22.95	17.61, 33.55	5.80	2.26, 7.95	0.68	0.39, 0.84
Force(5s)avg3	Mean	51.26	52.09	52.58	51.98	Session 2-1	3.03	-6.65, 13.70	18.53	14.28, 26.87	6.44	3.40, 8.50	0.79	0.58, 0.90
	SD	18.16	17.31	16.89	17.46	Session 3-2	1.23	-8.99, 12.61	20.16	15.51, 29.32	5.44	2.38, 7.37	0.70	0.43, 0.86

[#]:outlier removed; *:smallest effect from pure SD; CI: Confidence interval: CV: Coefficient of variation; SD: standard deviation

Table 6.13. Measures of reliability in the nondominant hand of healthy participants without vision during the plateau phase of 5s

		Session 1	Session 2	Session 3	Mean 3 sessions		Change in mean (%)	90% CI	CV (%)	90% CI	Smallest effect(%)*	90% CI	ICC	90% CI
Pressure/kPa														
Pres(5s)max	Mean	41.14	43.11	42.11	42.12	Session 2-1	5.12	0.40, 10.06	8.24	6.41, 11.73	4.72	3.14, 5.92	0.91	0.80, 0.96
	SD	9.60	9.30	9.94	9.62	Session 3-2	-2.60	-8.51, 3.69	11.41	8.85, 16.33	4.43	2.74, 5.66	0.82	0.63, 0.92
Pres(5s)avg2	Mean	38.23	40.64	39.18	39.35	Session 2-1	5.68	-0.78, 12.56	11.49	8.91, 16.45	4.80	2.94, 6.14	0.84	0.67, 0.93
	SD	8.81	9.94	8.75	9.18	Session 3-2	-3.00	-8.27, 2.58	10.12	7.86, 14.45	4.94	3.13, 6.27	0.88	0.74, 0.94
Pres(5s)avg3	Mean	38.17	40.25	39.53	39.32	Session 2-1	5.38	0.74, 10.24	8.08	6.29, 11.50	4.98	3.28, 6.25	0.92	0.82, 0.96
	SD	8.97	9.40	8.90	9.09	Session 3-2	-1.48	-6.88, 4.24	10.21	7.93, 14.59	4.68	2.98, 5.94	0.86	0.71, 0.94
Force/N														
Force(5s)max	Mean	56.82	52.87	54.80	54.83	Session 2-1	-5.41	-12.37, 2.10	14.09	10.90, 20.26	6.48	3.82, 8.37	0.87	0.72, 0.94
	SD	20.02	16.50	19.08	18.59	Session 3-2	2.72	-6.96, 13.40	18.61	14.33, 26.99	5.63	2.76, 7.52	0.74	0.50, 0.88
Force(5s)avg2	Mean	51.49	47.16	49.87	49.51	Session 2-1	-6.91	-15.39, 2.43	17.92	13.81, 25.95	6.18	3.27, 8.17	0.79	0.58, 0.90
	SD	18.51	15.64	16.44	16.91	Session 3-2	5.60	-3.41, 15.45	16.62	12.83, 24.02	5.59	2.97, 7.37	0.78	0.56, 0.90
Force(5s)avg3	Mean	50.98	47.91	50.16	49.68	Session 2-1	-4.61	-12.30, 3.77	15.62	12.07, 22.53	6.17	3.48, 8.05	0.83	0.65, 0.92
	SD	17.67	15.16	16.92	16.61	Session 3-2	3.85	-4.87, 13.37	16.33	12.61, 23.60	5.73	3.10, 7.54	0.79	0.58, 0.90

*:smallest effect from pure SD; CI: Confidence interval: CV: Coefficient of variation; SD: standard deviation

Table 6.14. Summary of evaluation of measures of maximal tactile pressures and forces against the reliability criteria in the dominant hand of healthy participants

Sessions	Measures of maximal tactile pressure/force over complete grasp duration	Complete grasp duration (8s) with vision			*Complete grasp duration (8s) without vision*			Measures of maximal tactile pressure/force over plateau phase	*Plateau phase (5s) with vision*			*Plateau phase (5s) without vision*		
		Change in mean (%)	CV (%)	ICC	Change in mean (%)	CV (%)	ICC		Change in mean (%)	CV (%)	ICC	Change in mean (%)	CV (%)	ICC
Session 2-1	Pres(8s)max	very good	acceptable	good	very good	acceptable	x	Pres(5s)max	very good	acceptable	good	very good	acceptable	x
Session 3-2		very good	acceptable	good	very good	acceptable	x		very good	acceptable	good	very good	acceptable	x
Session 2-1	Pres(8s)avg2	very good	acceptable	good	very good	acceptable	x	Pres(5s)avg2	very good	acceptable	x	very good	acceptable	x
Session 3-2		very good	good	very good	very good	acceptable	x		very good	good	good	very good	acceptable	x
Session 2-1	Pres(8s)avg3	very good	acceptable	good	very good	acceptable	x	Pres(5s)avg3	very good	acceptable	good	very good	acceptable	x
Session 3-2		very good	good	good	very good	acceptable	x		very good	good	good	very good	acceptable	x
Session 2-1	Force(8s)max	very good	x	x	very good	acceptable	good	Force(5s)max	very good	x	good	very good	acceptable	good
Session 3-2		very good	x	x	good	x	x		very good	x	x	good	x	good
Session 2-1	Force(8s)avg2	very good	x	x	very good	x	x	Force(5s)avg2	very good	x	x	very good	x	x
Session 3-2		very good	x	x	good	x	x		very good	x	x	good	x	x
Session 2-1	Force(8s)avg3	good	x	good	very good	x	good	Force(5s)avg3	good	x	good	very good	acceptable	good
Session 3-2		very good	x	x	good	x	x		very good	x	x	good	x	good

Table 6.15. Summary of reliability criteria in the non-dominant hand of healthy participants

Sessions	Measures of maximal tactile pressure/force over complete grasp duration	Complete grasp duration (8s) with vision			Complete grasp duration (8s) without vision			Measures of maximal tactile pressure/force over complete grasp duration	*Plateau phase (5s) with vision*			*Plateau phase (5s) without vision*		
		Change in mean (%)	CV (%)	ICC	Change in mean (%)	CV (%)	ICC		Change in mean (%)	CV (%)	ICC	Change in mean (%)	CV (%)	ICC
Session 2-1	Pres(8s)max	good	good	good	good	good	good	Pres(5s)max	good	good	good	good	good	very good
Session 3-2		good	x	x	very good	acceptable	good		good	x	x	very good	acceptable	good
Session 3-2[#]		Very good	acceptable	good					very good	acceptable	good			
Session 2-1	Pres(8s)avg2	good	acceptable	good	very good	acceptable	good	Pres(8s)avg2	good	acceptable	good	good	acceptable	good
Session 3-2		very good	x	x	very good	acceptable	good		very good	x	x	very good	acceptable	good
Session 3-2[#]		very good	acceptable	good					very good	acceptable	good			
Session 2-1	Pres(8s)avg3	good	acceptable	good	good	good	very good	Pres(5s)avg3	good	acceptable	good	good	good	very good
Session 3-2		good	x	x	very good	acceptable	good		good	x	x	very good	acceptable	good
Session 3-2[#]		very good	acceptable	good					very good	acceptable	good			
Session 2-1	Force(8s)max	very good	x	good	good	x	good	Force(5s)max	very good	x	good	good	acceptable	good
Session 3-2		very good	x	x	very good	x	x		very good	x	x	very good	x	x
Session 2-1	Force(8s)avg2	good	x	x	good	x	x	Force(5s)avg2	good	x	x	good	x	good
Session 3-2		very good	x	x	acceptable good	x	good		very good	x	x	good	x	good
Session 2-1	Force(8s)avg3	very good	x	good	very good	x	good	Force(5s)avg3	very good	x	good	very good	x	good
Session 3-2		very good	x	x	very good	x	good		very good	x	x	very good	x	good

[#]:outlier removed;

6.4.2.2 Reliability of values of maximal tactile pressures/forces in participants with stroke

The results for the test-retest reliability of measures of maximal tactile pressures and forces in people with stroke are summarised in Table 6.16-6.23. A summary of the evaluation of measures of maximal tactile pressures and forces against the reliability criteria are summarised in Table 6.24-6.25.

For measures of maximal tactile pressure in the affected hand, the reliability criteria for changes in mean were good, coefficients of variation were acceptable and ICCs were very good for within-day sessions with vision using Pres(8s)avg3. Using other measures of maximal tactile pressure, changes in mean and ICCs were good to very good but coefficients of variations were unsatisfactory for within-day sessions with and without vision. For between-day sessions, changes in mean and ICC were very good and coefficients of variation were acceptable without vision using Pres(8s)avg3 and Pres(5s)avg3. Using other measures of maximal tactile pressure for between-day sessions, changes in mean and ICCs were good to very good but coefficients of variations were unsatisfactory without vision while both coefficients of variations and ICC were unsatisfactory with vision.

For measures of maximal tactile force in the affected hand, the reliability criterion for changes in mean were good, coefficients of variation were acceptable and ICCs very good in within-day sessions with vision using Force(8s)avg3 and Force(5s)avg3. For between-day sessions, changes in mean were good, coefficients of variation were acceptable and ICCs were very good using Force(8s)max, Force(5s)avg2 and Force(5s)avg3 without vision.

For measures of maximal tactile pressure in the less affected hand, the reliability criterion for changes in mean were good to very good, coefficients of variations were acceptable and ICCs were good to very good for between-day sessions with and without vision using Pres(5s)avg3 and Pres(8s)avg3. Changes in mean and coefficients of variations were good and ICCs were very good for within-day sessions without vision using Pres(5s)max and

Pres(5s)avg2. For within-day sessions with vision, changes in mean were good to very good but coefficients of variations and ICCs were unsatisfactory using Pres(8s)max and Pres(8s)avg2.

For measures of maximal tactile force in the less affected hand, the reliability criterion for changes in mean, coefficients of variations and ICCs were good to very good for within-day and between-day sessions without vision using Force(5s)max, Force(5s)avg2 and Force(5s)avg3. For between-day sessions, changes in mean were good, coefficients of variation acceptable and ICCs very good with vision using Force(8s)avg2 and Force(8s)avg3.

Changes in mean in between-day sessions were smaller than within-day sessions for measures of maximal tactile pressures in both hands with and without vision. For measures of maximal tactile forces, differences in changes in mean between within-day sessions and between-day sessions were inconsistent in both hands, with and without vision.

Table 6.16. Measures of reliability in the affected hand of participants with stroke with vision during complete grasp duration (8s)

		Session 1	Session 2	Session 3	Mean 3 sessions		Change in mean (%)	90% CI	CV (%)	90% CI	Smallest effect (%)*	90% CI	ICC	90% CI
Pressure/kPa														
Pres(8s)max	Mean	31.29	34.62	33.25	33.05	Session 2-1	9.30	-4.51, 25.12	19.11	13.80, 32.12	10.01	3.96, 13.79	0.91	0.74, 0.97
	SD	11.89	12.24	11.14	11.76	Session 3-2	0.59	-17.78, 23.06	29.81	21.27, 51.54	7.68	-2.31, 11.32	0.71	0.34, 0.89
						Session 3-2[#]	-8.99	-17.55, 0.46	12.80	9.18, 21.92	9.09	4.06, 12.35	0.94	0.84, 0.98
Pres(8s)avg2	Mean	28.85	31.74	29.85	30.15	Session 2-1	10.04	-4.51, 26.80	20.14	14.52, 33.95	10.08	3.88, 13.92	0.90	0.73, 0.96
	SD	11.53	11.55	8.95	10.74	Session 3-2	-1.08	-18.32, 19.80	28.12	20.10, 48.40	7.55	-1.97, 11.06	0.73	0.36, 0.90
						Session 3-2[#]	-10.01	-18.18, -1.02	12.31	8.84, 21.05	8.84	3.96, 12.01	0.95	0.84, 0.98
Pres(8s)avg3	Mean	29.40	31.41	30.58	30.46	Session 2-1	6.89	-4.03, -19.06	14.97	10.86, 24.88	10.47	4.64, 14.26	0.94	0.84, 0.98
	SD	11.64	11.18	9.49	10.81	Session 3-2	2.30	-15.27, 23.51	27.61	19.74, 47.46	7.62	-1.76, 11.12	0.74	0.38, 0.90
						Session 3-2[#]	-7.18	-13.84, 0.01	9.52	6.86- 16.14	9.00	4.24, 12.12	0.97	0.90, 0.99
Force/N														
Force(8s)max	Mean	46.00	46.73	43.66	45.46	Session 2-1	5.62	-5.49, 18.03	15.46	11.21, 25.74	12.54	5.71, 17.06	0.96	0.88, 0.99
	SD	23.23	18.79	11.59	18.50	Session 3-2	0.02	-13.74, 15.97	21.10	15.20, 35.67	8.69	2.80, 12.14	0.86	0.63, 0.95
Force(8s)avg2	Mean	39.58	42.73	39.97	40.76	Session 2-1	10.87	0.00, 22.91	14.28	10.37, 23.69	13.86	6.47, 18.83	0.97	0.91, 0.99
	SD	18.89	17.65	13.12	16.74	Session 3-2	0.08	-15.80, 18.95	25.05	17.96, 42.78	10.25	3.29, 14.35	0.86	0.63, 0.95
Force(8s)avg3	Mean	40.52	43.15	39.83	41.17	Session 2-1	9.73	-0.15, 20.58	12.98	9.44, 21.47	13.28	6.25, 18.01	0.97	0.92, 0.99
	SD	20.20	17.97	11.66	17.00	Session 3-2	-0.65	-15.84, 17.28	23.95	17.19, 40.78	9.40	2.84, 13.19	0.85	0.61, 0.95

[#]:outlier removed; *:smallest effect from pure SD; CI: Confidence interval: CV: Coefficient of variation; SD: standard deviation

Table 6.17. Measures of reliability in the affected hand of participants with stroke without vision during complete grasp duration (8s)

