The Effect of Sensory-Motor Training on Brain Activation and Functional Recovery in Chronic Stroke Survivors

by

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Declaration

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Abstract

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Introduction: Functional loss is greatly determined by postural control impairment in chronic stroke survivors causing reduced ability to execute activities of daily living, impaired mobility and increases the risk of falling. It is known that the basal ganglia network play an important role in postural control, however the effect of sensory-manipulated balance training on structural connectivity in chronic stroke survivors remains unknown.

Objective: To assess the influence of sensory-manipulated balance training, i.e. sensory-motor training (SMT), on structural connectivity and functional recovery in chronic stroke survivors.

Study design: Double-blind randomised controlled trial.

Methods: Twenty-two individuals with chronic stroke ($\geq$ 6 months post-stroke) were randomly divided into two groups, namely the sensory-motor training (SMT; n = 12) and attention-matched control group (CON; n = 10). The SMT group participated in task-specific balance training, which focused on manipulating the visual, vestibular and somatosensory systems, three times a week for 45 to 60-minute sessions, over an eight-week period. The CON group attended educational talks regarding various lifestyle topics for the same duration as the SMT group. Both interventions were delivered by experienced clinical exercise therapists and were executed in a group setting. Primary outcome measures included changes in structural connectivity strength (diffusion tensor magnetic resonance imaging (MRI) scan), postural sway and sensory dependency (modified Clinical Test for Sensory Interaction and Balance (m-CTSIB)), as well as functional mobility (Timed-Up and Go (TUG)).

Structural connectivity strength was specifically investigated between the two subcortical basal ganglia nuclei, caudate and lentiform nucleus, with other regions of interest. Furthermore, the m-CTSIB and TUG tests were executed with APDM's Mobility Lab^{TM} body-worn inertial sensors. Secondary outcome measures were health-related quality of life (Short Form Health Survey (SF-36)) and fall efficacy (Fall Efficacy Scale - International (FES-I)). Participants were tested pre- and post-intervention.

Results: Diffusion tensor MRI results showed interaction effects for increased connectivity strength between the basal ganglia and sensory-motor fronto-parietal areas in the SMT group (n = 5; $p < 0.05$), whereas the CON group (n = 4) presented increased structural connectivity in the higher cognitive orbito-temporal and frontal lobe areas ($p < 0.05$). For the behavioural outcome measures, interaction effects were found for turning performance ($p = 0.02$), perceived physical functioning ($p = 0.005$) and fall efficacy ($p = 0.03$). Moreover, the SMT group (n = 12) showed improved postural sway when standing on a foam pad with eyes open ($p = 0.04$, ES = 0.61^{M}, 95% CI = -0.27 to 1.36), reduced somatosensory dependence ($p = 0.02$, ES = 0.63^{M}, 95% CI = -0.24 to 1.40), improved turning performance ($p \leq 0.05$) as well as improvements in perceived physical ($p = 0.01$, ES = 0.52^{M}, 95% CI = -0.33 to 1.29) and social functioning ($p = 0.02$, ES = 1.03^{L}, 95% CI = 0.11 to 1.80) after participating in the SMT programme. Lastly, a group difference was observed for perceived physical ($p = 0.003$, ES = 0.90^{L}, 95% CI = -0.05 to 1.70) and social functioning ($p = 0.02$, ES = 1.01^{L}, 95% CI = 0.04 to 1.81) at post-intervention.

Conclusions: This study highlights postural control-related improvements induced by SMT, which may be associated with structural connectivity changes in chronic stroke survivors. Therefore, the preliminary results support the notion that the human brain has the ability to undergo activity-dependent neuroplasticity.

Uittreksel

Die Effek van Sensories-Motoriese Oefening op Brein Aktivering en Funksionele Herstel in Individue met Kroniese Beroerte

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Inleiding: Funksionele verlies word grootliks bepaal deur aantasting van postuurbeheer in individue met kroniese beroerte, wat veroorsaak dat die vermoë om alledaagse aktiwiteite uit te voer verswak, mobiliteit aangetas word en valrisiko verhoog. Dit is bekend dat die basale ganglia 'n belangrike rol in postuurbeheer speel, maar die effek van sensories-gemanipuleerde balansoefening op strukturele konnektiwiteit in individue met kroniese beroerte bly onbekend.

Doelwit: Om die invloed van sensories-gemanipuleerde balansoefening, d.i. sensories-motoriese oefening (SMO), op strukturele konnektiwiteit en funksionele herstel te evalueer in individue met kroniese beroerte.

Studie ontwerp: Dubbelblind ewekansige gekontroleerde proefneming.

Metodes: Twee-en-twintig individue met kroniese beroerte ($\geq$ 6 maande gelede) is ewekansig in twee groepe verdeel, naamlik die sensories-motoriese oefening (SMO; n = 12) en gelyke-aandag kontrolegroep (KON; n = 10). Die SMO-groep het drie keer per week in 45- tot 60 minuut sessies deelgeneem aan taak-spesifieke balansoefeninge, wat gefokus het op die manipulering van die visuele, vestibulêre en somatosensoriese stelsels oor 'n tydperk van agt weke. Die KON-groep het opvoedkundige praatjies met betrekking tot verskeie onderwerpe oor lewenstyl bygewoon vir dieselfde tydsduur as die SMO-groep. Beide intervensies was deur ervare kliniese oefenterapeute gelewer en in groepsverband uitgevoer. Primêre uitkomstes het die sterkte van strukturele konnektiwiteit (*diffusion tensor magnetic resonance imaging (MRI) scan*), postuurswaai en sensoriese afhanklikheid (*modified Clinical Test for Sensory*

Interaction and Balance (m-CTSIB)), sowel as funksionele mobiliteit (*Timed-Up and Go (TUG)*) ingesluit. Die sterkte van strukturele konnektiwiteit was spesifiek ondersoek tussen die twee subkortikale basale ganglia kerne, koudaat en lensvormige kern, met ander areas van belang. Verder was die *m-CTSIB* en *TUG*-toetse uitgevoer met *APDM* se *Mobility Lab*^{TM} traagheidsensors. Sekondêre uitkomstes was gesondeheidsverwante lewenskwaliteit (*Short Form Health Survey (SF-36)*) en valpersepsie (*Fall Efficacy Scale - International (FES-I)*). Deelnemers was voor- en na-intervensie getoets.

Resultate: Diffusion tensor MRI resultate het interaksie effekte vir verhoogde konnektiwiteitsterkte tussen die basale ganglia en sensories-motoriese fronto-pariëtale areas in die SMO-groep (n = 5; $p < 0.05$) getoon, terwyl die KON-groep (n = 4) verhoogde strukturele konnektiwiteit in die hoër orbito-temporale- en frontale lobareas ($p < 0.05$) getoon het. Vir die gedragsuitkomste was interaksie effekte gevind vir omdraai-prestasie (p = 0.02), self-waargenome fisiese funksionering (p = 0.005) en valpersepsie (p = 0.03). Verder het die SMO-groep (n = 12) die volgende getoon: verbeterde postuurswaai wanneer daar op 'n sponsmat met oop oë gestaan word (p = 0.04, ES = 0.61^{M}, 95% CI = -0.27 to 1.36), verlaagde somatosensoriese afhanklikheid (p = 0.02, ES = 0.63^{M}, 95% CI = -0.24 to 1.40), verbeterde omdraai-prestasie ($p \leq 0.05$) sowel as 'n verbetering in self-waargenome fisiese- (p = 0.01, ES = 0.52^{M}, 95% CI = -0.33 to 1.29) en sosiale funksionering (p = 0.02, ES = 1.03^{L}, 95% CI = 0.11 to 1.80) na deelname aan die SMO-program. Laastens was 'n groepsverskil opgemerk vir waargenome fisiese- (p = 0.003, ES = 0.90^{L}, 95% CI = -0.05 to 1.70) en sosiale funksionering (p = 0.02, ES = 1.01^{L}, 95% CI = 0.04 to 1.81) na-intervensie.

Gevolgtrekkings: Hierdie studie beklemtoon postuurbeheer verwante verbeteringe wat deur SMO geïnduseer is, en word geassosieer met veranderinge in strukturele konnektiwiteit in individue met kroniese beroerte. Die voorlopige resultate ondersteun daarom die idee dat die menslike brein die vermoë het om aktiwiteits-afhanklike neuroplastisiteit te ondergaan.

Zusammenfassung

Zum Effekt von sensomotorischem Training auf die Gehirnaktivierung und die Wiederherstellung der Körperfunktionen bei chronischen Schlaganfall-Überlebenden

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Einleitung: Funktionsverlust bei chronischen Schlaganfall-Überlebenden wird maßgeblich durch die Beeinträchtigung posturaler Kontrolle bestimmt und führt zur reduzierten Fähigkeit, Alltagsaktivitäten durchzuführen, eingeschränkter Mobilität und erhöhtem Sturzrisiko. Es ist allgemein bekannt, dass dem Netzwerk der Basalganglien eine bedeutende Rolle bei der posturalen Kontrolle zukommt. Allerdings ist die Wirkung von sensorisch-manipuliertem Gleichgewichtstraining auf strukturelle Konnektivität bei chronischen Schlaganfall-Überlebenden nicht bekannt.

Zielsetzung: Ziel ist es ist, den Einfluss von sensorisch-manipuliertem Gleichgewichtstraining bzw. sensomotorischem Training (SMT) auf die strukturelle Konnektivität und die Wiederherstellung der Körperfunktion bei chronischen Schlaganfall-Überlebenden zu untersuchen.

Untersuchungsdesign: Eine doppelt verblindete randomisierte, kontrollierte Studie.

Verfahren: Zweiundzwanzig Individuen mit chronischem Schlaganfall ($\geq$ 6 Monate) wurden willkürlich in zwei Gruppen aufgeteilt, nämlich das sensomotorische Trainings- (SMT; n = 12) und eine *attention-matched* Kontrollgruppe (CON; n = 10). Die SMT-Gruppe beteiligte sich an aufgabenspezifischem Gleichgewichtstraining, dessen Fokus die Manipulation der visuellen, vestibulären und somatosensorischen Systeme bildetet. Dies erfolgte dreimal die Woche für 45-60 Minuten pro Sitzung und verlief über einen Zeitraum von

acht Wochen. Die CON-Gruppe besuchte für die gleiche Zeitdauer Beratungsgespräche über verschiedene Lifestyle-Themen. Beide Interventionen wurden durch erfahrene klinische Bewegungstherapeuten durchgeführt und erfolgten im Gruppenverband. Die primären Ergebnismessungen beinhalteten Veränderungen in der Intensität der strukturellen Konnektivität (*diffusion tensor magnetic resonance imaging (MRI) scan*), Körperhaltung und -bewegung und sensorische Abhängigkeit (*modified Clinical Test for Sensory Interaction and Balance (m-CTSIB)*) sowie funktionale Mobilität (*Timed-Up and Go (TUG)*). Die Intensitität der strukturellen Konnektivität wurde vor allem zwischen den zwei subkortikalen Nuclei basales, den Nucleus caudatus und Nucleus lentiformis untersucht, mit zusätzlichen Interessenbereichen. Des Weiteren wurden die *m-CTSIB*- und *TUG*-Tests mit APDMs Mobility Lab^{TM} am Körper getragenen Inertialsensoren durchgeführt. Sekundäre Ergebnismessungen waren gesundheitsbezogene Lebensqualität (*Short Form Health Survey (SF-36)*) und sturzassoziierte Selbstwirksamkeit (*Fall Efficacy Scale - International (FES-I)*). Die Beteiligten wurden vor und nach der Intervention geprüft.

Ergebnisse: Die Diffusions-Tenor-MRI-Ergebnisse zeigen Interaktionseffekte für eine erhöhte Intensität der Konnektivität zwischen den Basalganglien und sensomotorisch-frontalparietalen Bereichen bei der SMT-Gruppe (n = 5; $p < 0.05$), wohingegen die CON-Gruppe (n = 4) eine erhöhte strukturelle Konnektivität im höheren kognitiven orbitotemporalen und Frontallappenbereichen präsentierte ($p < 0.05$). Hinsichtlich der verhaltensbezogenen Ergebnismessung wurden Interaktionseffekte bei der Drehfähigkeit ($p = 0.02$), der wahrgenommenen körperlichen Funktionsfähigkeit ($p = 0.005$) und sturzassoziierter Selbstwirksamkeit ($p = 0.03$) festgestellt. Außerdem zeigte die SMT-Gruppe (n = 12) nach ihrer Beteiligung am SMT-Programm eine verbesserte posturale Stabilität beim Stehen auf einem Schaumstoffkissen mit geöffneten Augen ($p = 0.04$, ES = 0.61^{M}, 95% CI = -0.27 to 1.36), eine reduzierte somotosensorische Abhängigkeit ($p = 0.02$, ES = 0.63^{M}, 95% CI = -0.24 to 1.40), eine gesteigerte Drehfähigkeit ($p \leq 0.05$) sowie eine Verbesserung in der wahrgenommenen körperlichen ($p = 0.01$, ES = 0.52^{M}, 95% CI = -0.33 to 1.29) und sozialen Funktionsfähigkeit ($p = 0.02$, ES = 1.03^{L}, 95% CI = 0.11 to 1.80). Nicht zuletzt wurde nach der Intervention ein Gruppenunterschied bei der wahrgenommen körperlichen ($p = 0.003$, ES = 0.90^{L}, 95% CI = -0.05 to 1.70) und sozialen Funktionsfähigkeit ($p = 0.02$, ES = 1.01^{L}, 95% CI = 0.04 to 1.81) beobachtet.

Fazit: In der Studie werden die Verbesserungen der Körperhaltung und -bewegung hervorgehoben, die durch SMT induziert wurden. Dies mag mit Änderungen der strukturellen Konnektitvität bei chronischen Schlaganfall-Überlebenden assoziiert sein. Die vorläufigen Ergebnisse unterstützen somit die Annahme, dass das menschliche Gehirn die Fähigkeit besitzt, sich einer aktivitätsabhängigen Neuroplastizität zu unterziehen.

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"The future belongs to those who believe in the beauty of their dreams."
- Eleanor Roosevelt

Dedications

This thesis is dedicated to the memory of my grandfather Frans Hendrik Viljoen (27 November 1935 - 06 August 2018) whose love for teaching and education was contagious.

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Abbreviations

ABC:	Activities-specific Balance Confidence
AD:	Axial diffusion
ADL:	Activities of daily living
BBS:	Berg Balance Scale
BOLD:	Blood-oxygen-level-dependent
BOS:	Base of support
CBF/V:	Cerebral blood flow/volume
CI:	Confidence intervals
CNS:	Central nervous system
COG:	Centre of gravity
COM:	Centre of mass
CON:	Attention-matched control group
COP:	Centre of pressure
DMN:	Default mode network
DTI:	Diffusion tensor imaging
DWI:	Diffusion weighted imaging
EPI:	Echo planar imaging
ES:	Effect size
FA:	Fractional anisotropy
FES-I:	Fall Efficacy Scale - International
fMRI:	Functional magnetic resonance imaging
FOV:	Field of view
FT:	Fiber tracking
IMI:	Intrinsic Motivation Inventory
iTUG:	instrumented Timed-Up and Go
LSD:	Least Significant Difference
M1:	Primary motor cortex

MBI:	Magnitude-based inference
MD:	Mean diffusivity
m-CTSIB:	modified Clinical Test for Sensory Interaction and Balance
MRI:	Magnetic resonance imaging
MoCA:	Montreal Cognitive Assessment
NDT:	Neurodevelopmental-theory-based treatment
NHP:	Nottingham Health Profile
PEDro:	Physiotherapy Evidence Database
PFC:	Prefrontal cortex
PMC:	Premotor cortex
RAPA:	Rapid Assessment of Physical Activity
RD:	Radial diffusion
RPE:	Rate of Perceived Exertion
S1:	Primary somatosensory cortex
SD:	Standard deviation
SEM:	Standard Error of the Mean
SF-36:	Short Form Health Survey
SIT:	Sensory integration training
SMA:	Supplementary motor area
SMT:	Sensory-motor training
SOT:	Sensory Organization Test
TBM:	Tensor-based morphometry
TE:	Echo time
TR:	Repitition time
TUG:	Timed-Up and Go
VAS:	Visual Analogue Scale
VBM:	Voxel-based morphometry

Glossary

Activity-dependent neuroplasticity: Reorganisation of the central nervous system (CNS) in response to goal-directed therapy [1, 2, 3].

Base of support (BOS): The base of support for standing on a flat, firm surface is defined as the area contained within the perimeter of contact between the surface and the two feet. This area is nearly square when the feet are placed comfortably apart while the person is quietly standing [4, 5].

Centre of mass (COM): This is a point that relates to the centre of the total body mass, where the body is in perfect equilibrium [4].

Centre of gravity (COG): This is the vertical projection of the COM to the ground, usually located in the lower abdominal area of the trunk [4].

Ellipse sway area (95%): The area of the 95% confidence ellipse encompassing the sway trajectory in the transverse plane [6].

Jerkiness: This is the relative smoothness of postural sway, reflecting the amount of active postural corrections, and is interpreted as a measure of dynamic stability [7].

Functional recovery: The improved ability of an individual to execute activities of daily living (ADL) and perform mobility independently [8].

Neurplasticity: Ability of the CNS to reorganise itself and adopt a new structural or functional state in response to intrinsic and extrinsic factors [9, 10, 11].

Postural control: The ability to maintain COM within the limits of stability, therefore keeping to the BOS [12]. It contains a complex organisation that controls the orientation and equilibrium of the body when standing upright [13].

Sensory-motor system: The process whereby sensory input gets integrated by the CNS, to facilitate and implement motor program execution [14].

Overview

The current dissertation followed a PhD by publication format and focussed on clinical and practical implications of the research conducted, based on the specified research aims and objectives. Chapter 1 serves as an introduction, providing background information on stroke as well as knowledge regarding sensory-motor principles, neuroplasticity and functional recovery. Chapter 2 presents an in depth overview of the core concepts and previous research conducted that relates to this dissertation. This includes aspects of stroke and the human brain, postural control-related functional recovery, activity-dependent neuroplasticity, the sensory-motor training (SMT) programme utilised and the dynamic systems theory. This chapter also contains a review on previously conducted intervention studies that focussed on the effect of sensory-manipulated balance training on structural neuroplasticity and postural control-related functional recovery in chronic stroke survivors. Additionally, the problem statement, research hypothesis as well as aims and objectives are discussed at the end of Chapter 2. Chapters 3-5 each contain a research article, however a unified style is used throughout this dissertation. Therefore, one reference list can be found at the end of the dissertation, after the Appendices. Lastly, Chapter 6 contains a general discussion and conclusion, which includes the study limitations, recommendations for future research, as well as implications for clinical practice. The Vancouver (numeric) referencing style was used throughout this dissertation and all additional documentation can be found in the Appendices attached.

Chapter 1

Introduction

1.1 Background

Stroke is a neurological disorder causing one in ten deaths globally and has shown to be the second-leading cause of death worldwide [15]. According to a Global Burden of Disease Study, by 2030 there will be 20 million stroke deaths yearly and 70 million stroke survivors living with disability worldwide [16]. Survivors are affected by the long-term consequences of stroke, which impact individuals, health systems and society [17]. Research on the incidence and prevalence of stroke is particularly scarce, especially from developing countries.

In South Africa, stroke is a significant cause of death, however very little research has been done on the epidemiology of stroke in South Africa [18, 19, 20]. Bertram and colleagues [21] stated that stroke causes 25 000 deaths yearly in South Africa and that 95 000 stroke survivors live with disability. Calculations established that in 2011, the cost of vascular disease in South Africa would be 13-16 billion Rand (840 million to 1 billion Euro) annually, creating a high health and economic burden [21].

During the acute ($<$ 3 months post-stroke) and subacute (3 to 6 months post-stroke) phases of stroke, spontaneous recovery is generally evident and a large heterogeneity is seen among survivors [22, 23, 24]. During the chronic phase of stroke ($\geq$ 6 months post-stroke), heterogeneity persists, however the effects of exercise are unlikely to be influenced by spontaneous neurological recovery, and should therefore emphasise the research importance [25]. It is imperative to develop feasible methods for individuals to engage in exercise programmes, independently, to improve their quality of life. Exercise may be a cost-effective and simple way to promote independent living in chronic stroke individuals.

1.2 Sensory-Motor Principles

Dr. Vladimir Janda, a physician and neurologist from the Czech Republic (1928-2002), studied the control of human movement and noted that it is impossible to separate the motor and sensory systems. He started using the term sensorimotor (also referred to as sensory-motor) system and defined it as the process whereby sensory input gets integrated by the central nervous system (CNS), to facilitate and implement motor programme execution [14].

Postural control is a complex sensory-motor process that allows an individual to maintain their balance through feedback and feed-forward mechanisms from the visual, vestibular and somatosensory systems [26]. Following stroke, postural control can be compromised due to insufficiencies within the various systems responsible for postural stability [27, 13]. Furthermore, one of the major culprits causing impaired postural control in chronic stroke survivors is the lack of sensory integration and reweighting, i.e. the ability to choose and rely on the appropriate visual, vestibular and somatosensory input under different contextual conditions [13, 28]. Therefore, these individuals struggle to mobilise available sensory systems when one of the other sensory inputs are missing or insufficient [29]. According to Carey [30], deficits in the sensory systems are present in more than half of stroke survivors and influences motor function, which could limit participation in activities of daily living (ADL) and affect independent living [31].

The sensory-motor training (SMT) programme in this dissertation entails task-specific balance training in combination with manipulating the visual, vestibular and somatosensory systems. Examples of sensory manipulation include head, hand and eye movements, removing or disrupting visual input (i.e. blindfolding, closing eyes, moving the visual surround) or changing the surface area (i.e. foam and/or incline surfaces) to disrupt somatosensory and vestibular input. The SMT programme utilised will be discussed in more detail throughout Chapter 2-5 and can be found in Appendix A.

1.3 Neuroplasticity and Functional Recovery

During childhood the brain goes through extraordinary changes and it preserves the ability to adapt throughout life. Brain plasticity, also known as neuroplasticity, is the ability of the brain and other parts of the CNS to reorganise itself in response to sensory input, experience and learning [9, 10]. During the chronic stage of stroke, spontaneous plasticity mostly subsides and shifts towards activity-dependent plasticity, i.e. brain changes in response to goal-directed therapy [32, 1, 2, 3, 11]. Fortunately, advances in structural and functional magnetic resonance imaging (MRI) data analysis has made it pos-

sible to measure activity-dependent neuroplasticity in humans [33].

Stroke critically disrupts the homeostasis within the motor network when a lesion either directly affects the cortical or subcortical areas or damages-related white matter tracts [34]. Consequently, this could lead to slow, uncoordinated, weak and abnormal postural control, and at worst, movement cannot be produced altogether. Fortunately, the damaged CNS has the ability to adapt and repair itself through neuroplasticity, induced by physical activity [3]. Plasticity after stroke occurs at a neurological level that is overall associated with structural and functional reorganisation of the brain [35].

Brain reorganisation is the ability of the brain to modify its own structure and function, plays an important role in functional recovery [36] and incorporates alterations in both the sensory and motor areas [37]. These alterations enable new functions or compensate for lost functions following stroke [38]. Research shows that standing balance is a strong predictor of functional recovery [39, 40], walking capacity [23, 41] and fall risk [42], which all give an indication of ADL performance. Functional recovery is the improved ability of an individual to execute ADL and perform mobility independently [8]. Thus, functional recovery is exceedingly important for stroke survivors as this can aid them in achieving a level of functional independence to return and reintegrate into their community.

1.4 Conclusion

Postural control impairment is one of the leading causes of functional loss among stroke survivors causing impaired movement, reduced ability to execute ADL and increased risk of falling [43]. Balance interventions executed under sensory manipulation, are being recognised as a strategy to improve the functional status of chronic stroke individuals. Research indicates that following several weeks of sensory-manipulated balance training, chronic stroke survivors have shown significant improvements in balance, functional mobility, walking speed, endurance and muscle activity [44, 29, 28]. To date, no research has been done on the effect of balance training on brain connectivity in chronic stroke survivors.

To conclude, rehabilitation is the most common treatment modality to provide stroke survivors with the highest likely level of physical and psychological performance [45]. Balance training with sensory system manipulation shows promise in improving functionality in chronic stroke survivors. Therefore, this study sets out to investigate the effect of SMT on structural brain connectivity and functional recovery in chronic stroke survivors.

Chapter 2

Core Concepts and Literature Review

This chapter provides an overview of the core concepts related to this dissertation and sets the context of the literature review. The chapter starts by giving a brief description of stroke, which is followed by the different brain structures important for sensory-motor processing and integration. The focus then shifts to the concepts of postural control, based on the systems framework for postural control, and how stroke affects these domains. The next three sections describe activity-dependent neuroplasticity, the principles used to design the sensory-motor training (SMT) programme utilised and why the dynamic systems theory was applied. Thereafter, a review of previous research is provided, specifically interventions that investigated the effect of sensory-manipulated balance training on neuroplasticity and functional recovery in chronic stroke survivors. Lastly, the problem statement is specified with the stipulated aims and objectives for the current dissertation, setting the scene for the three article formulated chapters.

2.1 The Brain after Stroke

The brain is highly dependent on sufficient blood supply, as only seconds without adequate oxygen can cause neurological symptoms, and minutes can cause irreversible neuronal damage. The brain is protected by cerebral vasculature, which have special anatomical and physiological functions to protect the brain. When the cerebral vasculature fails to protect the brain, the result is a cerebrovascular accident, more commonly known as a stroke [46]. The timeline of stroke can be split into three phases, namely the acute phase ($<$ 3 months post-stroke), subacute phase (3 to 6 months post-stroke) and chronic phase of stroke ($\geq$ 6 months post-stroke) [22, 23, 24, 25].

Stroke can be divided into two main categories namely, ischemic (infarc-

tion) or haemorrhagic (bleeding) cerebral insult. An ischemic stroke occurs when insufficient blood supply is being delivered to the brain due to an obstruction in a blood vessel(s). Depending on where the obstruction occurs, it can further be divided into (1) thrombotic stroke; blood vessel obstruction inside the brain, or arteries in the neck, or (2) embolic stroke; blood vessel obstruction elsewhere in the body which travels to the brain [47, 48, 46]. Haemorrhagic stroke occurs due to the rupture of a blood vessel in or around the brain. These are also further subdivided into (1) intracerebral haemorrhage; blood vessel rupture within the brain itself, or (2) intracranial haemorrhage; blood vessel rupture between the brain and the skull [47, 46]. Ischemic stroke occurs more frequently than haemorrhagic stroke, roughly accounting for 70% to 80% of all strokes [47]. For detailed classification of stroke subtypes, please refer to Amarenco and colleagues [49].

Stroke is a heterogeneous disease causing various neurological signs and symptoms, which are not only defined by the type of stroke, but also the lesion site and the extent of cerebral insult [49, 50]. Interestingly, the side of lesion remains a matter of controversy in whether it is a key element of balance impairment after stroke [26]. Researchers have found that right cerebral hemisphere lesions present with a greater amount of balance impairment [51, 52, 53, 54], which could be explained by the function of the right posterior parietal lobe [52]. However, lesions of the left hemisphere have not shown any difference [55, 56] or contrasting results [22] with worse outcomes of static and dynamic balance ability. Thus, more research is warranted about the possible effects of the side of lesion after stroke.

An intact sensory-motor system is essential in practicing activities of daily living (ADL), as it is responsible for processing sensory information and generating the appropriate motor output [57]. Following stroke, the sensory-motor system might be impaired due to the loss of neural tissue, which induces neurophysiological changes throughout the brain, and leads to various functional impairments [58]. These impairments do not only occur due to the specific lesioned area, but also due to the inability of the rest of the brain to maintain normal functioning [59]. The next section will look at what the sensory-motor system entails and what functions could be lost due to stroke-related damage.

2.2 Sensory-Motor Brain Structures

Humans are capable of various types of movements that originate from the activity of 640 skeletal muscles, which are all controlled by the central nervous system (CNS). For these movements to occur the CNS needs to process and integrate sensory information from the visual, vestibular and somatosensory systems to form an internal representation of the body and its surroundings

[13, 60]. The motor centres in turn, utilise the internal representation and execute coordinated and purposeful movements [46, 61].

Each section of the brain is responsible for different functions, therefore, according to researchers, the brain is organised in a functional hierarchy [62]. The prefrontal cortex (PFC) is the highest level, which is concerned with the purpose of movement [63]. The next level involves the interaction between the parietal lobe and premotor cortex (PMC), leading to the formation of a motor plan [63, 64]. The parietal lobe provides sensory information regarding the environment and body position in space to the PMC, which specifies the spatial characteristics of a movement. The lowest level contains the primary motor cortex (M1), brain stem and spinal cord, which coordinate and define the muscle contractions needed to execute a purposeful movement [46, 63].

This section provides an overview of the most important cortical and subcortical sensory-motor areas with regards to anatomy and function. Most attention is paid to the basal ganglia because it is the primary focus of Chapter 3, Article 1. The main reasoning for this is that it plays an important role in and has shown to be predictive of postural control [65, 66].

2.2.1 Primary Somatosensory Cortex

The primary somatosensory cortex (S1; Brodmann Area 3,1 & 2), also known as somatic sensory cortex, is located within the postcentral gyrus in the parietal lobe. It is responsible for the extraction of sensory information regarding the visual movement of objects, their location in space and in relation to oneself. The S1 does not only extract relevant sensory information, but also organises the information relative to the situation or context. This contextual processing allows for goal-orientated behaviour to occur by relaying the information to the PMC [67].

2.2.2 Premotor Cortex

The PMC (Brodmann Area 6, laterally) can be found in the frontal lobe of the brain and lies just anterior to the M1. The PMC is responsible for motor control, decision-making, strategy formation as well as selection of correct movement responses relative to available sensory input [68, 50]. More specifically, it is involved in the integration of sensory information with regards to the environment as well as object and body position in space [69]. After sensory information is extracted and filtered in the S1, it is projected to the PMC from which these projections are then sent to the M1 for further integration and analysis [68, 50].

2.2.3 Primary Motor Cortex

The M1 (Brodmann Area 4) is a strip of angular cortex within the precentral gyrus in the frontal lobe. For a long time, researchers believed that the M1 is solely responsible for the control of voluntary movements. However, more recently it has been found that the M1 contains a heterogeneous population of neurons that assist in the planning of a movement and more importantly, the execution of said movement [70]. The motor neurons in the spinal cord function to encode the different muscle activity patterns received form the M1. Thus, the M1 is a dynamic map, which forms part of a network of cortical motor areas, each responsible for different aspects of the control of voluntary movement [50, 67, 71].

2.2.4 Supplementary Brain Areas

The supplementary brain area (SMA; Brodmann Area 6, medially) is situated in front of the M1 and medial to the PMC in the frontal lobe. The superior frontal gyrus is considered to be included in the SMA and is connected with the middle frontal gyrus [72, 73]. It forms part of a centre of behavioural organisation and is involved in the planning, execution and control of motor actions. A popular hypothesis is that the SMA is concerned with internal and self-guided behaviour, whereas the PMC mostly controls externally guided behaviour. Furthermore, the SMA functions to switch between different actions or strategies and is primarily concerned with the acquirement of a motor skill rather than the performance [74, 50]. The SMA also plays an important role in postural control [75, 76] and is suggested to be a crucial area for balance recovery in stroke survivors [77].