		Session 1	Session 2	Session 3	Mean 3 sessions		Change in mean (%)	90% CI	CV (%)	90% CI	Smallest effect (%)*	90% CI	ICC	90% CI
Pressure/kPa														
Pres(8s)max	Mean	32.02	33.69	31.81	32.50	Session 2-1	11.15	-2.52, 26.73	18.50	13.37, 31.06	8.36	2.98, 11.59	0.88	0.68, 0.96
	SD	14.64	10.82	12.01	12.59	Session 3-2	-7.08	-17.18, 4.24	16.05	11.63, 26.75	7.06	2.46, 9.78	0.87	0.66, 0.95
Pres(8s)avg2	Mean	30.05	31.10	29.85	30.34	Session 2-1	8.10	-5.52, 23.68	19.03	13.74, 31.99	9.63	3.74, 13.29	0.90	0.73, 0.97
	SD	14.40	11.51	11.27	12.47	Session 3-2	-3.48	-14.59, 9.08	17.15	12.41, 28.68	8.04	2.97, 11.12	0.89	0.69, 0.96
Pres(8s)avg3	Mean	29.56	30.69	29.69	29.98	Session 2-1	9.38	-4.02, 24.65	18.42	13.31, 30.91	8.99	3.41, 12.41	0.89	0.71, 0.96
	SD	13.97	10.46	10.88	11.87	Session 3-2	-3.66	-13.36, 7.13	14.72	10.69, 24.46	7.55	2.97, 10.37	0.90	0.73, 0.97
Force/N														
Force(8s)max	Mean	49.46	47.58	42.58	46.54	Session 2-1	0.86	-13.65, 17.81	22.26	16.01, 37.74	11.91	4.76, 16.44	0.91	0.76, 0.97
	SD	25.53	21.03	14.65	20.88	Session 3-2	-7.39	-16.80, 3.08	14.87	10.79, 24.71	9.91	4.34, 13.51	0.94	0.83, 0.98
Force(8s)avg2	Mean	40.01	46.07	39.99	42.02	Session 2-1	18.68	3.72, 35.79	19.04	13.75, 32.01	11.61	4.91, 15.92	0.93	0.80, 0.98
	SD	17.86	20.06	13.83	17.44	Session 3-2	-10.95	-18.20, -3.05	11.62	8.46, 19.14	10.11	4.69, 13.69	0.96	0.89, 0.99
Force(8s)avg3	Mean	42.21	45.08	38.85	42.04	Session 2-1	11.31	-4.45, 29.67	21.84	15.72, 36.98	11.69	4.68, 16.13	0.91	0.76, 0.97
	SD	20.22	19.51	13.02	17.88	Session 3-2	-10.91	-19.41, -1.51	13.86	10.07, 22.96	9.81	4.36, 13.34	0.94	0.84, 0.98

*:smallest effect from pure SD; CI: Confidence interval: CV: Coefficient of variation; SD: standard deviation

Table 6.18. Measures of reliability in the affected hand of participants with stroke with vision during the plateau phase (5s)

		Session 1	Session 2	Session 3	Mean 3 sessions		Change in mean (%)	90% CI	CV (%)	90% CI	Smallest effect (%)*	90% CI	ICC	90% CI
Pressure/kPa														
Pres(5s)max	Mean	39.33	41.26	41.00	40.53	Session 2-1	4.35	-7.28, 17.43	16.52	11.96, 27.57	10.40	4.46, 14.22	0.93	0.81, 0.98
	SD	15.20	14.66	13.92	14.60	Session 3-2	3.94	-14.38, 26.17	28.51	20.37, 49.13	7.87	-1.79, 11.48	0.74	0.38, 0.90
						Session 3-2#	-5.68	-13.89, 3.31	11.74	8.44, 20.04	9.15	4.17, 12.39	0.95	0.86, 0.98
Pres(5s)avg2	Mean	35.17	39.64	37.13	37.31	Session 2-1	11.92	-0.65, 26.07	16.66	12.07, 27.83	10.67	4.60, 14.59	0.93	0.82, 0.98
	SD	14.29	14.99	10.57	13.43	Session 3-2	0.16	-17.61, 21.75	28.74	20.53, 49.54	7.61	-2.09, 11.17	0.72	0.35, 0.90
						Session 3-2#	-9.48	-16.02, -2.42	9.58	6.90, 16.25	9.13	4.31, 12.32	0.97	0.90, 0.99
Pres(5s)avg3	Mean	36.07	38.27	37.87	37.40	Session 2-1	6.19	-5.04, 18.76	15.57	11.29, 25.92	10.75	4.74, 14.66	0.94	0.84, 0.98
	SD	14.65	13.95	11.81	13.52	Session 3-2	4.44	-13.93, 26.73	28.44	20.32, 48.99	7.76	-1.88, 11.33	0.74	0.38, 0.90
						Session 3-2#	-5.45	-12.57, 2.25	10.02	7.21, 17.01	9.17	4.30, 12.38	0.97	0.89, 0.99
Force/N														
Force(5s)max	Mean	56.91	58.50	54.54	56.65	Session 2-1	7.09	-4.28, 19.80	15.63	11.33, 26.02	12.78	5.83, 17.40	0.96	0.88, 0.99
	SD	28.76	23.66	15.01	23.18	Session 3-2	-0.31	-13.43, 14.79	20.03	14.44, 33.75	9.02	3.21, 12.52	0.88	0.68, 0.96
Force(5s)avg2	Mean	49.06	53.54	48.96	50.52	Session 2-1	11.05	0.85, 22.27	13.27	9.64, 21.95	14.50	6.85, 19.68	0.98	0.93, 0.99
	SD	24.13	24.33	15.88	21.81	Session 3-2	-0.32	-16.83, 19.47	26.40	18.91, 45.25	10.60	3.33, 14.88	0.86	0.62, 0.95
Force(5s)avg3	Mean	50.38	53.91	49.74	51.34	Session 2-1	9.78	0.19, 20.29	12.56	9.14, 20.74	13.70	6.48, 18.57	0.97	0.93, 0.99
	SD	25.20	23.47	15.11	21.71	Session 3-2	-0.11	-15.76, 18.44	24.67	17.70, 42.08	9.74	2.97, 13.67	0.85	0.61, 0.95

#:outlier removed; *:smallest effect from pure SD; CI: Confidence interval: CV: Coefficient of variation; SD: standard deviation

Table 6.19. Measures of reliability in the affected hand of participants with stroke without vision during the plateau phase (5s)

		Session 1	Session 2	Session 3	Mean 3 sessions		Change in mean (%)	90% CI	CV (%)	90% CI	Smallest effect (%)*	90% CI	ICC	90% CI
Pressure/kPa														
Pres(5s)max	Mean	39.90	41.80	39.48	40.39	Session 2-1	11.10	-2.86, 27.06	18.97	13.70, 31.89	8.89	3.27, 12.30	0.89	0.69, 0.96
	SD	19.12	14.42	14.48	16.15	Session 3-2	-6.30	-16.61, 5.29	16.29	11.80, 27.17	7.27	2.57, 10.07	0.87	0.67, 0.96
Pres(5s)avg2	Mean	36.65	38.32	36.90	37.29	Session 2-1	9.65	-2.90, 23.83	17.04	12.33, 28.48	10.20	4.30, 13.97	0.93	0.79, 0.97
	SD	18.72	14.93	12.70	15.65	Session 3-2	-1.43	-12.84, 11.46	17.24	12.48, 28.85	7.91	2.86, 10.94	0.88	0.68, 0.96
Pres(5s)avg3	Mean	36.45	37.74	36.91	37.04	Session 2-1	9.35	-4.42, 25.11	19.03	13.74, 31.99	9.35	3.56, 12.91	0.89	0.72, 0.96
	SD	17.69	13.39	13.29	14.93	Session 3-2	-2.07	-11.61, 8.50	14.18	10.30, 23.52	7.76	3.16, 10.63	0.91	0.76, 0.97
Force/N														
Force(5s)max	Mean	61.56	59.60	53.46	58.21	Session 2-1	1.92	-13.40, 19.94	23.45	16.85, 39.88	12.36	4.90, 17.08	0.91	0.75, 0.97
	SD	33.38	27.52	19.11	27.30	Session 3-2	-6.97	-16.86, 4.09	15.65	11.35, 26.07	10.30	4.48, 14.05	0.94	0.82, 0.98
Force(5s)avg2	Mean	50.78	57.35	50.23	52.78	Session 2-1	16.06	0.90, 33.49	19.85	14.32, 33.44	12.26	5.21, 16.82	0.93	0.81, 0.98
	SD	23.67	26.69	18.42	23.18	Session 3-2	-9.48	-16.94, -1.36	11.77	8.57, 19.39	10.70	4.99, 14.49	0.96	0.90, 0.99
Force(5s)avg3	Mean	52.58	56.00	48.81	52.46	Session 2-1	11.14	-5.14, 30.22	22.75	16.36, 38.62	12.07	4.80, 16.67	0.91	0.75, 0.97
	SD	26.02	25.36	16.92	23.14	Session 3-2	-9.60	-18.26, -0.03	13.91	10.10, 23.06	10.15	4.55, 13.80	0.95	0.85, 0.98

*:smallest effect from pure SD; CI: Confidence interval: CV: Coefficient of variation; SD: standard deviation

Table 6.20. Measures of reliability in the less affected hand of participants with stroke with vision during complete grasp duration (8s)

		Session 1	Session 2	Session 3	Mean 3 sessions		Change in mean (%)	90% CI	CV (%)	90% CI	Smallest effect (%)*	90% CI	ICC	90% CI
Pressure/kPa														
Pres(8s)max	Mean	42.55	36.90	36.93	38.80	Session 2-1	-8.75	-27.21, 14.40	33.99	24.14, 59.37	6.84	-3.61, 10.57	0.61	0.16, 0.85
	SD	21.99	11.74	10.97	15.73	Session 3-2	1.07	-8.13, 11.19	13.15	9.56, 21.74	7.21	2.95, 9.86	0.91	0.76, 0.97
Pres(8s)avg2	Mean	40.30	35.57	34.98	36.95	Session 2-1	-7.96	-26.05, 14.55	32.73	23.27, 56.99	6.83	-3.40, 10.47	0.62	0.18, 0.86
	SD	20.03	11.62	10.72	14.73	Session 3-2	-0.57	-8.5, 8.11	11.43	8.33, 18.82	7.36	3.21, 10.01	0.93	0.81, 0.98
Pres(8s)avg3	Mean	40.22	34.82	34.86	36.63	Session 2-1	-9.00	-26.78, 13.08	32.47	23.10, 56.51	6.79	-3.37, 10.41	0.63	0.19, 0.86
	SD	20.53	10.86	10.69	14.76	Session 3-2	0.75	-7.53, 9.77	11.73	8.54, 19.33	7.19	3.09, 9.79	0.93	0.80, 0.98
Force/N														
Force(8s)max	Mean	50.91	45.04	49.16	48.37	Session 2-1	-11.29	-25.01, 4.94	24.28	17.43, 41.38	7.49	-0.13, 10.76	0.78	0.45, 0.92
	SD	18.98	16.79	14.43	16.83	Session 3-2	11.52	-0.27, 24.70	15.55	11.27, 25.89	7.50	2.83, 10.34	0.89	0.70, 0.96
Force(8s)avg2	Mean	47.56	42.86	46.02	45.48	Session 2-1	-9.53	-23.91, 7.56	25.10	18.00, 42.87	7.14	-1.43, 10.37	0.75	0.40, 0.91
	SD	17.61	15.65	15.10	16.16	Session 3-2	8.27	-1.66, 19.21	13.25	9.64, 21.93	7.80	3.28, 10.64	0.92	0.78, 0.97
Force(8s)avg3	Mean	46.70	41.79	45.05	44.51	Session 2-1	-9.35	-23.71, 7.70	24.99	17.93, 42.68	7.22	-1.30, 10.46	0.75	0.41, 0.91
	SD	17.66	14.73	14.29	15.63	Session 3-2	8.81	-0.67, 19.20	12.52	9.11, 20.67	7.52	3.20, 10.25	0.92	0.79, 0.97

*:smallest effect from pure SD; CI: Confidence interval: CV: Coefficient of variation; SD: standard deviation

Table 6.21. Measures of reliability in the less affected hand of participants with stroke without vision during complete grasp duration (8s)

		Session 1	Session 2	Session 3	Mean 3 sessions		Change in mean (%)	90% CI	CV (%)	90% CI	Smallest effect (%)*	90% CI	ICC	90% CI
Pressure/kPa														
Pres(8s)max	Mean	36.44	37.25	35.10	36.26	Session 2-1	7.36	-3.03, 18.87	14.08	10.23, 23.36	10.37	4.66, 14.11	0.95	0.85, 0.98
	SD	17.37	13.49	8.99	13.71	Session 3-2	-1.78	-12.48, 10.24	16.11	11.67, 26.86	7.20	2.55, 9.98	0.87	0.67, 0.96
Pres(8s)avg2	Mean	34.49	36.07	32.09	34.22	Session 2-1	11.67	-0.57, 25.41	16.21	11.74, 27.03	10.82	4.72, 14.77	0.94	0.83, 0.98
	SD	17.68	13.16	9.79	13.93	Session 3-2	-8.70	-15.79, -1.02	11.02	8.03, 18.12	8.25	3.74, 11.18	0.95	0.86, 0.98
Pres(8s)avg3	Mean	34.16	34.37	32.47	33.67	Session 2-1	6.94	-5.07, 20.48	16.67	12.07, 27.84	10.46	4.48, 14.30	0.93	0.81, 0.98
	SD	17.15	12.12	8.93	13.17	Session 3-2	-2.38	-10.68, 6.69	12.19	8.87, 20.11	7.72	3.34, 10.50	0.93	0.81, 0.98
Force/N														
Force(8s)max	Mean	46.39	50.16	44.49	47.01	Session 2-1	4.45	-7.46, 17.89	16.96	12.28, 28.35	10.25	4.34, 14.04	0.93	0.80, 0.97
	SD	17.93	25.30	13.57	19.54	Session 3-2	-5.02	-17.35, 9.17	19.73	14.23, 33.22	9.02	3.25, 12.50	0.88	0.68, 0.96
Force(8s)avg2	Mean	42.79	47.82	40.85	43.82	Session 2-1	11.52	-2.13, 27.07	18.40	13.30, 30.87	11.23	4.76, 15.39	0.93	0.80, 0.98
	SD	20.28	24.68	12.71	19.85	Session 3-2	-8.24	-20.54, 5.97	20.47	14.75, 34.53	9.20	3.27, 12.78	0.88	0.68, 0.96
Force(8s)avg3	Mean	42.78	45.25	40.86	42.96	Session 2-1	5.04	-5.96, 17.34	15.40	11.16, 25.63	10.56	4.65, 14.40	0.94	0.84, 0.98
	SD	18.64	21.47	12.33	17.89	Session 3-2	-4.09	-15.62, 9.01	18.02	13.03, 30.21	8.86	3.38, 12.22	0.89	0.72, 0.96

*:smallest effect from pure SD; CI: Confidence interval: CV: Coefficient of variation; SD: standard deviation

Table 6.22. Measures of reliability in the less affected hand of participants with stroke with vision during the plateau phase (5s)

		Session 1	Session 2	Session 3	Mean 3 sessions		Change in mean (%)	90% CI	CV (%)	90% CI	Smallest effect (%)*	90% CI	ICC	90% CI
Pressure/kPa														
Pres(5s)max	Mean	50.06	44.39	45.23	46.56	Session 2-1	-8.96	-26.80, 13.24	32.62	23.20, 56.79	7.34	-3.13, 11.08	0.66	0.24, 0.87
	SD	23.38	14.81	13.22	17.71	Session 3-2	4.34	-8.05, 18.40	17.77	12.85, 29.77	7.38	2.40, 10.28	0.86	0.63, 0.95
Pres(5s)avg2	Mean	48.56	42.92	42.64	44.70	Session 2-1	-8.87	-27.71, 14.89	34.95	24.80, 61.20	7.17	-3.63, 11.03	0.62	0.18, 0.85
	SD	23.12	14.65	12.58	17.39	Session 3-2	1.96	-9.51, 14.89	16.70	12.09, 27.89	7.33	2.54, 10.17	0.87	0.66, 0.95
Pres(5s)avg3	Mean	48.06	41.69	42.90	44.22	Session 2-1	-10.51	-27.98, 11.19	32.44	23.08, 56.45	7.27	-3.13, 10.98	0.66	0.24, 0.87
	SD	22.90	13.76	12.89	17.12	Session 3-2	5.04	-6.30, 17.75	15.92	11.54, 26.54	7.38	2.70, 10.20	0.88	0.69, 0.96
Force/N														
Force(5s)max	Mean	62.39	55.20	60.84	**59.48**	Session 2-1	-11.95	-25.58, 4.18	24.32	17.45, 41.45	7.77	0.97, 11.11	0.79	0.48, 0.92
	SD	22.45	19.99	17.67	**20.13**	Session 3-2	13.40	1.28, 26.97	15.75	11.41, 26.24	7.73	2.95, 10.64	0.89	0.71, 0.96
Force(5s)avg2	Mean	57.13	50.33	56.72	54.73	Session 2-1	-13.17	-26.94, 3.20	25.04	17.96, 42.76	7.75	0.32, 11.12	0.78	0.46, 0.92
	SD	20.95	19.78	18.16	19.66	Session 3-2	15.79	3.89-29.06	15.07	10.93, 25.05	8.24	3.35, 11.29	0.91	0.76, 0.97
Force(5s)avg3	Mean	57.06	50.59	56.51	54.72	Session 2-1	-11.18	-25.20, 5.46	24.88	17.85, 42.47	7.85	0.82, 11.25	0.78	0.47, 0.92
	SD	21.30	18.49	17.83	19.27	Session 3-2	14.14	3.26, 26.16	13.84	10.05, 22.93	7.96	3.32, 10.88	0.92	0.78, 0.97

*:smallest effect from pure SD; CI: Confidence interval: CV: Coefficient of variation; SD: standard deviation

Table 6.23. Measures of reliability in the less affected hand of participants with stroke without vision during the plateau phase (5s)

		Session 1	Session 2	Session 3	Mean 3 sessions		Change in mean (%)	90% CI	CV (%)	90% CI	Smallest effect (%)*	90% CI	ICC	90% CI
Pressure/kPa														
Pres(5s)max	Mean	44.72	45.41	43.46	44.53	Session 2-1	7.16	-3.69, 19.24	14.82	10.75, 24.63	10.67	4.76, 14.53	0.95	0.85, 0.98
	SD	21.18	16.38	11.23	16.76	Session 3-2	-0.15	-10.99, 12.01	16.03	11.62, 26.73	7.28	2.62, 10.08	0.88	0.68, 0.96
Pres(5s)avg2	Mean	41.86	42.78	39.81	41.48	Session 2-1	7.63	-3.27, 19.75	14.81	10.75, 24.61	10.89	4.88, 14.82	0.95	0.85, 0.98
	SD	20.98	15.94	12.07	16.73	Session 3-2	-3.80	-12.59, 5.86	13.19	9.59, 21.82	8.41	3.65, 11.46	0.93	0.81, 0.98
Pres(5s)avg3	Mean	41.56	41.52	40.15	41.08	Session 2-1	6.10	-5.42, 19.01	16.03	11.61, 26.72	10.52	4.57, 14.36	0.94	0.82, 0.98
	SD	20.57	14.64	11.07	15.92	Session 3-2	0.00	-8.43, 9.20	12.06	8.78, 19.89	7.72	3.36, 10.50	0.93	0.81, 0.98
Force/N														
Force(5s)max	Mean	56.69	60.92	54.89	57.50	Session 2-1	3.95	-8.40, 17.97	17.78	12.86, 29.79	10.34	4.30, 14.18	0.92	0.78, 0.97
	SD	22.45	30.86	17.31	24.19	Session 3-2	-3.50	-15.99, 10.85	19.64	14.17, 33.07	9.09	3.31, 12.60	0.88	0.69, 0.96
Force(5s)avg2	Mean	52.36	56.70	51.11	53.39	Session 2-1	6.98	-7.25, 23.39	20.28	14.62, 34.20	11.45	4.70, 15.75	0.92	0.77, 0.97
	SD	24.70	30.51	15.35	24.33	Session 3-2	-1.47	-15.47, 14.84	21.93	15.78, 37.15	9.19	3.03, 12.83	0.86	0.64, 0.95
Force(5s)avg3	Mean	52.19	54.87	50.60	52.56	Session 2-1	4.23	-7.17, 17.04	16.18	11.72, 26.98	10.55	4.58, 14.41	0.94	0.82, 0.98
	SD	22.79	26.42	15.65	22.08	Session 3-2	-1.98	-13.71, 11.35	17.93	12.97, 30.06	8.90	3.42, 12.28	0.90	0.72, 0.96

*:smallest effect from pure SD; CI: Confidence interval: CV: Coefficient of variation; SD: standard deviation

Table 6.24. Summary of evaluation of measures of maximal tactile pressures/forces against reliability criteria in the affected hand of participants with stroke

Sessions	Measures of maximal tactile pressure/force over complete grasp duration	Complete grasp duration (8s) with vision			Complete grasp duration (8s) without vision			Measures of maximal tactile pressure/force over complete grasp duration	Plateau phase (5s) with vision			Plateau phase (5s) without vision		
		Change in mean (%)	CV (%)	ICC	Change in mean (%)	CV (%)	ICC		Change in mean (%)	CV (%)	ICC	Change in mean (%)	CV (%)	ICC
Session 2-1	Pres(8s)max	good	x	very good	x	x	good	Pres(5s)max	very good	x	very good	x	x	good
Session 3-2		very good	x	x	good	x	good		very good	x	x	good	x	good
Session 3-2#		good	acceptable	very good					good	good	Very good			
Session 2-1	Pres(8s)avg2	good	x	very good	good	x	very good	Pres(8s)avg2	x	x	very good	good	x	very good
Session 3-2		very good	x	x	very good	x	very good		very good	x	x	very good	x	very good
Session 3-2#		good	acceptable	very good					good	good	Very good			
Session 2-1	Pres(8s)avg3	good	acceptable	very good	good	x	very good	Pres(5s)avg3	very good	x	very good	good	x	very good
Session 3-2		very good	x	x	very good	acceptable	very good		very good	x	x	very good	acceptable	very good
Session 3-2#		good	acceptable	very good					good	good	Very good			
Session 2-1	Force(8s)max	good	x	very good	very good	x	very good	Force(5s)max	very good	x	very good	very good	x	very good
Session 3-2		very good	x	good	good	acceptable	very good		very good	x	good	good	x	very good
Session 2-1	Force(8s)avg2	x	acceptable	very good	x	x	very good	Force(5s)avg2	x	acceptable	very good	x	x	very good
Session 3-2		very good	x	good	x	acceptable	very good		very good	x	good	good	acceptable	very good
Session 2-1	Force(8s)avg3	good	acceptable	very good	x	x	very good	Force(5s)avg3	very good	acceptable	very good	x	x	very good
Session 3-2		very good	x	good	x	acceptable	very good		very good	very good	good	good	acceptable	very good

#:outlier removed;

Table 6.25. Summary of evaluation of measures of maximal tactile pressures/forces against reliability criteria in the less affected hand of participants with stroke

Sessions	Measures of maximal tactile pressure/force over complete grasp duration	Complete grasp duration (8s) with vision			Complete grasp duration (8s) without vision			Measures of maximal tactile pressure/force over complete grasp duration	Plateau phase (5s) with vision			Plateau phase (5s) without vision		
		Change in mean (%)	CV (%)	ICC	Change in mean (%)	CV (%)	ICC		Change in mean (%)	CV (%)	ICC	Change in mean (%)	CV (%)	ICC
Session 2-1	Pres(8s)max	good	x	x	good	good	very good	Pres(5s)max	good	x	x	good	good	very good
Session 3-2		very good	acceptable	good	very good	x	good		very good	x	good	very good	x	good
Session 2-1	Pres(8s)avg2	good	x	x	x	x	very good	Pres(5s)avg2	good	x	x	good	good	very good
Session 3-2		very good	acceptable	very good	good	good	good		very good	x	good	very good	good	very good
Session 2-1	Pres(8s)avg3	good	x	x	good	x	very good	Pres(5s)avg3	x	x	x	good	good	very good
Session 3-2		very good	acceptable	very good	very good	good	good		very good	x	good	very good	good	very good
Session 2-1	Force(8s)max	x	x	good	very good	x	very good	Force(5s)max	x	x	good	very good	good	very good
Session 3-2		x	x	good	very good	x	good		x	x	good	very good	good	good
Session 2-1	Force(8s)avg2	good	x	good	x	x	very good	Force(5s)avg2	x	x	good	good	good	very good
Session 3-2		good	acceptable	very good	good	x	good		x	x	very good	very good	good	good
Session 2-1	Force(8s)avg3	good	x	good	very good	x	very good	Force(5s)avg3	x	x	good	very good	good	very good
Session 3-2		good	acceptable	very good	very good	x	good		x	good	very good	very good	good	good

6.4.2.3 Most reliable measures of maximal tactile pressures or forces

A visual inspection of the scatter plots of the test-retest raw scores indicated that the test performance of one healthy participant (ID26C) in the nondominant hand and one participant with stroke (IDK11S) in the affected hand were outliers for testing session 3 with vision. When these outliers were removed, the indices of reliability were acceptable to very good using all measures of maximal tactile pressures for between-day sessions with vision. The indices of reliability and reliability criteria were reported without the outlier data in Tables 6.10, 6.12, 6.15, 6.16, 6.18 and 6.24. A larger number of indices of reliability that met the reliability criteria were observed in healthy participants than those with stroke.

In healthy participants, the number of indices of reliability that met the reliability criteria was greater for measures of maximal tactile pressures than measures of maximal tactile forces in both the dominant and nondominant hands. In the dominant hand, there was better reliability with vision than without vision whereas in the nondominant hand, reliability was similar with and without vision for maximal tactile pressure measures. For both hands, reliability was similar for within-day and between-day sessions for measures of maximal tactile pressures. For both hands, reliability was similar during the complete grasp duration (8s) and during the plateau phase (5s) for measures of maximal tactile pressures. Using the highest value, mean of two or three trials, the indices of reliability met the reliability criteria, though the highest value and the mean of three trials to estimate maximal tactile pressures had greater reliability than the mean of two trials. Therefore, in healthy individuals, Pres(8s)max, Pres(8s)avg3 , Pres(5s)max and Pres(5s)avg3 were most reliable for within and between-day sessions.

In participants with stroke, the number of indices of reliability that met the reliability criteria was greater for measures of maximal tactile pressures than measures of maximal tactile forces in both the affected (pressures|forces:54|51) and less affected hands (pressures|forces: 52:48). In the affected hand, there was better reliability with vision than without vision while in the less affected hand, reliability was greater without vision than with vision for measures of maximal tactile pressures. In the affected hand, reliability was greater

for between-day sessions than within-day sessions for measures of maximal tactile pressures. For both hands, reliability was similar during the complete grasp duration(8s) and during the plateau phase(5s) for maximal tactile pressures. Using the mean of three trials to estimate maximal tactile pressure had greater reliability that the highest value or the mean of two trials. Therefore, in people with stroke, Pres(8s)avg3 and Pres(5s)avg3 were most reliable for between-day sessions.

Measures of maximal tactile pressure using Pres(8s)avg3 was found to be the most consistently reliable across healthy participants and participants with stroke in all conditions, except in the less affected hand of people with stroke during within-day sessions with vision. Therefore, for the purpose of this study (and chapter 5), measures using Pres(8s)avg3 were used for further analysis. The raw scores of Pres(8s)avg3 of healthy participants and participants with stroke are reported in Appendix 6.2.

6.4.2.4 Systematic error

The systematic error was evaluated for measures of pressure using the average of three repetitions during the complete grasp duration (8s) in healthy participants and those with stroke, with or without vision for within-day and between-day sessions. The systematic errors in the healthy participants were not statistically significant for either pair of consecutive sessions in both hands with vision (range of systematic error: -2.68, 5.29%; range p value: 0.30, 1.00) or without vision (range of systematic error: -1.81, 5.38%; range p value: 0.10, 0.410). In participants with stroke, the systematic errors were not statistically significant for either pair of consecutive sessions in both hands with vision (range of systematic error:-9.43, 6.67%; range p value: 0.44, 0.72) or without vision (range of systematic error: -3.73, 8.97%; range p value: 0.19, 0.31). Table 6.26 summarises the statistical significance of the Student t-test analyses of the difference in means (log-transformed data) between the two consecutive testing occasions. Inspections of the scatter plots for both pairs of consecutive testing sessions in healthy participants and those with stroke showed that the points were all clustered close to the regression line, more evident in healthy people. Two examples are illustrated of the dominant hand in healthy participants (figure 6.2) and the affected hand in people with stroke (figure 6.3) without vision for within-day sessions.

Table 6.26. Average difference between consecutive sessions

Group	Upper limb		Average difference between consecutive sessions		P value
			Session 2-1	Session 3-2	
Healthy	Dominant	Vision	-2.68	2.01	0.30
		No vision	2.85	-1.63	0.41
	Nondominant	Vision*	6.84	-0.10	0.13
		No vision	5.38	-1.81	0.10
Stroke	Affected	Vision*	6.67	-7.45	0.07
		No vision	8.97	-3.73	0.19
	Less affected	Vision	-9.43	0.75	0.44
		No vision	7.10	-1.79	0.31

*Outlier removed

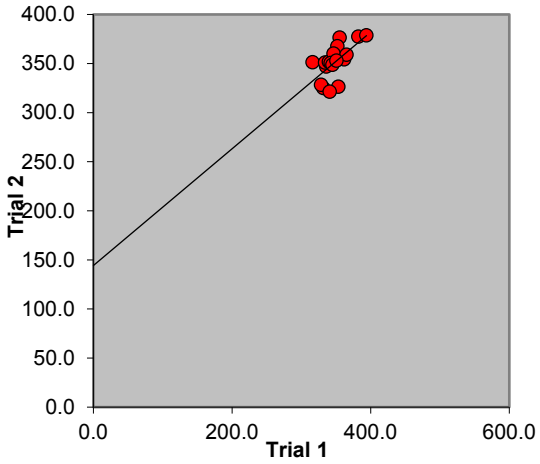


Figure 6.2. Scatter plot of log-transformed data of dominant hand of healthy participants without vision during complete grasp duration(8s)

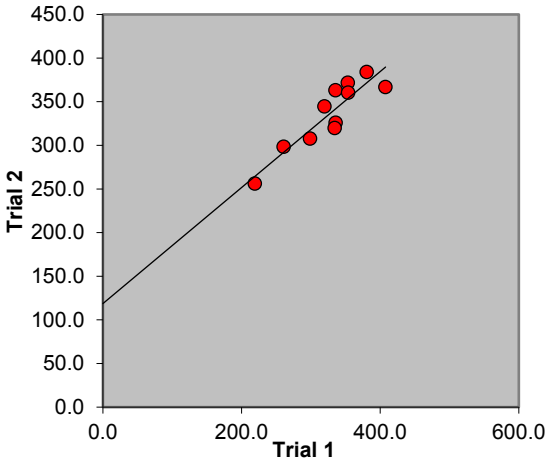


Figure 6.3. Scatter plot of log-transformed data of affected hand of participants with stroke without vision during complete grasp duration(8s)

6.4.2.5 Heteroscedasticity

Measures of pressure using the average of three trials during the complete grasp duration (8s) were examined for heteroscedasticity. The analysis revealed that there was a uniform scatter of maximal tactile pressures values after log-transformation of the data in the scatterplots in both populations, with or without vision for within-day and between-day sessions. Two examples are illustrated representing the dominant hand in healthy participants (figure 6.4) and the affected hand in people with stroke (figure 6.5) without vision for within-day sessions.