2.2.5 Cerebellum

Various areas of the CNS project to different regions of the cerebellum, which in turn project to the motor cortex. Even though the cerebellum cannot initiate motor activity independently, it is crucial for coordinated motor control execution [70]. Due to the cerebellum's input and output organisation, it is known that the cerebellum primarily functions to generate corrective signals in order to make movements as accurate as possible. The cerebellum does this by comparing the intended movement, received by internal feedback systems, with the actual movement, received by external feedback systems. Therefore, a continuous inflow of information exists from the motor and sensory cortices [70]. These corrective signals are mostly anticipatory actions, which mean a great deal of movement planning has to be done in advance. Thus, motor and cognitive learning also play an important part in the cerebellum, and are dependent on repeated practise [50, 78]. Additionally, the cerebellum is impli-

cated in motor learning, postural equilibrium and somatosensory processing [70].

2.2.6 Basal Ganglia

The basal ganglia are located deep within the cerebral hemispheres, and consists of five subcortical groups of nerve cells (nuclei), namely the caudate, putamen, globus pallidus, substantia nigra and subthalamic nucleus [79]. The striatum is a major input structure of the basal ganglia and consists of the caudate nucleus and putamen. Furthermore, the putamen and globus pallidum together form the lentiform nucleus [80, 67, 81]. The basal ganglia network has been shown to play a great role in postural control, motor learning and motor control [77, 81], and has previously been a focus point in balance training studies [82, 81].

Traditionally, it was believed that the basal ganglia largely play a role in motor functions for two reasons; (1) Parkinson's disease and Huntington's disease originate from basal ganglia impairment and are characterised as movement disorders, and (2) the basal ganglia exclusively send its output neurons to the motor cortex. More recently it was made clear that the basal ganglia are not only involved in motor functions, but also assist in storing and executing motor plans automatically, adapting to environmental changes, processing sensory information, regulating muscle tone, controlling automatic postural responses and contribute in higher-order aspects of mood, behaviour, emotion, reward and executive functioning [65, 83, 50].

To conclude, an intact sensory-motor system is essential for the neural control of movement. The functioning of the brain occurs through integration, no matter how simple the activity or movement is. Therefore, damage in one region of the brain not only affects the associated specialised centres, but also causes the entire brain to suffer due to the loss of input from the injured part [84]. Taken together from the section above, it is clear that the sensory-motor structures play a big role in postural control, which is the focus of the next section.

2.3 Overview of Postural Control

Postural control is the ability to maintain balance in a gravitational environment, and requires the interaction of multiple sensory-motor processes [85]. It is usually referred to when discussing the neural and musculoskeletal subsystems that contribute to balance function [12]. These neural systems include, the spinal cord, brainstem, cerebellum, basal ganglia and cerebral cortex in a hierarchical manner [77]. Therefore, the CNS filters, compares, weighs, stores

and processes sensory information from the visual, vestibular and somatosensory systems, to implement the correct timing, direction and amplitude for the desired postural action [86].

Postural control consists of two main functional goals, namely (1) postural orientation, and (2) postural equilibrium [13]. The first, postural orientation, involves the interpretation of the visual, vestibular and somatosensory systems to actively control body tone and alignment. Secondly, postural equilibrium is the ability to maintain the centre of gravity (COG) within the body's base of support (BOS), by means of coordination between the sensory-motor strategies [13, 87]. Postural equilibrium can further be divided into static or dynamic equilibrium. Static equilibrium involves the capability to keep the centre of mass (COM) within the BOS, and thus maintaining a stable position. Whereas, during dynamic equilibrium, an unstable position exists because the COM is disrupted and cannot be kept within the BOS [87]. Postural equilibrium is essential during the maintenance of static postural positions, i.e. sitting or standing, moving between structures, as well as when reacting to external disturbances, such as slipping or tripping [88].

Maintaining postural control requires effective interaction between the motor, sensory and neural systems [89]. Therefore, a systems framework for postural control was described by Horak [13], which entails six major components that are crucial for the maintenance of postural control (Table 2.1). With aging and disease, complications in any one of these components can occur, leading to postural instability and increased risk for falling. The next section will discuss the resources important for postural control as well as the effect of stroke induced constraints on the postural control system.

Table 2.1: Resources required for postural stability and orientation.

Domains in Systems Framework for Postural Control	Summarised components in each domain
Biomechanical Constraints	Degrees of freedom, strength, limits of stability
Movement Strategies	Reactive balance, anticipatory and voluntary postural strategies
Sensory Strategies	Sensory integration, sensory reweighting
Orientation in Space	Perception, gravity, verticality
Control of Dynamics	Gait, proactive control
Cognitive Processing	Attention, learning

Adapted from Horak [13]

2.4 Postural Control Resources and Stroke

Individuals that have suffered a stroke present with impaired postural control due to deficits in the different domains and systems responsible for postural stability [27, 13]. Research indicates that 75% of stroke survivors regain their independent standing-balance ability, however, asymmetry in weight-bearing activities and increased postural sway remains of a concern [90]. Due to the scope of this dissertation and outcome measures used, three of the six domains (Biomechanical Constraints, Sensory Strategies and Control of Dynamics) in the systems framework for postural control will be discussed, as well as the impact of stroke on each domain. Outcome measures regarding Movement Strategies, Orientation in Space and Cognitive Processing were not assessed in this dissertation due to time constraints and logistical difficulties.

2.4.1 Biomechanical Constraints

The ability to maintain the COG within the limits of the BOS gives an indication of postural stability [26]. According to Horak [13], the most crucial biomechanical constraint to postural control is the size and quality of the BOS. Limits of stability can be defined as the ability to move the COM in the anterior-posterior and medial-lateral direction without losing balance [26]. This is achieved by the formation of an internal representation by the CNS, namely a cone of stability, to determine how much AP and ML movement can be executed to sustain balance [13]. Therefore, if an individual's postural sway exceeds their limits of stability, the individual would have to give a step if the movement is controlled, or they would experience a fall. In this dissertation, the outcome measure, Jerkiness (m^2/s^5), was measured in the anterior-posterior direction, which gives an indication of the relative smoothness of postural sway, reflecting the amount of active postural corrections made [7]. Furthermore, the 95% ellipse sway area (m^2/s^4) was also measured, which is the circle containing 95% of the sway area in the transverse plane [6].

Chronic stroke-related balance impairments include increased postural sway as well as reduced limits of stability [55, 27, 43]. Furthermore, signs and symptoms seen in stroke individuals, such as pain, weakness, reduced muscle control and decreased range of motion, can alter an individual's BOS [56]. Postural instability is an unavoidable feature of stroke involving both static and dynamic postural equilibrium. Therefore, abnormalities in the postural control system increase postural instability which will consequently affect functionality of stroke individuals [91]. Lastly, reduced postural stability can lead to falls in stroke individuals causing high economic costs and social problems [92].

2.4.2 Sensory Strategies

As mentioned earlier, sensory-motor interaction is essential for postural control. This refers to the process whereby the CNS integrates sensory input, used for assisting or implementing motor programme execution [93, 57]. The visual, vestibular and somatosensory systems are the three main sensory modalities involved in postural control [26]. Therefore, the ability of the brain to use multiple sensory inputs and transfer it into usable functional outputs, is referred to as sensory processing and integration [94, 95].

Another important function of the CNS to maintain postural control is sensory reweighting, which enables an individual to scale the relative importance of sensory cues in an ever-changing environment [96, 13, 12]. When in an upright position, the CNS gives priority to one system over another to control balance when multiple sources are available [97]. For example, if an individual is standing on an unstable surface with their eyes open, the somatosensory system will be disrupted, and the CNS will use the accurate visual and vestibular information available to maintain postural control. Consequently, any abnormal interactions between the sensory systems could be the source of impaired postural control [55]. The Modified Clinical Test for Sensory Interaction and Balance (m-CTSIB) was used to quantify how well participants were able to shift the importance and select the most suitable or accurate sensory information (visual, vestibular and/or somatosensory) for the situation.

When standing in a controlled environment with feet in contact with the floor with a firm BOS, healthy individuals tend to rely 70% on somatosensory information, 20% on vestibular information and 10% on visual information to maintain postural control [98]. Following stroke, sensory integration and reweighting has been shown to be impaired and that these individuals mainly rely on visual feedback to maintain postural control [55, 43, 99, 100]. According to Bonan and colleagues [55], individuals with stroke show worse performance under conditions of inaccurate somatosensory and visual feedback. Furthermore, they demonstrate reduced multisensory integration with excessive reliance on visual input during the chronic stages of stroke [55]. Unfortunately, the visual system becomes impaired with aging, which means these individuals are relying on an inappropriate sensory system. This in turn results in individuals having poor postural control, causing decreased independence in ADL and an increased risk for falling [55, 101].

2.4.3 Control of Dynamics

Mobility is the ability of changing and maintaining posture while moving oneself from one position to another [102]. During gait, the COM is not within the BOS and requires a complex control of balance. Forward postural stabil-

ity is defined as placing the swinging limb under the falling COM during gait, whereas the combination of lateral trunk control and lateral foot placement is defined as lateral postural stability [103, 13]. The extent of functional recovery after stroke is greatly determined by dynamic postural equilibrium [104].

Gait abnormalities among stroke survivors hold long term implications such as decreased efficiency, reduced activity levels and musculoskeletal injury [105]. According to researchers, stroke individuals have higher energy expenditure during gait as well as very low activity levels compared to healthy controls [106, 107]. In everyday life, various situations require an individual to change direction or turn while walking, i.e. walking in crowded areas, performing household tasks, grocery shopping, etc. Interestingly, more than 20% of steps taken at home are turns [108], and both walking and turning contribute to the risk of falling [109, 110]. Unfortunately, gait abnormalities place even more strain on turning difficulties in stroke survivors. Thus, regaining home- and community-based dynamic postural equilibrium is an important rehabilitation goal for chronic stroke survivors [106]. The Timed-Up and Go (TUG) was used to assess performance of four functional movements, namely sit-to-stand, gait, turning 180°, and turn-to-sit [111].

In summary, stroke individuals present with various postural control impairments, specifically in limits of stability, postural sway, sensory integration and reweighting, as well as aspects of dynamic postural equilibrium. Impairments in postural control directly affect functional recovery, i.e. the ability to execute ADL and perform mobility independently. Nonetheless, rehabilitation is an efficient treatment modality to provide stroke survivors with improved functional recovery by means of activity-dependent neuroplasticity [45]. The next section will discuss the neural strategies responsible for functional improvement in stroke survivors.

2.5 Activity-Dependent Neuroplasticity

Neuroplasticity is the ability of the CNS to reorganise itself and adopt a new functional or structural state in response to intrinsic and extrinsic influences (i.e. sensory input, experience and learning) [9, 10, 11]. Therefore, when the CNS is damaged, it is able to repair itself, make changes as well as adapt through nerve regeneration and neuroplasticity [3]. Activity-dependent neuroplasticity can occur in the healthy and injured brain in response to goal-directed therapy through formation, removal as well as remodelling of synapses and dendritic connections [1, 2, 3].

Stroke is associated with the loss of neural tissue and produces great neurophysiological changes in the entire brain leading to a wide range of behavioural

impairments, such as postural control deficiencies [27, 59]. Following stroke, there is usually some spontaneous recovery over the first few months, however it subsides after some time [24]. When this occurs, activity-dependent neuroplasticity becomes important in order to induce functional recovery in chronic stroke survivors [23, 11]. Neuroplasticity after stroke occurs at a neurological level that is overall associated with structural and functional reorganisation of the brain [35]. Structural neuroplasticity refers to brain structure changes by means of white or gray matter changes, while functional neuroplasticity refers to various brain pattern changes based upon learning and memory processes [112]. Nonetheless, structural and functional neuroplasticity will always be linked to one another because any structural changes will induce brain pattern changes. Magnetic resonance imaging (MRI) is a non-invasive method which has been shown to be effective in researching the effect of exercise interventions on brain changes [63]. Table 2.2 summarises the different structural and functional MRI analysis techniques available for investigating activity-dependent neuroplasticity [63].

Focussing on activity-dependent neuroplasticity, an important question to ask is what are the training principles necessary to induce activity-dependent neuroplasticity in neurological disorders? According to researchers, the answer could lie in task-specific training, therefore, training which focusses on improving functional performance through goal-directed practice and repetition [113, 2]. Task-specific training should utilise everyday tasks to achieve optimal function in undertaking ADL. Some research has been done on neuromotor interventions in chronic stroke survivors [114], and findings suggest that task-specific training can influence neuroplasticity and functional recovery. Bayona and colleagues [115] stress the importance of task-orientated therapy and highlight the positive effects thereof on functional improvements in chronic stroke individuals.

The current dissertation uses task-specific SMT as intervention regime to investigate the effect thereof on structural neuroplasticity and functional recovery in chronic stroke survivors. In the following section, this SMT programme will be discussed in more detail, specifically how it was designed and implemented.

2.6 Sensory-Motor Training

The ability of an individual to maintain postural control is dependent on the efficiency of the sensory-motor system. It is impossible to separate the sensory and motor system from one another when interpreting the control of human movement [14]. Any changes within the sensory or motor systems will cause adaptations elsewhere in the system because it functions as a unit.

Table 2.2: MRI analysing techniques targeting the relationship between physical activity and brain structures and functions.

Method	Application
Cerebral blood flow/volume (CBF/V) Diffusion	Measurement of (regional) cerebral blood flow, e.g. the difference between precontrast and postcontrast images to access (regional) CBV map.
Diffusion tensor imaging (DTI); diffusion weighted imaging (DWI) only MD	Mapping of the diffusion process of water molecules in the brain revealing microscopic details about tissue architecture; different measurement parameters: (a) mean diffusivity (MD): average rate of water diffusion across all three eigenvalues, independent of direction (b) axial diffusion (AD): refers to the eigenvalue of the primary axis, (c) radial diffusion (RD): average of the two perpendicular eigenvalues, (d) fractional anisotropy (FA): scalar value that refers to the coherence of the orientation of water diffusion, independent of rate, (e) fiber tracking (FT): depicts white matter connectivity of the brain measurement.
Functional magnetic resonance imaging (fMRI)	Measurement of brain activity by detecting associated changes in cerebral blood flow, primary form uses the blood-oxygen-level-dependent (BOLD) contrast; applicable during the execution of a task (e.g., motor or cognitive task) or during rest (resting fMRI).
Manual morphometry Tensor-based	Determination of, e.g., gray/white matter volume or volume of white matter lesions/hyperintensities on neuroanatomic images by manually tracing regions of interest.
Tensor-based morphometry (TBM)	Deformation-based morphometry; measurement of focal differences in brain anatomy using non-linear algorithms, statistical analyses are performed on deformation fields (automated/half-automated morphometry version).
Voxel-based morphometry (VBM)	Measurement of voxel-wise differences in brain anatomy using statistical parametric mapping, images are registered to a template (automated/half-automated morphometry version).

Taken from Voelcker-Rehage et al. [63]

In 1970, Dr Vladimir Janda developed a SMT programme for rehabilitation of the lower extremities and spine [116], which progressively challenges the sensory-motor system and places emphasis on postural control. The basis of the programme is built on the importance of proprioception and therefore focusses on delivering input into the sensory-motor system from the feet to cervical spine [116, 117]. According to Janda, there are three locations in the body, which house large amounts of proprioceptors, namely the foot, the sacroiliac joint and the cervical spine. Therefore, the basis of SMT is to increase proprioceptive input from these locations to increase postural control and facilitate coordinated movement by stimulating subcortical routes.

Once an individual has learned the proper positioning of these three locations the SMT can continue. Individuals progress through static, dynamic, and functional balance exercise phases, and within each phase they progress through various postures, BOS as well as COG positions [117]. The static phase focusses on the development of a stable core, which can be built on when progressing to the next phases. Accordingly, once that is achieved more challenges can be placed on their limits of stability, forcing them to move beyond their cone of stability during the dynamic phase. The programme lastly ends off with a functional phase where individuals are challenged with ADL whilst maintaining a stable core and moving through different postures and positions.

Together with using the principles from Janda's SMT [116, 117], Horak and Nashner's [118] three movement strategies (i.e. ankle, hip and stepping strategies, Figure 2.1 [4]) to maintain balance were also incorporated. The first is the ankle strategy, which is used during small disturbances to the COG. When utilising this strategy, individuals are usually standing on a large, firm and supporting surface in a stable position. Second is the hip strategy, which comes into play when the disturbance to the COG is too large and the individual has to use flexion and extension of the hip to maintain balance. When executing hip strategy, individuals are usually standing on an uneven, narrow or moving surface. Lastly, is the stepping strategy, which is used due to large forces that display the COM beyond an individual's BOS. The individual has to give a step to maintain their balance and then forms a new BOS when in a stable position.

The last element of this dissertation's SMT programme was adding a multisensory component. Thus, the balance exercises throughout each phase were task-specific and focused on manipulating the visual, vestibular and somatosensory systems. Examples of sensory manipulation include blindfolding the individual, asking them to close their eye(s), implementing head, hand and eye movements, moving the visual surround or changing the surface area underneath their feet. The major reasoning behind this was that we live in a dynamic world where environmental changes and adaptations are inevitable.

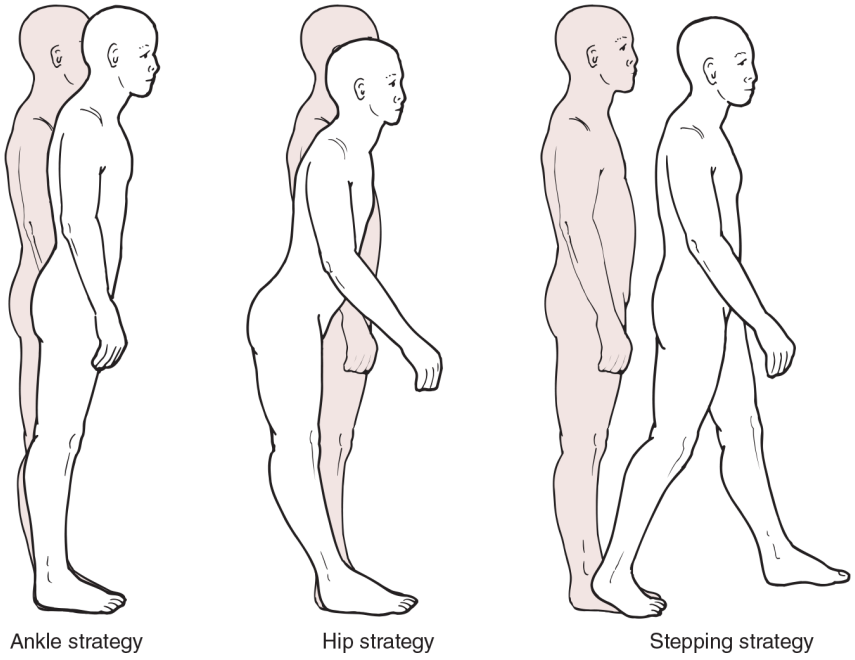

Figure 2.1: Ankle, hip and stepping strategies©.

Therefore, the dynamic systems theory was utilised in this dissertation and is discussed in the following section.

2.7 Dynamic Systems Theory

Mosby's medical dictionary defines motor control as the "systematic transmission of nerve impulses from the motor cortex to motor units, resulting in coordinated contractions of muscles". Roller and colleagues [3] further extended this definition and stated that an individual accesses sensory information from the environment, observes the conditions and chooses an appropriate movement plan to successfully meet the outcome goals of the task. The dynamic systems theory originates from the field of mathematics, however, it is a general theory based on studying change and can be applied to almost any field. Specific to motor control, the dynamic systems theory is defined as nonlinear changes in motor behaviour, as well as movement patterns that emerge or self-organise, as a function of the ever-changing constraints placed upon it [119, 120, 121]. According to Thelen [122], functional synergies develop naturally through experience and implement the coordination of multiple muscle and joint movements at the same time.

According to the dynamic systems theory, movement behaviour results spontaneously from the complex interaction between different subsystems, namely: the person, the task at hand, and the environment [3, 123]. The

person refers to all bodily structures, whether functional or not, as well as bodily functions that interact with each other. The task is typically the challenge or problem that needs to be solved with goal-directed behaviour. Lastly, the environment entails everything outside of the body and exists in the external world [3]. All three of these constraints vary and are dynamic in their interaction with each other during learning and movement execution.

The dynamic systems theory allows therapists to identify any difficulties in motor performance, develop treatment strategies for these performance difficulties and assess the effectiveness of interventions in practice [124]. According to a review by Holt and colleagues [125], the dynamic systems theory has various implications for rehabilitation. For example, we must consider the impact of the task and environment in relation to the constraints of the person if we wish to understand the relationship between deficits and compromised body functions. Consequently, we have to ask the questions, what are the individual's resources and what should the requirements of the task and environment entail.

In summary, the term SMT will be used throughout this dissertation, which entails balance exercises that focus on manipulating the sensory systems, namely the visual, vestibular and somatosensory systems. Familiarisation and progressions were adapted from Janda's SMT principles [116, 117] and followed the three different movement strategies to maintain balance described by Horak and Nashner [118]. Furthermore, the dynamic systems theory supports the use of SMT to improve functional recovery in chronic stroke survivors because it follows a task-oriented intervention. The SMT programme is orientated around goal-directed behaviour, which focuses on fundamental functional tasks to restore some degree of postural control. Appendix A shows a sample of the SMT programme implemented in this dissertation.

The next section involves a review of previous research conducted on chronic stroke survivors executing sensory-manipulated balance training on structural neuroplasticity and functional recovery.

2.8 Sensory-Motor Training in Chronic Stroke

This section aimed to summarise the results of previously conducted controlled trials which utilised sensory-manipulated balance training interventions on chronic stroke individuals. The focus was on outcome measures, which include; (1) structural neuroplasticity, and (2) functional recovery, based on postural control outcome measures mentioned in Section 2.4. Due to the limited research on structural neuroplasticity in chronic stroke survivors, the effect of balance training, with or without the manipulation of the sensory systems,

on other neurological diseases and healthy population is mentioned. However, the functional recovery section only focused on sensory-manipulated balance training and the chronic phase of stroke ($\geq$ 6 months post-stroke).

The studies that focused on functional recovery were evaluated by the Physiotherapy Evidence Database (PEDro), to assess the quality of the randomised controlled trials (Appendix B) [126]. This scale functions to determine the impact of physical therapy on functional outcomes after stroke [127]. Articles that scored six points or higher were classified as high quality, scores of five or four points were classified as lower quality, and articles with scores below four were excluded from the dissertation. [128].

2.8.1 Neuroplasticity

Stroke can be associated with motor and sensory abnormalities which arise from disrupted connectivity between different regions of the brain [129, 58]. Fortunately, neuroimaging studies in humans have shown that the brain has the ability to reorganise throughout a person's lifespan [130]. According to Donoghue [131], reorganisation or neuroplasticity may include lasting changes in structural cortical properties and play an important role in recovery after injury to the CNS. Various neuroimaging methods are available and make it possible to study the human brain in healthy individuals as well as those affected by injury or disease [132]. More specifically to this dissertation, structural MRI techniques, such as diffusion MRI, aids in the understanding of the relationship between structural changes and behavioural deficits [133].

To the researcher's knowledge, no studies have been executed on acute, subacute or chronic stroke individuals regarding the effect of balance training, with or without sensory manipulation, on structural brain changes. Training regime's that have been evaluated using structural connectivity include constraint induced movement therapy, hand-motor therapy, physiotherapy training with or without brain computer inference and sensory discrimination training in chronic stroke individuals [133].

With regards to other neurological populations, Sehm and colleagues [134] assessed the association between morphometric brain changes and balance training in Parkinson's disease individuals. Researchers included 20 individuals with Parkinson's disease (EXP; age: 62.9 $\pm$ 7.1 years) and 16 healthy matched controls (CON; age: 64.9 $\pm$ 6.8 years). Both groups learned a whole-body dynamic balance task over a period of six weeks. The participants were asked to stand with both feet on a movable platform for 30 seconds with the goal being to keep it in a horizontal position for as long as possible. Outcome measures included balance testing and structural MRI assessment before and after two, four, and six weeks of training. Results indicated balance improvements in

both groups ($p < 0.05$), as well as a correlation between balance task training improvements and gray matter changes in the frontal, parietal and temporal areas in EXP group. Additionally, the CON group showed learning-dependent gray matter changes in the left hippocampus, whereas the EXP group revealed time-dependent gray matter changes in the right cerebellum. Therefore, the researchers provided evidence that balance improvements induced by balance training could be associated with specific structural brain plasticity patterns, which serves as new evidence for activity-dependent neuroplasticity in neurological diseases such as Parkinson's disease.

In the healthy population, most MRI studies have applied aerobic or cardiorespiratory exercise interventions, and fewer studies have investigated other exercise paradigms, such as coordination (i.e. balance, eye-hand and leg-arm coordination, spatial orientation and reaction time) and resistance training [63]. Similar to the previous Parkinson's disease study [134], Taubert and colleagues [82] investigated the effect of learning a whole-body dynamic balance task on structural brain changes in healthy individuals. The study included 14 healthy individuals (age: 25.9 ± 2.8 years) who participated in the balance task training and 14 age- and gender-matched healthy controls. The balance task required the participants to stand with both feet on a platform and keep it in a horizontal position as long as possible for a 30 seconds duration. The balance task training consisted of one training session for 45 minutes over six consecutive weeks and testing occured before and after two, four, and six weeks of training. Researchers utilised T1-weighted images together with diffusion tensor imaging (DTI) and found increased gray matter volume in the frontal and parietal areas after two sessions of practising the whole-body balancing task. Furthermore, the researchers found a correlation between performance improvements and gray matter volume in the PFC during the six weeks. Researchers concluded that the adult brain structure may be affected by modifications made in the ever-changing environment and confirm that a causal relationship exists between structural reorganisation and behavioural adaptation.

More recently, Magon et al. [81] investigated the effects of slackline balance training on morphological changes and functional connectivity in healthy elderly population by means of MRI analysis. Twenty-eight healthy individuals were randomly divided into two groups, namely balance-intervention group ($n = 14$; age: 62.3 ± 5.4 years) or control group ($n = 14$; age: 61.8 ± 5.3 years). The intervention group received slackline balance training three times a week for six weeks, and the control group attended three educational sessions (90 minutes) regarding neuromuscular training for fall prevention. Participants underwent a standing balance task and an MRI session before and after the intervention. During the MRI session, resting-state MRI data and T1 weighted images were acquired. Researchers found that participants improved in the

standing balance tasks ($p < 0.05$), however MRI data showed no structural or functional differences on the whole sample after the intervention or between groups ($p > 0.05$). Nevertheless, researchers further divided participants into subgroup of responders, and found that this group ($n = 8$; age: 61.7 ± 5.8) showed decreased functional connectivity of the caudate and putamen compared to other brain areas after the intervention ($p < 0.05$). No morphological changes were observed in the responder subgroup ($p > 0.05$). Researchers concluded that slackline balance training has the ability to improve balance performance and that it is associated with increased efficiency of the striatal network. Hence, the basal ganglia network is involved in brain reorganisation following a balance training programme because of its involvement in motor learning and postural control.

To conclude, research regarding the effect of balance training, with or without sensory manipulation, is very limited not only in chronic stroke survivors but also in other populations. Consequently, this is the first MRI study which set out to investigate the effect of an eight-week SMT programme, focussed on pure balance exercises with sensory manipulation, on structural connectivity changes in chronic stroke individuals.

2.8.2 Functional Recovery

Functional recovery has previously been defined as the improved ability of an individual to execute ADL and perform mobility independently [8]. For this to occur, efficient postural control is essential, and from Section 2.3 we know that postural control consists of various functional goals. A variety of systematic reviews and meta-analyses exist in the literature, focussed on the effects of exercise-based rehabilitation, specifically balance training on balance and gait in chronic stroke survivors [135, 136, 128, 137, 25]. Due to the scope of this dissertation, this section reports on outcome measures targeting sensory integration and reweighting, static as well as dynamic postural equilibrium, and the effect sensory-manipulated balance training has on it in chronic stroke survivors.

Bonan and colleagues [44] investigated the effect of a four week balance training programme with and without visual cue deprivation in chronic stroke participants. Twenty participants were assigned to either the vision-deprived group ($n = 10$; age: 49.5 ± 10 years; 20.5 ± 25 months post-stroke) or to the free vision group ($n = 10$; age: 49 ± 17 years; 20.5 ± 10 months post-stroke). Both of the rehabilitation programmes lasted 20 sessions and were similar in design, except that the eyes of the vision-deprived group were blinded with a mask during the exercise session. The primary outcome measure included the Sensory Organisation Test (SOT), whereas secondary outcome measures focused on gait parameters, namely gait velocity, timed stair climbing and

self-assessed ease of gait. Lastly, quality of life was also assessed with the Nottingham Health Profile (NHP). Results indicated that participants in both groups improved in balance, gait velocity, and self-assessment of gait ($p < 0.05$). Furthermore, gait velocity ($p = 0.03$) and timed stair climbing ($p = 0.01$) significantly correlated with balance. Researchers concluded that balance improved more in the visual-deprived group compared to free vision group because the visual deprivation encouraged the participants to increase the use of somatosensory and vestibular information. Thus, physical therapy programmes should include vision-deprived balance exercises to improve balance control in chronic stroke survivors.

Marigold et al. [138] compared the effects of two different community-based group exercise programmes in 61 older adults with chronic stroke. Participants were randomly assigned to either an agility group ($n = 30$; age: 68.1 ± 9.0 years; 3.6 ± 1.8 years post stoke) or a stretching/weight-shifting group ($n = 31$; age: 67.5 ± 7.2 years; 3.8 ± 2.4 years post stoke). The agility group performed exercises in various postures and many tasks were executed with eyes closed conditions and on foam surfaces. Measurements included Berg Balance Scale (BBS), TUG test, step reaction time, Activities-specific Balance Confidence (ABC), NHP, as well as standing postural reflexes and induced falls evoked by a translating platform. Additionally, from the start of the interventions falls were tracked for one year. Participants were tested at pre- and post-intervention, as well as after a retention period of one month. Both groups improved all clinical outcome measures, however, the agility group showed greater improvement in step reaction, postural reflexes and platform induced falls ($p < 0.05$). According to results, both exercise interventions show promise to improve postural reflexes, functional balance, and mobility as well as fall reduction in chronic stroke individuals. However, researchers encourage the use of dynamic balance training with emphasis on a multisensory component. Researchers hypothesised that neuronal circuitry remodelling could have contributed to the neurophysiological and functional changes observed in the study.

Bayouk and colleagues [139] investigated the effects of a task-orientated exercise programme with and without altered sensory input on postural stability in chronic stroke individuals. Sixteen subjects were randomly divided into either a control group ($n = 8$; age: 62.0 ± 4.6 years; 5.7 ± 6.9 years post-stroke) or an experimental group ($n = 8$; age: 68.4 ± 7.1 years; 7.1 ± 12.5 years post-stroke). The control group performed task-orientated exercises, whereas the experimental group performed the same exercises under different sensory conditions. Exercise sessions were 60 minutes in duration and were done twice per week for a total of eight weeks. Outcome measures were tested at pre- and post-assessment and included centre of pressure (COP) displacement during double-legged stance, a 10-metre walking test, and sit-to-stand under four

sensory conditions: (1) eyes open, firm surface; (2) eyes open, soft surface; (3) eyes closed, firm surface; and (4) eyes closed, soft surface. Researchers found significant improvements for the experimental group in COP displacement under sensory conditions (1) and (2) ($p < 0.05$). Additionally, both groups significantly improved in the 10-metre walking test ($p < 0.05$). Researchers concluded that additional sensory manipulation with task-oriented exercise is more effective than conventional task-oriented exercise to improve standing balance in chronic stroke subjects. According to the researchers, improvements could be due to sensory compensation that improved sensory-motor integration of postural control in the CNS, which in turn assisted with the coordination of motor processes.