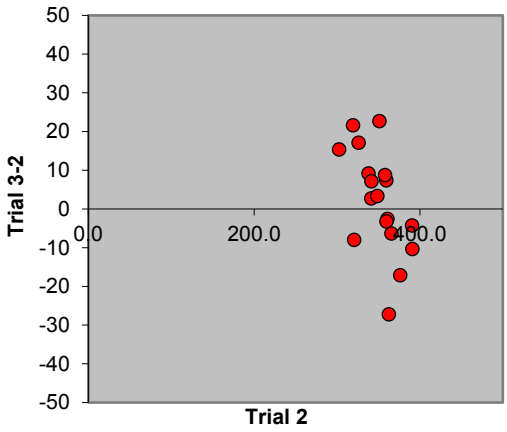


Figure 6.4. Scatter plot of log-transformed data of dominant hand of healthy participants without vision during complete grasp duration(8s)

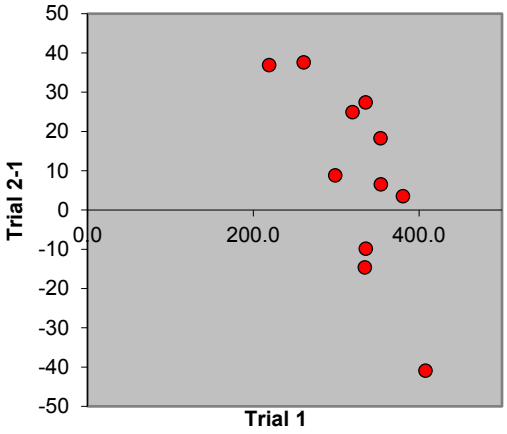


Figure 6.5. Scatter plot of log-transformed data of affected hand of participants with stroke without vision during complete grasp duration(8s)

6.4.3 Results of secondary objectives

6.4.3.1 Differences in maximal tactile pressures between vision conditions and between hands

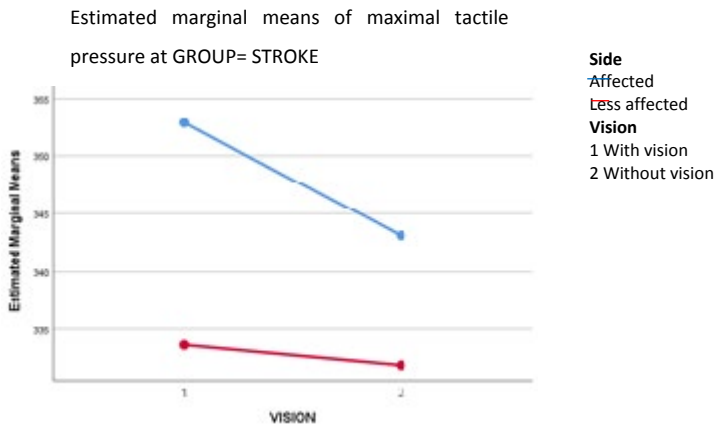
In healthy participants, a 2 (VISION) X 2 (SIDE) X 3 (SESSION) ANOVA for repeated measures on all three factors indicated no statistically significant effects except for that due to VISION, i.e., mean maximal tactile pressures tested with vision were significantly higher than those without vision ($F(1,17) = 10.79$, $p = 0.00$). There were no significant differences between the dominant and nondominant hand ($p=0.13$). There were no significant interactions between laterality effects and vision conditions ($p= 0.56$).

In participants with stroke, 2 (VISION) X 2 (SIDE) X 3 (SESSION) ANOVA for repeated measures on all three factors indicated no statistically significant effects except for that due to SIDE, i.e., mean maximal tactile pressures were significantly lower when performing with the affected side compared to the less affected side ($F(1,10) = 7.94$, $p = 0.02$). In addition, significant interactions effects were found with VISION; maximal tactile pressures were significantly higher in tests with vision than those without ($F(1,10) = 11.76$, $p = 0.01$). There were no interaction effects between laterality and vision conditions ($p= 0.24$).

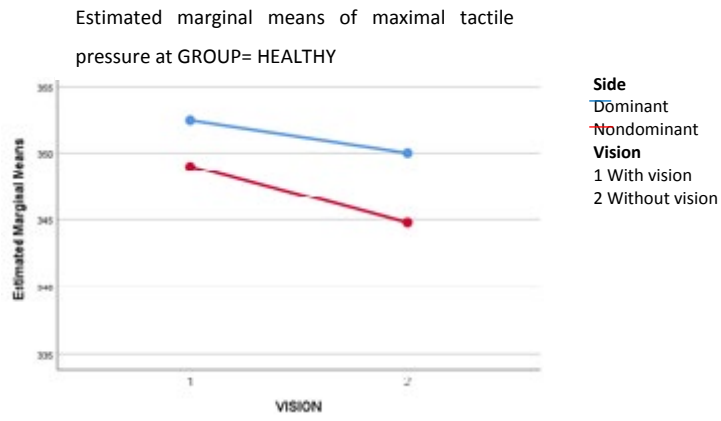
Higher mean maximal tactile pressures were observed in the less affected side (mean:348; standard error: 8; CI:331, 365) compared to the affected side (mean: 332; standard error: 9; CI: 314, 352) in the group with stroke and the dominant side (mean: 351; standard error: 7; CI: 338, 365) compared to the nondominant side (mean: 347; standard error: 7; CI: 332, 362) in the healthy group, based on log-transformed data. The laterality effect based on pathology, i.e., affected versus less affected side in the group with stroke (4.5%) was 3.7 times more pronounced than the laterality effect based on dominance, i.e., dominant versus nondominant side in the healthy (1.2%) (figures 6.6 a and b).

6.4.3.2 Investigation of values of maximal tactile pressures between healthy participants and participants with stroke

There was no significant difference between the affected side in people with stroke and the nondominant side in healthy people, although the difference closely approached accepted standards of statistical significance ($F(1,27) = 4.03$, $p = 0.06$). A statistically significant laterality effect ($F(1,27) = 12.87$, $p = 0.001$) was found when pooling over both groups, i.e., pooled data from the dominant side in healthy people and less affected side in those with stroke compared with nondominant side in healthy people and affected side in group with stroke. A statistically significant effect of vision was also observed when pooled over both groups ($F(1,27) = 24.36$, $p < 0.001$). An effect of testing with vision appears more pronounced for the less affected side than for the more affected side in the group with stroke whereas in the healthy group, there is little apparent effect of vision on the dominant and nondominant values (figure 6.6 a and b). This apparent interaction of the nature of laterality effect with vision [2 (GROUPS) x 2 (SIDE) x 2 (VISION)] did not yield a significant interaction effect to confirm it ($F(1,27) = 2.77$, $p = 0.11$).



a



b

Figures 6.6 a and b. Estimated marginal means of pressure measures in the group with stroke and healthy group

6.5 DISCUSSION

This study evaluated the reliability indices of measures of maximal tactile pressures and forces during sustained grasp task using a TactArray cyclinder device in healthy individuals and those with stroke.

6.5.1 Changes in mean

In healthy individuals, no significant changes in means were observed in the dominant hand but some changes were found in the nondominant hand for within-day sessions. For instance, the confidence intervals overlapped zero in measures using Pres(8s)avg3 without vision and using Pres(5s)max with vision. These observations could suggest a learning or fatigue effect after the second testing session. It is noteworthy that the lower limits of the confidence intervals of these indices approached the value zero, suggesting that the lack of statistical significance could be due to the small sample size[284]. This was further supported by the analysis of the systematic errors indicating no significant change between the within-day sessions. Systematic error resulting from some degree of learning are not surprising because none of the participants had any previous experience with performing maximal voluntary contractions using the TactArray device or performing these contractions without vision. Consequently, one practice trial is suggested prior to testing maximal tactile pressures with a TactArray device as recommended in other studies on measurement of grip strength to ensure higher reliability of the measures by minimising any learning effects and allowing familiarisation with the task prior to real evaluation[601]. Future trials could investigate the impact of practice-based improvements on repeated maximal tactile pressures in larger samples.

There were no significant changes in mean for any measures of maximal tactile pressures in people with stroke in either hand for within-day or between-day sessions, suggesting no important learning or fatigue effects. This was surprising as one might have expected some fatigue effects in stroke survivors, particularly for the within-day assessments. This implied that this testing protocol using the TactArray device was appropriate for people with stroke with little or no confounding effect of fatigue.

6.5.2 Coefficients of variation

Typical errors, expressed as coefficients of variations, reflect the amount of variation in an individual participant's score from one testing session to another and are therefore critically important in enhancing the reliability of measures[281,283,284]. In this study, none of the

coefficients of variation in either groups were < 5%, which is the target recommended by Hopkins[283,284]. For instance, in the group with stroke, the coefficients of variation ranged from 11.73-14.72% for both hands for between-day sessions using Pres(8s)avg3. One reason for these coefficients of variations (typical errors) being > 5% could be that the trials included in estimating maximal tactile pressures using a mean of two or three trials did not consider the magnitude of the relative difference between each trial assessed within each testing session for each participant. Consequently, this could have reduced the reproducibility of the trials within each testing session, which could have contributed to an overestimation of the typical errors. Any variation greater than 10 to 15% between the repeated trials is likely to compromise the statistical stability of the measures[604]. In the absence of other studies reporting the coefficients of variation of pressure sensor-based devices, it is difficult to determine whether the criteria for coefficient of variation set in this study (<15% as acceptable) is typical of measures provided by other sensor-based devices or of maximal grip strength in general. Given that fluctuations in functional performance over short intervals have been reported after stroke[322,325,536], setting the coefficient of variation at < 5% could be too stringent and not realistic for people with stroke. Therefore, to increase the reproducibility of repeated trials within a testing session, it is suggested that the relative difference in maximal tactile pressure between the trials are within 10%. Otherwise, additional trials are proposed until the trials are reproducible[255]. Furthermore, future studies should clearly state criteria that they use in their assessments of reliability.

It is also possible that the coefficients of variations were larger than 5% due to variations resulting from the randomisation of the order of hand testing. It has been suggested that randomisation of testing order reduces the impact of learning or practice effects[255], however randomisation of testing order may compromise performance, particularly in a population with stroke where task performance with the less affected hand first could serve as an appropriate form of learning to facilitate task performance with the affected hand. Consequently, the randomisation of testing order is likely to introduce inconsistencies in the assessment procedure, potentially increasing measurement errors. Hence, it is suggested that future trials evaluating repeatability of measures of maximal tactile pressures use the same order of testing across all testing sessions for more stable measures.

The coefficients of variations were satisfactory, according to the set criteria, in healthy individuals between the consecutive testing sessions using Pres(8s)avg3 in both hands with and without vision. Large differences in coefficients of variation were observed in the stroke group across the testing sessions, indicating inconsistent responses from the participant. For instance, in people with stroke, coefficients of variation were larger (approximately twice) in between-day sessions than in within-day sessions using Pres(8s)avg3 in the affected hand with vision and without vision. The differences in coefficients of variations between the consecutive testing sessions in the affected hand were smaller without vision than with vision. For instance, 10 out of 11 participants with stroke showed variations in the magnitude of maximal tactile pressure > 10% in at least one of the 3 trials in one of the 3 testing sessions using Pres(8s)avg3 with the affected hand with vision (range of variations in contact area between trials: 0.06, 30.37%) and without vision (range of variations in contact area between trials: 0.44, 28.27%). In the less affected hand, the differences in coefficients of variation were smaller (approximately half) in between-day sessions than in within-day sessions using Pres(8s)avg3 with vision. The differences in coefficients of variations between the consecutive testing sessions in the less affected hand were smaller without vision than with vision. The differences between the affected and the less affected hand could be due to the lack of ability to perform the task in a consistent manner due to more pronounced deficits in grasp performance in the affected hand than in the less affected hand. These observations suggest that in people with stroke, evaluating both hands without vision could provide more comparable measures for within-day and between-day sessions.

This study found that some measures of maximal tactile pressures had very good ICCs with unsatisfactory coefficients of variations, such as in the affected hand of the group with stroke using Pres(8s)max and Pres(8s)avg2 with and without vision. The good reliability indicated by the ICCs could result from the extent of heterogeneity of the sample, i.e., if participants' scores vary from each other (wide range of scores), the ICC values will likely be high, even when measurement errors are large[281,283,285]. Therefore, knowledge of coefficients of variation are necessary for appropriate interpretation of changes in task performance. To

state that a participant's performance has changed from the last assessment, the measured change needs to be larger than the measurement error[605]. For example, for the dominant hand of healthy people, a difference in the within-day session needs to be more than 11.15% when assessed with vision and 11.59% without vision to exceed the measurement error, so as to detect a genuine change in 90% of the observations. When assessed on different days, changes in maximal tactile pressures need to be more than 9.83% when assessed with vision and 12.75% without vision to be considered meaningful. In people with stroke, if the intention is to use measures of maximal tactile pressures for the affected hand before and after an intervention, the post-intervention change needs to be greater than 9.52% when assessed with vision and 14.72% without vision to be considered as true change. Therefore, the coefficients of variation could help identify people who truly respond to an intervention so as to gain better understanding of the interaction between participants' characteristics and the intervention components[606].

In most studies investigating object manipulation and grasp strength, it is measures of force that are predominantly reported[607]. In this study, the coefficients of variation were relatively large and unsatisfactory for measures of maximal tactile forces as compared to the higher reliability for measures of maximal tactile pressures in both groups. Inconsistency in the magnitudes of maximal tactile forces could be due to the variability in the contact area across the trials since finger positioning was not restricted to specific locations on the TactArray sensors. For instance, in the dominant hand of healthy participants, 17 of the 18 participants have shown variations in contact area greater > 10% in at least one of the 3 trials of the three testing sessions (range of variations in contact area between trials: 0.47, 59.00%). This variability across trials could indicate that the central nervous system is not limited to performing the task in one unique way but makes provision for co-variations in variables required to satisfy the task goals[608]. Moreover, based on the concept of motor abundance[609,610], the total grip force during the task could be consistent in each trial due to force sharing, despite the different contribution of individual fingers [611,612]. Thus, normalising the tactile force to the contact area could have resulted in large random errors. Alternately, to obtain the tactile pressures, the contact areas were controlled such that the extent of variations in measures of maximal tactile pressure were minimised resulting in satisfactory

reliability. Other studies using tactile sensor arrays in a data sensor glove[613] and robotics[614] also found that pressure measurements were more appropriate than force measurements to evaluate performance during grasping. Additionally, evaluation of grip strength commonly use power grips or grips[393,615,616] with restrict finger positioning and contact areas[617,618] to maintain the internal consistency of task performance but limit the ecological validity of grasping. These observations suggested that the TactArray device provided more reliable maximal tactile pressures as compared to tactile force measures when performing a cylindrical grasping task.

The analysis of the log-transformed data provided the best estimate of typical error which was appropriately expressed as percent typical error or CV%[284,503]. This was demonstrated by the absence of heteroscedasticity, as evident by the even spread of maximal tactile pressures/forces values after log-transforming the data indicating that the percent typical error (CV%) was independent of the magnitude of maximal tactile pressures/forces obtained, i.e., test-retest error was similar for all participants within the healthy group.

6.5.3 Smallest detectable change

The smallest detectable changes were smaller than the coefficients of variations in both groups. Consequently, the smallest detectable change value obtained cannot necessarily be interpreted as a meaningful change. Instead, it is suggested that the coefficients of variations are used as the threshold to interpret whether the magnitudes of change in measures of maximal tactile pressures are meaningful after an intervention. Accordingly, a participant who demonstrates a change in maximal tactile pressures more than the coefficients of variation is viewed as benefitting from the intervention. It is also suggested that future trials evaluate the magnitudes of the smallest detectable changes and the coefficients of variations in a larger sample or more testing sessions are required to reduce the extent of measurement error[284].

6.5.4 ICCs

Intra-day and inter-day reliability of performance measures are commonly evaluated because of the differences in their applications in research trials and clinical practice. ICCs evaluate agreement between repeated measurements such that a high ICC can result from participants preserving their rank in a sample of test-retest scores[619]. This is appropriate for determining the reliability of data to be used in observational studies but has less application to the reliability required to evaluate the effects of an intervention. ICCs are also influenced by outlier scores[619]. This was evident in this study because exclusion of the outliers from the reliability analysis resulted in much higher ICC values.

The reliability of a measure varies under different experimental conditions such as the properties of the task, the order of task administration, and the number of trials[620]. The current study indicated that the behaviour of the ICCs varied with regards to the estimate of maximal grasp, side tested, the visual conditions and the group in which the test was being conducted as reported in Tables 6.6-6.25. For instance, in people with stroke, differences in the magnitude of ICCs were not particularly evident between hands or between visual conditions except for the less affected hand with vision where ICCs for within-day sessions had a smaller ICC than in the other measures. Furthermore, in people with stroke, the ICCs were similar or smaller for within-day sessions than for between-day sessions in both hands, with and without vision using Pres(8s)avg3. The higher ICCs could result from participants' performance being more consistent such that there was a reduction in between-tests variances arising from a decrease in measurement errors over the repeated measurements. Therefore, the findings of this study indicate that ICCs are subject to methodological variations that need to be specified when estimating the ICCs.

6.5.5 Complete grasp duration and plateau phase

Few studies have compared the differences in grip performance after stroke compared to healthy individuals using short duration maximum voluntary contractions[252,574,575]. This study therefore addresses a gap in the literature in exploring differences in sustained grip performance between these groups. In this study, maximal

tactile pressures during complete grasp duration and during the plateau phase were reliable in both groups. Similarly, reliability of grasp measures during the plateau phase of a sustained grasp was demonstrated using a multiaxis profile dynamometer[594]. Other studies have emphasised the need to assess other aspects of grip strength besides instantaneous maximum voluntary contractions[571,621]. Findings from this study highlight the importance of evaluating sustained grasp performance over complete grasp duration to identify specific grip control deficits during the build-up phase (from object contact up to stabilisation of grip) and during object release. The pressure sustained across the plateau phase could be used to characterise grip endurance, which is required to perform activities of daily living such as carrying a shopping bag and mopping the floor[622].

6.5.6 Number of trials

The findings of this study indicate that the repetition with the highest value of maximal tactile pressure and the average pressure of the three repetitions have demonstrated high reliability during complete grasp duration with vision in both hands in the healthy group. For instance, maximal tactile pressures using Pres(8s)max was higher (6.72%) than using Pres(8s)avg3 in the dominant hand with vision. Similarly, amongst people with stroke, maximal tactile pressures using Pres(8s)max was higher (5.92%) than using Pres(8s)avg3 in the less affected hand with vision. Other studies evaluating maximum voluntary isometric contractions have demonstrated the suitability of both these methods to maximise test-retest reliability using hand dynamometers with short and sustained durations[252,595,623]. Therefore, these findings emphasize the importance of reporting the method used to analyse the sensor data, i.e., whether the highest pressure or an average pressure was used, due to the difference in maximal tactile pressure between both methods.

6.5.7 Impact of testing with and without vision

The development of maximal voluntary contractions during grasping could be influenced by visual conditions. This study found significantly larger magnitudes of maximal tactile pressures with vision compared to without vision conditions in both healthy individuals and those with stroke, with the effects more evident after stroke. These observations are

consistent with another study in healthy young adults that demonstrated that there was significantly greater force production during isometric contractions of the index finger in the presence of visual feedback[577]. This could be because when both vision and tactile stimuli are present, they compete for access to processing and attention resources of the brain[624] whereby the impact of vision is more powerful than tactile perception because the neural representations of visual correlates elicit higher levels of activation in the brain as compared to tactile stimulus[625]. Consequently, this could imply that in the absence of vision, tactile somatosensory information alone might induce brain activity levels insufficient to optimise maximal voluntary contractions, especially in those with impaired somatosensation thereby resulting in smaller motor output.

6.5.8 Differences in values of maximal tactile pressures between sides in healthy participants and participants with stroke

This study found a significant difference in the magnitude of maximal tactile pressures between the affected and less affected sides in the stroke group but no significant difference between the dominant and nondominant sides in healthy people, consistent with other studies[239,252,571]. A comparison between the affected hand in the stroke group and the non-dominant hand in heathy people showed a lack of statistical difference. This finding was contradictory to other studies that found a significant difference in grip maximal voluntary contractions between the paretic hand after stroke and the dominant or nondominant hand in healthy group[252,574,575]. It is noteworthy that in this study the difference between the affected hand in stroke and non-dominant hand in healthy was close to acceptable standards of statistical significance indicating that it is possible that the difference could be significantly more pronounced if a larger sample size is used.

It could be argued that the difference between the group with stroke and the healthy group in this study could have been due to hand dominance and not due to deficits post-stroke. However, this is unlikely since the affected side in the group with stroke was the dominant side in 5 of the 11 cases such that the effect of dominance in the stroke sample was in effect controlled by averaging over this 5:6 split. This was reinforced by the laterality effects

based on deficits post-stroke being 3.69 times more pronounced than the laterality effect based on dominance. These findings suggested the TactArray device could be useful in characterising deficits in grip strength after stroke. A larger study with statistical power is required to clarify the difference between the affected hand after stroke and the nondominant hand in healthy people. Further analysis could also be done to explore the difference between the less affected hand after stroke with the nondominant hand in healthy people to determine any ipsilateral deficits.

Another reason for the lack of difference between the group with stroke and the healthy group in this study could be due to gender differences in grip strength. Both groups had gender bias since the healthy group contained predominantly women (66.7%) while the group with stroke contained predominantly men (63.6%). Previous studies have demonstrated that female grip strength was 60% to 70% less than male grip strength during a power grip with the Jamar dynamometer in younger adults (19-62 years)[626] and in older adults (68-88 years)[627]. Additionally, given that males have larger hand sizes than females[628], the size of the fingerpads are likely to be proportionally larger which is expected to contribute to larger tactile pressures in the group with stroke as compared to the healthy group. However, the outcome assessments in this study did not incorporate anthropometric measures with regards to hand size. It is noteworthy that analysis of hand anthropometric indices have provided conflicting findings on whether larger hand size with regards to the hand length, hand width, wrist circumference and palm length produce stronger total grip strength, as compared to a smaller hand[622,626,629,630]. It is therefore suggested that future studies explore the influences of anthropometric variations and gender influences on grip strength evaluations.

6.5.9 Implications for research and clinical practice

The TactArray device provides reliable intra-day and inter-day measures of maximal tactile pressures. Therefore, it could be used to monitor incremental changes in grip performance in stroke survivors during a rehabilitation session as well as evaluating participants' or patients' responses to the effect of an intervention over a period of time. Grip

strength data provided by the TactArray sensors could be useful to inform decisions in clinical practice and in cross-sectional studies investigating effectiveness of intervention. Pressure array data is considered sufficiently robust to be used as primary outcome measures in clinical trials[631,632].

The pressure-time profile provided by TactArray could be dissected to provide information on the pressure build-up from point of contact to the plateau phase, pressure distribution over the plateau phase, maximum pressure exerted across the grip, and pressure variability during the plateau phase. The customised MATLAB script is appropriate and useful for data processing. The script provides the momentary tactile pressures and forces over every second of the grip duration to identify variability in grasp performance. Additionally, the display of the pressure distribution maps by the TactArray enables the estimation of the contributions to each finger involved in the grip[274,566] which could be extracted by modifying the current Matlab script. Therefore, the TactArray sensors can help identify which aspects of grip strength are affected so that interventions can be tailored to target those specific deficits. This is valuable for clinical practice and research trials as standard clinical tools like the Jamar cannot provide information on sustained grip strength variations but report only maximum instantaneous force of exertion[255].

6.5.10 Limitations

This study was limited by the sample size utilised and the three testing sessions conducted. Hopkins[284] recommends a sample size of 50 participants and at least four testing sessions to minimise the extent of typical errors. Furthermore, this study was limited to only a cylindrical object as it could easily be wrapped with pressure sensors such as the TactArray[633-635]. Moreover, only measures of normal pressures and forces were obtained using the TactArray because it is unable to separately quantify tangential or shear forces during loading. The cylindrical grasping task utilised in the current study differed from commonly performed grasping because the participants were instructed to use only the fingerpads without any palm contact.

6.5.11 Recommendations for future trials

To determine the difference in maximal tactile pressures between healthy people and those with stroke, a sample size with sufficient statistical power is required. A larger sample size will also help to establish normative data in the healthy group to facilitate characterisation of deficits in grasp performance in stroke survivors. It is desirable for the sample to have a balanced proportion of male and female participants to minimise gender bias effects. Additionally, it would be valuable to evaluate other psychometric properties such as the floor and ceiling effects as well as the responsiveness of maximal tactile pressures in people with stroke. Validity studies could also be carried out to evaluate the strength of correlations between maximal tactile pressures and gold standard measures, such as grip strength using the Jamar dynamometer. To further increase clinical utility of maximal tactile pressures, future studies could evaluate the minimal clinically important differences for maximal tactile pressures. Future trials could also explore the reliability of other measures such as minimal tactile pressures and preferred tactile pressures or over longer time frames.

The development of the measures of maximal tactile pressures using the TactArray pressure distribution system and the evaluation of their psychometric properties are in line with the recommendations of the Stroke Recovery and Rehabilitation Roundtable[519]. Maximal tactile pressures could provide a novel means of objective quantification of grasp strength.

6.6 CONCLUSION

A customised TactArray cyclinder device demonstrates satisfactory reliability for measures of maximal tactile pressures during complete grasp duration using an average of three trials with and without vision, for within-day and between-day testing sessions, in healthy people and those with stroke. This study reinforces the importance of reporting indices of absolute reliability such as changes in mean and coefficients of variation, along with ICCs for appropriate interpretation of reliability results. Further studies with sufficient statistical power are required to explore the differences in maximal tactile pressures between healthy people and stroke survivors.

Appendix 6.1

Data processing procedure of raw TactArray data

Prior to obtaining the measures using TactArray, the raw sensor data need to be pre-processed on customised MatLab script through a series of steps in order to be converted into the appropriate format for subsequent data analysis. These preprocessing steps include:

1. Removing default lines from csv files from TactArray raw data
2. Identification of features such as sensors activated, number of grips, start of grip, end of grip to write MatLab script(see script below)
3. Data reduction by
    a. Excluding sensors with non-zero values or with noise on MatLab
4. Calculation of contact area, mean pressure and mean force using running averages over 1 second over the duration of the grip on Matlab
5. Importation of data for each trial onto Excel
6. Computation of maximal tactile pressures and forces over (1) complete grasp duration and (2) plateau phase for the following:
    a. Measure with the highest value amongst the three trials
    b. Mean of two trials
    c. Mean of three trials
7. Reliability analysis