Smania and colleagues [29] performed a pilot study which aimed to evaluate whether postural stability and/or walking ability in chronic stroke patients could be improved by balance exercises performed under various sensory input conditions. Seven chronic hemiparetic patients (mean age: 63.1 years; mean onset time: 14.8 months) were recruited to take part in the study and participated in 20 one-hour daily sessions consisting of several balance exercises. Patients performed the SOT as well as the 10 metre walking test, pre- and post-intervention, as well as one week after the end of training. After the treatment, performance of balance on compliant surfaces showed significant improvement ($p = 0.018$) and walking speed increased significantly ($p = 0.018$). Furthermore, this improvement was maintained for one week ($p < 0.05$). Researchers concluded that balance rehabilitation for chronic stroke patients should include exercises performed under sensory conflict conditions. Consequently, rehabilitation of sensory-motor integration deficits can improve balance in chronic stroke participants due to the improved ability of the participants to change their sensory strategy to maintain their standing posture.

Yelnik and colleagues [140], investigated the effect of two rehabilitation strategies to improve balance after stroke. Sixty-eight participants were divided into either a conventional neurodevelopmental-theory-based treatment group (NDT; $n = 35$; age: 54.9 ± 11.8; 218 ± 93.4 days post stroke) or multisensorial rehabilitation group ($n = 33$; age: 55.5 ± 11.6; 217 ± 92.9 days post stroke). Researchers defined chronic stroke as more than three months post-stroke. The NDT-based treatment focussed on global sensorimotor rehabilitation described by the Bobath therapy, whereas the multisensorial training was based on the manipulation of the sensory information required to maintain balance. Participants received 20 sessions over four weeks, and were assessed pre-intervention, post-intervention and after a 30-day retention period. Assessments included BBS, posturography, gait, functional independence measure, and NHP. Results showed that both groups improved significantly in balance and gait parameters ($p < 0.05$). Furthermore, no differences between groups were found regarding the main dependent variable, BBS post-intervention.

Secondary outcome measures showed slight improvement in the experimental group compared to the NDT group, however, differences were not likely to be clinically relevant. Researchers concluded that there is no evidence indicating that multisensorial rehabilitation is superior to NDT-based training in chronic stroke individuals. Researchers attributed the findings to several reasons mostly related to study design aspects, i.e. sampling, choice of outcome measures, training duration and so forth.

Lastly, Jang and Lee [28] recently investigated the impact of sensory integration training on muscle activity and limits of stability among chronic stroke patients. Twenty-eight patients were recruited for the study and were randomly divided into one of two groups, namely sensory integration training (SIT) or control group (CON). The CON group ($n = 15$; age: 67.47 ± 13.00; onset time: unknown) received 30 minutes general balance training whereas the SIT group ($n = 13$; age: 64.77 ± 11.27; onset time: unknown) received an additional 30 minutes of sensory integration training. Both groups trained five days a week for a total of four weeks. Results indicated that the erector spinae and gluteus medius activity improved significantly more in the SIT group ($p < 0.05$) compared to the CON group ($p < 0.05$). Additionally, limits of stability improvements in the affected and forward side were significantly higher over time in the SIT group ($p < 0.05$) compared to the CON group ($p < 0.05$). Researchers made the conclusion that sensory integration training has the ability to improve impaired balance ability in chronic stroke patients by reinforcing muscle activity in the erector spinae and gluteus medius.

2.8.3 Summary

To date, no research has been done on the effect of balance training combined with sensory manipulation on structural neuroplasticity, and only a few studies have investigated the effects on postural control related functional recovery in chronic stroke. Above-mentioned studies focussed on various outcome measures, such as sensory integration and reweighting, postural stability, various gait parameters, functional measures, as well as quality of life, fall risk and perceived balance confidence. The average duration of the interventions reviewed were 21 ± 5 sessions and were on average 60 ± 6 minutes long. Taken together, results are mostly positive, showing improved functioning in terms of sensory integration and reweighting, static as well as dynamic postural equilibrium. Improvements are observed after the various balance interventions within groups, however, only a few studies show significant between group differences. This could be due to the effect of exericse in general being beneficial overall.

This chapter ends off with the problem statement of this dissertation as well as the aims and objectives set out for Article 1 (Chapter 3), Article 2

(Chapter 4) and Article 3 (Chapter 5).

2.9 Problem Statement

Postural control depends on the ability of an individual to combine input from the visual, vestibular and somatosensory systems in combination with the automatic and voluntary motor systems [141]. Following a stroke, the sensory integration process may become more difficult due to impairments of the sensory-motor system. Thus, individuals may present with reduced postural orientation as well as the inability to maintain static and dynamic postural equilibrium, leading to inefficient postural control [91]. Impairments in dynamic postural equilibrium stem from the inability to control postural stability and orientate oneself while moving from one position to another [87]. The cerebral cortex plays a crucial role in postural control, however the cortical mechanisms underlying postural control and its recovery still remain unclear [142, 56, 143, 77].

Impairments within the sensory systems are a big concern following stroke, being reported between 11% and 60%, and are closely related to functional recovery [30]. Previous research has shown that stroke individuals without sensory deficit spend an average of 68 days in the hospital as an inpatient, whereas those with sensory deficit spend an average of 236 days in inpatient rehabilitation settings [144]. The clinical importance of sensory impairments in chronic stroke survivors has received little research attention when compared with cognitive and motor impairments [31]. Additionally, the detailed mechanism of the interaction between sensory and motor recovery in chronic stroke survivors remains unknown [145].

Balance impairment is an important consideration in chronic stroke survivors since the number of falls can be as high as five per year in the first year post-stroke [146]. From a rehabilitation point of view, more research is required to investigate the effect of balance training that utilises the manipulation of the visual, vestibular and somatosensory systems in chronic stroke individuals. Sensory-motor training may be a cost-effective and simple way to improve quality of life in chronic stroke survivors. This training method requires little equipment and it can be executed in a group setting, which facilitates social interaction.

To conclude, there is still uncertainty on this specific topic and more research is warranted. Individuals with stroke need lifelong management, which can be very expensive. As a result, it is important to develop ways that are more feasible for individuals to engage in physical activity, independently, which will lead to improved quality of life. A better understanding of the

underlying mechanisms of activity-dependent neuroplasticity and functional recovery is wanted. Thus, by examining the relationship between structural changes and functional outcomes, the gap between research and practice can be bridged.

2.9.1 Aims

The primary aim of this dissertation is to establish whether an eight-week SMT programme can induce structural brain changes and functional recovery in chronic stroke survivors. The research hypothesis is that SMT will induce structural neuroplasticity by means of reorganisation and compensation processes, which will lead to functional recovery in chronic stroke individuals.

2.9.1.1 Article 1

To investigate the effect of an eight-week SMT programme on structural brain changes and balance in chronic stroke survivors. Specifically, the goal of this study was to examine whether SMT could induce changes in structural connectivity between the two subcortical basal ganglia nuclei, caudate and lentiform nucleus, with other regions of interest.

2.9.1.2 Article 2

To assess the influence of SMT on sensory reweighting in chronic stroke survivors. Additionally, health-related quality of life and intrinsic motivation were assessed. The research hypothesis is that eight weeks of SMT may improve postural sway in individuals with chronic stroke due to better sensory reweighting capacity.

2.9.1.3 Article 3

To evaluate whether SMT can alter functional mobility in chronic stroke survivors. Additionally, the study also set out to evaluate fall efficacy. The researchers hypothesise that if SMT could improve key mobility components and perceived fall efficacy, functional recovery could be increased in chronic stroke survivors.

2.9.2 Objectives

The above-mentioned aims were achieved by using the following objectives. Measurements were taken before (pre-test) and after (post-test) the intervention, unless specified otherwise.

2.9.2.1 Article 1

- Measure structural brain connectivity changes with MRI using DTI analysis (Appendix C).
- Measure postural sway (jerkiness (m^2/s^5)) with APDM's Mobility Lab^{TM} (Portland, Oregon, USA) body-worn inertial sensor.

2.9.2.2 Article 2

- Measure postural sway (95% ellipse sway area (m^2/s^4)) with APDM's Mobility Lab^{TM} (Portland, Oregon, USA) body-worn inertial sensor using the m-CTSIB.
- Assess health-related quality of life with the Short Form Health Survey (SF-36; Appendix D).
- Assess intrinsic motivation with Intrinsic Motivation Inventory (IMI; Appendix E), only after intervention.

2.9.2.3 Article 3

- Measure functional mobility with APDM's Mobility Lab^{TM} (Portland, Oregon, USA) body-worn inertial sensors using the instrumented Timed-Up and Go (iTUG) test.
- Assess concern for falling with the Fall Efficacy Scale - International (FES-I; Appendix F).

Various aspects are novel and original within this dissertation, specifically the outcome measures utilised and executing it under randomised controlled study design conditions. Therefore, this was the first study to investigate the effect of SMT on (1) structural connectivity using MRI measures; (2) sensory orientation using APDM's Mobility Lab^{TM}; and (3) the individual components of the TUG test using APDM's Mobility Lab^{TM}. Additionally, this was the first study to assess the subjective experiences of participants after intervention. Article 1 set out to establish clinical changes induced by training whereas Article 2 and Article 3 focussed on behavioural aspects related to targeted activity. These last two behavioural articles were written as separate articles to ensure that a detailed report could be given on both static and functional outcome measures. Both aspects are of utmost importance for chronic stroke survivors and should be discussed in detail. All of these components are of high importance in the field of rehabilitation as it aids in the objective measurement of structural neuroplasticity and aspects of postural control. Therefore, objective and accurate conclusions can be made on the specific changes induced by exercise in chronic stroke survivors.

2.9.3 Descriptive Outcome Measures

The following information was aquired before commencing with the intervention:

- Obtain informed consent (Appendix G) and personal health information (Appendix H).
- Assess mild cognitive impairment with the Montreal Cognitive Assessment (MoCA; Appendix I).
- Assess physical activity status with the Rapid Assessment of Physical Activity (RAPA; Appendix J).
- Assess functional capacity with Fugl-Meyer questionnaire [147, 58].

The Institutional Health Research Ethics Committee (S16/07/128) approved the study and all tests were conducted with professionalism and in accordance with the Declaration of Helsinki.

2.10 Conclusion

Stroke critically disturbs the balance within the different structures in the brain [34]. After CNS injury, brain reorganisation lays the foundation for motor learning, new skill achievement as well as functional recovery [148]. Rehabilitation facilitates brain reorganisation and incorporates adaptations in both the sensory and motor areas [37].

To date, no clinical trials have been done on the effect of sensory-manipulated balance training on structural brain changes and only a few on functional recovery in chronic stroke survivors. As a result, it is important to research effective practise design methods, such as SMT, which could promote structural neuroplasticity and lead to functional recovery in chronic stroke individuals.

The next three chapters present the investigation into whether eight weeks of SMT could influence structural neuroplasticity (Chapter 3; Article 1), sensory orientation (Chapter 4; Article 2) and functional mobility (Chapter 5; Article 3) in chronic stroke survivors.

Chapter 3

Article 1

Structural Connectivity Changes within the Basal Ganglia after Eight Weeks of Sensory-Motor Training in Chronic Stroke Survivors: A Randomised Controlled Pilot Study

3.1 Abstract

Background: Stroke survivors can present with impaired postural control and sensory integration. The basal ganglia are involved in postural control and sensory processing, however the effect of sensory-manipulated balance training on brain connectivity in chronic stroke individuals remains unknown.

Objective: To examine structural connectivity brain changes and balance after eight weeks of sensory-motor training (SMT), i.e. balance training under sensory-manipulated conditions, in chronic stroke survivors.

Methods: Nine individuals with chronic stroke ($\geq$ 6 months post-stroke) participated in the study and were randomly assigned into the SMT group (n = 5) and attention-matched control group (CON; n = 4). Both interventions were 45 to 60-minute group sessions, three days a week. The SMT consisted of balance training while manipulating the visual, vestibular and somatosensory systems, while the CON group received educational talks. Outcome measures included changes in structural connectivity strength from probabilistic whole brain tractography derived from a diffusion tensor magnetic resonance imaging (MRI) scan, and jerkiness in the anterior-posterior direction (m^2/s^5) while standing on a foam pad for 30 seconds, pre- and post-test.

Results: Diffusion tensor MRI analysis revealed interaction effects for increased connectivity strength between the basal ganglia network and sensory-motor fronto-parietal areas in the SMT group ($p < 0.05$), whereas the CON group showed increased structural connectivity in visual processing and higher cognitive orbito-temporal and frontal lobe areas ($p < 0.05$).

Conclusions: This proof-of-concept study demonstrates that SMT may improve the effectiveness of the basal ganglia network, which in turn could in-

dicate improved postural control-related restorative effects on structural connectivity.

Keywords: Postural control; Stroke; Neurorehabilitation; Reorganization; Structural neuroplasticity

3.2 Introduction

Postural control is the ability of a person to maintain equilibrium and orient themselves in the existence of gravity [85]. The term postural control usually referes to the neural and musculoskeletal systems that contribute to balance function [12]. Neural systems involved in postural control include the spinal cord, brainstem, cerebellum, basal ganglia and cerebral cortex in a hierarchical manner [77]. Therefore, these neural systems receive sensory information from the visual, vestibular and somatosensory systems in response to various physiological, task and environmental cues [149, 27]. In turn, the central nervous system (CNS) filters, compares, weighs, stores and processes the information to implement the correct timing, direction and amplitude for the desired postural action [86].

Individuals that have suffered a stroke can present with impaired postural control due to deficits in the different domains and systems responsible for postural stability [27, 13]. Research indicates that 75% of stroke survivors regain their independent standing-balance ability, however, asymmetry in weight-bearing activities and increased postural sway remains a concern [90]. Furthermore, stroke survivors struggle with sensory integration and reweighting of the visual, vestibular and somatosensory systems, i.e. to mobilise available sensory systems when one or more of the other sensory inputs are missing or insufficient [29, 28].

To date, a few studies have shown that balance training focused on sensory manipulation may improve balance ability, functional mobility and muscle activity in chronic stroke survivors [44, 139, 29, 28]. However, neuroimaging studies examining the effect of balance training on structural brain changes in chronic stroke individuals are very limited. Previous research that focused on changes in structural connectivity utilised constraint-induced movement therapy, hand-motor therapy, physiotherapy training with or without brain computer inference and sensory discrimination training in chronic stroke patients ($\geq$ 6 months post-stroke) [133]. Magon and colleagues [81] investigated the effect of a six-week slackline balance training programme on striatal functional connectivity in a healthy elderly population and found that a subgroup of responders showed functional connectivity changes between the striatum

and other brain regions.

The basal ganglia consist of five subcortical nuclei namely the caudate, putamen, globus pallidus, substantia nigra and subthalamic nucleus [79]. Together the putamen and globus pallidus form the lentiform nucleus, while the caudate and putamen are also named the striatum [80, 67, 81]. These have been shown to be key structures in motor learning and motor control [79, 81]. Specifically, the caudate can be referred to as the associative portion and is involved in the early phase of learning, whereas the putamen consists of the sensorimotor portion, which is involved in the later phase of learning [81]. The globus pallidus has furthermore shown to have somatosensory properties [150]. Other functions of the basal ganglia include; (1) storing and executing motor plans automatically; (2) motor flexibility, thus adapting to environmental changes; (3) sensory processing; (4) regulating muscle tone; (5) control of automatic postural responses; and (5) cognition, motivation, and emotional behavior [65].

Therefore, this is the first randomised controlled pilot trial set out to investigate the effect of an eight-week sensory-motor training (SMT) programme, focused only on balance exercises with sensory system manipulation, on structural brain connectivity in chronic stroke survivors. Specifically, the purpose of this study was to examine whether SMT could induce any changes in structural connectivity between the two subcortical basal ganglia nuclei, caudate and lentiform nucleus, with other regions of interest. The research hypothesis was that eight weeks of SMT may improve postural control in chronic stroke survivors due to improved efficiency of the basal ganglia network.

3.3 Methods

3.3.1 Participants

Nine chronic stroke survivors were included in the study and were randomly divided into the SMT group or attention-matched control (CON) group. The inclusion criteria were men and women 18 years and older, clinically diagnosed with stroke six or more months ago [24, 25], the ability to maintain standing balance for 30 seconds and ambulate independently for at least 7 metres. Participants were excluded if they had more than one stroke, any neurological conditions other than stroke (Parkinson's disease, Alzheimer's disease, etc.), any visual, vestibular and/or auditory impairment, as well as muscular injuries in the previous six months. Additionally, participants had to obtain an attendence rate of at least 80% at the end of the intervention. Written informed consent was received by all participants and the study was approved by the institutional Health Research Ethics Committee (S16/07/128). The

present study complied with the Declaration of Helsinki and followed CONSORT guidelines [151].

3.3.2 Study Design

This was a double-blind randomised controlled pilot trial, which included a magnetic resonance imaging (MRI) scan and balance assessment within one week before and after the interventions. Demographic information was obtained before the intervention and included age, sex, body mass, height, time since stroke, number of strokes, lesion side, type of lesion and global cognition by means of Montreal Cognitive Assessment (MoCA) [152]. The SMT group executed task-specific balance training under sensory-manipulated conditions, whereas the CON group listened to educational talks. Both interventions occurred in a group setting, three times a week for 45 to 60-minute sessions over an eight-week period. Participants were blinded to the true purpose of the study until the end and allocation was concealed. Individual clinical exercise therapists were responsible for group allocation, data collection and intervention execution, thus each were blinded.

3.3.3 Interventions

The SMT programme was built on the principles of Janda's sensory-motor training guides [117] as well as Horak and Nashner's movement strategies [118]. Overall, participants progressed through eight weeks of balance training while the visual, vestibular and somatosensory systems were manipulated. The first three sessions focused on posture and alignment, specifically on providing input to the sensory-motor system from the ground up. According to Janda [117], sensory information being integrated by the CNS should be optimum at the foot, sacroiliac joint and cervical spine because of the large amount of proprioceptors in these areas. By increasing somatosensory (proprioceptive and tactile) input, subcortical pathways can be stimulated to facilitate coordinated movements [117]. Session four to nine focused on static balance; therefore, maintaining postural stability while progressing to eyes closed conditions, with head movements as well as on unstable surfaces. Additionally, the ankle and hip strategies were also incorporated [118]. Session 10 to 15 progressed to dynamic balance, which added arm and leg movements while maintaining postural stability also while manipulating the three sensory systems as above. The final nine sessions (16-24) executed functional balancing movements, which included activities of everyday life under sensory manipulation and dual tasking conditions. During the dynamic and functional phases, ankle, hip and stepping strategies were utilised [118]. The intensity of each session was measured with a Visual Analogue Scale (VAS) using a cut-off score of ≥ 6.5; thus, moderate-high intensity. Additionally, exertion was measured using a Rate of Perceived Exertion (RPE) scale, with a cut-off score of ≤ 5;

thus, low-moderate exertion [153]. The reasoning behind these measures was to ensure that the sessions were intense enough, however not fatiguing. Results can be viewed in Appendix K.

Participants included in the CON group attended educational talks on the importance of living a healthy lifestyle. The use of an attention-matched control group was to control and balance for nonspecific intervention effects (i.e. attention, intervention contact, social support, etc.) [154]. Topics included the different facets of wellness, risk factors for stroke, awareness of the various signs of stress and management thereof, therapies to enhance a healthy lifestyle and lastly components of bodily and nutritional health. Both interventions were led by qualified clinical exercise therapists.

3.3.4 MRI Protocol

Diffusion tensor imaging (DTI) data were measured using an echo planar imaging (EPI) whole brain sequence using the following parameters: echo time (TE) = 83ms, repetition time (TR) = 10000ms, bandwidth = 1776 Hz/Px, FOV read 256mm^2, 69 axial slices, 2.0mm slice thickness, therefore the isotropic voxel size was 2.0×2.0×2.0mm^3, gradient pulses along 64 different directions with a b-value of 1500s/mm^2. Non-diffusion weighted image (b = 0s/mm^2) were acquired afterwards to guide registration of individual diffusion.

3.3.5 MRI Data Analysis

FSL software package 5.1 (https://fsl.fmrib.ox.ac.uk/fsl/fslwiki) was used to analyse diffusion-weighted images, also, eddy currents and head motion corrections were done for all datasets. A standard freesurfer parcellation scheme and probabilistic whole-brain tractography was used for structural connectome reconstruction [155, 156]. Using the Desikan-Killiany Atlas for automated anatomical segmentation and labelling, 72 regions (36 in each hemisphere) of interest were created (Table 3.1) [157].

3.3.6 Standing Balance Task

Postural sway, a characteristic of standing balance, was measured with the APDM's Mobility Lab^{TM} (Portland, Oregon, USA) body-worn inertial sensor, strapped at the fifth lumbar spine (Figure 3.1) [158, 159]. The participants were asked to stand on a foam pad (Airex Balance pad, Airex AG, Sins, Switzerland: 6.4×40.6×50.8cm, Density: 55kg/m^3 with ICC = 0.41-0.81 [160]) with their eyes open (EO+Foam), without shoes, for 30 seconds. During this balance task, the participants mainly used visual and vestibular inputs because somatosensory information is distorted when standing on a compliant

Table 3.1: Cortical parcellation of cortical and subcortical structures using freesurfer software.

Banks superior temporal sulcus	Parahippocampal gyrus
Caudal anterior-cingulate cortex	Pars opercularis
Caudal middle frontal gyrus	Pars orbitalis
Caudate nucleus	Pars triangularis
Cuneus cortex	Pericalcarine cortex
Frontal pole	Postcentral gyrus
Fusiform gyrus	Posterior-cingulate cortex
Inferior parietal cortex	Precentral gyrus
Inferior temporal gyrus	Precuneus cortex
Insula	Rostral anterior-cingulate cortex
Isthmus-cingulate cortex	Rostral middle frontal gyrus
Lateral occipital cortex	Superior frontal gyrus
Lateral orbital frontal cortex	Superior parietal cortex
Lentiform nucleus	Superior temporal gyrus
Lingual gyrus	Supramarginal gyrus
Medial orbital frontal cortex	Temporal pole
Middle temporal gyrus	Thalamus
Paracentral lobule	Transverse temporal cortex

surface. As mentioned earlier, the basal ganglia play an important role in sensory processing and postural control [150, 65]. Jerkiness (m^2/s^5) was measured in the anterior-posterior direction, which is the relative smoothness of postural sway, reflecting the amount of active postural corrections made [7]. The Mobility Lab objectively measures various components of balance and is a valid and reliable test for patients with neurological disorders [159, 161]. A smaller value indicates a better outcome for postural sway.

3.3.7 Statistical Analysis

STATISTICA for Windows version 13 (StatSoft, Inc., Tulsa, OK, USA) software was used for clinical and behavioral statistical analysis. Data was assessed using normal probability plots and log transformations were done where data was not normally distributed. In some cases with outliers, the variables were winsorized which reduced the effects of the outliers without having to remove the outliers. The standing balance task and connectivity strength between both the caudate and lentiform with the other regions of interest, were analysed between groups (SMT vs. CON) and within groups (pre vs. post) by

Figure 3.1: APDM's Mobility Lab^{TM} inertial sensor placement on the fifth lumbar spine$^{©}$.

using a mixed model repeated measures ANOVA with Fisher Least Significant Difference (LSD) post-hoc test. Group, time and group x time were set as fixed effects. The latter gave an indication of changes over time within the groups. Subjects were treated as random effect. Due to the small sample size, Cohen's d effect sizes (ES; i.e. 0.2^{S}: Small, 0.5^{M}: Medium and 0.8^{L}: Large [162]) and magnitude-based inference (MBI; i.e. substantially positive, trivial and substantially negative [163]) statistics were added to supplement the traditional inferential statistics. Statistical significance was designated by $p \leq 0.05$.

3.4 Results

Out of 15 individuals who met the inclusion criteria, only nine completed the study, five in the SMT group and four in the CON group. No significant differences were found for demographic results between the groups ($p > 0.05$; Table 3.2). On average the attendance rate for the SMT group was 98.40 ± 2.19 (%) and for the CON group 90.22 ± 2.17 (%) after intervention. Progress from enrollment to analysis of the groups are shown in the CONSORT flow diagram, Figure 3.2.

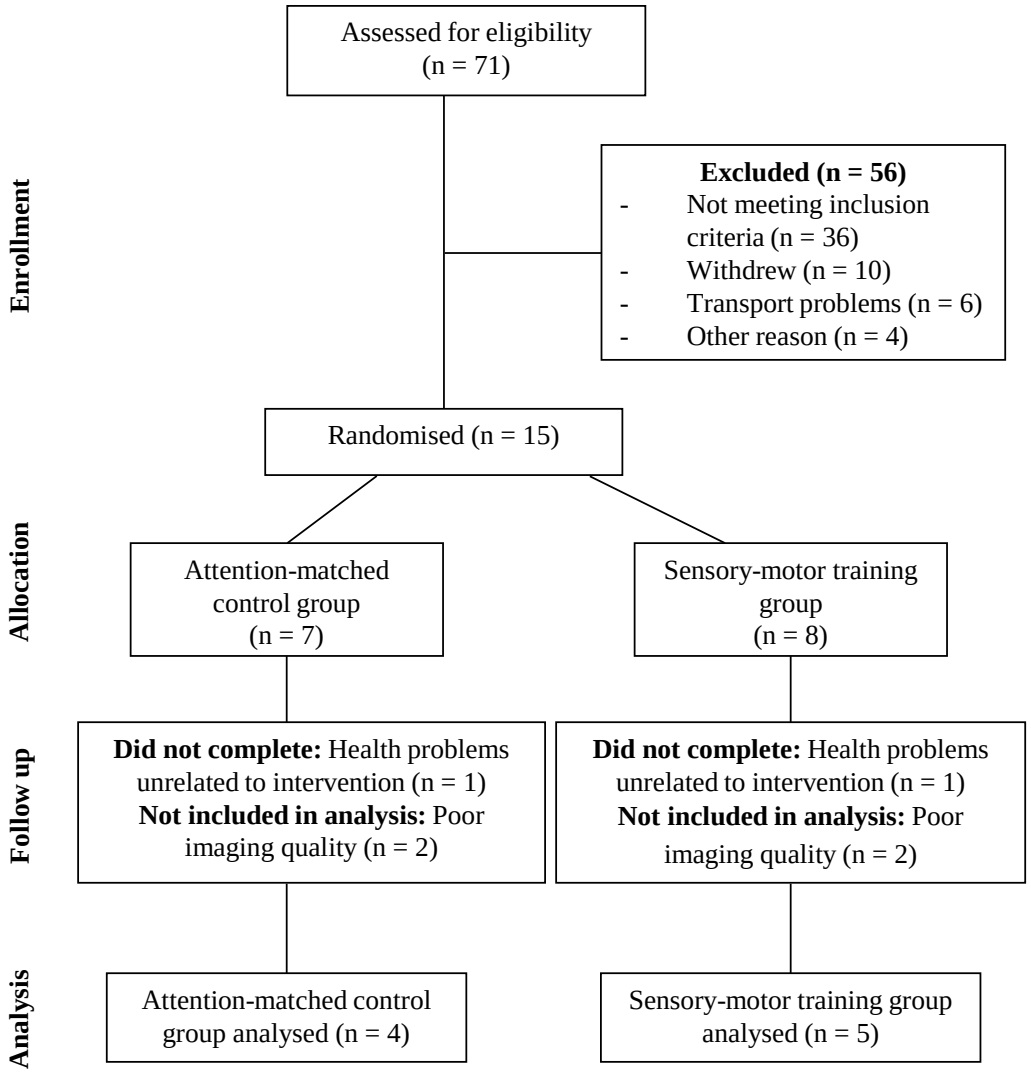

Figure 3.2: CONSORT flow diagram.

3.4.1 MRI Analysis

Repeated measures ANOVA revealed interaction effects for structural connectivity strength between both the caudate and lentiform with other regions of interest. Significant between group and over time changes were also found. Furthermore, the MBI results supported the findings from the inferential statistics, which can be viewed in Appendix L.

3.4.1.1 Caudate Nucleus

The SMT group showed increased structural connectivity between the left caudate and contralateral and ipsilateral caudal anterior cingulate cortex. Furthermore, increased structural connectivity was seen between the right caudate

Table 3.2: Demographic characteristics of participants in SMT and CON groups (mean ± SD).

Variable	SMT group (n = 5)	CON group (n = 4)	p-value
Age (years)	68 ± 19	75 ± 10	0.58
Sex: men (%)	60	50	0.80
Body mass (kg)	63.90 ± 21.62	76.30 ± 24.20	0.74
Height (m)	1.72 ± 0.11	1.68 ± 0.18	0.83
Time since stroke (years)	5.92 ± 6.13	6.75 ± 6.29	0.84
Lesion side (R/L)	4/1	3/1	
Lesion type (cortical/subcortical)	2/3	2/2	
MoCA	25.20 ± 1.79	25.25 ± 3.40	0.98

CON, Attention-matched control; L, Left; MoCA, Montral Cognitive Assesment; R, Right; SD, Standard deviation; SMT, Sensory-motor training

with the contralateral paracentral lobule and rostral middle frontal gyrus, as well as with ipsilateral fusiform gyrus, superior frontal gyrus and parahippocampal gyrus (Table 3.3). The CON group revealed reduced structural connectivity between the left caudate and the ipsilateral parsopercularis and superior frontal gyrus. Furthermore, the CON group showed increased structural connectivity between the left caudate with the ipsilateral lingual gyrus and between the right caudate and the contralateral inferior temporal gyrus and cuneus (Table 3.3).

3.4.1.2 Lentiform Nucleus

The SMT group showed increased structural connectivity between the left lentiform and the contralateral and ipsilateral isthmus cingulate cortex, as well as between the right lentiform and contralateral temporal pole, inferior parietal cortex and precuneus cortex (Table 3.3). Lastly, the CON group showed an increased connectivity between the left lentiform with the ipsilateral rostral anterior cingulate cortex (Table 3.3).

3.4.2 Standing Balance Task

Repeated measures ANOVA showed no significant interaction effect for jerkiness during EO+Foam balance task (p = 0.20). Post-hoc analysis further showed no between group difference at pre- (p = 0.41; ES = 0.59^{M}; ES 95% CI = -0.87 to 1.80) or post-test (p = 0.40; ES = 0.80^{L}; ES 95% CI = -0.74 to 1.95), as well as over time for the SMT group (pre = 0.24 ± 0.45 vs. post = 0.04 ± 0.04; p = 0.28; ES = 0.70^{M}; ES 95% CI = -0.70 to 1.83) and CON group

Table 3.3: Structural connectivity strength between the caudate and lentiform with other regions of interest for SMT and CON groups.