Customised MatLAb script for TactArray data processing

```
clc;
clear all;

% parameters setting
latency = 1; % measurement latency
areaFactor=25e-3; %sensor area in m2 allowing for kPa
%load file
%rootname='/IDA1S Aff Vis Max cleaned';
rootname='ID3\Intervention\ID3 IntAss1 Aff Vis Max Cleaned';
Datafilename=strcat(rootname,'.csv');
Outputfilename=char(strcat(rootname,'.mat'));
Pressure=csvread(Datafilename);

time=Pressure(1:end,1);        % get time values
timeinterval=(time(end)-time(1))/size(time,1);
Pressure(:,1)=[];              %delete time values from pressure array

%baseline adjust and threshold
baseline=mean(Pressure(1:10,:),1);      % find baseline values for each sensor
for i=1:size(Pressure,2);Pressure(:,i)=Pressure(:,i)-baseline(i);end %subtract off baseline
[N,edges]=histcounts(Pressure(Pressure~=0),(-5:.1:5));
peak = edges(N==max(N));RMS=std(Pressure(Pressure<5 & Pressure~=0)); %get peak and
standard deviation of baseline (exclude zeros)
threshold = peak+3*RMS;                                  % threshold for sensor activity

%figure (1)
%hist(Pressure(Pressure<5 & Pressure~=0),(-5:.1:5));                    % check histogram
of values aropnd baseline

%total pressure timecourse & define active sensors overall
template=Pressure>threshold;                              % all sensor readings above threshold
active = template;
for i=1:size(template,2);active(:,i)=sum(template(:,i))>10;end; %sensor considered active if
10 points rise above threshold
totalPressure=sum(Pressure.*active,2);                  %total pressure of all active sensors
Nactive=max(sum(active,2));

%grip identification
episodes=medfilt1(totalPressure,101)>max(totalPressure/5);          %grip = 1 where a grip
has occured, filter used to rid of short gaps
grip=episodes==1;
gripN=sum(abs(diff(grip)))/2;                  % number of grips
gripStarttimes=time(diff(grip)==1)+latency;                          %grip start times
gripEndtimes=time(diff(grip)==-1)-latency;                          %grip start times
```

```
gripStartpoints=find(diff(grip)==1)+round(latency/timeinterval);                    %grip
startpoints
gripEndpoints=find(diff(grip)==-1)-round(latency/timeinterval);                     %grip
startpoints

griptemplate=zeros(size(time,1),gripN);
for i=1:gripN; griptemplate(gripStartpoints(i):gripEndpoints(i),i)=1;end     % position of each
grip

%gap identification
gapN=gripN+1;
gapStarttimes=time(diff(grip)==-1)+latency;                          %grip start times
gapEndtimes=time(diff(grip)==1)-latency;                           %grip start times
gapStartpoints=find(diff(grip)==-1)+round(latency/timeinterval);                    %grip
startpoints
gapEndpoints=find(diff(grip)==1)-round(latency/timeinterval);
gapStartpoints=vertcat(1,gapStartpoints);
gapEndpoints=vertcat(gapEndpoints,size(time,1));


gaptemplate=zeros(size(time,1),gapN);
for i=1:gapN; gaptemplate(gapStartpoints(i):gapEndpoints(i),i)=1;end   % position of each gap

%  define active sensors within each grip
template=Pressure>threshold;                              % all sensor readings above threshold
active1 = template;
for j=1:gripN;
   for
i=1:size(template,2);active1(gripStartpoints(j):gripEndpoints(j),i)=sum(template(gripStartpoi
nts(j):gripEndpoints(j),i))>10;end; %sensor considered active if 10 points rise above threshold
active1N(j)=sum(active1(gripStartpoints(j),:));
end

%mean total pressure within grips
GripTotalPressure=zeros(gripN,1);
GapTotalPressure=zeros(gapN,1);
for
i=1:gripN;GripTotalPressure(i)=sum(totalPressure.*griptemplate(:,i))/sum(griptemplate(:,i));
end
%mean total pressure between grips
for
i=1:gapN;GapTotalPressure(i)=sum(totalPressure.*gaptemplate(:,i))/sum(gaptemplate(:,i));e
nd

%baseline adjust using interpolation of baseline
gaps=zeros(2*gapN,2);  % gaps contains time and pressure values to interpolate
gaps(2:end-1,1)=vertcat(gapStarttimes,gapEndtimes);
```

```
gaps(end,1)=time(end);
gaps=sort(gaps);
for i=1:gapN;gaps(2*i-1,2)=GapTotalPressure(i);gaps(2*i,2)=GapTotalPressure(i);end;
PressureTotalBase=interp1(gaps(:,1),gaps(:,2),time);

%baseline adjusted pressure
totalPressureAdj=totalPressure-PressureTotalBase;

%Total presure baseline adjust using interpolation of baseline
gaps=zeros(2*gapN,2);  % gaps contains time and pressure values to interpolate
gaps(2:end-1,1)=vertcat(gapStarttimes,gapEndtimes);
gaps(end,1)=time(end);
gaps=sort(gaps);
for i=1:gapN;gaps(2*i-1,2)=GapTotalPressure(i);gaps(2*i,2)=GapTotalPressure(i);end;
PressureTotalBase=interp1(gaps(:,1),gaps(:,2),time);

hold on
%plot(time,PressureBase)

figure (1)
plot(time,totalPressureAdj)
hold on
plot(time,griptemplate*max(totalPressure/5))
plot(time,gaptemplate*max(totalPressure/5))

%Output total pressure variables
range=round(1/timeinterval);
for i = 1:gripN
  gripData=totalPressureAdj(gapEndpoints(i):gapStartpoints(i+1));
  cnt=0;
  for j = fix(range/2)+1:range:fix(size(gripData,1)-range/2);
     cnt=cnt+1;
     griprange=gripData(j-fix(range/2):j+fix(range/2));
     timeblock(cnt,i)=j*timeinterval+gapEndtimes(i);
     meanTotalForce(cnt,i)=areaFactor*mean(griprange(griprange>threshold));
     maxTotalForce(cnt,i)=areaFactor*max(griprange(griprange>threshold));
     minTotalForce(cnt,i)=areaFactor*min(griprange(griprange>threshold));
  end
end

% timecourse of active sensors
active2N=zeros(size(time,1),1);

for i = 1 : size(time,1)
   active2N(i)= sum(Pressure(i,:)>threshold);
end
```

```
%Output mean pressure variables

for i = 1:gripN
  gripData=totalPressureAdj(gapEndpoints(i):gapStartpoints(i+1));
  active3N=active2N(gapEndpoints(i):gapStartpoints(i+1));
  cnt=0;
  for j = fix(range/2)+1:range:fix(size(gripData,1)-range/2);
     cnt=cnt+1;
     griprange=gripData(j-fix(range/2):j+fix(range/2));
     activesensor(cnt,i)=max(active3N(j-fix(range/2):j+fix(range/2)));
     meanPressure(cnt,i)=mean(griprange(griprange>threshold))/activesensor(cnt,i);
     maxPressure(cnt,i)=max(griprange(griprange>threshold))/activesensor(cnt,i);
     minPressure(cnt,i)=min(griprange(griprange>threshold))/activesensor(cnt,i);

  end
end

% figure (2)
% hold on
% for i = 1 : size(time,1)
%     a= Pressure(i,:);
%     b= reshape(a,27,16);
%     surf(b)
%     zlim([-5 50])
%     pause(0.1)
%     view([0,0,1])
% end
save(Outputfilename,'timeblock','meanTotalForce','maxTotalForce','minTotalForce','meanPr
essure','maxPressure','minPressure','gripStarttimes','gripEndtimes','activesensor');
```

Appendix 6.2

Raw scores of Pres(8s)avg3 in healthy participants

Participants	Dominant hand						Nondominant hand					
	Vision			No Vision			Vision			No Vision		
	Session 1 /kPa	Session 2 /kPa	Session 3 /kPa	Session 1 /kPa	Session 2 /kPa	Session 3 /kPa	Session 1 /kPa	Session 2 /kPa	Session 3 /kPa	Session 1 /kPa	Session 2 /kPa	Session 3 /kPa
ID21C	26.00	26.10	30.97	27.59	25.81	27.77	19.29	18.61	23.16	20.73	19.01	20.42
ID22C	36.05	38.76	36.38	37.26	34.52	34.04	36.10	37.04	35.79	31.92	35.84	33.63
ID23C	28.22	36.92	35.98	23.62	33.53	37.14	29.12	39.96	38.55	33.83	36.90	35.07
ID24C	27.58	29.39	32.21	34.28	26.15	37.43	30.22	28.88	34.88	25.86	27.41	35.28
ID25C	28.05	24.36	30.24	28.77	32.09	28.08	26.67	27.69	36.02	25.80	26.71	34.30
ID26C	24.16	20.62	24.05	26.70	26.64	24.98	16.38	20.41	49.90	17.85	19.83	19.52
ID27C	37.47	43.10	36.32	34.95	43.10	31.66	37.42	36.89	35.09	32.92	39.65	34.40
ID28C	51.93	49.72	47.65	45.71	43.53	50.15	45.90	46.90	49.90	43.48	42.30	44.97
ID29C	37.68	36.38	39.18	28.32	33.45	37.60	31.32	32.98	35.60	33.55	35.28	33.58
ID30C	31.84	37.53	28.59	29.88	33.74	26.16	27.15	32.56	24.15	28.95	33.57	25.02
ID31C	41.71	35.83	39.11	33.77	39.46	34.63	41.79	40.31	38.33	36.25	42.35	42.76
ID32C	30.87	36.50	35.33	31.98	36.62	34.25	24.64	32.79	28.82	20.53	27.17	25.94
ID33C	50.19	49.88	44.98	51.37	44.09	37.36	40.11	48.36	44.22	41.19	44.02	37.43
ID34C	32.80	30.46	32.71	30.64	33.26	31.42	35.09	36.02	30.10	32.98	34.10	35.99
ID35C	29.36	24.72	22.82	30.23	24.86	27.11	27.89	24.99	23.70	27.24	29.03	23.99
ID36C	36.82	33.53	42.07	38.56	36.20	42.64	38.33	39.58	45.46	42.69	38.80	42.27
ID37C	37.15	30.37	31.21	31.48	32.71	26.56	34.45	35.05	33.58	36.45	38.25	31.48
ID38C	43.53	32.71	33.83	33.36	34.09	36.44	35.60	28.87	30.97	33.07	25.64	28.30

Raw scores of Pres(8s)avg3 in participants with stroke

Participants	Affected hand						Less affected hand					
	Vision			No Vision			Vision			No Vision		
	Session 1 /kPa	Session 2 /kPa	Session 3 /kPa	Session 1 /kPa	Session 2 /kPa	Session 3 /kPa	Session 1 /kPa	Session 2 /kPa	Session 3 /kPa	Session 1 /kPa	Session 2 /kPa	Session 3 /kPa
IDA1S	34.17	41.37	34.49	28.70	26.01	38.84	39.95	36.94	36.78	38.99	36.98	39.24
IDB2S	36.81	35.39	34.88	58.97	39.17	29.17	89.41	39.43	41.16	69.36	46.64	40.45
IDC3S	13.76	19.96	15.81	13.58	19.77	16.28	22.85	35.06	37.17	19.22	29.24	29.29
IDD4S	20.53	21.88	23.14	19.85	21.68	19.49	17.62	24.19	19.57	16.09	21.01	21.31
IDE5S	40.69	37.49	38.33	34.28	41.15	38.98	43.63	51.92	42.28	49.97	51.74	38.45
IDF6S	27.97	29.59	29.80	28.36	24.50	27.59	51.92	30.94	32.70	33.77	31.66	32.78
IDG7S	26.13	39.18	30.52	28.68	37.73	33.40	33.15	31.62	32.55	25.21	31.85	31.54
IDH8S	44.03	44.42	50.04	44.93	46.54	50.90	56.89	41.07	48.76	43.31	47.28	39.82
IDI9S	27.68	30.89	27.15	24.45	31.36	26.80	29.27	30.75	25.84	30.14	29.65	25.99
IDJ10S	42.76	38.30	33.31	34.43	36.76	31.28	36.93	48.32	49.36	41.08	41.23	43.24
IDK11S	8.93	7.00	18.94	8.95	12.95	13.90	20.82	12.79	17.26	8.65	10.82	15.03

CHAPTER 7: THESIS DISCUSSION

7.1 OVERVIEW

This thesis aimed to address the overarching research question, *"Can combined somatosensory and motor training improve upper limb recovery after stroke?"* Four distinct but complementary studies were conducted, each investigating a specific research question and corresponding aim to address this overarching question (figure 7.1). Chapters 3-6 presented and discussed the findings from each individual study. The aim of this chapter is to provide a synthesis of overall key findings and discuss findings consistent with the overarching research question.

The systematic scoping review identified few studies that investigated the effects of combined somatosensory and motor training interventions. These individual studies provide some evidence that these interventions have potential to improve upper limb recovery after stroke if they incorporate active ingredients and appropriate dosage. Findings from the feasibility study on COMPoSE indicated that training with the combination of somatosensory and motor variables synchronously was feasible although modifications to allow more specific tailoring to participant deficits is recommended. This thesis also found that TactArray device demonstrates satisfactory reliability for measures of maximal tactile pressures during complete grasp duration of 8s for within-day and between-day testing sessions using an average of three trials with and without vision, in healthy people and those with stroke. This chapter also provides recommendations for research informed by the findings of this thesis.

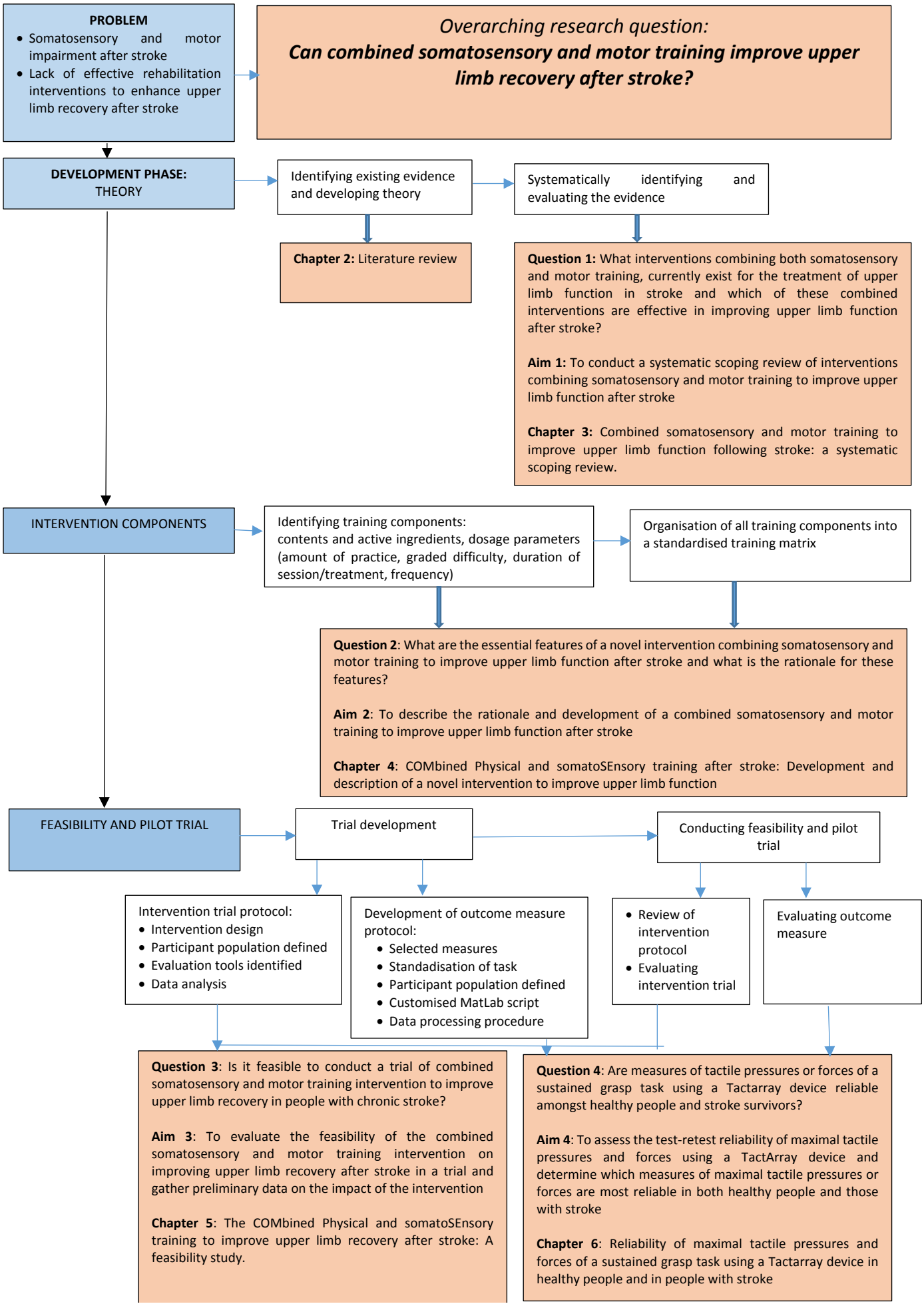


Figure 1.1 Structure of thesis from overarching research question, specific research questions, thesis aims and thesis chapters

7.2 SUMMARY OF FINDINGS

7.2.1 Summary of findings from systematic scoping review (Research question 1, Thesis aim 1 and Chapter 3)

Chapter 3 reported the results from a systematic scoping review of studies that identified combined somatosensory and motor training and their training components to improve upper limb function after stroke. Additionally, this review aimed to evaluate the efficacy of the combined interventions.

The main findings from Chapter 3 are summarised below:

- Ten studies were included in this review, comprising three randomised controlled trials, two pre-post studies with non-randomised comparison groups, three single-case experimental studies, and two case reports.
- Five groups of intervention combinations were identified including tactile stimulation/discrimination, proprioceptive stimulation/discrimination, haptic object discrimination/recognition, movement training, and functional training.
- All studies, except one, combined their training components predominantly in a sequential manner. Some integrated somatosensory and motor training was incorporated in seven studies, but involved at most two training tasks.
- The total number of treatment sessions ranged from 8-30 sessions delivered in nine studies; one study delivered 104 sessions. The amount of time scheduled per therapy sessions ranged from 0.25 to 3 hours. The total duration of scheduled therapy time over the treatment period ranged from 7 to 72 hours.
- Only one group study, a non-randomised controlled trial with multiple active components and the largest dose of treatment (72 hours found significant improvements in fine motor and somatosensory measures. One single-case experimental study found improvements in the Action Research Arm Test and the Motricity index (arm) in all participants. Two single-case experimental studies and case reports found improvements in some participants on some motor and somatosensory

measures. No significant improvements were found in any of the RCTs or the pre-post study.

Overall, this systematic scoping review found heterogeneity across studies with regards to intervention content and dosage, participant characteristics, and outcome measures. Relatively few "combined somatosensory and motor training" interventions were reported. Evidence of efficacy of these interventions to improve somatosensory and motor capacity and UL function is limited at present but has potential. Future trials are encouraged to provide complete reporting of the intervention contents and the training dosage to facilitate optimisation of interventions. RCTs with sufficient statistical power are required to evaluate the efficacy of "combined somatosensory and motor training".

7.2.2 Summary of findings from the development and description of the COMPoSE intervention (Research question 2, Thesis aim 2 and Chapter 4)

The purpose of this chapter was to describe the rationale and development of the COMPoSE intervention designed to improve somatosensory and motor deficits in the upper limb after stroke. Chapter 4 reports the developmental stages and the essential features of the COMPoSE intervention.

The main findings from Chapter 4 are summarised below:

- The COMPoSE intervention focused on combining somatosensory and motor training to be delivered synchronously and within the same tasks.
- The essential features of COMPoSE include: use of combined somatosensory-motor training variables (grasp pressure, distance, object size, crushability, surface texture and friction); feedback and calibration using a haptic device providing measures of grasp pressure; varied practice; and high dose repetitive task practice. The somatosensory-motor task involves reach-to-grasp and lift-and-hold of the stationary cylindrical object. The tasks were organised into progressive and systematic grading

of levels of difficulty under two conditions of practice (i.e., with vision and without vision).

- There is a total of 36 combinations of somatosensory-motor tasks within a session, each with 6 repetitions (216 repetitions in total).
- The standardised training matrix was developed to facilitate the delivery of the COMPoSE intervention as it explicitly and systematically incorporates all the combinations of somatosensory-motor parameters, conditions of practice, feedback delivery focused on somatosensory and motor aspects, as well as adaptive pressure outputs.
- Each session lasts approximately 1.5 hours (with rest). It was planned for ten treatment sessions to be delivered over 3 weeks to trial this intervention.
- A novel aspect of this intervention involves using a TactArray device as a means of retraining sensorimotor function for scaling of grasp forces, which is crucial for dexterity.

In summary, the COMPoSE intervention offers a learning based intervention approach that involves processing of multisensory information from the tactile, proprioceptive and visual systems, which are simultaneously integrated with motor function.It is proposed that this integrated somatosensory-motor retraining approach could optimise processes that drive reorganisation of brain activation and neural connectivity to a greater extent leading to maximal functional improvement in the paretic upper limb compared to training somatosensory and motor function sequentially, which may be a less effective approach to relearn functional movements.

7.2.3 Summary of findings from the feasibility study of the COMPoSE intervention to improve upper limb recovery after stroke (Research question 3, Thesis aim 3 and Chapter 5)

This study evaluated the feasibility of the COMPoSE intervention trial on upper limb recovery after stroke. Additionally, this study gathered preliminary data on the impact of the intervention. Chapter 5 presented the findings of a feasibility trial using a single case

experimental design that evaluated the feasibility of the COMPoSE intervention trial with regards to the feasibility of the recruitment of participants, the feasibility of intervention protocol and study design, the acceptability of the intervention and trial, the appropriateness of data collection procedures, the resources required and the preliminary impact on participants.

The main findings from Chapter 5 are summarised below:

- Over a period of 24 months, 36 potential participants identified through various recruitment routes were screened, of which 22 met the inclusion criteria. This study recruited 6 participants, of which 5 chronic stroke survivors (62-89 years) completed the COMPoSE intervention trial. The participants were heterogenous with regards to types and severity of somatosensory and motor deficits.

- Enrolment of participants in the study was limited by the burden of attendance at intervention and assessment sessions

- The combination of somatosensory and motor variables synchronously, within the same tasks was feasible. The standardised training matrix facilitated the delivery of the COMPoSE intervention, however modifications to allow more specific tailoring to participant deficits is recommended.

- Provision of real-time feedback on selected tactile pressures using the TactArray device was useful to retrain the control of finger forces.

- The graded difference in the physical characteristics of the object properties between the two variables of the somatosensory parameters was relatively large.

- All participants attended 90-100% of intervention sessions.

- The amount of practice ranged from 108-360 repetitions/session across all intervention sessions and across all participants. The scheduled training duration ranged from 90 to 120 minutes, with 90 minutes of actual training duration.

- All participants reported that they were satisfied (range score out of 10: 6-10) with the intervention.
- Three participants attended all assessment sessions. There was a total of 14 assessment sessions scheduled across the COMPoSE trial and duration of assessment sessions ranged between 2-4 hours.
- Measures of maximal tactile pressures showed a trend in improvement in 4 participants (12.0-62.5%) between baseline and post-intervention, with vision and without vision conditions.
- Across the group, improvements were observed in the WMFT score, WMFT time, BBT, MAL-AS, MAL-HW, grip strength, WPST, TDT, SIS-strength, SIS-hand, SIS-participation and SIS-stroke recovery at post-intervention (range: 3.0-50.3%) as compared to baseline. No changes were observed in FTORT (0%). Deteriorations were observed in FMT, SIS-ADL and FAS at post-intervention as compared to baseline (0.2- 7.4%).

Overall, this feasibility trial showed that the target number of somatosensory-motor combinations (36 combinations per session) and amount of practice (216 repetitions per session) were feasible, at least to some extent. The COMPoSE intervention prioritised delivering a relatively high number of repetitions, while allowing sufficient time for feedback to be delivered. The overall data collection was time and labour intensive. Improvements were observed in all participants following the COMPoSE intervention but varied across the outcome measures. The findings from this study suggest that COMPoSE could be beneficial to people with mild to severe somatosensory and motor deficits after stroke. The contents of the COMPoSE intervention and its dosage parameters need to be adjusted, prior to subsequent trials in order to maximise somatosensory and motor improvements in the upper limb after stroke.

7.2.4 Summary of findings from an exploratory study on the reliability of maximal tactile pressures and forces during sustained grasp task using aTactArray device in healthy people and in people with stroke (Research question 4, Thesis aim 4, Chapter 6)

This study investigated the test-retest reliability of measures of maximal tactile pressures and forces during sustained grasp task using a TactArray device and determined which measures of maximal tactile pressures or forces were most reliable in both healthy people and in people with stroke. Both arms were tested in within-day sessions and between-day sessions, with vision and without vision. Reliability was determined using changes in mean, coefficients of variation and intraclass correlation coefficients.

The main findings from Chapter 6 are summarised below:

- Healthy participants (n= 18; mean age: 62.2 ± 9.9 years) and participants with stroke (n=11; mean age: 64.1 ± 9.0 years) were evaluated.

- In healthy individuals, changes in mean were very good, coefficient of variation were good to acceptable and ICCs were very good to good for maximal tactile pressures, using Pres(8s)max, Pres(8s)avg3, Pres(5s)max and Pres(5s)avg3 in the dominant hand with and without vision, and in the nondominant hand without vision for within-day and between-day sessions.

- In people with stroke, changes in mean were good, coefficients of variation were acceptable and ICC were very good for maximal tactile pressures using Pres(8s)avg3 in the affected hand with vision and without vision for within-day sessions, and without vision for between-day sessions. In the less affected hand, changes in mean were good to very good, coefficients of variation were acceptable and ICCs were good to very good for maximal tactile pressures using Pres(5s)avg3 and Pres(8s)avg3 for between-day sessions, with and without vision.

- Maximal tactile pressure using Pres(8s)avg3 was found to be most reliable across healthy participants and participants with stroke in all conditions, except in the less affected hand of people with stroke during within-day sessions with vision.

This study also sought to evaluate the difference between vision and no vision conditions in each hand as well as the difference between both hands, with and without vision. The findings are summarised below:

- Interaction effects were found with vision such that mean maximal tactile pressures measures tested with vision were significantly higher than those without vision in healthy participants ($p = 0.004$) and those with stroke ($p = 0.01$).
- In healthy participants, there were no significant differences between the dominant and nondominant hand ($p=0.131$) while interaction effects were found due to side such that mean maximal tactile pressures were significantly lower when performing with the affected side compared to the less affected side ($p = 0.02$).

Additional analysis was used to evaluate any difference between the affected hand in people with stroke and the nondominant hand in healthy people. There was no significant difference between the affected side in people with stroke and the nondominant side in healthy people, though the difference closely approached accepted standards of statistical significance ($p = 0.06$).

In general, the TactArray device demonstrates satisfactory reliability for measures of maximal tactile pressures during complete grasp duration for within-day and between-day testing sessions using an average of three trials, with and without vision, in healthy people and those with stroke. One practice trial is recommended prior to actual testing with the TactArray device to allow familiarisation with the task whilst minimising any learning effect. Visual conditions could influence the development of maximal voluntary contractions during grasping. Further studies with sufficient statistical power are required to identify any differences in maximal tactile pressures between healthy people and stroke survivors.

7.3 OVERALL DISCUSSION

The combined findings from the studies in this thesis indicate that combined somatosensory and motor training has the potential to improve upper limb recovery in people with mild to severe motor and somatosensory deficits post-stroke. Chapters 3, 4 and 5 showed that the characteristics of rehabilitation interventions and dosage constitute the

main factors influencing upper limb recovery. Additionally, these chapters also showed that complex interaction between the intervention and the participants' characteristics, such as time post-stroke, and types and severity of somatosensory and motor deficits, also need to be considered when evaluating the effectiveness of rehabilitation interventions since they are likely to influence the extent of upper limb recovery on post-stroke. Chapters 3 and 5 caution that interpretation of findings on the efficacy of studies included should consider the impact of the methodological rigour of the studies in terms of the study design, statistical power of the sample size, choices of outcome measures as these could limit the internal and external validity of the studies. Chapter 3 also found that comparisons between studies combining somatosensory and motor training interventions to improve upper limb function following stroke need to be interpreted with caution due to the heterogeneity across studies. Chapter 6 further reinforced the importance of using reliable and sensitive outcome measures to quantify grasp deficits after stroke.

7.3.1 Strengths and limitations of intervention development

This thesis follows the UK Medical Research Council framework for the development of complex interventions and exemplifies that the staging of pilot studies constitutes a crucial step in the development of combined somatosensory and motor training interventions after stroke. The assessment of the feasibility of the intervention and the operational aspects of an intervention trial have been strongly recommended during the early stages of intervention development[55,56]. Other studies have also demonstrated that exploratory trials provide an opportunity to test a combination of treatment strategies aiming to improve the upper limb after stroke[322,636,637]. Three studies[322,323,327]included in the systematic scoping review (Chapter 3) demonstrated the value of evaluating a novel intervention using single-case experimental studies in a sub-acute and chronic population with stroke before assessing the dose-response in a randomised-controlled trial in a sub-acute population. However, these studies[322,323,327] did not modify the components of the combined mobilisation and tactile stimulation, which could be a missed opportunity for optimising the intervention. By adhering to a systematic development of the COMPoSE intervention, determining and assembling the components of the intervention as well as the feasibility phases (Chapters 4 and 5) allowed identification of

intervention components that could be modified and allowed assessment of the feasibility of COMPoSE. It is noteworthy that there is insufficient guidance from the MRC (UK) framework on the conduct of feasibility and pilot studies to gather preliminary data on the efficacy of a novel intervention.

7.3.2 Strengths and limitations of single-case experimental designs

Single-case experimental designs were used in small pilot studies included in the systematic scoping review (Chapter 3) and in the COMPoSE trial (Chapter 5). These studies showed that single-case experimental designs are valuable to optimise the components of interventions that are likely to produce beneficial effects, inform the most appropriate outcome measures, provide proof-of-concept data and evaluate dose-response effects[536].

The baseline-intervention (AB) phases design was suitable to determine the individual impact of the COMPoSE intervention over time amongst people with stroke[66], though it is acknowledged that the baseline-intervention phases design has limited experimental control[638]. A withdrawal phase with repeated measures would increase the burden of assessments and was therefore purposefully not incorporated in this study. It is acknowledged that the baseline-intervention phases design with one follow-up assessment used in the COMPoSE trial cannot provide definitive evidence of treatment effectiveness[405], but was valuable for the preliminary evaluation of this novel intervention[480,639].

The addition of a withdrawal phase with repeated measures beyond the intervention phase, such as studies with a baseline-intervention-withdrawal (A-B-A) phases design, could offer a robust experimental control[640], now that certain knowledge has been gained. However, the changes in a withdrawal phase should be carefully interpreted in studies that are based on principles of learning mechanisms[370] such as combined somatosensory and motor training interventions. This is because it is possible that participants do not 'unlearn' the behaviour after the intervention is stopped such that performance might not return to pre-intervention levels after the intervention is withdrawn[640]. Alternatively, a single case experimental study with a multiple baseline design could be useful when an intervention is likely to permanently change a person's ability such that return to baseline performance is

not feasible[641]. In multiple baseline designs, the COMPoSE intervention would be staggered across time such that the intervention effects are separated from effects of experience, learning or practice[642].

7.3.3 Strengths and limitations of participation selection criteria

The COMPoSE trial included participants with varied severity across somatosensory and motor deficits, which is typical of people with stroke. One participant with mild deficits in both somatosensory and motor function showed that he was less likely to benefit from COMPoSE (Chapter 5). Although the small sample size of the COMPoSE trial means this observation has limited external generalisability at present, it is a factor that should be considered in population selection for further investigations of COMPoSE. The extent of upper limb improvement should also consider the time post-stroke for accurate predictions of recovery as the capacity to improve decreases with time. For instance, the lack of improvement in some measures in the COMPoSE trial could be due to reduced potential of recovery in the chronic phase of stroke since the participants were between 11-192 months post-stroke. In support of this, a study investigating the integrity of the corticospinal tract using TMS and functional MRI found meaningful improvements in the upper limb at 3 years post-stroke which declined with increase in time post-stoke[179]. Other factors that are likely to adversely affect response to the COMPoSE intervention include ageing[539,549] and cognitive impairments[550] which also need to be considered when evaluating expected improvement after an intervention.

7.3.4 Strengths and limitations of combined somatosensory and motor training interventions

Prior to determining the contents of a combined somatosensory and motor training intervention, it is critical to determine the goal of the intervention, i.e., to target restoration, substitution or compensation based on the specific needs of the patient. Interventions included in the systematic scoping review (Chapter 3) and the COMPoSE trial (Chapters 4 and 5) primarily aimed at processes of recovery by restoring the ability to perform a task in the same way it was performed prior to stroke, rather than compensatory mechanisms[44].