			Sensory-motor training group (n = 5)			**Attention-matched control group (n = 4)**			**Group differences**		**Interaction effect**
	Lobes	Region of interest	Pre-test mean (SD) {95% CI}	Post-test mean (SD) {95% CI}	p-value (ES) {ES 95% CI}	Pre-test mean (SD) {95% CI}	Post-test mean (SD) {95% CI}	p-value (ES) {ES 95% CI}	Pre-test p-value (ES) {ES 95% CI}	Post-test p-value (ES) {ES 95% CI}	p-value
Left caudate	Frontal	Left caudal cingulate cortex, anterior	0.67 (0.26) {0.38 to 0.95}	1.05 (0.24) {0.77 to 1.33}	0.05 (1.7^{H}) {-0.1 to 2.75}	0.63 (0.25) {0.31 to 0.94}	0.53 (0.32) {0.21 to 0.85}	0.60 (0.39^{S}) {-1.09 to 1.70}	0.82 (0.19^{S}) {-1.18 to 1.46}	0.02 (2.11^{H}) {0.14 to 3.19}	0.08
		Right caudal cingulate cortex, anterior	0.62 (0.38) {0.25 to 0.98}	1.15 (0.22) {0.79 to 1.52}	0.01 (1.92^{H}) {0.13 to 2.95}	0.54 (0.32) {0.13 to 1.94}	0.48 (0.44) {0.08 to 0.89}	0.74 (0.16^{S}) {-1.25 to 1.52}	0.74 (0.26^{S}) {-1.12 to 1.52}	0.02 (2.3^{H}) {0.24 to 3.34}	**0.02**
		Left pars opercularis	0.10 (0.12) {-0.06 to 0.26}	0.15 (0.22) {-0.01 to 0.31}	0.47 (0.33^{S}) {-0.99 to 1.50}	0.32 (0.15) {0.14 to 0.50}	0.11 (0.09) {-0.07 to 0.29}	0.03 (2.04^{H}) {-0.09 to 3.04}	0.07 (1.93^{H}) {-0.02 to 2.94}	0.70 (0.27^{S}) {-1.12 to 1.52}	**0.03**
		Left superior frontal gyrus	0.48 (0.17) {0.21 to 0.74}	0.55 (0.29) {0.29 to 0.82}	0.32 (0.37^{S}) {-0.98 to 1.51}	0.56 (0.32) {0.26 to 0.85}	0.37 (0.21) (0.07 to 0.66)	0.05 (0.81^{L}) {-0.81 to 2.03}	0.65 (0.36^{S}) {-1.03 to 1.61}	0.30 (0.83^{L}) {-0.73 to 1.96}	**0.04**
	Occipital	Left lingual gyrus	0.007 (0.006) {-0.001 to 0.015}	0.005 (0.004) {-0.003 to 0.013}	0.41 (0.50^{M}) {-0.90 to 1.60}	0.005 (0.006) {-0.004 to 0.014}	0.013 (0.013) {0.003 to 0.022}	0.05 (0.82^{L}) {-0.74 to 2.11}	0.72 (0.37^{S}) {-1.03 to 1.62}	0.19 (0.94^{L}) {-0.58 to 2.15}	**0.05**
Right caudate	Frontal	Left paracentral lobule	0.02 (0.02) {-0.01 to 0.05}	0.05 (0.04) {0.02 to 0.08}	0.008 (1.05^{L}) {-0.44 to 2.15}	0.01 (0.003) {-0.02 to 0.04}	0.012 (0.01) {-0.02 to 0.04}	0.68 (0.59^{M}) {-0.93 to 1.88}	0.51 (0.85^{L}) {-0.65 to 2.05}	0.06 (1.36^{VL}) {-0.32 to 2.50}	0.09
		Left rostral middle frontal gyrus	0.006 (0.005) {-0.002 to 0.014}	0.017 (0.011) {0.01 to 0.025}	0.01 (1.51^{H}) {-0.18 to 2.50}	0.005 (0.007) {-0.003 to 0.014}	0.006 (0.004) {-0.003 to 0.014}	0.92 (0.07^{N}) {-1.24 to 1.54}	0.90 (0.13^{N}) {-1.17 to 1.47}	0.05 (1.53^{H}) {-0.29 to 2.53}	**0.05**
		Right superior frontal gyrus	0.08 (0.09) {0.0004 to 0.15}	0.14 (0.09) {0.06 to 0.21}	0.02 (0.75^{L}) {-0.76 to 1.87}	0.07 (0.04) {-0.015 to 0.16}	0.05 (0.01) {-0.03 to 0.14}	0.48 (0.67^{M}) {-0.82 to 2.01}	0.90 (0.1^{N}) {-1.19 to 1.44}	0.12 (1.34^{VL}) {-0.25 to 2.59}	**0.04**
	Temporal	Left inferior temporal gyrus	0.003 (0.003) {0.001 to 0.006}	0.003 (0.002) {0.001 to 0.006}	0.46 (0.15^{S}) {-1.11 to 1.37}	0.001 (0.001) {-0.002 to 0.004}	0.002 (0.002) {-0.0003 to 0.005}	0.05 (0.96^{L}) {-0.86 to 1.96}	0.20 (1.04^{L}) {-0.50 to 2.25}	0.74 (0.28^{S}) {-0.93 to 1.73}	**0.05**
		Right fusiform gyrus	0.005 (0.004) {0.001 to 0.009}	0.01 (0.005) {0.006 to 0.014}	0.05 (1.1^{L}) {-0.32 to 2.31}	0.002 (0.001) { -0.002 to 0.007}	0.004 (0.003) {-0.0005 to 0.009}	0.45 (0.79^{L}) {-0.66 to 2.21}	0.29 (1.17^{VL}) {-0.51 to 2.23}	0.06 (1.4^{VL}) {-0.18 to 2.69}	0.37
		Right parahippocampal gyrus	0.0004 (0.0004) {-0.0004 to 0.0012}	0.002 (0.001) {0.0008 to 0.002}	0.03 (1.37^{VL}) {-0.76 to 1.75}	0.0002 (0.0001) {-0.0007 to 0.001}	0.0005 (0.0004) {-0.0004 to 0.001}	0.50 (1.21^{VL}) {-0.56 to 2.35}	0.63 (0.98^{L}) {-1.26 to 1.37}	0.07 (1.2^{VL}) {0.14 to 3.19}	0.23
	Occipital	Left cuneus cortex	0.0007 (0.0007) {-0.0002 to 0.0015}	0.0007 (0.0008) {-0.0002 to 0.0015}	0.94 (0.04^{N}) {-1.11 to 1.37}	0.0003 (0.0003) {-0.0007 to 0.0012}	0.0014 (0.0012) {0.0005 to 0.0024}	0.03 (1.54^{H}) {-0.39 to 2.58}	0.50 (0.81^{L}) {-0.64 to 2.07}	0.23 (0.81^{L}) {-0.64 to 2.07}	0.09
Left lentiform	Frontal	Left rostral cingulate cortex, anterior	0.7 (0.46) {0.25 to 1.14}	0.46 (0.44) {0.01 to 0.91}	0.17 (0.58^{M}) {-0.76 to 1.76}	0.32 (0.34) {-0.18 to 0.82}	0.79 (0.43) {0.29 to 1.29}	0.03 (1.4^{VL}) {-0.43 to 2.53}	0.23 (1.02^{L}) {-0.55 to 2.19}	0.29 (0.86^{L}) {-0.66 to 2.05}	**0.02**
	Parietal	Right isthmus cingulate cortex	0.12 (0.05) {0.04 to 0.2}	0.18 (0.11) {0.1 to 0.26}	0.04 (0.83^{L}) {-0.64 to 1.90}	0.09 (0.05) {-0.01 to 0.18}	0.12 (0.08) {0.03 to 0.22}	0.20 (0.68^{M}) {-1.01 to 1.79}	0.54 (0.75^{L}) {-0.81 to 1.87}	0.30 (0.68^{M}) {-0.80 to 1.88}	0.53
Right lentiform	Temporal	Left temporal pole	0.006 (0.005) {-0.001 to 0.01}	0.014 (0.008) {0.007 to 0.02}	0.02 (1.31^{VL}) {-0.25 to 2.4}	0.006 (0.007) {-0.002 to 0.01}	0.008 (0.008) {0.00004 to 0.02}	0.48 (0.32^{S}) {-1.16 to 1.62}	0.94 (0.07^{N}) {-1.26 to 1.38}	0.25 (0.86^{L}) {-0.68 to 2.02}	0.19
	Parietal	Left inferior parietal cortex	0.005 (0.003) {-0.004 to 0.014}	0.016 (0.012) {0.007 to 0.025}	0.02 (1.43^{VL}) {-0.20 to 2.47}	0.006 (0.008) {-0.004 to 0.016}	0.009 (0.008) {-0.001 to 0.019}	0.56 (0.38^{S}) {-1.07 to 1.72}	0.80 (0.31^{S}) {-1.16 to 1.47}	0.26 (0.75^{L}) {-0.75 to 1.94}	0.19
		Left precuneus cortex	0.06 (0.04) {0.001 to 0.13}	0.12 (0.09) {0.06 to 0.19}	0.03 (0.92^{L}) {-0.51 to 2.06}	0.06 (0.03) {-0.01 to 0.13}	0.07 (0.05) {0.004 to 0.15}	0.47 (0.50^{M}) {-1.18 to 1.60}	0.85 (0.25^{S}) {-1.12 to 1.52}	0.27 (0.71^{M}) {-0.75 to 1.93}	0.24
		Right isthmus cingulate cortex	0.27 (0.15) {0.04 to 0.5}	0.47 (0.29) {0.24 to 0.7}	0.01 (1.00^{L}) {-0.50 to 2.01}	0.26 (0.2) {0.004 to 0.52}	0.22 (0.21) {-0.04 to 0.48}	0.51 (0.24^{S}) {-1.56 to 1.22}	0.98 (0.03^{N}) {-1.26 to 1.37}	0.13 (1.11^{VL}) {-0.52 to 2.23}	**0.02**

CI, Confidence Intervals; ES, Effect Size; ^{N}Negligible; ^{S}Small; ^{M}Medium; ^{L}Large; ^{VL}Very Large; ^{H}Huge; SD, Standard Deviation

(pre = 0.06 ± 0.08 vs. post = 0.22 ± 0.40; p = 0.43; ES = 0.66^{M}; ES 95% CI = -0.92 to 1.89). However, MBI analysis showed that clinically, the over time improvement seen in the SMT group is likely a substantial positive result (77.8%) and the group difference after intervention is possibly a substantial positive result (72.8%).

3.5 Discussion

The present study set out to assess the effect of eight weeks of SMT on structural brain changes and balance in chronic stroke survivors. The analysis of the structural MRI data revealed significant interaction effects together with significant between and within group results after the intervention. The SMT group showed interaction effects for increased connectivity after the training between the caudate and lentiform with other brain regions such as: caudal anterior cingulate, rostral middle frontal, superior frontal gyrus and the isthmus cingulate cortex. The SMT group showed better balance, though not statistically significant when looking at the p-value statistics. Nonetheless, the MBI analysis showed promising results from a clinical point of view, which should not be disregarded as this is an important finding to take into practise.

Results indicated an increased connectivity in the SMT group between the left caudate and contralateral anterior caudal cingulate cortex, whereas the CON group also showed increased connectivity strength between the left lentiform and ipsilateral anterior rostral cingulate cortex. The anterior cingulate cortex forms part of the basal ganglia network [164] and according to previously reported results, activity in the caudal anterior cingulate cortex correlates with sensory-motor regions, and plays an important role in motor control, while the rostral anterior cingulate cortex correlates with prefrontal regions [165, 81]. In the SMT group, majority of participants had left hemisphere lesions, which could explain the improved connectivity strength seen across the hemispheres. Additionally, a tendency for increased connectivity was seen between the left caudate and ipsilateral anterior caudal cingulate cortex, indicating improved connectivity strength within the hemisphere as well. Therefore, this could be an indication of improved sensory-motor function [64]. The prefrontal cortex is responsible for higher mental functions, such as executive functioning, attention, inhibition, memory as well as language and emotional processing [63]. Consequently, the educational talks could have contributed to improved cognitive functioning in the CON group.

Furthermore, an interaction effect for increased connectivity was seen between the right caudate and contralateral rostral middle frontal gyrus and ipsilateral superior frontal gyrus in the SMT group. Interestingly, the CON group showed reduced structural connectivity between the left caudate and

ipsilateral frontal lobe areas (parsopercularis and superior frontal gyrus). The frontal lobe can be subdivided into the superior frontal gyrus, middle frontal gyrus and inferior frontal gyrus [166]. The superior frontal gyrus is considered to be comprised of the supplementary motor area (SMA) and is connected with the middle frontal gyrus [72, 73]. According to MRI studies, the SMA plays a large role in postural control [75, 76], and is supported by previous research that reported significant gray matter volume increases in the SMA and superior frontal gyrus after six weeks of dynamic balance task training [82]. These areas are involved with various brain functions, such as sequencing and initiation of actions, motor learning and motor control [167, 73].

With regards to the lentiform, no significant interaction effects were found between the left lentiform and regions of interest, however, an interaction effect for increased structural connectivity was observed between the right lentiform and ipsilateral isthmus cingulate cortex. Additionally, statistically significant over time changes were found in the SMT group between the lentiform and other parietal lobe regions. The isthmus cingulate includes involvement of the medial and inferior lateral parietal areas and has been used to study the default mode network (DMN) as it shows characteristic features of the DMN [168, 64]. Connectivity within the DMN is associated with various functions such as integration and processing of emotions and cognition, monitoring the world around us, mind wandering, and can be modulated by the basal ganglia through the dopamine system [169, 170, 171, 81].

Some increased connectivity changes were also discovered in the CON group, specifically between the caudate and occipital lobe as well as temporal lobe regions. The lingual gyrus, in the occipital lobe, comprises of the primary visual cortex which plays an important role in visual processing [67]. Additionally, the inferior temporal gyrus, in the temporal lobe, is connected behind the inferior occipital gyrus and also plays a role in the higher levels of visual processing [172]. Therefore, increases within these areas in the CON group could be due to the nature of the intervention, which solely consisted of educational talks using Microsoft PowerPoint presentations. A relationship has been shown to exist between the basal ganglia and visual processing, as the output of the basal ganglia targets the occipitotemporal processing pathways within the inferiortemporal cortex [173].

This is the first pilot study set out to investigate structural connectivity between the basal ganglia and other brain regions of interest in chronic stroke survivors. Taken together, there seems to be potential for increased connectivity strength between the basal ganglia nuclei and fronto-parietal areas after participating in a SMT programme. These findings are in line with previous reported studies on a healthy population [63]. Although the sample size is small, which could be perceived as a limitation, statistically and practically

significant results were found for postural control-related restorative effects on structural neuroplasticity. This is a proof-of-concept study to indicate that desirable results could be achieved by participating in a SMT programme. Future researchers should replicate the study and aim to establish whether structural connctivity changes are similar and whether the size of the sample has an effect on the outcome measures. If a larger group of participants can be recruited it might also be worthwhile for future researchers to divide participants into subgroups according to lesion side as well as type of lesion to investigate the impact thereof on activity-dependent neuroplasticity.

To conclude, SMT shows promise to improve effectiveness of the basal ganglia network, which in turn could indicate improved ability to store and execute motor plans automatically, adapt to environmental changes, process sensory information, regulate muscle tone and control automatic postural responses.

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Conflict of Interest The authors declare that they have no conflict of interest.

Chapter 4

Article 2

Efficiency of Sensory-Motor Training on Sensory Reweighting and Perceived Quality of Life in Individuals with Chronic Stroke: A Randomised Controlled Trial

4.1 Abstract

Background: Balance is a complex sensory-motor process, which allows an individual to maintain their postural control by feedback and feed-forward mechanisms through the visual, vestibular and somatosensory systems. These mechanisms become compromised in individuals with chronic stroke causing impaired movement and reduced quality of life.

Objective: To assess the influence of sensory-manipulated balance training on sensory reweighting in individuals with chronic stroke. Additionally, health-related quality of life and intrinsic motivation were assessed.

Design: A double-blind randomised controlled trial.

Methods: Twenty-two individuals with chronic stroke ($\geq$ 6 months post-stroke) were randomly divided into two groups i.e. sensory-motor training (SMT; n = 12) and attention-matched control group (CON; n = 10). The SMT included task-specific balance training, which focused on manipulating the visual, vestibular and somatosensory systems, and the CON group listened to educational talks. Both interventions were delivered in a group setting, three times a week for 45 to 60-minute sessions over an eight-week period for a total of 24 sessions. Postural sway was measured with APDM's Mobility Lab^{TM} body-worn inertial sensors using the modified Clinical Test for Sensory Interaction and Balance (m-CTSIB). The m-CTSIB was measured for one 30 second trial under four different sensory conditions: (1) eyes open on firm surface, (2) eyes closed on firm surface, (3) eyes open on foam surface and (4) eyes closed on foam surface. Health-related quality of life was measured with the Short Form Health Survey (SF-36) and intrinsic motivation with the Intrinsic Motivation Inventory (IMI). Participants were evaluated one week before beginning the intervention (pre-test) and within one week after completing the intervention (post-test).

Results: The SMT group improved their sway area during condition three (p = 0.04, ES = 0.61^{M}, 95% CI = -0.27 to 1.36) and showed a reduction in somatosensory dependence (p = 0.02, ES = 0.63^{M}, 95% CI = -0.24 to 1.40) after the intervention. An interaction effect was identified for physical functioning (p = 0.005). Additionally, the SMT group showed improvements in physical (p = 0.01, ES = 0.52^{M}, 95% CI = -0.33 to 1.29) and social functioning (p = 0.02, ES = 1.03^{L}, 95% CI = 0.11 to 1.80) after training. Lastly, a group difference for physical functioning (p = 0.003, ES = 0.90^{L}, 95% CI = -0.05 to 1.70) and social functioning (p = 0.02, ES = 1.01^{L}, 95% CI = 0.04 to 1.81) was observed at post-test.

Conclusions: A balance training programme under sensory-manipulated conditions shows promise to improve sensory reweighting and health-related quality of life in individuals with chronic stroke.

Keywords: Postural control; Rehabilitation; Sensory manipulation; Stroke

4.2 Introduction

Maintaining posture and balance requires the interaction between the sensory (visual, vestibular and somatosensory) and motor systems [26]. These systems provide vital information with regards to position and body orientation within the environment by integrating with each other to draw a complete picture for the central nervous system (CNS) to process [60]. Based on the sensory reweighting hypothesis of Nashner [96], an individual is able to scale the relative importance of sensory cues (visual, vestibular, and somatosensory) for postural control under different contextual conditions [13, 12]. Thus, abnormal interactions between the visual, vestibular and somatosensory systems could be the source of abnormal postural control [55].

Following stroke, sensory-motor integration and reweighting may be impaired, and previous research has shown that these individuals predominantly rely on visual feedback to maintain postural control [55, 99, 100]. Even though most of these studies only include individuals with acute stroke, others have also reported that chronic stroke individuals perform worse in conditions where somatosensory information is distorted (like uneven or pliable surfaces) and/or when visual information is absent [55].

The exact reason why individuals with stroke develop visual dependency after an event is unclear. Researchers have suggested that this shift in sensory dominance might be a compensatory mechanism, due to faulty sensory orientation [174, 175], that it could be due to the specific lesion area that is affected [99], or even that the person might have been visually dominant prior to the event [176]. Other researchers have found that visual dependence in individ-

uals with stroke does not necessarily entail any neglect of somatosensory and vestibular information [100]. Subsequently, researchers have suggested that therapeutic interventions should focus on multisensory training techniques i.e. where these sensory systems are manipulated, withheld or disrupted, in order to ensure the use of another sense [177, 175, 99, 100].

Neuroplasticity can occur in the healthy and injured brain in response to goal-directed therapy through formation, removal as well as remodelling of synapses and dendritic connections in the cortex [1, 2, 3]. During the acute ($<$ 3 months post-stroke) and subacute (3 to 6 months post-stroke) phases of stroke spontaneous neuroplasticity occurs [22, 23, 24], whereas during the chronic phase of stroke ($\geq$ 6 months post-stroke) spontaneous recovery subsides and shifts more towards activity-dependent neuroplasticity [25]. The effect of a therapeutic intervention on reorganisation in the chronic stage of stroke is worthwhile to study, because during this stage spontaneous recovery is negligible, and any functional improvements would be due to the effects of the intervention [178].

One of the primary objectives for rehabilitation following stroke is the restoration of postural control [140]. Balance training programmes have been found to be effective in re-establishing postural control in individuals with chronic stroke [25]. In the literature, only two randomised controlled trials have been carried out to evaluate the effectiveness of balance training under sensory-manipulated conditions on static and dynamic balance in individuals with chronic stroke ($\geq$ 6 months post-stroke) [44, 139]. In both studies, a significant improvement in overall balance and gait was noted after training. More specifically to this study, a previous pilot trial showed that balance performance on a foam surface was improved by balance training under various sensory conditions in individuals with chronic stroke (mean time from onset: 14.9 $\pm$ 3.08 months; range: 12-20 months) [29].

Only a few studies to date have researched balance training under sensory manipulated conditions, specifically how it affects sensory-motor integration during a postural control task in individuals with chronic stroke. Therefore, the primary objective of the present study was to assess whether sensory-motor training (SMT), i.e. balance training under sensory-manipulated conditions, can alter sensory reweighting in individuals with chronic stroke. The researchers hypothesised that eight weeks of SMT may improve postural sway in individuals with chronic stroke due to better sensory reweighting capacity. Stroke is accompanied with long-term consequences such as physical disability, cognitive impairment, fatigue as well as depression and anxiety [179, 180, 181]. Consequently, the study also explored the effect on health-related quality of life as a secondary objective. To the researchers knowledge, this is the first study that included randomisation and double-blind evaluations.

4.3 Methods

4.3.1 Design Overview

This was a double-blind randomised controlled trial. The random allocation sequence was generated through stratified randomisation according to sex and an independent researcher assigned participants to either the SMT group or attention-matched control (CON) group through sealed envelopes. Independent researchers performed the screening process, participant enrolment and data collection throughout the study, thus allocation was concealed. Separate clinical exercise therapists oversaw the interventions in teams of two, either administering the SMT sessions or presenting the educational talks. Participants were blinded to the true purpose of the study. The institutional Health Research Ethics Committee (S16/07/128) approved the study. All participants provided written informed consent and assessments were conducted with professionalism as well as in accordance with the Declaration of Helsinki. Lastly, CONSORT guidelines were followed [151].

4.3.2 Setting and Participants

Participants were recruited by means of local newspapers, radio interviews and stroke support groups. Inclusion criteria were age $\geq$ 18 years; clinical diagnosis of stroke six or more months ago [24, 25]; ability to maintain standing balance for 30 seconds; ability to walk 7 metres independently; and physician approval for participation. Exclusion criteria were any other neurological conditions (Alzheimer disease, Parkinson's disease, etc.); mental health problems; visual, vestibular or auditory impairment; musculoskeletal injuries in previous six months; inability to travel to the intervention location; and less than 80% attendance at the end of the intervention. Above-mentioned information was obtained by means of patient history and clinical examination. Data collection and interventions were executed in a community hall at two different retirement villages, to assure comfortable driving distance for participants. The only requirement for the community halls were that they needed to have a walking distance of 8 metres with a firm surface as well as enough space and chairs for safety reasons.

4.3.3 Interventions

The SMT and educational talks were delivered in a group setting, three times a week for 45 to 60-minute sessions over an eight-week period for a total of 24 sessions. The SMT included task-specific balance training, which focused on manipulating the visual, vestibular and somatosensory sensory systems. The aim of week 1 was to focus on posture and alignment, specifically foot, sacroiliac joint and cervical spine alignment. Week 2-3 focussed on static balance,

week 4-5 on dynamic balance and week 6-8 on functional balance. Each session per week had a central theme; session 1 concentrated on posture, session 2 on base of support (BOS) and session 3 on centre of gravity (COG). Sessions started with 10-minute warm-up and ended with five minutes cool-down and relaxing techniques. Familiarisation and progressions were adapted from Janda's sensory-motor training principles [117] and followed the three different movement strategies described by Horak and Nashner [118] i.e. ankle, hip and stepping strategies. Even though the sessions were performed in a group, the therapist still catered for individual needs according to participant capabilities. A Visual Analogue Scale (VAS) for intensity and Rate of Perceived Exertion (RPE) scale were used to ensure that the sessions remained challenging and met individual needs [153]. Researchers set cut-off scores of ≥ 6.5 (moderate-high intensity) for the VAS and ≤ 5 (low-moderate exertion) for the RPE scale (Appendix K). Table 4.1 shows an outline of the SMT programme.

Table 4.1: Outline of sensory-motor training programme.

Week	**Sensory-motor training examples**
1	Short-foot training; toe abduction, adduction, curling; towel dragging; transverse abdominis activation; pelvic tilt (sitting/standing), head nods; chin-to-chest, shoulder rolls.
2-3	Seated and standing balance (trunk leans, reaching, catching, throwing); modified/normal tandem stance; single leg stance; over the moon; weight shifting.[#]
4-5	Repeat previous weeks and add: Walking (normal, high knees, butt kicks, sideways); tandem walking; weight shifts with stepping strategy; agility ladders; follow the light.[#]
6-8	Repeat previous weeks and add: Walking backwards, line walking; sit-to-stands; walking with direction and obstacles; reaching and walking; 360° turns; swiss ball sitting and reaching; dual task conditions.[#]

[#]Repeated under sensory-manipulated conditions: dimmed lights, dark glasses, eye(s) closed, soft/compliant surface, head tilts, sloped surface, etc.

The educational talks, in the CON group, focussed on wellness, risk factors, stress, complementary and alternative medicine therapies, bodily health and nutrition topics. The CON group was used to control for nonspecific effects of the intervention, thus balancing attention, intervention contact, social support and nonspecific therapist effects [154]. Table 4.2 summarises the educational talks for each session. Both interventions were planned and designed before

commencement and care providers adhered to the protocol of the SMT and educational talks.

Table 4.2: Outline of educational talks.

Week	Session	Educational topics
1	1	Introduction to stroke talks
	2	Group activity
	3	**Wellness:** Introduction to wellness. Why it matters?
2	4	**Wellness:** Physical, Emotional & Intellectual wellness
	5	**Wellness:** Social, Financial & Spiritual wellness
	6	**Wellness:** Environmental, Occupational wellness
3	7	**Risk factors:** What is a stroke?
	8	**Risk factors:** Blood pressure
	9	**Risk factors:** Cholesterol
4	10	**Risk factors:** Diabetes
	11	**Risk factors:** Disease management
	12	**Risk factors:** Disease management
5	13	**Stress:** Introduction
	14	**Stress:** Trauma
	15	**Stress:** Management (breathing & heart-rate variability)
6	16	**Complimentary & alternative medicine therapies**
	17	**Complimentary & alternative medicine therapies**
	18	**Complimentary & alternative medicine therapies**
7	19	**Your body:** Sleep
	20	**Your body:** Effects of aging
	21	**Your body:** Genes
8	22	**Nutrition**
	23	**Nutrition**
	24	Closing talk

4.3.4 Outcome Measures

Participants were evaluated one week before beginning the intervention (pre-test) and within one week after completing the intervention (post-test). Descriptive measures entailed age, sex, body mass, height, Body Mass Index (BMI), time since stroke, number of strokes, affected side and Fugl-Meyer assessment for Sensation [182]. Primary outcome measures included postural sway and sensory dependency during standing balance. Secondary outcome measures included health-related quality of life and intrinsic motivation.

4.3.4.1 Modified Clinical Test for Sensory Interaction and Balance (m-CTSIB)

The stability underlying standing quietly is referred to as standing balance and characterised by the amount of postural sway [183]. The m-CTSIB was used to assess postural sway and sensory dependency with APDM's Mobility Lab^{TM} (Portland, Oregon, USA) body-worn inertial sensor, strapped to the back at the height of the fifth lumbar spine [159]. The Mobility Lab has been shown to be a valid and reliable test for patients with neurological disorders and is an ideal instrument as it is a portable, low-cost alternative to dynamic posturography and objectively measures various components of balance [159, 161]. The m-CTSIB consists of four 30-second standing balance tasks under different sensory conditions: (1) eyes open on firm surface, (2) eyes closed on firm surface, (3) eyes open on foam surface and (4) eyes closed on foam surface [184, 60, 185]. The purpose of the test is to quantify how well participants are able to shift the emphasis and choose the most appropriate or accurate sensory information (visual, vestibular and/or somatosensory) for the situation. During condition one, eyes open on firm surface, participants have all three systems available to maintain balance. During condition two, eyes closed on firm surface, participants don't receive any visual feedback, and thus they mainly use vestibular and somatosensory inputs. During condition three, eyes open on foam surface, the participant mainly uses visual and vestibular inputs because somatosensory information is distorted. Lastly, during condition four, eyes closed on foam surface, participants only use vestibular input, as visual input is absent and the somatosensory system is distorted [101, 185]. The 95% ellipse sway area (m^2/s^4), which is the area of the 95% confidence ellipse encompassing the sway trajectory in the transverse plane, was used to measure postural sway [6]. From this measure visual dependence (%), somatosensory dependence (%) and vestibular loss (%) were calculated. For the m-CTSIB a lower score indicates a better outcome. For more information on calculations please see Appendix M.

4.3.4.2 Short Form Health Survey (SF-36)

The SF-36 is a health-related quality of life instrument assessing physical, psychological and social functions [186]; and focuses on the impact of health status on quality of life [187]. This is a self-administered questionnaire containing 36-items and measures a participant's perception of health on eight multi-item dimensions. The RAND 36-Item Health Survey 1.0 scoring system was used, dividing the items into the following eight dimensions; physical functioning, role limitations due to physical health, role limitations due to emotional problems, energy/fatigue, emotional well-being, social functioning, pain and general health. Each item is scored on a 0 to 100 range and all items are scored so that a higher score indicates a better outcome [188]. The validity and reliability for SF-36 in stroke has previously been established [189, 190].

4.3.4.3 Intrinsic Motivation Inventory (IMI)

The IMI assesses subjective experiences related to targeted activity [191], and was used to evaluate how the participants experienced the SMT and educational talks. It was used in both groups, however considered slightly different categories due to the nature of the two interventions. The SMT group completed a 20-item version of the IMI, which assessed five categories namely, Interest/Enjoyment; Perceived Competence; Effort/Importance; Pressure/Tension; and Value/Usefulness. The CON group completed a 17-item version of the IMI, which assessed 3 categories namely, Interest/Enjoyment; Value/Usefulness; and Perceived Choice. To score the IMI, all negatively worded statements in the questionnaire were inversely translated by subtracting the participant's score from 8. Following this, the average score for each category was calculated and converted into a percentage [192]. A higher percentage indicates a better outcome. The IMI was only done at post-test.

4.3.5 Power Analysis

A priori power analysis (G*Power 3.1.9.3 Software for Windows, Germany) [193] using difference between two dependent means (matched pairs) revealed that a total of 4 participants were needed to achieve 95% power. The m-CTSIB data from the pilot study done by Smania and colleagues [29] was used for sample size calculation. The pilot study utilised a one-group pre-post study design and evaluated the total duration of each condition. This was the best available data seeing as this is the first two-group pre-post study design focussed on balance training under sensory-manipulated conditions.

4.3.6 Data Analysis

Statistical analysis was performed using the STATISTICA for Windows version 13 (StatSoft, Inc., Tulsa, OK, USA) software. Data was assessed using

normal probability plots and all data were normally distributed. Descriptive statistics are reported as mean and standard deviation (SD), graphs as mean and Standard Error of the Mean (SEM), furthermore primary and secondary outcome measures are reported as mean, SD and 95% Confidence Intervals (CI). Baseline differences between groups were calculated with a two-sample t-test assuming unequal variances. Mixed model repeated measures ANOVA was conducted with group and time as fixed effects, and the participants as random effect. The group $\times$ time interaction effect was used to test whether changes over time were similar for the SMT and CON groups. Fisher Least Significant Difference (LSD) post-hoc testing was used to test for differences between groups and over time within each group. A significance level of $p \leq 0.05$ was used, and $p < 0.10$ designating trends. Lastly, Cohen's d effect sizes (ES) are also reported i.e. 0.2^{S}: Small, 0.5^{M}: Medium and 0.8^{L}: Large [162].

4.4 Results

4.4.1 Baseline Participant Characteristics

Out of 25 volunteers who met the inclusion criteria, only 22 completed the study, 12 in the SMT group and 10 in the CON group. Demographic characteristics of the participants are presented in Table 4.3, and no differences were found between groups ($p > 0.05$). Participants completed all assessments, except for one individual in the CON group and another in the SMT group. These two individuals did not complete condition 3 and 4 (foam conditions) in the m-CTSIB due to fear of falling. The CONSORT flow diagram displays the progress of all participants throughout the study and is demonstrated in Figure 5.1. No adverse events were reported.

4.4.2 Modified Clinical Test for Sensory Interaction and Balance (m-CTSIB)

Post-hoc analysis revealed a significant improvement in sway area during condition three, eyes open on foam surface, for the SMT group only. Participants reduced their sway area with 36.7% from pre- to post-test ($p = 0.04$; ES = 0.61^{M}; Figure 4.2), while the CON group changed by 0.4% ($p = 0.99$; ES = 0.01^{N}). Moreover, there was a tendency for group difference during this condition ($p = 0.09$; ES = 0.42^{M}), yet no interaction effect was reported for 95% ellipse sway area for condition three ($p = 0.15$). A tendency for an interaction effect was found for somatosensory dependency ($p = 0.06$). Post-hoc analysis revealed that the SMT group showed a significant 50.8% reduction in somatosensory dependence ($p = 0.02$; ES = 0.63^{M}) as well as a 38.6% tendency for less vestibular loss ($p = 0.08$; ES = 0.77^{M}) after the intervention. The CON group showed 27.6% increase in somatosensory dependence ($p = 0.65$;

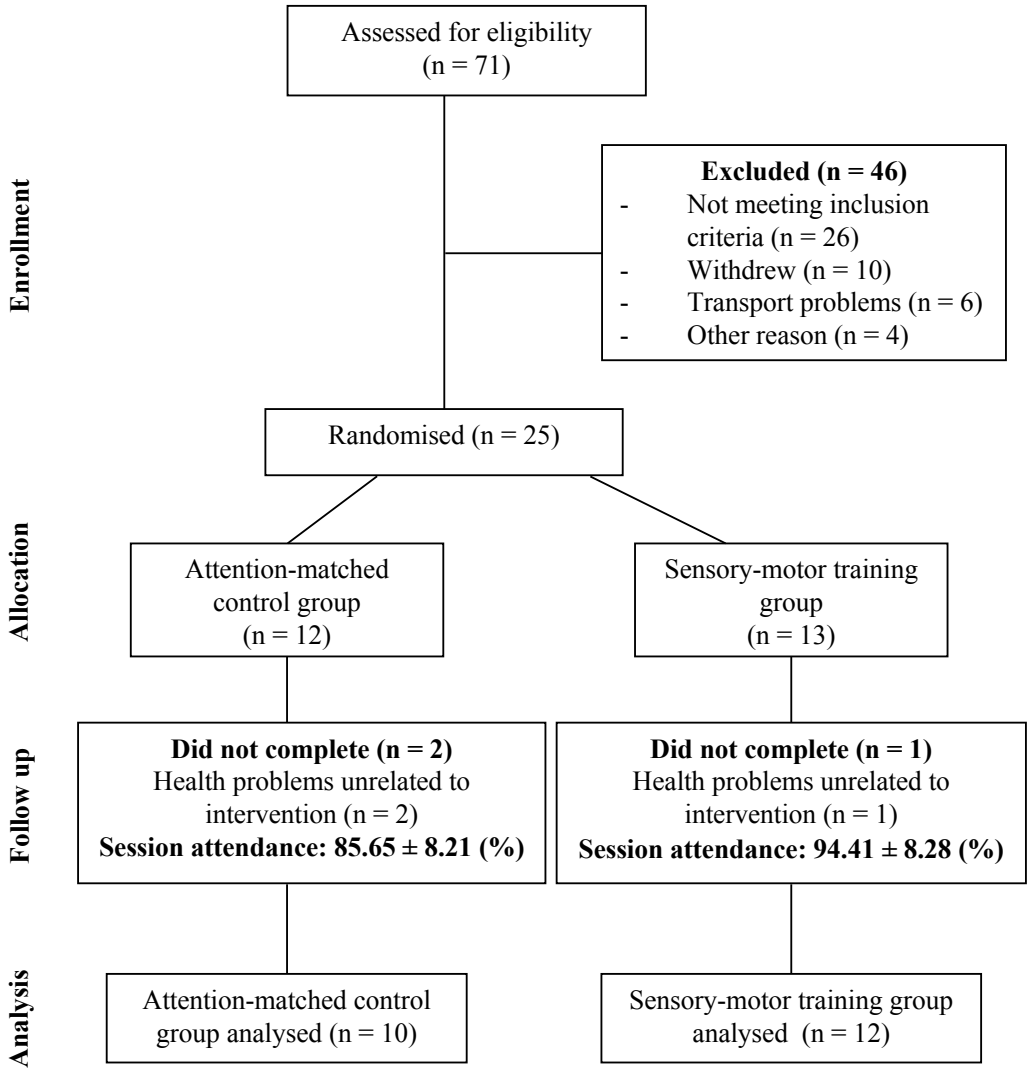

Figure 4.1: CONSORT flow diagram.

ES = 0.33^{S}) and 6.3% increase in vestibular loss (p = 0.84; ES = 0.08^{N}). Group performances for the m-CTSIB are shown in Table 4.4.

4.4.3 Short Form Health Survey (SF-36)

A significant interaction effect was identified for physical functioning (p = 0.005). According to post-hoc analysis the SMT group showed a significant 20.1% improvement in physical functioning (p = 0.01; ES = 0.52^{M}) after training, whereas the CON group showed a weak tendency for deterioration of 14.0% (p = 0.10; ES = 0.35^{S}). Additionally, a significant group difference for physical functioning (p = 0.003; ES = 0.90^{L}) was observed at post-test. Lastly, the SMT group also showed a significant 29.9% improvement in social functioning

Table 4.3: Demographic characteristics of participants (mean [SD]).

Variable	SMT group (n = 12)	CON group (n = 10)	p-value
Age (years)	68 [13]	71 [11]	0.53
Sex: men (%)	66.67	60.00	0.76
Body mass (kg)	86.89 [17.23]	81.54 [17.63]	0.48
Height (m)	1.69 [0.10]	1.70 [0.10]	0.80
Body mass index (kg/m^2)	30.58 [6.51]	28.55 [7.79]	0.52
Time since stroke (years)	10.72 [8.59]	6.98 [7.17]	0.28
Number of strokes	1 [0.89]	1 [0.48]	0.91
Affected side (R/L/both)	5/7	5/4/1	
Fugl-Meyer assessment for Sensation (24)	22.08 [1.56]	21.89 [1.62]	0.79

CON, Attention-matched control; L, Left; R, Right; SD, Standard deviation; SMT, Sensorymotor training

after the intervention (p = 0.02; ES = 1.03^{L}), and a significant group difference was seen after the intervention (p = 0.02; ES = 1.01^{L}) due to the CON group showing no change after the intervention (p = 0.80; ES = 0.09^{N}). A significant group difference was found at pre-test for energy/fatigue (p = 0.01; ES = 0.93^{L}), however over time the SMT group stayed consistent (p = 0.0.98; ES = 0.01^{N}) and the CON group improved somewhat (p = 0.16; ES = 0.46^{M}). SF-36 scores for the SMT and CON group are shown in Table 4.4.

4.4.4 Intrinsic Motivation Inventory

The IMI results revealed that the SMT group enjoyed and were interested in the exercises (83.3 ± 11.9%), they felt competent (71.4 ± 16.1%), saw the importance (81.0 ± 9.3%) and usefulness (98.9 ± 4.1%) of the exercises; however, they did feel some pressure/tension (58.3 ± 18.7%) during the intervention. Similarly, the CON group also enjoyed and were interested in the educational talks (95.7 ± 6.9%), saw the value and usefulness (91.4 ± 15.4%) and felt that they wanted to be there (94.3 ± 10.0%).

4.5 Discussion

The present study demonstrates that, when following a balance training programme under sensory-manipulated conditions, sensory reweighting and hence the ability to shift between more appropriate sensory inputs tend to improve.

Table 4.4: Group performances for all outcome measures.

	Experimental group (n = 12)			Attention-matched control group (n = 10)			Group differences		Interaction effect
Outcome	Pre-test mean (SD) {95% CI}	Post-test mean (SD) {95% CI}	p-value (ES) {ES 95% CI}	Pre-test mean (SD) {95% CI}	Post-test mean (SD) {95% CI}	p-value (ES) {ES 95% CI}	Pre-test p-value (ES) {ES 95% CI}	Post-test p-value (ES) {ES 95% CI}	p-value
95% Ellipse sway area (m^2/s^4) & Sensory dependence									
Eyes open on firm surface	0.03 (0.06) {-0.0009 to 0.06}	0.03 (0.06) {-0.002 to 0.06}	0.87 (0.02^{N}) {-0.77 to 0.83}	0.03 (0.03) {-0.02 to 0.07}	0.03 (0.02) {-0.01 to 0.07}	0.30 (0.32^{S}) {-0.58 to 1.18}	0.92 (0.04^{N}) {-0.82 to 0.86}	0.38 (0.17^{S}) {-0.66 to 1.03}	0.38
Eyes closed on firm surface	0.06 (0.07) {-0.01 to 0.10}	0.06 (0.10) {-0.02 to 0.10}	0.71 (0.07^{N}) {-0.77 to 0.83}	0.06 (0.06) {-0.03 to 0.12}	0.06 (0.05) {-0.03 to 0.12}	0.98 (0.01^{N}) {-0.86 to 0.89}	0.36 (0.05^{N}) {-0.76 to 0.92}	0.52 (0.03^{N}) {-0.80 to 0.87}	0.81
Eyes open on foam surface[#]	0.14 (0.11) {-0.09 to 0.19}	0.09 (0.06) {-0.04 to 0.13}	0.04 (0.61^{M}) {-0.27 to 1.36}	0.11 (0.06) {-0.08 to 0.19}	0.11 (0.07) {-0.08 to 0.19}	0.99 (0.01^{N}) {-0.86 to 0.89}	0.89 (0.30^{S}) {-0.56 to 1.13}	0.09 (0.42^{M}) {-0.49 to 1.20}	0.15
Eyes closed on foam surface[#]	0.48 (0.26) {-0.30 to 0.68}	0.37 (0.31) {-0.19 to 0.57}	0.26 (0.40^{M}) {-0.44 to 1.18}	0.57 (0.39) {-0.39 to 0.80}	0.52 (0.34) {-0.34 to 0.76}	0.66 (0.13^{N}) {-0.75 to 1.01}	0.35 (0.30^{S}) {-0.58 to 1.11}	0.14 (0.51^{M}) {-0.40 to 1.30}	0.66
Visual dependence (%)	123.42 (131.94) {-57.28 to 187.56}	84.73 (69.45) {-18.59 to 148.86}	0.33 (0.38^{S}) {-0.45 to 1.16}	64.98 (88.34) {-11.26 to 130.76}	126.14 (146.24) {-49.89 to 191.91}	0.16 (0.53^{M}) {-0.41 to 1.37}	0.16 (0.54^{M}) {0.36 to 1.34}	0.40 (0.39^{S}) {-0.49 to 1.21}	0.10
Somatosensory dependence (%)[#]	882.62 (940.62) {-485.83 to 1223.1}	434.09 (480.80) {-37.30 to 774.5}	0.02 (0.63^{M}) {-0.24 to 1.40}	333.46 (307.30) {-98.21 to 894.30}	425.58 (293.80) {-190.33 to 986.40}	0.65 (0.33^{S}) {-0.59 to 1.17}	0.11 (0.79^{M}) {-0.14 to 1.59}	0.40 (0.02^{N}) {-0.82 to 0.86}	**0.06**
Vestibular loss (%)[#]	3139.34 (1977.60) {-2056.25 to 4282.49}	1927.35 (1258.02) {-844.27 to 3070.51}	0.08 (0.77^{M}) {-0.12 to 1.53}	2307.81 (2188.07) {-1217.08 to 3663.58}	2453.96 (1750.48) {-1363.23 to 3909.73}	0.84 (0.08^{N}) {-0.81 to 0.95}	0.33 (0.42^{M}) {0.46 to 1.23}	0.40 (0.37^{S}) {-0.51 to 1.18}	0.18
SF-36 categories									
Physical functioning	58.75 (25.24) {-40.32 to 66.72}	70.56 (22.17) {-52.13 to 78.52}	0.01 (0.52^{M}) {-0.33 to 1.29}	57.55 (21.54) {-41.80 to 69.22}	49.50 (27.23) {-33.75 to 61.17}	0.10 (0.35^{S}) {-0.57 to 1.19}	0.72 (0.05^{N}) {-0.79 to 0.89}	0.003 (0.90^{L}) {-0.05 to 1.70}	**0.005**
Role limitations due to physical health	52.08 (32.78) {-28.32 to 68.22}	64.58 (32.78) {-40.82 to 80.72}	0.26 (0.40^{S}) {-0.44 to 1.18}	35.00 (39.44) {-9.45 to 52.68}	45.00 (34.96) {-19.45 to 62.68}	0.41 (0.28^{S}) {-0.63 to 1.13}	0.19 (0.50^{M}) {-0.39 to 1.31}	0.13 (0.61^{M}) {-0.30 to 1.41}	0.88
Role limitations due to emotional health	61.14 (37.16) {-40.03 to 83.60}	80.58 (26.42) {-59.47 to 103.10}	0.15 (0.63^{M}) {-0.23 to 1.40}	56.67 (44.58) {-30.31 to 77.90}	66.63 (38.52) {-40.28 to 87.80}	0.50 (0.25^{S}) {-0.65 to 1.11}	0.60 (0.12^{N}) {-0.73 to 0.95}	0.25 (0.45^{M}) {-0.43 to 1.23}	0.63
Energy/fatigue	70.28 (21.34) {-57.39 to 80.50}	70.42 (15.14) {-57.53 to 80.64}	0.98 (0.01^{N}) {-0.79 to 0.81}	50.67 (23.07) {-37.06 to 62.07}	60.50 (21.92) {-46.89 to 71.90}	0.16 (0.46^{M}) {0.47 to 1.30}	0.01 (0.93^{L}) {-0.02 to 1.73}	0.20 (0.56^{M}) {-0.34 to 1.37}	0.31
Emotional well-being	77.00 (16.64) {-65.32 to 84.40}	78.33 (17.68) {-66.66 to 85.74}	0.76 (0.08^{N}) {-0.73 to 0.88}	68.40 (15.25) {-57.11 to 77.43}	69.60 (17.51) {-58.31 to 78.63}	0.80 (0.08^{N}) {0.81 to 0.95}	0.16 (0.56^{M}) {-0.34 to 1.37}	0.15 (0.52^{M}) {-0.37 to 1.33}	0.98
Social functioning	69.79 (27.93) {-53.59 to 82.30}	90.67 (10.81) {-74.46 to 103.2}	0.02 (1.03^{L}) {0.11 to 1.80}	65.00 (20.24) {-47.25 to 78.60}	67.50 (33.95) {-49.75 to 81.10}	0.80 (0.09^{N}) {-0.79 to 0.96}	0.61 (0.20^{S}) {-0.65 to 1.03}	0.02 (1.01^{L}) {0.04 to 1.81}	0.17
Pain	87.54 (19.89) {-73.58 to 99.11}	81.29 (21.15) {-67.33 to 92.86}	0.42 (0.32^{S}) {-0.51 to 1.10}	81.25 (19.48) {-66.86 to 94.69}	76.80 (25.63) {-62.41 to 90.24}	0.60 (0.21^{S}) {-0.69 to 1.06}	0.52 (0.33^{S}) {-0.54 to 1.15}	0.66 (0.20^{S}) {0.66 to 1.03}	0.87
General health	70.83 (20.65) {-56.84 to 79.03}	72.50 (18.28) {-58.50 to 80.70}	0.74 (0.09^{N}) {-0.72 to 0.88}	61.00 (19.83) {-47.36 to 71.03}	66.00 (21.38) {-52.36 to 76.03}	0.38 (0.25^{S}) {-0.65 to 1.11}	0.17 (0.51^{M}) {-0.38 to 1.12}	0.39 (0.34^{S}) {-0.53 to 1.16}	0.66

[#]One participant in each group could not complete balance task (Experimental n = 11; Attention-control n = 9). CI, Confidence Intervals; ES, Effect Size; ^{N}Negligible; ^{S}Small; ^{M}Medium; ^{L}Large; SD, Standard Deviation; SF, Short Form.

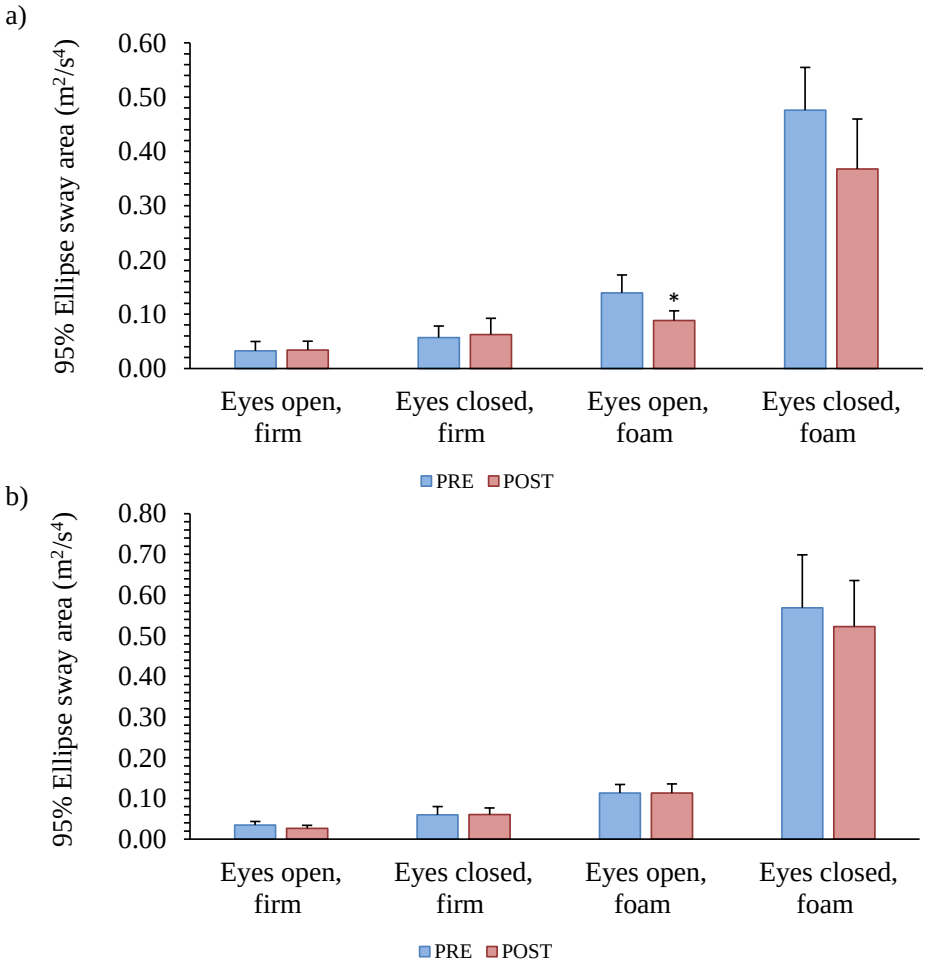

Figure 4.2: a) 95% Ellipse sway area during pre and post-test for SMT group (mean and SEM); b) 95% Ellipse sway area during pre and post-test for CON group (mean and SEM).

In addition, participants improved their perceptions of health-related quality of life for physical and social functioning.

Sensory reweighting is critical for the recovery of postural control in individuals who had a stroke [100]. During condition three, participants stood with their eyes open on a foam surface, resulting in accurate visual and vestibular feedback but distorted somatosensory input from the environment. The ability to utilise sensory integration and reweighting allows a person to overcome sensory conflicts generated by faulty afferent information [13, 12]. Thus, the over time improvement seen during condition three in the SMT group could mainly be attributed to the participants being able to override the faulty somatosensory input and focus on the accurate visual and vestibular inputs available to them [29]. This is supported by the reduction observed in somatosensory de-

pendence and vestibular loss. When a participant is somatosensory dependent, they need sensory input from a stable surface to maintain their balance. Thus, the opposite would be that if the participant is less somatosensory dependent, they are able to stand on an unstable platform (e.g. foam) and still be able to maintain their balance since they will shift the emphasis to the more accurate senses like the visual and vestibular systems. Hence, the individual is able to continuously shift between various types of sensory input for efficient, flexible and context-dependent postural control [100]. Balance training under sensory-manipulated conditions might therefore have helped participants to override the faulty somatosensory input available, leading them to be less dependent on somatosensory input and showing better sensory reweighting abilities.

Another possible explanation for the findings is provided by Sober and Sabes [194], who suggested that the weighting of vision and somatosensation reflects a strategy of minimising errors, or economising the neural input during the coordination task. Typically, before somatosensory feedback can be used, it must be transformed into visual coordinates, and this may result in transformation errors [194]. Consequently, the nervous system might still have preferred visual or possibly vestibular feedback to somatosensory inputs, for maintaining standing balance under conditions of sensory conflict since it was the input that resulted in the least transformation errors.

Similar results were found with the previously mentioned pilot trial by Smania and colleagues [29], with the exception that they found significant improvement in all somatosensory conflicting conditions. In the current study, no significant improvement was found when standing with eyes closed on the foam surface (condition four), however it should be noted that there was a medium effect size after the intervention for the SMT group as well as a tendency for less vestibular loss. Therefore, even with the positive reduction in vestibular loss, the vestibular input did not fully compensate for the lack of the visual feedback [194]. Another possible reason for this could be that the participants may not have exercised under visual conflict conditions intensely enough, due to their fear of falling. Attentional shifts have previously been shown to affect sensory integration [194]. In other words, during the intervention the participants may have purposefully shifted their attention on what they deemed the more salient feedback (i.e. visual and/or vestibular inputs), instead of being forced to use the somatosensory inputs.

Furthermore, health-related quality of life showed improvements in physical and social functioning categories for the SMT group. Health-related quality of life refers to the aspects that are affected by disease [195]. According to researchers, the component physical well-being (i.e., SF-36 physical functioning and role physical scales) is the most affected after stroke [189, 195]. Thus, it is very important to find ways to improve physical functioning in individuals

who have had a stroke. The conclusion can be made that SMT helped the individuals to perceive themselves to function better physically. Schinkel-Ivy et al. [196] found that individuals with chronic stroke who demonstrate low balance confidence exhibited impaired control of standing balance as well as walking. Similarly, Salbach et al. [197] also reported that improved perceived balance efficacy lead to better perceptions of health status and physical functioning. Additionally, social functioning improved over time in the SMT group more than in the CON group. This could be attributed to the exercise sessions taking place in groups and some of the activities had to be done with partners, facilitating social interaction. Even though the educational talks were also executed in a group setting, the participants did not interact with each other and rather only listened to the speaker. Previously Lai et al. [198] stated that social functioning is an important part of assessing recovery after stroke and should be monitored when implementing rehabilitative interventions.

Both groups indicated very good intrinsic motivation towards the SMT and educational talks, which correlated with the high session attendance percentages and low dropout rates. This is a very important factor to take into consideration when planning an intervention study seeing as a high dropout rate could influence results quite noticeably. The findings from the IMI also support the notion, that the incorporation of a CON group balanced out possible influences on outcome variables through attention, contact and social support [154].

The present study has a few limitations. Firstly, the sample size might be too small for inertial sensor data, which could have increased the chances of type two error. Future studies should focus on including a larger sample size to investigate further findings. Secondly, the type of stroke and lesion site could not be established for inclusion criteria. Previously, research has reported that some lesion sites such as the right hemisphere middle cerebral artery infarcts are associated with visual dependency for postural sway [99]. Thus, future studies should repeat this study and focus on recruiting participants according to stroke type and lesion site. Thirdly, in addition to using the VAS and RPE scales to monitor intensity and exertion, it might be viable to further divide the participants (via stratified randomisation) into groups according to balance capability to ensure maximal effort. Future studies could investigate the influence of a retention period, to establish whether improvements can be maintained over time or include a perturbation-based approach for more extensive explanation.

To conclude, results of this study demonstrate that there is value for individuals with stroke to participate in a balance training programme under sensory-manipulated conditions. The SMT group showed improved sensory reweighting as well as better perceived physical and social functioning over

time. Balance impairment is one of the leading causes for functional loss and commonly leads to impaired movement, reduced ability to execute activities of daily living (ADL) and increased risk of falling in individuals with chronic stroke. Exercise interventions, focussed on sensory manipulation, are being recognised as a strategy to improve the functional status of stroke individuals and should be a topic researched further.

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Conflict of Interest The authors declare that they have no conflict of interest.

Chapter 5

Article 3

Effects of Sensory-Motor Training on Turning Performance and Fall Efficacy in Chronic Stroke Survivors: A Randomised Controlled Trial

5.1 Abstract

Background: Postural control impairment is one of the leading causes of functional loss among chronic stroke survivors causing impaired mobility, reduced ability to execute activities of daily living (ADL) and increased risk of falling. The primary aim was to assess whether sensory-motor training (SMT), i.e. balance training under sensory-manipulated conditions, can alter functional mobility in chronic stroke survivors. Additionally, the study also set out to evaluate fall efficacy as a secondary outcome measure.

Design: A double-blind randomised controlled trial.

Methods: Chronic stroke participants ($\geq$ 6 months post-stroke) were divided into two groups namely, sensory-motor training (SMT; n = 12) and attention-matched control group (CON; n = 10). Both interventions were executed three times a week for 45 to 60-minute sessions over an eight-week period. The SMT consisted out of task-specific balance exercises while manipulating the sensory systems (i.e. visual, vestibular and somatosensory). Functional mobility was tested using the instrumented Timed-Up and Go (iTUG) test, which includes four functional movements, namely sit-to-stand, gait, turning, and turn-to-sit. Therefore, specific outcomes included (1) Total duration (sec); (2) Sit-to-stand duration (sec); (3) Turn: step time (sec); (4) Turn: number of steps; and (5) Turn-to-sit (sec). Additionally, concern for falling was measured with the Fall Efficacy Scale - International (FES-I). Participants were evaluated pre- and post-test.

Results: An interaction effect was identified with Turn: number of steps (p = 0.02) and fall efficacy (p = 0.03). Furthermore, the SMT group reduced their Turn: number of steps (p = 0.05, ES = 0.33^{S}, 95% CI = -0.51 to 1.10), however increased their Turn: step time (p = 0.02, ES = 0.59^{M}, 95% CI = -0.51 to 1.10) after the intervention.

Conclusion: Sensory-motor training can improve turning performance and fall efficacy in chronic stroke survivors. The SMT group executed turning with increased accuracy, indicating better postural control and functional mobility.

Keywords: Dynamic balance; Functional recovery; Fall risk; Rehabilitation; Stroke

5.2 Introduction

Stroke survivors struggle with an array of physical, social and emotional disabilities [199]. Physical disabilities cause long-term motor and sensory impairments in the body's physical function. The most common motor impairments following stroke include hemiparesis, poor balance and coordination as well as spasticity [200], whereas sensory impairments include somatosensory (touch and proprioception) impairment and somatic sensation deficits (temperature and pain) [201, 202]. Due to improved disease awareness and acute stroke care ($<$ 6 months post-stroke), stroke is shifting away from being a major cause of death to being a long-term chronic disease ($\geq$ 6 months post-stroke), leaving survivors with lasting impairments [203, 17]. Postural control impairment is one of the leading causes of functional loss among stroke survivors causing impaired mobility, reduced ability to execute activities of daily living (ADL) and increased risk of falling [43].

Mobility is the ability of changing and maintaining posture while moving oneself from one position to another [102]. The Timed-Up and Go (TUG) test is highly reliable in assessing daily sequential mobility activities in chronic stroke survivors [204, 111]. To execute the TUG, the participant has to stand up from the chair, walk 3 metres, turn around (180°), walk back to the chair, and sit back down [111]. One of the key mobility components of the TUG is turning, and research indicates that poor turning capability is associated with an increased risk for falls in elderly [205] and chronic stroke individuals [109, 206, 207]. Previous research has shown that chronic stroke survivors take longer to turn with more steps when turning-while-walking compared to healthy controls [208]. Additionally, performance measures such as a longer turning time and increased number of steps while turning suggest turning difficulty [209]. Fall injuries are eight times more likely to occur during turning events compared to straight forward walking in the elderly population [210]. Turning while walking is not an automatic movement but requires the integration and processing of information from the visual, vestibular and somatosensory systems, to adjust the body accordingly [211, 12]. Following stroke, the processing and integration of these sensory systems can be impaired [55, 13]. Therefore, when the integration and processing of one of these systems fail, the individual is likely to lose their balance and fall.

Balance training programmes have been found to be effective in improving functional mobility in chronic stroke survivors [135]. Two randomised control trials [44, 139] and one pilot study [29] evaluated the effect of sensory-manipulated balance training on walking speed in chronic stroke participants ($\geq$ 6 months post-stroke), however only one study found a significant improvement in walking speed after the intervention [29]. Marigold and colleagues [138] investigated the effect of multisensory agility training on functional mobility on chronic stroke survivors (> 12 months post-stroke) by means of the TUG test. Researchers only looked at the total duration of the TUG and found a trend ($p = 0.08$) for an interaction effect. Therefore, research is vague with regards to the effect of balance training on daily sequential mobility activities in chronic stroke survivors, and more research is needed.

This is the first study to look at the effect of balance training under sensory-manipulated conditions, from here on known as SMT, on daily mobility skills in chronic stroke survivors. The researchers hypothesise that if SMT could improve key mobility components and perceived fall efficacy, functional recovery could be increased in chronic stroke survivors. Thus, the primary aim of the present study was to evaluate whether SMT can alter functional mobility in chronic stroke survivors. Additionally, the study also set out to evaluate fall efficacy after the intervention as a secondary aim.

5.3 Methods

5.3.1 Study Design

This was a double-blind randomised controlled trial with assessments pre- and post-intervention. Participants were randomly divided into either the SMT or attention-matched control (CON) group by using sealed envelopes. Using impartial researchers for randomisation, participant enrolment and data collection, allocation was concealed. The participants knew they would be allocated to a group after pre-test, but were unaware of the differences between the groups. The institutional Health Research Ethics Committee approved the study (S16/07/128). Lastly, assessments were conducted in agreement with the Declaration of Helsinki and followed CONSORT guidelines [151].

5.3.2 Participants

Seventy-one individuals with chronic stroke were recruited to take part in the study, though only 25 individuals met the study inclusion criteria (Figure 5.1). Local newspapers, radio interviews and stroke support groups were utilised for participant recruitment. All participants provided written informed consent

before commencing with the study. Table 5.1 specifies the inclusion and exclusion criteria for all participants.