Based on findings from the systematic scoping review (Chapter 3) and the COMPoSE trial (Chapters 4 and 5), this thesis found that there is limited evidence on the effectiveness of combined somatosensory and motor training interventions to improve upper limb recovery after stroke. There is considerable heterogeneity across the studies included with regards to characteristics of the intervention. Consequently, there was insufficient evidence to delineate an optimal type or dosage of somatosensory and motor training strategies to maximise upper limb recovery after stroke. Overall, this thesis points out that the effects of combined somatosensory and motor training interventions can be optimised by a combination of several active ingredients delivered at the appropriate dosage. Active ingredients in the COMPoSE intervention described here incorporated such as integrated somatosensory-motor tasks[297,643], specificity of training with regards to targeted somatosensory and motor deficits, varied practice[398], augmented feedback[157], practice conditions such as with vision and without vision[133,140,387,388], and intensive repetitions[62,209]. Additionally, systematic progression in grading difficulty of tasks are crucial to maintain continued improvement in upper limb recovery[435].

Findings from this thesis (Chapters 3, 4 and 5) suggest that the mode of combination of somatosensory and motor training, i.e., sequentially or integrated, is likely to influence the extent of upper limb recovery after stroke. Previous studies (Chapter 3) primarily delivered distinct somatosensory and motor training sequentially, thus addressing the somatosensory and motor impairments separately. In addition to sequential somatosensory and motor training, some interventions included in the systematic scoping review (Chapter 3) incorporated training tasks that integrated somatosensory and motor training. The systematic scoping review (Chapter 3) indicates that sequential combination of somatosensory and motor training can improve upper limb deficits to some extent but are not necessarily optimal for recovery. The COMPoSE trial delivered integrated rather than sequential somatosensory and motor tasks and found potential benefits in enhancing somatosensory-motor integration. Integrated and fast somatosensory-motor interactions are essential for accurate and precise motor control of complex tasks and for exploration of tactile interactions with objects[297,643].

Therefore, the findings of this thesis reinforce the importance of further investigating integrated somatosensory and motor training approaches to improve upper limb recovery.

Results from this thesis suggest that stroke survivors having somatosensory and motor deficits in their upper limbs may first require interventions targeting impairments, followed by interventions that progressively target functional deficits. In the COMPoSE trial, four participants with either substantial motor impairment or severe somatosensory impairment with or without important functional deficits highlighted the need to address impairments post-stroke. Therefore, the COMPoSE trial showed that it could be more beneficial to prioritise impairment-oriented approaches to target specific somatosensory and motor deficits due to their individual characteristics, rather than directly focusing on functional training. Other studies have found that impairment-oriented training could be more effective than functional training after severe stroke[357,644,645]. It is suggested that following improvement in somatosensory and motor deficits, task-oriented or task-specific approaches can be delivered to enhance the transfer of somatosensory and motor improvement to performing functional tasks in daily living[370,646]. Therefore, COMPoSE could be useful to address somatosensory and motor deficits using a goal-oriented approach, prior to task-oriented or task-specific approaches.

7.3.5 Strengths and limitations of dosage parameters

Comprehensive reporting of dosage parameters is necessary to facilitate replication of interventions and appropriate comparison across studies. These include scheduled and actual duration of one treatment session, scheduled and actual duration of overall treatment, frequency of treatment sessions, time of exposure to stimuli and the number of repetitions per session. The COMPoSE trial showed that these parameters are likely to impact on the extent of learning and fatigue. Hence, monitoring these parameters could assist in optimising the delivery of the intervention at an optimal learning pace with minimal fatigue. Also, because the systematic scoping review (chapter 3) was conducted in parallel with the COMPoSE trial, the findings on effective dosage of combined somatosensory and motor

interventions from the systematic scoping review (chapter 3) could not inform the choice for the overall dosage of 15 hours of the COMPoSE intervention (chapter 5) in a timely manner.

7.3.6 Strengths and limitations of outcome measures

It was beneficial that the COMPoSE trial directly assessed somatosensory and motor impairments as the COMPoSE intervention targeted specific somatosensory and motor deficits. The COMPoSE trial also assessed motor function using measures such as the Wolf Motor Function Test but these were not sufficiently sensitive to directly evaluate impairments. Nevertheless, measures of function can be useful to monitor whether improvements in impairments translate into skill acquisition. It is therefore suggested that future trials evaluating combined of somatosensory and motor training interventions prioritise outcome measures according to the goal of the intervention.

The COMPoSE trial found that a heavy burden of assessments could result in fatigue which in turn could confound potential improvement. The impact of data collection procedures should therefore be considered when evaluating the efficacy of an intervention to avoid false negative results and to inform the choice of outcome measures for subsequent trials.

A review of the literature highlighted a need for sensitive measures to evaluate tactile pressures and forces in stroke rehabilitation trials. Consequently, a novel measure evaluating tactile pressures and forces using the TactArray device was developed and evaluated to measure changes in scaling of grasp forces. The measures were tailored to the COMPoSE intervention which incorporated selected graded pressures as part of the training tasks. The reliability study on measures of tactile pressures and forces reported in this thesis (Chapter 6) reinforces the importance of conducting advanced statistical calculations to comprehensively evaluate indices of absolute reliability, in addition to indices of relative reliability to assist in the appropriate interpretation of changes in performance while considering the limitations of the tool.

Chapter 6 focused on the assessment of the reliability of maximal tactile pressures during sustained grasp as part of outcome tool development. On this basis, only maximal tactile pressures were evaluated in the COMPoSE trial while changes in preferred and minimal grasp were not assessed. Future studies are required to investigate the reliability of measures of preferred and minimal tactile pressures for further evaluation of deficits in control of finger pressures or forces after stroke. Additionally, the COMPoSE trial (Chapter 5) and the reliability study (Chapter 6) showed that evaluation of tactile pressures were limited in people with severe deficits with control of finger opening and closure who required assistance during grasping. It is therefore suggested that for people with such deficits, the data analysis of tactile pressures be adjusted to exclude the phase during which assistance is provided. This will help to extend the usefulness of the COMPoSE trial to people with severe deficits in grasp control which are common in real-world practice.

7.4 CLINICAL IMPLICATIONS

The clinical implications of the four studies included in this thesis have been discussed in Chapters 3, 4, 5, and 6. Overall, based on findings from the systematic scoping review (Chapter 3) and the COMPoSE trial (Chapters 4 and 5), this thesis indicates that there is insufficient evidence on the effectiveness of combined somatosensory and motor training interventions on somatosensory and motor deficits in the upper limb after stroke. Therefore, these interventions cannot yet be recommended for clinical practice. Larger studies with sufficient statistical power are required to evaluate the effectiveness of these interventions. The study on the reliability of measures of maximal tactile pressures (Chapter 6) found that the TactArray device can be used to quantify deficits during sustained grasp after stroke.

7.5 RECOMMENDATIONS FOR FUTURE RESEARCH ON THE COMPOSE INTERVENTION

The findings from this thesis will help inform the subsequent stages of the development of the COMPoSE intervention with regards to the intervention protocol, as well

as the study design and methods of the COMPoSE trial. A series of feasibility and pilot trials are required to systematically evaluate variations of the COMPoSE protocol, identify responders and evaluate the preliminary efficacy of COMPoSE with respect to participants' characteristics such as types and severity of somatosensory and motor deficits, phase of recovery (acute, sub-acute or chronic) and dosage parameters, prior to a larger definitive RCT. The next part of this chapter will suggest details for a future series of trials of the COMPoSE intervention.

7.5.1 Refinement of study design

Based on the Medical Research Council (UK) framework[54], it is suggested that the next phase of the COMPoSE intervention could be a single case experimental study using a multiple baseline design[640] to collect data on preliminary efficacy the COMPoSE intervention to improve somatosensory and motor impairments and upper limb function after stroke. Before delivering the COMPoSE intervention, it is critical for measures to be repeated regularly until the participant reaches a plateau[536,537] on at least 5 data points[457,647].

7.5.2 Refinement of participants' selection criteria

To identify responders, it is essential that the COMPoSE trial is investigated in well-characterised populations such as in people with chronic stroke having a combination of specific deficits. These include tactile somatosensory deficits, such as difficulties in discriminating texture, and slipperiness of object features, such as crushability, slipperiness, weight and shape; motor deficits, such as difficulties in achieving reaching distance, difficulty opening fingers for sufficient grasp aperture, deficits in control of finger opening and closure; and difficulties in scaling finger forces.

Characterising the target population is essential so as to not to include participants who are unlikely or cannot respond to the COMPoSE intervention in a larger Phase III study which could yield misleading results[648]. Stroke survivors having a combination of mild, moderate or severe somatosensory and motor deficits could be included to represent a real-

world sample and to identify responders to the COMPoSE intervention. Participants with mild deficits in both somatosensory and motor function will be lower in priority as they are less likely to benefit from COMPoSE (Chapter 5). Stratification of participants according to severity of impairments or functional deficits using measures such as the Fugl-Meyer (upper limb)[649] and Motor Activity Log[348,401] will help increase the generalisability of findings to people with similar specific deficits and help determine the participants' characteristics for which COMPoSE could be most beneficial.

7.5.3 Refinement of COMPoSE intervention protocol

Evaluation of the COMPoSE trial has demonstrated that the current intervention protocol needs to be modified to maximise upper limb recovery after stroke. Findings from this thesis emphasised the importance of tailoring the active ingredients and dosage parameters of the COMPoSE intervention towards the participants' characteristics with regards to the specificity and severity of deficits. This reinforces a personalised training approach according to the needs of the participant, which is recommended in rehabilitation trials post-stroke[650]. It is suggested that choices of somatosensory and motor variables directly match the targeted deficits. For example, if a participant has no deficits in discriminating slipperiness of object surfaces but has difficulty with discriminating between object shapes, then trials with training of discrimination of slipperiness need not be performed and instead, training with shape discrimination could be incorporated. The grading of difficulty of tasks needs to be adjusted according to the severity level to maintain continued learning to enhance recovery. For example, materials with smaller differences in texture could be used for people with moderate deficits in tactile somatosensation and larger differences for those with severe deficits. Specifying the participants' characteristics and detailing the components of COMPoSE to use will enable clinicians to evaluate how and with whom COMPoSE can be delivered in clinical settings.

7.5.4 Refinement of dosage parameters

Observations from the COMPoSE trial (Chapter 5) showed that it was appropriate to adjust the number of repetitions performed per session to the tolerability of each individual

participant. The COMPoSE trial (Chapter 5) also showed that dosage parameters need to be tailored to the severity of deficits to avoid over-exertion. Training with specific combinations of somatosensory and motor variables could be adjusted to emphasise deficits that are more severe. For example, if a patient has more severe deficits in control of finger forces than in discriminations of surface textures, then training with selected graded pressures could be emphasised. Additionally, findings from the systematic scoping review (Chapter 3) found that an overall treatment duration of 72 hours of combined somatosensory and motor training showed positive outcomes in improving somatosensory and motor deficits after stroke. For the next phase of COMPoSE, it is suggested that parameters of dosage include 72 hours of actual training duration, delivered 3 x per week over 16 weeks for 1.5 hours actual training duration/session (total of 48 treatment sessions; up to 96 hours of scheduled training duration) for people in the chronic phase with moderate somatosensory and motor deficits.

7.5.5 Refinement of outcome measures

The choice of outcome measures plays a significant role in appropriately reflecting the goals and the potential benefits of the COMPoSE intervention. The outcome measures should be not only objective and standardised with good reliability, responsiveness and validity but should also evaluate variables that were specifically trained in the COMPoSE intervention. For the subsequent phases of COMPoSE trial, the primary outcome measures could prioritise assessment of impairments using laboratory measures that are more likely to reflect small changes such as kinematic assessments using 3D motion analysis for the motor domain and measures of tactile pressures for the integrated somatosensory-motor domain.

It is suggested that clinical measures are aligned with the goals of the intervention and chosen based on their responsiveness to severity of deficits. To measure motor impairment, the Fugl-Meyer upper limb assessment is recommended, as it is sensitive to people with mild, moderate and severe deficits[649]. To evaluate motor function, the Box and Block test is recommended for people with mild to moderate motor deficits but having limited responsiveness among those with severe functional motor deficits[526]. It is noteworthy that measures to evaluate motor function are limited for those with severe deficits. Clinical

somatosensory measures are currently limited in rehabilitation trials post-stroke[248]. Based on available tools, the Tactile Discrimination Test is recommended to evaluate somatosensory impairments and the functional tactile recognition test for functional assessment. These tests could be completed within an hour and are required to be administered periodically, but not excessively, across the baseline, intervention and withdrawal phase.

It is also recommended to conduct MRI analysis to evaluate the impact of COMPoSE with regards to the site of lesion and the extent of damage along the corticospinal tract. This is because lesion location is reported to influence brain adaptation in response to rehabilitation interventions[651,652]. Additionally, lesion-specific recovery could also explain changes in the motor or somatosensory outcome measures. This was observed in one study[322] included in the systematic scoping review (Chapter 3) that reported significant improvements in motor measures in a participant with lesion in the right middle cerebral artery and 2 participants with left frontoparietal lesion but not in individuals with external capsule and lentiform nucleus or left upper pons or ganglionic region. Another study investigating the impact of lesion location following touch discrimination retraining found that activation patterns differed between people with the thalamic/capsular lesions and S1/S2 cortical somatosensory lesions even though improvements in touch discriminations were similar in both groups[653]. Additionally, the extent of lesion damage along the corticospinal tract was found to be a significant predictor of motor outcome in people with chronic stroke[541]. These findings suggest the value of assessing the corticospinal tract integrity to investigate whether might be useful to distinguish whether any lack of improvement following COMPoSE may be associate with a lack of viability of the corticospinal tract that limited potential recovery or due to effectiveness of the content or dosage of intervention per se.

7.5.6 Refinement of data analysis

It is recommended that changes in scores for each participant are represented as single patient data and analysed individually by visual inspection of plotted time-series data points to assess the magnitude of intervention effects[407,654,655].

7.5.7 Refinement of overall hypothesis

Based on the suggested changes in methods, it is hypothesised that 48 treatment sessions delivered over a 16 weeks period of COMPOSE intervention will result in an improvement of >1 standard deviation (SD) in measures of maximal tactile pressures, compared to baseline.

7.6 CONCLUSION

Findings from this thesis make an important contribution to advance our understanding on various factors that influence the effects of combined somatosensory and motor training interventions. So far, there is little consistency across "combined somatosensory and motor training" interventions to improve upper limb function after stroke. The individual studies in the systematic scoping review and the COMPoSE trials provided preliminary evidence that combined somatosensory and motor training interventions have potential to improve upper limb recovery after stroke, if they incorporate the optimal active ingredients and dosage. Findings from this thesis identified research gaps with regards to active ingredients, recruitment capability, responsiveness of outcome measures for people with severe deficits after stroke, individualised somatosensory-motor training, dosage and intensity of intervention. Furthermore, results from this thesis indicate that it could be beneficial to deliberately train for somatosensory and motor training synchronously to improve upper limb recovery after stroke. Additionally, a novel means of measuring maximal grasp pressures during a sustained grasp using the TactArray device has been evaluated, which can be further explored in larger trials. Recommendations have been provided on optimisation of the intervention contents and study design of COMPoSE in the future.

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