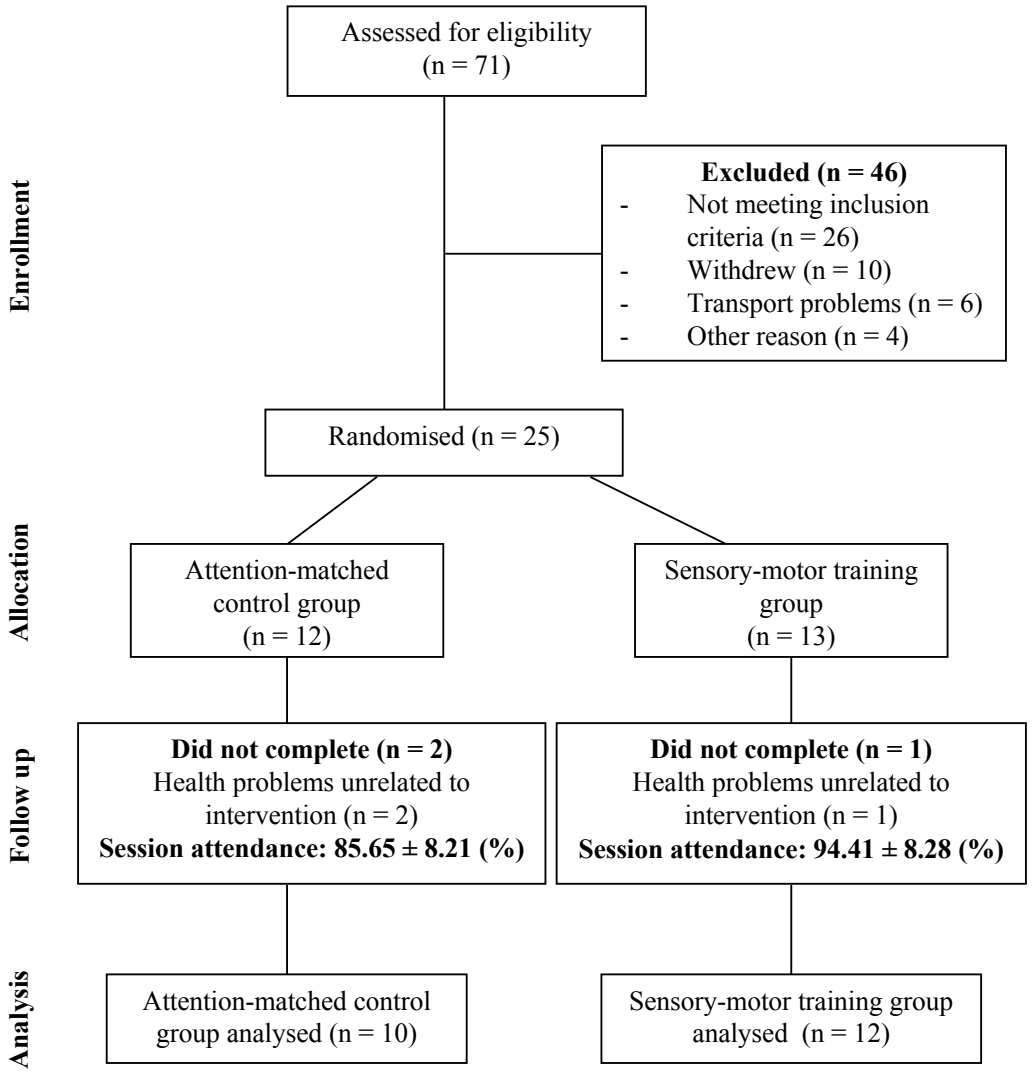

Figure 5.1: CONSORT flow diagram.

5.3.3 Procedures

At the start of the study and before randomisation, descriptive statistics were collected namely, age; sex; height; body mass; body mass index (BMI); time since stroke; number of strokes; affected side; physical activity status (Rapid Assessment of Physical Activity; RAPA [212]); and lower extremity motor function (Fugl-Meyer Assessment [147]). Data was collected at the same location pre- and post-test by the same assessor. Two community halls were

Table 5.1: Inclusion and exclusion criteria for all participants.

Inclusion criteria	Exclusion criteria
Men and women older than 18 years with clinically diagnosed stroke six or more months ago.	Any other neurological conditions (i.e. Parkinson's disease, Alzheimer's disease, etc.).
Ability to maintain standing balance for 30 seconds and walk 7 metres independently.	Visual, vestibular and/or auditory impairment.
Physician approval for participation.	Muscular injuries in previous six months.
Attendance rate of at least 80% at the end of the intervention.	Inability to travel to the treatment location.

utilised for the interventions, situated at a close driving proximity from the participants' homes. Community halls had 8 metres walking distance as well as a firm surface and enough space with chairs to ensure safe care for the participants. Experienced clinical exercise therapists oversaw the interventions and were not involved in the data collection phase.

5.3.4 Sensory-Motor Training Programme

Participants exercised three times a week for 45 to 60-minute sessions over an eight-week period. The eight weeks were divided into blocks, starting with posture and alignment, leading into static balance, moving to dynamic balance and ending off with functional balance. Table 5.2 summarises the aims and objectives for the blocked eight weeks. Sessions started with a 10-minute warm-up and ended with five minutes cool-down and relaxing techniques. The balance exercises were task-specific and focused on manipulating the visual, vestibular and somatosensory systems. These exercises included: seated and standing balance (trunk leans, reaching, catching, throwing); modified/normal tandem stance; single leg stance; over the moon; weight shifting; walking (normal, high knees, butt kicks, sideways, backwards); tandem walking; weight shifts with stepping strategy; agility ladders; line walking; sit-to-stands; walking with direction and obstacles; reaching and walking; 360° turns; swiss ball sitting and reaching. Thus, all exercises were executed under sensory-manipulated conditions, for example utilising dimmed lights, dark glasses, eye(s) closed, soft/compliant surface, head tilts, sloped surface, dual tasking, etc. Horak and Nashner's movement strategies [118] as well as Janda's sensory-motor training principles [117] were employed to ensure accurate progression throughout the SMT programme. Additionally, a Visual Analogue Scale (VAS) for intensity

and a Rate of Perceived Exertion (RPE) scale were used to tailor for individual needs according to participant capabilities [153]. The VAS was used to specifically monitor complexity and difficulty of the exercises, whereas the RPE scale was used to monitor fatigue and level of exertion. Researchers set cut-off scores of ≥ 6.5 for the VAS and ≤ 5 for RPE scale to assure that exercises were challenging enough, however not fatiguing (Appendix K).

Table 5.2: Outline of aims and objectives for sensory-motor training programme.

Week 1: Posture and alignment		
- Increase proprioceptive input to foot, sacroiliac joint and cervical spine to ensure proper positioning during exercise sessions.		
Session 1	**Session 2**	**Session 3**
Objective: Foot proprioception	Objective: Sacroiliac joint proprioception	Objective: Cervical spine proprioception
Week 2-3: Static balance		
- Maintain postural control on unstable surfaces and progress to weight shifting, eliminating vision or adding head movements.		
- Focus on using the ankle strategy during exercise sessions and introduce hip strategy.		
Session 1	**Session 2**	**Session 3**
Objective: Posture	Objective: Base of support	Objective: Centre of gravity
Week 4-5: Dynamic balance		
- Maintain postural control under sensory manipulated conditions while adding upper- and lower extremity movement.		
- Maintain ankle strategy, focus on hip strategy and start introducing stepping strategy in exercise sessions.		
Session 1	**Session 2**	**Session 3**
Objective: Posture	Objective: Base of support	Objective: Centre of gravity
Week 6-8: Functional balance		
- Perform functional movements of everyday life on under sensory manipulated conditions.		
- Maintain ankle and hip strategy and focus on stepping strategy in exercise sessions.		
Session 1	**Session 2**	**Session 3**
Objective: Posture	Objective: Base of support	Objective: Centre of gravity

5.3.5 Educational Talks

Participants in the CON group listened to educational talks, also three times a week for 45 to 60-minute sessions over an eight-week period. The talks covered various educational topics throughout the eight weeks, such as the different facets of wellness (physical, emotional, intellectual, etc.), risk factors associated with stroke, what stress entails and how to manage it, complementary and alternative medicine therapies, how to look after your body and lastly what a healthy nutritional diet entails. The reasoning for the CON group was to offset attention, intervention contact, social support and therapist effects, thus controlling for nonspecific intervention effects [154].

5.3.6 Primary Outcome Measure

The TUG is a clinical test used to evaluate balance and mobility, and has widely been employed in stroke population [111, 213, 207]. Furthermore, the TUG has been shown to be highly reliable (ICC = 0.96) as well as sensitive to real and clinical changes over time in chronic stroke [204, 111]. The TUG is a 3 metre time-based test used to assess performance of four functional movements, namely sit-to-stand, gait, turning 180°, and turn-to-sit [111]. These functional movements are complex activities on their own, therefore researchers proposed an instrumented TUG (iTUG) using portable inertial sensors, placed on the ankles, wrists, lumbar spine and trunk, to quantitatively evaluate these components [214]. The APDM's Mobility Lab™ (Portland, Oregon, USA; http://apdm.com) is a portable gait and balance system designed for clinicians and clinical researchers [159]. The iTUG automatically detects and separates the TUG components, providing detailed analysis of each [214, 159]. The Mobility Lab is a portable, low-cost alternative to dynamic posturography and has been shown to be a valid and reliable measure for individuals with neurological disorders [159, 161]. Therefore, the following outcomes were measured with the iTUG: (1) Total duration (sec); (2) Sit-to-stand duration (sec); (3) Turn: step time (sec); (4) Turn: number of steps; and (5) Turn-to-sit (sec).

5.3.7 Secondary Outcome Measure

The Fall Efficacy Scale - International (FES-I) was used to measure the level of concern for falling during ADL. This questionnaire is short, easy to administer and has shown to have excellent internal validity (Cronbach's alpha: 0.96) as well as test-retest reliability (ICC: 0.96) [215]. It targets older adults with or without a history of fear of falling and includes questions on physical and social activities. The level of concern is measured on a four point Likert scale (1: not at all concerned to 4: very concerned) [215]. Thus, a higher score indicates a greater concern for falling. The FES-I has been used on stroke survivors [216]

and a cut-off score of more than 27 points has been used to indicate a high concern for falling [217].

5.3.8 Statistical Analysis

A post-hoc power analysis (G*Power 3.1.9.3 Software for Windows, Germany [193]) using difference between two dependent means (matched pairs) revealed that a total of 20 participants achieved 92% power using the total duration TUG data. STATISTICA for Windows version 13 (StatSoft, Inc., Tulsa, OK, USA) was utilised for statistical analysis. Normal probability plots were used to assess data, and all data was normally distributed. Descriptive statistics are reported as mean and standard deviation (SD) and differences between groups were calculated with a two-sample t-test assuming unequal variances. Mixed model repeated measures ANOVA was executed with the participants as random effect and group and time as fixed effects. To evaluate whether changes over time were similar for the SMT and CON, a group x time interaction effect was employed. Fisher Least Significant Difference (LSD) post hoc testing was used to further test for differences over time within each group and between groups. The TUG and FES-I measures are reported as mean, SD and 95% Confidence Intervals (CI). Cohen's d effect sizes were used to determine any practical differences i.e. 0.2^{S}: Small, 0.5^{M}: Medium and 0.8^{L}: Large [162]. Lastly, the significance level was set at $p \leq 0.05$, and trends are described by $p < 0.10$.

5.4 Results

Twenty-two participants were included in the analysis, 12 in the SMT group and 10 in the CON group (Figure 5.1). The groups did not differ with respect to their demographic characteristics (Table 5.3) and outcome measures (Table 5.4) prior to the interventions, except for Turn: number of steps, which revealed a tendency for group difference at pre-test ($p = 0.06$; ES = 0.32^{S}). Unfortunately, one participant in each group could not be evaluated for iTUG measures due to equipment failure. No adverse events or side effects were reported.

5.4.1 Primary Outcome Measure

An interaction effect was identified with Turn: number of steps ($p = 0.02$). Furthermore, post-hoc analysis showed that over time the SMT group reduced their Turn: number of steps ($p = 0.05$; ES = 0.33^{S}), whereas the CON group increased their number of steps while turning ($p = 0.13$; ES = 0.27^{M}). Additionally, the SMT group increased their Turn: step time ($p = 0.02$; ES = 0.59^{M}) after the intervention, and the CON group didn't show noteworthy change

Table 5.3: Demographic characteristics of participants (mean ± SD).

Variable	SMT group (n = 12)	CON group (n = 10)	p-value
Age (years)	68 ± 13	71 ± 11	0.53
Sex: men (%)	66.67	60.00	0.76
Body mass (kg)	86.89 ± 17.23	81.54 ± 17.63	0.48
Height (m)	1.69 ± 0.10	1.70 ± 0.10	0.80
Body mass index (kg/m^2)	30.58 ± 6.51	28.55 ± 7.79	0.52
Time since stroke (years)	10.72 ± 8.59	6.98 ± 7.17	0.28
Number of strokes	1 ± 0.89	1 ± 0.48	0.91
Affected side (R/L/both)	5/7	5/4/1	
RAPA: Aerobic	2.75 ± 0.62	2.70 ± 0.67	0.86
RAPA: Strength and Flexibility	0.33 ± 0.78	0.80 ± 1.03	0.26
FM motor function lower extremity (34)	22.08 ± 9.52	21.22 ± 9.71	0.84

BMI: Body Mass Index; FM: Fugl-Meyer; RAPA: Rapid Assessment of Physical Activity (RAPA); RAPA Aerobic score: 1 = Sedentary; 2 = Under-active; 3 = Under-active regular - light activities; RAPA Strength & Flexibility score: 1 = Strength; 2 = Flexibility; 3 = Both; 0 = None

(p = 0.94; ES = 0.02^{N}). Group performances for the iTUG are presented in Table 5.4.

5.4.2 Secondary Outcome Measure

An interaction effect was identified for FES-I (p = 0.03). Post-hoc analysis showed a tendency for group difference (p = 0.06; ES = 0.32^{S}) at post-test, as the SMT group showed improved FES-I scores after the intervention (p = 0.19; ES = 0.27^{S}), while the CON group showed a strong tendency for higher concern for falling (p = 0.06; ES = 0.47^{M}). The FES-I scores for both groups are shown in Table 5.4.

5.5 Discussion

The main finding of the study is that SMT shows promise to improve turning performance and fall efficacy in chronic stroke survivors. From previous research, it is known that the processing and integration of the visual, vestibular and somatosensory systems may be impaired following stroke, which is fundamental for daily sequential mobility activities [55, 13]. Furthermore, falls are a

Table 5.4: Group performances for all outcome measures.

	Experimental group (n = 12)			Attention-matched control group (n = 10)			Group differences		Interaction effect
Outcome	Pre-test mean (SD) {95% CI}	Post-test mean (SD) {95% CI}	p-value (ES) {ES 95% CI}	Pre-test mean (SD) {95% CI}	Post-test mean (SD) {95% CI}	p-value (ES) {ES 95% CI}	Pre-test p-value (ES) {ES 95% CI}	Post-test p-value (ES) {ES 95% CI}	p-value
iTug variables[#]									
Total duration (sec)	17.38 (6.93) {-14.06 to 29.52}	18.09 (6.23) {-15.36 to 30.23}	0.51 (0.11^{N}) {-0.70 to 0.90}	19.08 (7.02) {-16.06 to 23.75}	19.05 (7.45) {-16.04 to 23.73}	0.98 (0.01^{N}) {-0.88 to 0.87}	0.35 (0.26^{S}) {-0.61 to 1.08}	0.87 (0.15^{N}) {-0.70 to 0.98}	0.51
Sit-to-stand duration (sec)	2.31 (0.57) {-2.07 to 2.62}	2.30 (0.26) {-2.05 to 2.61}	0.94 (0.03^{N}) {-0.78 to 0.82}	2.31 (0.52) {-1.99 to 2.60}	2.51 (0.38) {-2.19 to 2.80}	0.30 (0.46^{M}) {-0.47 to 1.30}	0.80 (0.01^{N}) {-0.84 to 0.84}	0.40 (0.69^{M}) {-0.23 to 1.49}	0.41
Turn: step time (sec)	0.57 (0.06) {-0.52 to 0.67}	0.64 (0.32) {-0.59 to 0.74}	0.02 (0.59^{M}) {-0.51 to 1.10}	0.63 (0.10) {-0.39 to 0.80}	0.63 (0.13) {-0.34 to 0.76}	0.94 (0.02^{N}) {-0.85 to 0.90}	0.19 (0.70^{M}) {-0.18 to 1.54}	0.59 (0.10^{N}) {-0.80 to 0.88}	0.13
Turn: number of steps	7.36 (2.82) {-6.05 to 8.81}	6.55 (2.39) {-5.23 to 7.99}	0.05 (0.33^{S}) {-0.51 to 1.10}	6.61 (2.04) {-5.04 to 7.89}	7.28 (3.15) {-5.71 to 8.56}	0.13 (0.27^{M}) {0.64 to 1.12}	0.06 (0.32^{S}) {-0.55 to 1.13}	0.29 (0.28^{S}) {-0.59 to 1.10}	0.02
Turn-to-sit duration (sec)	6.03 (2.42) {-5.25 to 8.37}	6.05 (1.88) {-5.27 to 8.39}	0.95 (0.01^{N}) {-0.79 to 0.81}	6.66 (3.40) {-5.19 to 8.38}	6.76 (3.41) {-5.29 to 8.48}	0.81 (0.03^{N}) {-0.85 to 0.90}	0.96 (0.23^{S}) {-0.63 to 1.05}	0.91 (0.28^{S}) {-0.58 to 0.10}	0.89
FES-I	28.50 (7.34) {-24.68 to 33.93}	26.25 (9.60) {-22.43 to 31.68}	0.19 (0.27^{S}) {-0.55 to 1.06}	25.60 (6.11) {-22.74 to 32.41}	29.20 (9.58) {-26.34 to 36.01}	0.06 (0.47^{M}) {-0.46 to 1.31}	0.42 (0.45^{M}) {-0.44 to 1.26}	0.06 (0.32^{S}) {-0.55 to 1.14}	0.03

[#]One participant in each group could not complete balance task (Experimental n = 11; Attention-matched control n = 9). CI, Confidence Intervals; ES, Effect Size; ^{N}Negligible; ^{S}Small; ^{M}Medium; ^{L}Large; SD, Standard Deviation; SF, Short Form.

common occurrence after stroke and continue into the chronic phase of stroke recovery [218]. Falls that occur during this phase contribute to individuals developing a fear of falling, increasing their dependence on external assistance and limiting their ability to execute ADL [219].

This study did not find that there was a statistically significant change in all TUG mobility components (i.e. total duration, sit-to-stand duration; and turn-to-sit duration), though turning performance presented significant results. However, the interaction effect found for the number of steps used during a turn should be interpreted lightly due to the tendency for groups to differ at pre-test. Nevertheless, post-hoc analysis did indicate that the SMT group used fewer steps to turn after the intervention, although surprisingly this was accompanied by an increase in step time while turning, thus turning slower after the intervention. During a turn there are four possibilities of executing the movement, (1) a quick turn with many steps, i.e. an uncontrolled shuffling gait pattern; (2) a slow turn with many steps, i.e. a controlled but hesitant gait movement; (3) a quick turn with fewer steps, i.e. a good gait pattern typically seen in healthy individuals; and (4) a slow turn with fewer steps, i.e. a controlled movement with more certainty [220, 221]. Before the SMT intervention, the SMT group turned quicker with more steps, while after the intervention they turned slower with fewer steps, which could indicate better control during turning. When turning a 180° the inner leg bears the entire body weight and acts as the turning axis, while the outer leg swings around to be placed on the ground [222]. Thus, when taking longer to step while turning and using less steps to make the turn, the ability of the inner leg to accept the entire body weight might improve while the distance of the outer leg to travel increases [208]. The use of fewer steps when turning could signify improved stability and coordination [209, 220].

When reflecting on the SMT programme used in this study, the participants were instructed to focus on executing the activities with better postural control instead of doing the activity as fast as they can. Therefore, this could be an explanation for the results found. In many perceptual-motor tasks, such as turning, there is a speed-accuracy trade-off where the individual has to decide between how fast they want to execute the activity and how many mistakes they want to make in performing the task [223]. Therefore, the possible conclusion can be made that because the participants were greatly focussed on executing the TUG with control, they mostly disregarded speed and preferred a slower self-selected gait speed [222], leading to the small improvements seen in the duration of the different mobility components of the TUG test. Nonetheless, with improved postural control comes improved functional mobility because the individual is able to change and maintain their posture better while moving from one position to another [102]. Additionally, the number of steps given during a 180° turn has been shown to correlate well

with functional ambulation and balance [224].

It has been reported that turning is one of the most frequent activities to cause a fall in stroke survivors [12, 208]. Therefore, if turning performance improves with SMT, it can result in reduced fall risk and furthermore improve concern for falling in chronic stroke survivors. This is demonstrated by the interaction effect for fall efficacy as well as the strong tendency for group difference after the intervention. Recently, a cut-off score of more than 27 points on the FES-I was used to discern high concern for falling from low concern for falling in stroke survivors ($>$ 3 months post-stroke) [217, 225]. Before the intervention commenced, the SMT group fell in the high concern for falling category and the CON group in the low concern for falling category. Yet, after the intervention the SMT group fell in the low risk of falling category and the CON group in the high risk of falling category.

The study had a few limitations. Results can only be compared to general community-dwelling chronic stroke survivors. Future studies should focus on recruiting participants specific to lesion site, number of strokes and stroke type. This study did not control for above-mentioned factors and could thus be interpreted as not being population specific enough. Furthermore, the sample size is relatively small. Future studies could aim to incorporate aspects focussed on speed into the SMT programme alongside postural control, to investigate further functional mobility changes.

To conclude, the results suggest that SMT could improve turning performance and fall efficacy in chronic stroke survivors. Taken together, the SMT group executed the movements with better precision, which could indicate better postural control and functional mobility. Sensory-motor training consists of low cost, easy to administer activities, with limited equipment. Therefore, the use of balance training under sensory-manipulated conditions should be encouraged in the rehabilitation procedure for chronic stroke survivors.

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Conflict of Interest The authors declare that they have no conflict of interest.

Chapter 6

General Discussion and Conclusion

The present dissertation evaluated the effect of a sensory-motor training (SMT) programme on structural brain changes and postural control-related functional recovery in chronic stroke survivors. The research hypothesis was that task-specific balance training, which focused on manipulating the visual, vestibular and somatosensory systems, could induce structural neuroplasticity through reorganisation and compensation, and in turn lead to the improved ability of chronic stroke individuals to execute activities of daily living (ADL) and perform mobility independently (i.e. improved functional recovery). The main findings of this dissertation showed that SMT may improve the connectivity strength between the basal ganglia network and sensory-motor fronto-parietal areas, sensory reweighting, turning performance as well as aspects of perceived quality of life and fall efficacy in chronic stroke survivors.

6.1 Baseline Characteristics

No differences were found in demographic characteristics between the SMT group and attention-matched control (CON) group. Consequently, this section will discuss the demographics of the participants collectively. However, there was a tendency for group difference at baseline for the number of steps taken during a 180° turn, which will be discussed later in this section.

Stroke can strike at any age, and research shows that the rate of stroke has increased in individuals under the age of 55 years old [226]. However, stroke is more likely to occur in individuals over the age of 55 years old and the risk thereof doubles each decade after that [227]. The average age for all of the participants in the current dissertation was 70 (SD 12) years old, and when dividing it into sex, men were on average 69 (SD 13) years old and women 71 (SD 10) years old. This is in line with previous research that established that men are at higher risk of experiencing a stroke at a younger age compared to women [228]. However, the mortality rate in women is greater than in men

due to women living longer and the increasing occurrence of stroke with aging [228]. Before the 1980's, stroke was considered to be primarily a disease of men, however since then stroke has emerged as a major health problem for women as well [229, 230].

Many risk factors exist for stroke, of which some include hypertension, smoking, diabetes mellitus, left ventricular hypertrophy and atrial fibrillation [231]. Obesity is a forerunner of hypertension and diabetes mellitus, which has been shown to play an important role in stroke epidemiology [232]. Body Mass Index (BMI; kg/m^2) was used in this dissertation to measure body composition and is based on weight relative to height. The conventional categories used for BMI include, normal weight (BMI of < 25 kg/m^2), overweight (BMI between 25 and 29.9 kg/m^2) and obese (BMI of ≥ 30 kg/m^2) [233]. The average BMI for all the participants in this dissertation was 29.7 (SD 7.0) kg/m^2, which places the average participant in the overweight category, borderline obese. According to researchers, an individual's risk of stroke increases by 22% when overweight and 64% when obese [232]. Furthermore, a higher body mass leads to increased balance instability, which is a key indicator of falling [234], and BMI has been shown to positively correlate with postural instability [235]. Therefore, this supports the importance for stroke survivors to participate in balance training programmes, as this will help improve postural stability and lower fall risk.

As mentioned, participants were only included if they experienced a stroke six or more months ago, which placed them in the chronic phase of their disease timeline. The average for all the chronic stroke survivors who participated in this current dissertation was 9 (SD 8) years post stroke. Researchers believe that the earlier a stroke survivor can start with rehabilitation, the more benefits will be gained [236]. However, margins for the rehabilitation process is still under debate due to many factors influencing the process, such as clinical, economical, and ethical consequences [237]. The school of thought is shifting away from the idea of a recovery plateau after six months and moving towards the belief that functional recovery can still occur after six months, through externally driven brain mechanisms [238]. This is supported by previous research that focused on postural control in the chronic phase of stroke [239]. Nonetheless, many differences exist between previous studies in terms of intervention, dosage and participants, which is preventing the exact classification of the effect of time since stroke in balance rehabilitation in the chronic phase of stroke [240].

Various factors impact the recovery process after stroke, such as the neuroanatomical details of stroke, i.e. lesion size, type and location [241, 239]. Stroke survivors are heterogeneous with regards to stroke etiology and baseline status, due to the high prevalence of comorbidity [242, 243]. In this disserta-

tion, only a small number of participants (n = 9) could undergo the necessary measures to obtain neuroanatomical details and thus heterogeneity could have influenced the results. This is a common occurrence in stroke research, and according to researchers, the problem in establishing whether any intervention in stroke rehabilitation is effective, is due to the large heterogeneity of the disease [242].

Another important aspect controlled for in this dissertation was global cognitive functioning. Cognitive impairment is very frequent following stroke and emerges in 40-70% of individuals of which half of the cases meet the criteria for dementia [244, 152]. Based on the Montreal Cognitive Assessment (MoCA) a cut-off score of ≤ 20 indicated moderate to severe cognitive impairment in the stroke survivors [152]. All of the participants together scored an average of 24.2 (SD 2.7) on the MoCA, indicating mild cognitive impairment. Therefore, the assumption could be made that the participants understood the tests that were executed and could easily follow either the SMT programme or educational talk sessions.

The Fugl-Meyer assessment also formed part of the demographic characteristic data collection to document motor functioning of the lower extremity as well as sensation of the participants. The Fugl-Meyer is a widely used and a clinically significant measure of body function impairment after stroke [182]. To date, no classifications exist for the different domains, however by executing the Fugl-Meyer assessment, body function impairment could be controlled for between groups. Motor and sensory losses contribute to movement limitations and restrict participation in ADL. Additionally, physical activity was noted with the Rapid Assessment for Physical Activity (RAPA) to ensure that physical activity levels stayed consistent and did not differ between groups. Therefore, participants were not allowed to participate in additional physical activity during the intervention.

The only difference observed between groups at baseline was a tendency for the number of steps taken during a turn in the Timed-Up and Go (TUG) test, however the effect size was small. With the demographic characteristics being similar between groups and controlling for confounding variables, little space is left for reasoning for this finding. However, during the TUG test the direction in which the participants turned was not controlled for, thus they could have chosen which way they wanted to make the turn. According to researchers, the turning direction during a TUG test does have an impact on performance, which is not related to hemiparesis, but to the fear of falling of the participants [245]. Conversely, there was no group difference at baseline for fall efficacy in this dissertation. Nonetheless, future studies should control the direction toward which the stroke participant turns when executing the TUG test, independent of the paretic or non-paretic side, and focus on the

fear of falling of the participant when executing a turn.

6.2 Activity-Dependent Neuroplasticity

Santiago Ramon y Cajal (1852-1934), a Spanish neuroscientist, once said: "Every man can, if he so desires, become the sculptor of his own brain". This quote emphasises what we now refer to as neuroplasticity, thus the ability of the brain to reorganise itself through experience and learning [9, 10, 11]. In this dissertation, the focus was placed on activity-dependent neuroplasticity, therefore, changes that occur in response to task-specific therapy. More specifically, does SMT change the structural connectivity strength between the basal ganglia network and other regions of interest in the brain. Various regions are of interest when investigating postural control, however for diverse reasons [66]. The basal ganglia were specifically chosen due to its ability to adjust postural responses relative to the particularities of the task at hand [65] and have been shown to be predictive of postural control [66].

Results indicated that the SMT group increased their structural connectivity strength between the basal ganglia network and fronto-parietal areas (i.e. caudal anterior cingulate cortex, rostral middle frontal gyrus, superior frontal gyrus and isthmus cingulate) after the SMT programme. In contrast, the CON group showed increased connectivity strength between the basal ganglia network with the orbito-temporal and frontal lobe areas (i.e. lingual gyrus, inferior temporal gyrus and rostral anterior cingulate cortex) after the educational talks. The areas that showed increased connectivity strength in the SMT group correlate with sensory-motor regions and are related to motor control, sensory-motor function, postural control and monitoring the world around us [165, 171, 167, 82, 73, 76, 81]. As for the CON group, the areas that indicated increased structural connectivity strength correlate with prefrontal areas and are related to higher cognitive and visual processing [172, 173, 67, 81]. Therefore, results from both groups are representative of the type of intervention executed.

Structural connectivity serves as the basis for inter-regional interactions in brain activity [246]. Therefore, the findings suggest that SMT could have postural control-related restorative effects on structural connectivity and support causal changes in activity-dependent neuroplasticity in chronic stroke survivors. Nevertheless, this was the first preliminary study regarding this topic and results should be interpreted with caution. The clinical implications of the changes in structural connectivity have across-the-board applications and shows that it is possible to produce postural control improvements long after stroke by means of SMT. As such, it is a topic that should be researched further.

6.3 Systems Framework for Postural Control

Stroke survivors present with impaired postural control due to deficits in the various domains responsible for postural stability [27, 13]. In Chapter 2, the systems framework for postural control was introduced, specifically the domains related to the outcome measures utilised in this dissertation. Thus, for the purpose of this discussion, the effect of SMT on the three domains of the postural control system will be discussed, namely Biomechanical Constraints, Sensory Strategies and Control of Dynamics.

6.3.1 Biomechanical Constraints

Postural stability depends on an individual's ability to keep the centre of gravity (COG) within the limits of the base of support (BOS) [26]. Therefore, while standing still the centre of mass (COM) is continuously moving (i.e. postural sway), and as long as it stays within the individual's limits of stability, a static position will be maintained. During the balance assessment, participants stood with feet slightly narrower than hip with apart, reducing the BOS slightly. However, no significant changes were observed in sway area when standing with eyes open on the floor. This condition is seen as the baseline condition of the Modified Clinical Test for Sensory Interaction and Balance (m-CTSIB) test because the participant can use all three sensory systems to maintain balance. Therefore, participants presented with good postural sway in the absence of sensory conflicted conditions and maintained it over time. The next section will discuss the effect of sensory conflict on postural sway in chronic stroke survivors.

6.3.2 Sensory Strategies

During quiet standing the ability to maintain postural control depends on the interaction between the visual, vestibular and somatosensory systems [93, 26]. The m-CTSIB consists of four balance tasks, i.e. (1) eyes open on firm surface, (2) eyes closed on firm surface, (3) eyes open on foam surface and (4) eyes closed on foam surface [184, 60, 185]. Therefore, this test quantifies how well a participant is able to shift their emphasis and choose the most suitable or correct sensory information (visual, vestibular and/or somatosensory) for the situation, also referred to as sensory reweighting [96, 13, 12]. Sway area improved significantly over time during condition three and somatosensory dependence was reduced after the intervention in the SMT group. A few tendencies for improvement were also found, i.e. group difference during condition three, an interaction effect for somatosensory dependency and over time reduction in vestibular loss.

By standing with eyes open on a foam pad, participants received accurate visual and vestibular feedback, however somatosensory input was distorted. According to previous research, postural control impairment in stroke survivors has been associated with the inability to select appropriate sensory input(s) [55, 44]. Moreover, somatosensation may be impaired in chronic stroke survivors, leading to the predominant reliance on the visual or vestibular systems [30, 247, 144]. Therefore, the conclusion can be made that the SMT programme helped participants to override the faulty somatosensory information and focus on the accurate visual and vestibular inputs available to them. This sensory compensation may have led to improved sensory-motor integration of postural control in the CNS, which facilitated the activation and coordination of proper motor processes [139]. Additionally, participants were able to shift their emphasis and choose the most suitable or correct sensory information for the given situation. To conclude, participants showed improved postural control which is essential for functional recovery of chronic stroke survivors as this aids them in executing ADL [248].

6.3.3 Control of Dynamics

As defined previously, functional recovery is the improved ability of chronic stroke individuals to execute ADL and perform mobility independently [8]. Accordingly, mobility is the capability to change and maintain postural control while moving from one point to another [102]. The TUG test was utilised in this dissertation as it assesses four daily sequential mobility activities, namely sit-to-stand, gait, turning 180° and turn-to-sit. Turning performance was the only variable to show significant change after the SMT programme. The SMT group used fewer steps to turn after the intervention, however increased their step time while turning. At first the increased step time was perceived as a strange result, together with the lack of change seen in the total duration, sit-to-stand duration, and turn-to-sit duration. Consequently, the test and intervention execution were examined which led to the discovery that participants were always instructed to complete movements with a self-selected gait speed and control. Therefore, a speed-accuracy trade-off element needs to be taken into consideration when interpreting the results [223]. Nonetheless, participants were able to turn with fewer steps and even though the step time increased, they had to spend more time on one leg to make the turn. The number of steps used to make a turn correlates with functional ambulation and postural control in chronic stroke survivors [224]. Therefore, this could be an indication of improved mobility and thus functional recovery.

6.4 Quality of Life and Fall Efficacy

Health-related quality of life and fall efficacy were assessed by means of questionnaires, which enabled individuals to document their perception of the impact and consequences illness has on their life. The SMT group showed an improved perception for physical and social functioning dimensions on the Short Form Health Survey (SF-36) after participating in the SMT programme. These results are favourable because after experiencing a stroke, individuals face a new reality associated with physical impairments, social isolation, increased dependency on others which leads to loss of identity and a lowered self-esteem [249, 250]. Therefore, the implications of this new reality can be devastating and often affect their perception of self-competence and ability to execute ADL [251]. A strong relationship exists between self-efficacy and functional recovery after stroke, which is mainly due to the positive association between self-efficacy and physical functioning [252, 253]. Therefore, the conclusion can be made that the SMT programme induced a higher perceived level of physical functioning, which in turn increased the participants' self-efficacy and created a state of improved functioning in daily living and overall well-being [254, 253]. Finally, the psychological and social problems stroke survivors experience are frequently overlooked [255, 256], however, due to the SMT session being executed in groups and facilitating partner interaction, the perception of social isolation was countered that led to higher perceived social functioning.

The Fall-Efficacy Scale International (FES-I) was used to assess fear of falling during ADL and a significant interaction effect was found together with a strong tendency for group difference after the intervention. Falling greatly affects functional recovery in stroke survivors [257], which leads to the reduced ability to execute ADL, i.e. eating, bathing, dressing and toileting [258]. Fear of falling defines a self-efficacy of falls as well as concern for falling and includes various aspects related to physical, psychological and functional impacts [259, 260]. Furthermore, fear of falling does not only occur in stroke survivors who have experienced a fall previously, but also in those who have not fallen before [109]. Consequently, this indicates that the fear of falling might be a more extensive problem than falls themselves and should be given more attention [216]. Therefore, SMT holds much potential to improve fall efficacy in chronic stroke survivors, which could improve the physical, psychological and functional aspects related to the disease. Overall, participants showed improved perception of the impact and consequences stroke has on their life after participating in the SMT programme.

To summarise the previous three sections, SMT has the ability to induce change in the functioning of chronic stroke survivors, which is supported by the dynamic systems theory. The changes observed in structural neuroplasticity and postural control-related functional recovery arose by changing the

nature of the task and environment in relation to the constraints of the person. Additionally, these changes had an impact on their perceived quality of life and fear of falling in everyday life. Therefore, by providing the right motivation, task and environment, the participants found good movement solutions by means of SMT, leading to the improved ability to execute ADL and move independently.

6.5 Limitations and Future Research

Each and every scientific research project has some limitations, an aspect that is unavoidable. Therefore, this section will highlight the conditions and circumstances, which may have influenced the outcome measures of the study. Recommendations for future research are also discussed accordingly.

Sample characteristics. Participants were recruited within a 70km radius from Stellenbosch University by means of local newspapers, local support groups and through word of mouth. Unfortunately, the sample size was relatively small, specifically for the MRI study. This is mainly due to the stringent MRI participants screening form, which ensures participant safety and prevents any interference during the MRI procedure. Also, participants were only included in the MRI study if they suffered one stroke previously, whereas the two behavioural outcome measure studies included individuals with multiple strokes. In general, the sample size was also small due to the disabling nature of stroke, which is a common problem in stroke intervention research [261]. One of the biggest obstacles to overcome in this dissertation was transport-related difficulties. In South Africa, the public transport system is not elderly friendly, which led to the participants having to get to and from the testing and intervention sessions by their own means. Most of these individuals were not able to drive themselves and did not have a caregiver to drive them around. Future research should focus on recruiting a larger sample to confirm the findings of this study, however, of more importance is raising awareness of the issues related to stroke participant recruitment, which might help other researchers with designing and conducting future research trials.

Neuroanatomical details. As mentioned above, not all participants could undergo an MRI analysis and additionally, the specific details regarding the history of the participant's stroke were not always available. Therefore, the neuroanatomical details of each participant's stroke could not be obtained, which could have influenced the results and also prevented the comparison of the findings to specific stroke subgroups. Subsequently, results can only be compared to general community-dwelling chronic stroke survivors. If possible, future research should endeavor to sub-divide participants according to

neuroanatomical details, which will allow for more specific conclusions to be made.

Testing equipment. The APDM's Mobility Lab^{TM} body-worn inertial sensors were used to assess postural sway and mobility in order to draw conclusions regarding postural control. Unfortunately, a force plate could not be used, which is the golden standard for postural control assessment. Nonetheless, the Mobility Lab has previously been validated against postural sway measured from centre of pressure displacement with a force plate [262] as well as with a motion analysis system in a gait laboratory [263, 264].

Systematic review and meta-analysis. This dissertation did not include a systematic review or meta-analysis, which is not necessarily a limitation but should be addressed. According to a recent investigation into the effects of exercise training on balance aspects in chronic stroke survivors, the systematic review and meta-analysis was limited by the number of studies included, which could have led to type 2 errors [25]. Only one randomised controlled trial [28] has been published since then, which led to the decision to rather provide a narrative review to present previous controlled trials executed within this topic. Therefore, future researchers should keep on investigating this topic as more randomised controlled trials are being executed, which could lead to more meaningful and insightful conclusions.

Sensory-motor training aspects. As mentioned earlier, the exercise sessions were executed in group sessions, which hold a variety of benefits. However, due to the heterogeneity of stroke one can't help to wonder whether individual sessions could yield better results. During the intervention the groups were kept small, ranging from three to five participants in a group. Additionally, measures such as the Visual Analogue Scale (VAS) for intensity and Rate of Perceived Exertion (RPE) were utilised to monitor and progress participants throughout the eight weeks accordingly. Therefore, the group sessions worked well for the purpose of this dissertation, however, it might be worthwhile for future research to investigate whether there is a difference between group and individual sessions.

Retention of outcomes. This dissertation did not investigate whether effects of participating in a SMT programme can be sustained, mainly due to logistical and financial reasons. However, it would be valuable to investigate whether improvements are retained at all as well as how long effects are maintained after finishing the SMT programme. Additionally, future research should investigate ways to encourage and support participants to continue with SMT after the supervised intervention, as well as the effectiveness of home training support. Sustainable methods need to be established and put

in place to ensure the maintenance of functional recovery in chronic stroke survivors.

6.6 Conclusion

Sensory-motor training consists of easy to administer exercises, which require little equipment and is a cost-effective option to induce activity-dependent neuroplasticity and functional recovery in chronic stroke survivors. This dissertation reduces the existing uncertainty regarding sensory-manipulated balance training for chronic stroke survivors, however more follow-up research is needed to confirm these findings. To conclude, there appears to be a relationship between structural connectivity and postural control-related functional recovery, which is a good start in bridging the gap between research and practice.

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Appendices

Appendix A

Sensory-Motor Training Programme

Safety guidelines for participants:

The following safety guidelines are tips to keep in mind while doing sensory-motor training. Please make yourself familiar with its contents before you start the eight weeks intervention program.

- Nothing should hurt. This is a simple rule, if it hurts inform the therapist. You should never get the idea that you should grin and just bear it. Nothing should hurt, cause physical problems or should make you feel uncomfortable or anxious.
- Arm's-length rule. Whenever you are not sitting, you should be no farther than an arm's length away from a balance support. This support will usually be a sturdy chair, but it could also be a walker or cane, handrail or counter, partner or assistant or even the therapist's hand.
- Ninety percent rule. This rule says that you should attempt only what you are ninety percent confident you can do safely - that is, what you are pretty sure you can do.
- Choose or refuse rule. Participation is always your own choice. If any activity makes you uncomfortable, stop and wait until you have the confidence to proceed.
- Signs to stop an activity immediately. Please inform the therapist if you experience any of the symptoms below:
  - Dizziness and/or nausea
  - Shortness of breath
  - Unusual fatigue

  - Heart racing or pounding
  - Uneasiness or anxiety
  - Blurred vision or slurred speech
  - Pain or tightness in chest, jaw or arm
  - Sudden paleness or clammy skin

- Medication, medication, medication. Please ensure that you take your medication as per your prescription. The exercise sessions should not serve as a substitution for your medication.

- Make sure you understand. Please inform the therapist if any of the exercises or movements are not completely understood. This will increase your chance of benefiting from the program.

- Good posture. The following points on posture should be maintained throughout the session:

  - Stand/sit up straight
  - Keep shoulders back
  - Keep abdomen tucked in
  - Keep feet flat on the floor

- In case of EMERGENCY. The following steps should be followed in case any participant becomes severely ill, disorientated, falls and/or gets injured:

  - Stop exercising immediately
  - Inform the therapist if necessary
  - Any participants standing should sit down
  - Clear the area around the injured participant
  - Make the participant as comfortable as possible

Warm-up and Cool-down before each session

Warm-up (10min)	Cool-down (5min)

• Session 1: Circle soccer
• Session 2: Balloon Volleyball
• Session 3: Shift around the clock and line passing
• Whole body stretches
  ○ Shoulder circles
  ○ Neck stretch
  ○ Arm stretch
  ○ Arm push
  ○ Arm circles
  ○ Back squeezes
  ○ Hugs
  ○ Wrist circles
  ○ Thumb to finger
  ○ Quadricep stretch
  ○ Hamstrings stretch
  ○ Calf stretch
  ○ Deep breathing
	• Muscular relaxation (seated on chair)
	  ○ Hands
	  ○ Arms
	  ○ Neck
	  ○ Face
	  ○ Chest
	  ○ Stomach
	  ○ Buttocks
	  ○ Legs
	• Deep breathing
	  ○ Chin-to-chest
	  ○ Chin-to-shoulder
	  ○ Trunk rotation
	  ○ Close eyes

Week 1

Session 1 - Foot alignment	Session 2 – SIJ alignment	Session 3 – Cervical spine alignment
• Cue Posture • Short foot training o Seated: Passive modelling or hand positioning o Standing: - Maintain short foot (SF) - Modified tandem stance with SF - One leg balance with SF - Pick foot up in air and maintain SF • Curl toes up and increase arch (pull towards heel) • Toe abduction (spreading) • Towel dragging o Inversion, Eversion o Plantar flexion o Marble pick ups	• Cue posture • Short foot training (recap) – 10min • SIJ training o Seated: - Pelvic tilt o Standing: - Pelvic tilt - Maintain SF - One leg balance with SF - Modified tandem stance with SF • Weight shifts with TA activation	• Cue posture • Short foot training (recap) • Cervical spine training with SIJ training • Repeat SIJ training with nodding movement of head • Roll shoulders, arms down, someone is pulling on your ears, chin in • Balance exercises on firm/foam surface o Seated balance: - Trunk leans in different directions - Reaching for objects - Catching and throwing objects (group)

Week 2

Session 1 - Posture	Session 2 – Base of Support	Session 3 – Centre of Gravity
• Cue Posture • Balance exercises on firm/foam surface o Seated balance: - Trunk leans in different directions - Reaching for objects - Catching and throwing objects (group) o Standing balance: - Eyes open - Trunk leans in different directions - Reaching for objects - Catching and throwing objects (group) o Modified Tandem stance: - Eyes open • Somatosensory activity o The ball game o Over the moon o Over the moon – rock forward, step up	• Cue posture • Balance exercises on firm/foam surface o Standing balance - Eyes open - Trunk leans in different directions - Reaching for objects - Catching and throwing objects (group) o Modified Tandem stance: - Eyes open - Trunk leans in different directions - Reaching for objects - Catching and throwing objects (group) o Single leg stance: - Eyes open • Somatosensory activity o Belly button training o Standing weight shifts	• Cue posture • Balance exercises on firm/foam surface o Standing balance: - Eyes open - Trunk leans in different directions - Reaching for objects - Catching and throwing objects (group) o Modified Tandem stance: - Eyes open - Dim room lights - Dark glasses o Single leg stance: - Eyes open - Dim room lights - Dark glasses • Somatosensory activity o Standing weight shifts o Making waves

Week 3

Session 1 - Posture	Session 2 – Base of Support	Session 3 – Centre of Gravity
• Cue Posture • Balance exercises on firm/foam surface o Seated balance: - Trunk leans in different directions - Reaching for objects - Catching and throwing objects (group) o Standing balance: - Trunk leans in different directions - Reaching for objects - Catching and throwing objects (group) o Modified Tandem stance: - Eyes open - Dark glasses - One eye closed - Both eyes closed • Somatosensory activity o Standing weight shifts o Making waves	• Cue posture • Balance exercises on firm/foam surface o Standing balance: - Trunk leans in different directions - Reaching for objects - Catching and throwing objects (group) o Modified Tandem stance: - Eyes open - Dark glasses - One eye closed - Both eyes closed o Single leg stance: - Eyes open - Dark glasses - One eye closed - Both eyes closed • Somatosensory activity o Keeping you on your toes	• Cue posture • Balance exercises on firm/foam surface o Standing balance: - Trunk leans in different directions - Reaching for objects - Catching and throwing objects (group) o Modified Tandem stance: - Eyes open - Dark glasses - One eye closed - Both eyes closed o Single leg stance: - Eyes open - Dark glasses - One eye closed - Both eyes closed • Somatosensory activity o Rock and walk

Week 4

Session 1 - Posture	Session 2 – Base of Support	Session 3 – Centre of Gravity
• Cue Posture • Balance exercises on firm/foam surface o Modified Tandem stance: - Eyes open - Dark glasses - One eye closed - Both eyes closed o Single leg stance: - Eyes open - Dark glasses - One eye closed - Both eyes closed o Walking (15m) - Normal walking - High knees walking - Butt kicks walking - Sideways walking • Somatosensory activity o Opposing circles and high fives	• Cue posture • Balance exercises on firm/foam surface o Modified Tandem stance: - Eyes open - Dark glasses - One and both eyes closed o Single leg stance: - Eyes open - Dark glasses - One eye closed - Both eyes closed o Walking (15m) - Normal walking - High knees walking - Butt kicks walking o Tandem Walking o Weight shifts with stepping strategy • Somatosensory activity o Follow the light	• Cue posture • Balance exercises on firm/foam surface o Single leg stance: - Eyes open - Dark glasses - One eye closed - Both eyes closed o Walking (15m) - Normal walking - High knees walking - Butt kicks walking - Sideways walking o Tandem Walking o Weight shifts with stepping strategy o Walking with reduced vision (15m) - High knees walking - Butt kicks walking - Sideways walking • Somatosensory activity o Agility ladders

Week 5

Session 1 - Posture	Session 2 – Base of Support	Session 3 – Centre of Gravity
• Cue Posture • Balance exercises on firm/foam surface o Single leg stance: - Eyes open - Dark glasses - One eye closed - Both eyes closed o Walking (15m) - Normal walking - High knees walking - Butt kicks walking - Sideways walking o Weight shifts with stepping strategy o Walking with reduced vision (15m) - Normal walking - High knees walking - Butt kicks walking - Sideways walking • Somatosensory activity o Opposing circles and high fives	• Cue posture • Balance exercises on firm/foam surface o Walking (15m) - Normal walking - High knees walking - Butt kicks walking - Sideways walking o Tandem Walking o Weight shifts with stepping strategy o Walking with reduced vision (15m) - Normal walking - High knees walking - Butt kicks walking - Sideways walking o Tandem Walking with reduced vision o Weight shifts with stepping strategy with reduced vision • Somatosensory activity o Follow the light	• Cue posture • Balance exercises on firm/foam surface o Walking (15m) - Normal walking - High knees walking - Butt kicks walking - Sideways walking o Tandem Walking o Weight shifts with stepping strategy o Walking with reduced vision (15m) - Normal walking - High knees walking - Butt kicks walking - Sideways walking o Tandem Walking with reduced vision o Weight shifts with stepping strategy with reduced vision • Somatosensory activity o Agility ladders

Week 6

Session 1 - Posture	Session 2 – Base of Support	Session 3 – Centre of Gravity
• Cue posture • Balance exercises on firm/foam surface o Recap Modified Tandem stance o Recap Single leg stance o Recap Walking (15m) o Tandem Walking o Weight shifts with stepping strategy o Recap Walking with reduced vision (15m) o Tandem Walking with reduced vision o Weight shifts with stepping strategy with reduced vision o Walking with reduced vision & head movements (15m) - Normal walking - High knees walking - Butt kicks walking - Sideways walking • Somatosensory activity o Opposing circles and high fives	• Cue posture • Balance exercises on firm/foam surface o Recap Walking (15m) o Tandem Walking o Weight shifts with stepping strategy o Recap Walking with reduced vision (15m) o Tandem Walking with reduced vision o Weight shifts with stepping strategy with reduced vision o Walking with reduced vision & head movements (15m) - Normal walking - High knees walking - Butt kicks walking - Sideways walking • Somatosensory activity o Follow the light	• Cue posture • Balance exercises on firm/foam surface o Recap Walking (15m) o Tandem Walking o Weight shifts with stepping strategy o Recap Walking with reduced vision (15m) o Tandem Walking with reduced vision o Weight shifts with stepping strategy with reduced vision o Walking with reduced vision & head movements (15m) - Normal walking - High knees walking - Butt kicks walking - Sideways walking • Somatosensory activity o Agility ladders

Week 7

Session 1 - Posture	Session 2 – Base of Support	Session 3 – Centre of Gravity
• Cue posture • Balance exercises on firm/foam surface o Recap Modified Tandem stance o Recap Single leg stance o Walking (15m) with added obstacles o Tandem Walking o Reaching exercises - Reaching high on shelf - Reaching shoulder height - Reaching down to ground o Weight shifts with stepping strategy o Walking with direction change *(t-test)* o Tandem Walking with reduced vision o Weight shifts with stepping strategy with reduced vision o Walking and counting (15m) o Group sit-to-stands in circle (move from chair 1 to chair 2)	• Cue posture • Balance exercises on firm/foam surface o Recap Modified Tandem stance o Recap Single leg stance o Walking (15m) with added obstacles o Tandem Walking o Reaching exercises - Reaching high on shelf - Reaching shoulder height - Reaching down to ground o Weight shifts with stepping strategy o Walking with direction change *(t-test)* o Tandem Walking with reduced vision o Weight shifts with stepping strategy with reduced vision o Walking and counting (15m) o Group sit-to-stands in circle (move from chair 1 to chair 2)	• Cue posture • Balance exercises on firm/foam surface o Recap Modified Tandem stance o Recap Single leg stance o Walking (15m) with added obstacles o Tandem Walking o Reaching exercises - Reaching high on shelf - Reaching shoulder height - Reaching down to ground o Weight shifts with stepping strategy o Walking with direction change (t-test) o Tandem Walking with reduced vision o Weight shifts with stepping strategy with reduced vision o Walking and counting (15m) o Group sit-to-stands in circle (move from chair 1 to chair 2)

Week 8

Session 1 - Posture	Session 2 – Base of Support	Session 3 – Centre of Gravity
• Cue posture • Balance exercises on firm/foam surface o Recap Modified Tandem stance o Recap Single leg stance o Walking with added obstacles and music o Tandem Walking o Reaching exercises with reduced vision - Reaching high on shelf - Reaching shoulder height - Reaching down to ground o Weight shifts with stepping strategy o Walking with direction change and obstacles (t-test) o Tandem Walking with reduced vision o Walking and counting backwards (15m) o Group sit-to-stands in circle (move from chair 1 to chair 2) o 360° turns	• Cue posture • Balance exercises on firm/foam surface o Walking with added obstacles and music o Tandem Walking o Weight shifts with stepping strategy o Walking with direction change and obstacles (t-test) o Tandem Walking with reduced vision o Walking and counting backwards (15m) o Group Sit-to-stands in circle (move from chair 1 to chair 2) o 360° turns o Sitting on Swiss Ball o Sitting on Swiss Ball + Reaching exercises - Reaching high on shelf - Reaching shoulder height - Reaching down to ground	• Cue posture • Balance exercises on firm/foam surface o Walking with added obstacles and music o Tandem Walking o Weight shifts with stepping strategy o Walking with direction change and obstacles (t-test) o Tandem Walking with reduced vision o Walking and counting backwards (15m) o Group Sit-to-stands in circle o (move from chair 1 to chair 2) o 360° turns o Sitting on Swiss Ball o Sitting on Swiss Ball + Reaching exercises - Reaching high on shelf - Reaching shoulder height - Reaching down to ground

Appendix B

Physiotherapy Evidence Database Review Table

Study	Participants	Design	CON group	EXP group	EX Frequency	EX Duration	Study Duration	Tests used	Main outcome variable	Main Findings	PEDro score (11)
Bonan et al. 2004 [44]	Stroke; at least 12 months post-stroke	RCT	Balance training with visual cues	Balance training without visual cues	5 times per week	60 minutes	4 weeks	SOT; gait parameters	Balance	Both groups improved in balance, gait velocity, and self-assessment of gait ($p<0.05$).	9
Marigold et al. 2005 [135]	Stroke; at least 12 months post-stroke	RCT	Stretching/ weight-shifting exercise	Multisensory agility exercise	3 times per week	60 minutes	10 weeks	BBS; TUG; step reaction time; ABC; NHP; postural reflexes; induced falls	Functional balance, mobility, postural reflexes, & falls	Both groups improved all clinical outcome measures. Agility group showed greater improvement in postural reflexes, functional balance, and mobility ($p<0.05$).	8
Bayouk et al. 2006 [136]	Stroke; at least 6 months post-stroke	RCT	Task-orientated exercise	Task-orientated exercise & sensory manipulation	2 times per week	60 minutes	8 weeks	COP; 10m walking	Postural stability	EXP COP improved & both groups' walking improved ($p<0.05$).	5

Study	Participants	Design	CON group	EXP group	EX Frequency	EX Duration	Study Duration	Tests used	Main outcome variable	Main Findings	PEDro score (11)
Smania et al. 2008 [29]	Stoke; at least 12 months post-stroke	Pilot study	None	Balance training	5 times per week	50 minutes	4 weeks	SOT; 10m walk test	Postural stability & walking ability	Balance on compliant surfaces improved ($p=0.018$) and walking speed increased ($p=0.018$).	4
Yelnik et al. 2008 [137]	Stroke; 3-15 months post-stroke (mean post-stroke time: 7 months)	Randomized parallel-group trial	Conventional Neuro-developmental-theory-based treatment (NDT)	Multi-sensorial training	5 times per week	60-70 minutes	4 weeks	BBS; posture-graphy; gait; FIM; NHP	Balance	Both groups improved in balance and gait ($p<0.05$). No difference between groups.	8
Jang & Lee et al. 2016 [28]	Stroke	RCT	General balance training	General balance & sensory integration training	5 times per week	CON: 30 minutes EXP: 60 minutes	4 weeks	LoS and muscle activity	Balance	Erector spinae & gluteus medius activity as well as LoS improved in the EXP group ($p<0.05$).	10

ABC: Activities-specific Balance Confidence; BBS: Berg Balance Scale; BI: Balance Index; CDP: Computerized Dynamic Posturography; CON: Control; COP: Centre Of Pressure; EX: Exercise; EXP: Experimental; FIM: Functional Independence Measure; JPS: Joint Position Sense; LoS: Limits of Stability; NHP: Nottingham Health Profile; NR: Not reported; PEDro: Physiotherapy Evidence Databse; RCT: Randomized Control Trial; RoM: Range of Motion; SOT: Sensory Organization Test; STS: Sit to Stand; TUG: Timed-Up and Go.

Appendix C

Diffusion Tensor Imaging Analysis

MRI acquisition and pre-processing information:

All imaging procedures took place at the Cape Universities Body Imaging Centre (CUBIC) which is based at the University of Cape Town's Medical Campus at the Groote Schuur Hospital. The centre hosts a 3T Siemens Skyra full body scanner. For more information regarding hardware/software solutions please refer to cubic.uct.ac.za.

The participants were asked to complete an *MRI Participant Screening Form* to ensure their safety and to prevent any interference during the MR procedure. Thereafter, participants were placed in the magnetic resonance scanner, the head coil was attached and head movement was reduced using patches between the ears/head and the coil.

Lastly, this appendix contains the Diffusion Tensor Imaging protocol utilised. A Freesurfer Analysis Pipeline was used for pre-processing of data and a detailed overview can be found at:

http://surfer.nmr.mgh.harvard.edu/fswiki/FreeSurferAnalysisPipelineOverview

\\Research\Tania&Karen\Routine\brain\BME_DTI_30gr_4b0_2mm_ISO_52sl_AP

TA: 11:22 PM: REF Voxel size: 2.0×2.0×2.0 mmPAT: 2 Rel. SNR: 1.00 : epse

Properties

Prio recon	Off
Load images to viewer	On
Inline movie	Off
Auto store images	On
Load images to stamp segments	Off
Load images to graphic segments	Off
Auto open inline display	Off
Auto close inline display	Off
Start measurement without further preparation	Off
Wait for user to start	Off
Start measurements	Single measurement

Routine

Slice group	1
Slices	69
Dist. factor	30 %
Position	L0.6 P1.2 H13.9 mm
Orientation	Transversal
Phase enc. dir.	A >> P
AutoAlign	---
Phase oversampling	0 %
FoV read	256 mm
FoV phase	81.3 %
Slice thickness	2.0 mm
TR	10000 ms
TE	83.0 ms
Averages	1
Concatenations	1
Filter	Prescan Normalize
Coil elements	HEA;HEP

Contrast - Common

TR	10000 ms
TE	83.0 ms
MTC	Off
Magn. preparation	None
Fat suppr.	Fat sat.
Fat sat. mode	Strong

Contrast - Dynamic

Averages	1
Averaging mode	Long term
Reconstruction	Magnitude
Measurements	1
Delay in TR	0 ms
Multiple series	Off

Resolution - Common

FoV read	256 mm
FoV phase	81.3 %
Slice thickness	2.0 mm
Base resolution	128
Phase resolution	100 %
Phase partial Fourier	6/8
Interpolation	Off

Resolution - iPAT

PAT mode	GRAPPA
Accel. factor PE	2

Resolution - iPAT

Ref. lines PE	24
Reference scan mode	EPI/separate

Resolution - Filter Image

Distortion Corr.	Off
Prescan Normalize	On
Dynamic Field Corr.	Off

Resolution - Filter Rawdata

Raw filter	Off
Elliptical filter	Off

Geometry - Common

Slice group	1
Slices	69
Dist. factor	30 %
Position	L0.6 P1.2 H13.9 mm
Orientation	Transversal
Phase enc. dir.	A >> P
FoV read	256 mm
FoV phase	81.3 %
Slice thickness	2.0 mm
TR	10000 ms
Multi-slice mode	Interleaved
Series	Interleaved
Concatenations	1

Geometry - AutoAlign

Slice group	1
AutoAlign	---
Position	L0.6 P1.2 H13.9 mm
Orientation	Transversal
Phase enc. dir.	A >> P
Initial Position	L0.6 P1.2 H13.9
L	0.6 mm
P	1.2 mm
H	13.9 mm
Initial Rotation	0.00 deg
Initial Orientation	Transversal

Geometry - Saturation

Fat suppr.	Fat sat.
Fat sat. mode	Strong
Special sat.	None

Geometry - Navigator

Geometry - Tim Planning Suite

Set-n-Go Protocol	Off
Table position	H
Table position	0 mm
Inline Composing	Off

System - Miscellaneous

Positioning mode	REF
Table position	H
Table position	0 mm
MSMA	S - C - T
Sagittal	R >> L

System - Miscellaneous

Coronal	A >> P
Transversal	F >> H
Coil Combine Mode	Adaptive Combine
Matrix Optimization	Off
AutoAlign	---
Coil Select Mode	Off - AutoCoilSelect

System - Adjustments

B0 Shim mode	Standard
B1 Shim mode	TrueForm
Adjust with body coil	Off
Confirm freq. adjustment	Off
Assume Dominant Fat	Off
Assume Silicone	Off
Adjustment Tolerance	Auto

System - Adjust Volume

Position	L0.6 P1.2 H13.9 mm
Orientation	Transversal
Rotation	0.00 deg
A >> P	208 mm
R >> L	256 mm
F >> H	179 mm
Reset	Off

System - pTx Volumes

B1 Shim mode	TrueForm
Excitation	Standard

System - Tx/Rx

Frequency 1H	123.261529 MHz
Correction factor	1
Gain	High
Img. Scale Cor.	1.000
Reset	Off
? Ref. amplitude 1H	0.000 V

Physio - Signal1

1st Signal/Mode	None
TR	10000 ms
Concatenations	1

Physio - PACE

Resp. control	Off
Concatenations	1

Diff - Neuro

Diffusion mode	MDDW
Diff. directions	64
Diffusion Scheme	Monopolar
Diff. weightings	2
b-value 1	0 s/mm²
b-value 2	1500 s/mm²
b-value 1	1
b-value 2	1
Diff. weighted images	On
Trace weighted images	Off
ADC maps	Off
FA maps	Off
Mosaic	On
Tensor	Off
Noise level	30

Diff - Body

Diffusion mode	MDDW
Diff. directions	64
Diffusion Scheme	Monopolar
Diff. weightings	2
b-value 1	0 s/mm²
b-value 2	1500 s/mm²
b-value 1	1
b-value 2	1
Diff. weighted images	On
Trace weighted images	Off
ADC maps	Off
Exponential ADC Maps	Off
FA maps	Off
Invert Gray Scale	Off
Calculated Image	Off
b-Value >=	0 s/mm²
Noise level	30

Diff - Composing

Inline Composing	Off
Distortion Corr.	Off

Sequence - Part 1

Introduction	On
Optimization	None
Multi-slice mode	Interleaved
Free echo spacing	Off
Echo spacing	0.65 ms
Bandwidth	1776 Hz/Px

Sequence - Part 2

EPI factor	104
RF pulse type	Normal
Gradient mode	Fast
Excitation	Standard

Sequence - pTX Pulses

Appendix D

Short Form Health Survey

Standard Form – 36 (SF-36)

Patient Name:	Date:

INSTRUCTIONS: This survey asks for views about your health. This information will help keep track of how you feel and how well you are able to do your usual daily activities. Answer every question marking the answer as indicated. If you are unsure about how to answer a question, please give the best answer you can.

1. In general, would you say your health is: (Circle One)	1. Excellent 2. Very Good 3. Good 4. Fair 5. Poor

2. Compared to one year ago, how would you rate your health in general at this time? (Circle One)	1. Much better now than one year ago 2. Somewhat better now than one year ago 3. About the same as one year ago 4. Somewhat worse that one year ago 5. Much worse now than one year ago

3. The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much? (Circle the appropriate number for each question)

Activities	Yes, limited a lot	Yes, limited a little	No, not limited
a. Vigorous activities, such as running, lifting heavy Objects, or participation in strenuous sports	1	2	3
b. Moderate activities, such as moving a table, Vacuuming, bowling or golfing	1	2	3
c. Lifting or carrying groceries	1	2	3
d. Climbing several flights of stairs	1	2	3
e. Climbing one flight of stairs	1	2	3
f. Bending, kneeling, or stooping	1	2	3
g. Walking more than a mile	1	2	3
h. Walking several blocks	1	2	3
i. Walking one block	1	2	3
j. Bathing or dressing yourself	1	2	3

4. During the past 4 weeks, have you had any of the following problems with your work or other regular activities as a result of your physical health? (Circle the appropriate number for each question)		
a. Cut down on the amount of time you spent on work or other activities	Yes = 1	No = 2
b. Accomplished less than you would like	Yes = 1	No = 2
c. Were limited in the kind of work or other activities	Yes = 1	No = 2
d. Had difficulty performing the work or other activities (For example – requiring an extra effort)	Yes = 1	No = 2

5. During the past four weeks, have you had any of the following problems with your work or other regular daily activities as result of any emotional problems (such as feeling depressed or anxious)? (Circle the appropriate number for each question)		
a. Cut down on the amount of time you spent on work or other activities	Yes = 1	No = 2
b. Accomplished less than you would like	Yes = 1	No = 2
c. Didn't do work or other activities as carefully as usual	Yes = 1	No = 2

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors or groups? (Circle one)	1. Not at all 2. Slightly 3. Moderately 4. Quite a bit 5. Extremely

7. How much bodily pain have you had during the past 4 weeks? (Circle one)	1. None 2. Very mild 3. Mild 4. Moderate 5. Severe 6. Very severe

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)? (Circle one)	1. Not at all 2. Slightly 3. Moderately 4. Quite a bit 5. Extremely

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks: (Circle one number on each line)

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time

a. Did you feel full of pep?	1	2	3	4	5	6
b. Have you been a very nervous person?	1	2	3	4	5	6
c. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
d. Have you felt calm and peaceful?	1	2	3	4	5	6
e. Did you have a lot of energy?	1	2	3	4	5	6
f. Have you felt downhearted and blue?	1	2	3	4	5	6
g. Did you feel worn out?	1	2	3	4	5	6
h. Have you been a happy person?	1	2	3	4	5	6
i. Did you feel tired?	1	2	3	4	5	6

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives etc.)? (Circle one)	1. All of the time 2. Most of the time 3. Some of the time 4. A little of the time 5. None of the time

11. How TRUE or FALSE is each of the following statements to you? (Circle one for each line).					
	Definitely True	Mostly True	Don't Know	Mostly False	Definitely False
a. I seem to get sick easier than other people	1	2	3	4	5
b. I am as healthy as anybody I know	1	2	3	4	5
c. I expect my health to get worse	1	2	3	4	5
d. My health is excellent	1	2	3	4	5

Appendix E

Intrinsic Motivation Inventory

Intrinsic Motivation Inventory: Sensory-motor training group

Name: _____ Date: _____

For each of the following statements, please indicate with regard to the exercises you have performed in the programme how true it is for you, using the following scale:

1 2 3 4 5 6 7

not true somewhat true very true

	Statement	**Score**
1	I enjoyed doing this exercise programme very much	
2	I think I am pretty good at the exercises	
3	I put a lot of effort into the exercises	
4	I was very relaxed while doing the exercises	
5	I believe the exercises could be of some value to me	
6	The exercises were fun to do	
7	I am satisfied with my performance of the exercises	
8	I tried very hard while doing the exercises	
9	I was anxious while doing these exercises	
10	I think that doing these exercises is good for my health and fitness	
11	I thought the exercises were boring	
12	I think I was pretty skilled at the exercises	
13	I didn't put much energy into the exercises	
14	I felt pressured while doing the exercises	
15	I believe doing the exercises could be beneficial to me	
16	I thought the exercises were quite enjoyable	
17	These are exercises that I couldn't do very well	
18	It was important to me to do well at the exercise	
19	I did not feel nervous at all while doing the exercises	
20	I would be willing to do the exercises again as they have some value to me	

Thank you for taking part in our research

Intrinsic Motivation Inventory: Attention-matched control group

Name: _____ Date: _____

For each of the following statements, please indicate with regard to the exercises you have performed in the programme how true it is for you, using the following scale:

1 2 3 4 5 6 7

not true somewhat true very true

	Statement	**Score**
1	I enjoyed doing these educational workshops/presentations very much.	
2	I believe these educational workshops/presentations could be of some value to me.	
3	While I was attending these educational workshops/presentations, I was thinking about how much I enjoyed it.	
4	I believe attending these educational workshops/presentations could be beneficial to me.	
5	I did these educational workshops/presentations because I wanted to.	
6	These educational workshops/presentations were fun to do.	
7	I would be willing to do this again because it has some value to me.	
8	I think that attending these educational workshops/presentations is useful for preventing future health problems	
9	I thought this was a boring activity.	
10	I think this is an important activity.	
11	These educational workshops/presentations did not hold my attention at all.	
12	I think this is important to do because it can help me educate others as well on the topics discussed/presented.	
13	I believe I had some choice about doing these educational workshops/presentations.	
14	I would describe these educational workshops/presentations as very interesting.	
15	I did these educational workshops/presentations because I had no choice.	
16	I think doing this activity could help me to make better health related choices in the future.	
17	I thought these educational workshops/presentations were quite enjoyable.	

Thank you for taking part in our research

Appendix F

Fall Efficacy Scale - International

Fall Efficacy Scale – International (FES-I)

For each of the following activities, please tick the opinion closest to your own to show how concerned you are that you might fall if you did this activity. Please reply thinking about how you usually do the activity. If you currently don't do the please answer to show whether you think you would be concerned about falling IF you did the activity.

Name: _____ **Surname:** _____ **Date:** _____	Not at all concerned 1	Somewhat concerned 2	Fairly concerned 3	Very concerned 4
Cleaning the house (e.g. sweep, dust)				
Getting dressed or undressed				
Preparing simple meals				
Taking a bath or shower				
Going to the shop				
Getting in or out of a chair				
Going up or down stairs				
Walking around in the neighbourhood				
Reaching for something above your head or on the ground				
Going to answer the telephone before it stops ringing				
Walking on a slippery surface (e.g. wet or icy)				
Visiting a friend or relative				
Walking in a place with crowds				
Walking on an uneven surface (e.g. rocky ground				
Walking up or down a slope				
Going out to a social event (e.g. family gathering, or club meeting)				
Total: **/64**				

Appendix G

Informed Consent Form

TITLE OF THE RESEARCH PROJECT: The Effect of Sensory-Motor Training on Brain Activation and Functional Recovery in Chronic Stroke Survivors.

REFERENCE NUMBER: S16/07/128

PRINCIPAL INVESTIGATOR: Tania Gregory

CONTACT NUMBER: 082 339 0787

You are being invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the study staff or doctor any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved. Also, your participation is **entirely voluntary** and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do agree to take part.

This study has been approved by the **Health Research Ethics Committee at Stellenbosch University** and will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research. For more information contact Dr Nicola Barsdorf, Head: Health Research Ethics Administration on Tel: 021 938 9075 or E-mail: nbarsdorf@sun.ac.za

What is this research study all about?

- *You are asked to participate in a research study conducted by Tania Gregory (Principle Investigator, Biokineticist) and Dr Karen Welman (Promotor & Biokineticist) from the Sport Science Department at Stellenbosch University.*
- *The research testing sessions will take place at Cape Universities Body Imaging Centre (CUBIC) at the Groote Schuur Hospital in Cape Town. However, the intervention will take place in public halls and center's close to participants' homes. These premises will be rented for the duration of the intervention. Researchers anticipate recruiting two groups of 10 - 15 participants to take part in the study.*
- *The main aim of this research study is to establish whether an 8-week intervention will influence brain activation and functional recovery in stroke survivors. The results will contribute to a research paper and PhD thesis as well as to the pool of knowledge on stroke disease, specifically on how to improve the quality of life in these individuals.*

Why have you been invited to participate?

- *You were selected as a possible participant in this study since you meet the inclusion criteria, of the study. To be included in the research study you need to meet the following criteria:*
  - *Male or female, aged > 18 years*
  - *Clinically diagnosed with stroke six or more months ago*
  - *No significant cognitive impairment or severe depression (determined by researchers)*
  - *Ability to execute dynamic balance activities (i.e. walking and sit –to –stand) without support other than customary walking aids*
  - *Participants must have 80% attendance at the end of the intervention*
  - *No other neurological conditions other than stroke (e.g. Diabetes, Parkinson's disease)*
  - *You should not have any visual, vestibular or hearing impairment, as well as neuropathy or muscular injuries in the previous six months*

What is the procedure and what will your responsibilities be?

- *You will be visited five times; unless unforeseen problems occur, then an additional visit will be scheduled at a convenient time for all parties involved. Each visit will last between 30 and 60-minutes.*
- *The first interaction will be done through a telephonic interview where the researcher will discuss the informed consent form with you and ask to verbally give consent to participate in the study as well as sign at the beginning of session 2. Additionally, a few questionnaires will be done telephonically as part of the screening process. Only after you have given consent and if you qualify for the inclusion criteria will you be included in the study.*
- *The second visit will either take place in the comfort of your own home or at public halls and center's close to participants' homes. During this session we will test your functional recovery and balance.*
- *The third visit will take place at the Groote Schuur Hospital in Cape Town where an MRI scan will be done.*
- *Due to the MRI being unfamiliar and foreign, you will be given the option to do a mock MRI screening session to make you feel comfortable and more at ease with the protocol.*
- *After the third visit the intervention will start. The intervention period will last 8 weeks and you will be required to complete 3 sessions per week. You will be allocated to a specific group.*
- *After the intervention session two and three will be repeated – thus functional ability and MRI will be assessed. This will serve as post-intervention assessment.*

Will you benefit from taking part in this research?

- *No monetary compensation will be given due to lack of funding. However, you will directly benefit by taking part in this study, by receiving rehabilitation for eight*

weeks. It should be noted that the average rate for a single biokinetics session is R250.00; nonetheless this program will be at no cost for you. Additionally, you will receive a massage treatment voucher at the value of R350.00 after the completion of your second visit. You will also be learning more about stroke and will contribute to the pool of knowledge on ways how to improve quality of life as well as functional recovery in stroke survivors.

Are there any risks involved in your taking part in this research?

- *The procedures used in this research project involve no serious risks. We will do all within our power to reduce possible risks. There is a possibility that you may experience a loss of balance or fall during some of the balance assessments. However, there will be a chair behind you and soft gymnastic mats will be placed around the testing area to prevent injury. You will be assessed away from obstacles and in a safe environment without distractions. You may also stop at any time if you feel that you cannot continue the activity. There will also be 1 or 2 research assistants, who are qualified biokinetici, to assist the researcher during activities. Furthermore, you will be more than welcome to alert us in case you experience any problems or discomfort. If you are not able to contact us for some reason, you are advised to contact your family doctor or go to the emergency department of your local hospital.*
- *Everyone involved in this project are competent and experienced in exercise testing and will not expose you to unnecessary risks or discomfort. Safety procedures are in place to deal with emergencies that may arise during the tests i.e. a first aid kit, as well as Netcare Stellenbosch (082 911) and/or Stellenbosch Medi Clinic (021 861 2000). The University of Stellenbosch is insured for emergencies during research interventions. Participants will be advised to contact Mr Van Kerwel (wvankerwel@sun.ac.za) at the University of Stellenbosch for information on the issue of compensation and coverage of medical expenses in the event of a research-related injury.*
- *We want to remind you that your participation is voluntary and that you are free to withdraw from the research at any time, with no prejudice or discrimination by Stellenbosch University or the researchers*

If you do not agree to take part, what alternatives do you have?

- *You can choose whether to be in this study or not. If you volunteer to be in this study, you may withdraw at any time without consequences of any kind. Alternatives include future research studies or going to your local biokineticist.*

Who will have access to your medical records?

- *Any information that is obtained in connection with this research study and that can be identified with you will remain confidential and will be disclosed only with your*

permission or as required by law. Confidentiality will be maintained by means of storing personal information and results from testing on a computer with a password. This computer is located inside the Motor Learning Laboratory in the Sport Science Department and access to it is limited to the researchers.

- *If a research article is published, your name will not be mentioned and all personal information will be kept anonymous. Results will be given as averages, percentages, etc. of the entire group and no exceptions will be made.*

What will happen in the unlikely event of some form injury occurring as a direct result of your taking part in this research study?

- *In the unlikely event of some form of injury due to this research study, Stellenbosch University the following cover is in place:*

    - *Primary General Liability (Broad form) insurance policy number 1000/28439 underwritten by Stalker Hutchison Admiral for a limit of R5 000 000.*
    - *Umbrella Liability insurance policy no 1000/22890 underwritten by Stalker Hutchison Admiral for a limit of R150 000 000.*
    - *Total Liability limit – R155 000 000*
    - *Professional Indemnity insurance policy number 4000/24901 underwritten by Stalker Hutchison and Admiral for a limit of ZAR 150 000 000.*
    - *The cover mentioned above is extended to include North American extension.*

Will you be paid to take part in this study and are there any costs involved?

No you will not be paid to take part in the study but your transport will be covered for each test session.

Is there any thing else that you should know or do?

- You should inform your family practitioner or usual doctor that you are taking part in a research study. (*Include if applicable*)
- You should also inform your medical insurance company that you are participating in a research study. (*Include if applicable*)
- You can contact Dr Karen Welman at tel 021 808 4733 if you have any further queries or encounter any problems.
- You can contact the Health Research Ethics Committee at 021-938 9207 if you have any concerns or complaints that have not been adequately addressed by your study doctor.
- You will receive a copy of this information and consent form for your own records.

Declaration by participant

By signing below, I ……..……. agree to take part in a research study entitled *The effect of a somatosensory training program on brain activation in stroke survivors and age-matched healthy individuals from South Africa*.

I declare that:

- I have read or had read to me this information and consent form and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this study is **voluntary** and I have not been pressurised to take part.
- I may choose to leave the study at any time and will not be penalised or prejudiced in any way.
- I may be asked to leave the study before it has finished, if the study doctor or researcher feels it is in my best interests, or if I do not follow the study plan, as agreed to.

Signed at (*place*) .....…..…….. on (*date*) ……...…….. 2017.

....

Signature of participant **Signature of witness**

Declaration by investigator

I *(name)* ……..…… declare that:

- I explained the information in this document to ……..
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understands all aspects of the research, as discussed above
- I did/did not use an interpreter. (*If an interpreter is used then the interpreter must sign the declaration below.*

Signed at (*place*) .....…..…….. on (*date*) ……...…….. 2017.

....

Signature of investigator **Signature of witness**

Declaration by interpreter

I *(name)* ……..…… declare that:

- I assisted the investigator (*name*) ……. to explain the information in this document to (*name of participant*) ……..…….. using the language medium of Afrikaans/English
- We encouraged him/her to ask questions and took adequate time to answer them.
- I conveyed a factually correct version of what was related to me.
- I am satisfied that the participant fully understands the content of this informed consent document and has had all his/her question satisfactorily answered.

Signed at (*place*) .....….....…….. on (*date*) ……...……..

....

Signature of interpreter **Signature of witness**

Appendix H

Personal Health Questionnaire

Name: _____ Surname: _____

Gender:_____ Age: _____

How long ago did you have a stroke? _____

Was this your first and only stroke? _____

Do you know what type of stroke you had? _____

Do you have any hemiparesis (weakness of the entire left or right side of the body?

_____

Most affected side (both sides/only one side, specify): _____

Has your doctor given you permission to participate in this study?_____

Please list your medication: _____

_____

_____

_____

Do you have any other neurological conditions other than stroke?
If yes, please specify: _____

Do you have any visual/colour blindness, vestibular, auditory impairment and or neuropathy?
If yes, please specify: _____

Have you had any orthopaedic and/or muscular injuries in the previous six months?
If yes, please specify: _____

Do you make use of any assistive devices e.g. walking frame? _____
Are you able to maintain your balance for 30seconds or when walking? _____

Thank you for taking part in our research

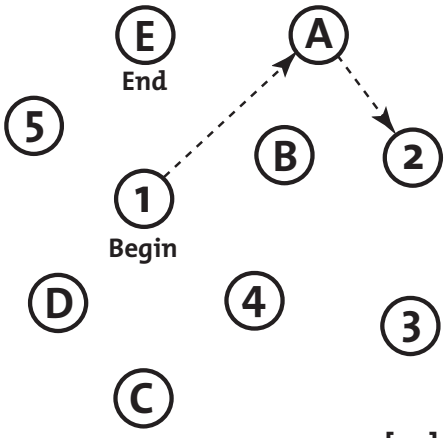
Appendix I

Montreal Cognitive Assessment

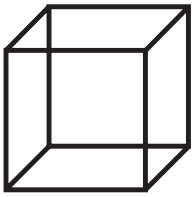
MONTREAL COGNITIVE ASSESSMENT (MOCA)

NAME :
Education : Date of birth :
Sex : DATE :

VISUOSPATIAL / EXECUTIVE



Copy cube



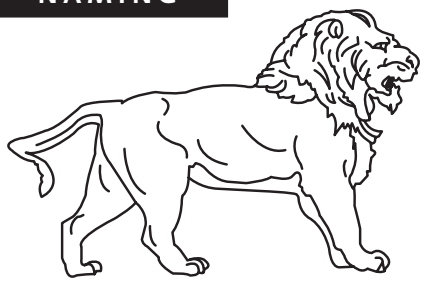
[ ] [ ]

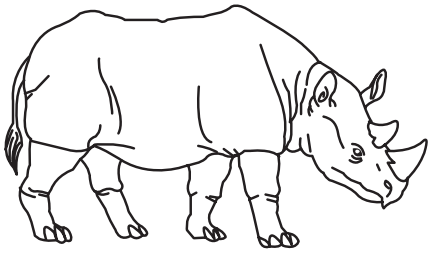
Draw CLOCK (Ten past eleven)
(3 points)

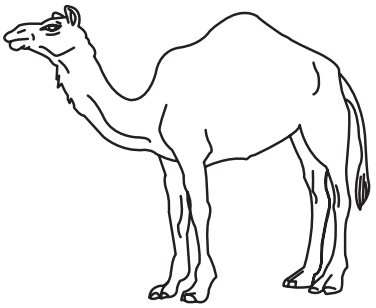
[ ] Contour [ ] Numbers [ ] Hands

POINTS ___/5

NAMING







[ ] [ ] [ ]

___/3

MEMORY

Read list of words, subject must repeat them. Do 2 trials. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION

Read list of digits (1 digit/ sec.). Subject has to repeat them in the forward order [ ] 2 1 8 5 4

Subject has to repeat them in the backward order [ ] 7 4 2

___/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

___/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**

___/3

LANGUAGE

Repeat : I only know that John is the one to help today. [ ]

The cat always hid under the couch when dogs were in the room. [ ]

___/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words)

___/1

ABSTRACTION

Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler

___/2

DELAYED RECALL

	Has to recall words WITH NO CUE	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]	Points for UNCUED recall only
Optional	Category cue						
	Multiple choice cue						

___/5

ORIENTATION

[ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

___/6

 Version 7.0 www.mocatest.org

Normal ≥ 26 / 30

TOTAL ___/30

Add 1 point if ≤ 12 yr edu

Administered by: _____

Appendix J

Rapid Assessment of Physical Activity

Rapid Assessment of Physical Activity

Physical Activities are activities where you move and increase your heart rate above its resting rate, whether you do them for pleasure, work, or transportation.

The following questions ask about the amount and intensity of physical activity you usually do. The intensity of the activity is related to the amount of energy you use to do these activities.

Examples of physical activity intensity levels:

<table>
<tr>
<td>Light activities
your heart beats slightly faster than normal
you can talk and sing</td>
<td> 
Walking Leisurely
 
Stretching
 
Vacuuming or Light Yard Work</td>
</tr>
<tr>
<td>Moderate activities
your heart beats faster than normal
you can talk but not sing</td>
<td> 
Fast Walking
 
Aerobics Class
 
Strength Training
 
Swimming Gently</td>
</tr>
<tr>
<td>Vigorous activities
your heart rate increases a lot
you can’t talk or your talking is broken up by large breaths</td>
<td> 
Stair Machine
 
Jogging or Running
 
Tennis, Racquetball, Pickleball or Badminton</td>
</tr>
</table>

How physically active are you? *(Check one answer on each line)*

			Does this accurately describe you?	
RAPA 1	1	I rarely or never do any physical activities.	Yes ☐	No ☐
	2	I do some **light** or **moderate** physical activities, but not every week.	Yes ☐	No ☐
	3	I do some **light** physical activity every week.	Yes ☐	No ☐
	4	I do **moderate** physical activities every week, but less than 30 minutes a day or 5 days a week.	Yes ☐	No ☐
	5	I do **vigorou**s physical activities every week, but less than 20 minutes a day or 3 days a week.	Yes ☐	No ☐
	6	I do 30 minutes or more a day of **moderate** physical activities, 5 or more days a week.	Yes ☐	No ☐
	7	I do 20 minutes or more a day of **vigorous** physical activities, 3 or more days a week.	Yes ☐	No ☐
RAPA 2 (3 = Both 1 & 2)	1	I do activities to increase muscle **strength**, such as lifting weights or calisthenics, once a week or more.	Yes ☐	No ☐
	2	I do activities to improve **flexibility**, such as stretching or yoga, once a week or more.	Yes ☐	No ☐

ID # _____

Today's Date _____

Appendix K

Visual Analogue Scale and Rate of Perceived Exertion Results

Table K.1: Weekly Rate of Perceived Exertion (RPE) and Visual Analogue Scale (VAS) for Intensity results (mean ± SD).

Week	Visual Analogue Scale (VAS)	Rate of Perceived Exertion (RPE)
1	4 ± 1	5.7 ± 1.6
2	4 ± 1	6.5 ± 1.4
3	4 ± 2	7.1 ± 1.6
4	5 ± 2	7.3 ± 1.3
5	5 ± 2	7.6 ± 1.5
6	4 ± 1	7.6 ± 1.6
7	5 ± 2	7.5 ± 1.7
8	4 ± 1	7.7 ± 1.6

Appendix L

Magnitude-based Inference statistics

			Within group difference over time: Sensory-motor training group		Within group difference over time: Attention-matched control group		Between group difference: After intervention	
	Lobes	Region of interest	p-value (ES) {ES 95% CI}	MBI	p-value (ES) {ES 95% CI}	MBI	p-value (ES) {ES 95% CI}	MBI
Left caudate	Frontal	Left caudal cingulate cortex, anterior	0.05 (1.7^{H}) {-0.1 to 2.75}	Positive: 96.3%, VL Negligible: 1.9%, VU Negative: 1.7%, VU	0.60 (0.39^{S}) {-1.09 to 1.70}	Positive: 21.2%, U Negligible: 19.9%, U Negative: 58.9%, P	0.02 (2.11^{H}) {0.14 to 3.19}	Positive: 98.4%, VL Negligible: 1.0%, VU Negative: 0.6%, VU
		Right caudal cingulate cortex, anterior	0.01 (1.92^{H}) {0.13 to 2.95}	Positive: 99.2%, VL Negligible: 0.4%, MU Negative: 0.3% MU	0.74 (0.16^{S}) {-1.25 to 1.52}	Positive: 23.4%, U Negligible: 30.1%, P Negative: 46.4%, P	0.02 (2.3^{H}) {0.24 to 3.34}	Positive: 98.4%, VL Negligible: 0.9%, VU Negative: 0.6%, VU
		Left pars opercularis	0.47 (0.33^{S}) {-0.99 to 1.50}	Positive: 58.3%, P Negligible: 29.6%, P Negative: 12.1%, U	0.03 (2.04^{H}) {-0.09 to 3.04}	Positive: 1.1%, VU Negligible: 0.9%, VU Negative: 98%, VL	0.70 (0.27^{S}) {-1.12 to 1.52}	Positive: 51.5%, P Negligible: 25.0%, U Negative: 23.5%, U
		Left superior frontal gyrus	0.32 (0.37^{S}) {-0.98 to 1.51}	Positive: 63.0%, P Negligible: 30.6%, P Negative: 6.4%, U	0.05 (0.81^{L}) {-0.81 to 2.03}	Positive: 1.3%, VU Negligible: 4.0%, VU Negative: 94.6%, VL	0.30 (0.83^{L}) {-0.73 to 1.96}	Positive: 77.3%, Li Negligible: 13.1%, U Negative: 9.6%, U
	Occipital	Left lingual gyrus	0.41 (0.50^{M}) {-0.90 to 1.60}	Positive: 50.0%, P Negligible: 43.0%, P Negative: 7.0%, U	0.05 (0.82^{L}) {-0.74 to 2.11}	Positive: 95.8%, VL Negligible: 2.6%, VU Negative: 1.6%, VU	0.19 (0.94^{L}) {-0.58 to 2.15}	Positive: 5.6%, U Negligible: 10.1%, U Negative: 84.3%, Li
Right caudate	Frontal	Left paracentral lobule	0.008 (1.05^{L}) {-0.44 to 2.15}	Positive: 98.9%, VL Negligible: 0.8%, VU Negative: 0.3%, VU	0.68 (0.59^{M}) {-0.93 to 1.88}	Positive: 60.7%, P Negligible: 10.2%, U Negative: 29.1%, P	0.06 (1.36^{VL}) {-0.32 to 2.50}	Positive: 95.0%, VL Negligible: 3.2%, VU Negative: 1.8%, VU
		Left rostral middle frontal gyrus	0.01 (1.51^{H}) {-0.18 to 2.50}	Positive: 98.9%, VL Negligible: 0.8%, VU Negative: 0.3%, VU	0.92 (0.07^{N}) {-1.24 to 1.54}	Positive: 49.2%, P Negligible: 9.5%, U Negative: 41.3%, P	0.05 (1.53^{H}) {-0.29 to 2.53}	Positive: 94.9%, VL Negligible: 3.9%, VU Negative: 1.2%, VU
		Right superior frontal gyrus	0.02 (0.75^{L}) {-0.76 to 1.87}	Positive: 97.1%, VL Negligible: 2.5%, VU Negative: 0.4%, VU	0.48 (0.67^{M}) {-0.82 to 2.01}	Positive: 18.6%, U Negligible: 12.0%, U Negative: 69.4%, P	0.12 (1.34^{VL}) {-0.25 to 2.59}	Positive: 91.0%, VL Negligible: 5.0%, VU Negative: 4.0%, VU
	Temporal	Left inferior temporal gyrus	0.46 (0.15^{S}) {-1.11 to 1.37}	Positive: 35.2%, P Negligible: 59.3%, P Negative: 5.5%, U	0.05 (0.96^{L}) {-0.86 to 1.96}	Positive: 92.2%, VL Negligible: 6.6%, U Negative: 1.1%, VU	0.74 (0.28^{S}) {-0.93 to 1.73}	Positive: 57.9%, P Negligible: 9.9%, U Negative: 32.2%, P
		Right fusiform gyrus	0.05 (1.1^{L}) {-0.32 to 2.31}	Positive: 96.7%, VL Negligible: 1.4%, VU Negative: 1.9%, VU	0.45 (0.79^{L}) {-0.66 to 2.21}	Positive: 73.1%, P Negligible: 8.2%, U Negative: 18.7%, U	0.06 (1.4^{VL}) {-0.18 to 2.69}	Positive: 95.3%, VL Negligible: 2.8%, VU Negative: 1.9%, VU
		Right parahippocampal gyrus	0.03 (1.37^{VL}) {-0.76 to 1.75}	Positive: 94.6%, VL Negligible: 4.9%, VU Negative: 0.5%, VU	0.50 (1.21^{VL}) {-0.56 to 2.35}	Positive: 70.8%, P Negligible: 7.9%, U Negative: 21.3%, U	0.07 (1.2^{VL}) {0.14 to 3.19}	Positive: 95.2%, VL Negligible: 2.3%, VU Negative: 2.5%, VU
	Occipital	Left cuneus cortex	0.94 (0.04^{N}) {-1.11 to 1.37}	Positive: 47.0%, P Negligible: 11.9%, U Negative: 41.1%, P	0.03 (1.54^{H}) {-0.39 to 2.58}	Positive: 97.5%, VL Negligible: 1.5%, VU Negative: 1.0%, VU	0.23 (0.81^{L}) {-0.64 to 2.07}	Positive: 7.9%, U Negligible: 8.6%, U Negative: 83.6%, Li
Left lentiform	Frontal	Left rostral cingulate cortex, anterior	0.17 (0.58^{M}) {-0.76 to 1.76}	Positive: 82.7%, Li Negligible: 11.9%, U Negative: 41.1%, P	0.03 (1.4^{VL}) {-0.43 to 2.53}	Positive: 97.6%, VL Negligible: 1.4%, VU Negative: 1.0%, VU	0.29 (0.86^{L}) {-0.66 to 2.05}	Positive: 9.6%, U Negligible: 11.7%, U Negative: 78.7%, Li
	Parietal	Right isthmus cingulate cortex	0.04 (0.83^{L}) {-0.64 to 1.90}	Positive: 94.8%, VL Negligible: 4.3%, VU Negative: 0.9%, VU	0.20 (0.68^{M}) {-1.01 to 1.79}	Positive: 77.7%, Li Negligible: 17.5%, U Negative: 4.8%, VU	0.30 (0.68^{M}) {-0.80 to 1.88}	Positive: 75.9%, Li Negligible: 15.2%, U Negative: 8.9%, U
Right lentiform	Temporal	Left temporal pole	0.02 (1.31^{VL}) {-0.25 to 2.4}	Positive: 97.6%, VL Negligible: 1.9%, VU Negative: 0.5%, VU	0.48 (0.32^{S}) {-1.16 to 1.62}	Positive: 55.9%, P Negligible: 31.9%, P Negative: 12.2%, U	0.25 (0.86^{L}) {-0.68 to 2.02}	Positive: 1.0%, VU Negligible: 99.0%, VL Negative: 0.0%, MU
	Parietal	Left inferior parietal cortex	0.02 (1.43^{VL}) {-0.20 to 2.47}	Positive: 98.0%, VL Negligible: 1.5%, VU Negative: 0.5%, VU	0.56 (0.38^{S}) {-1.07 to 1.72}	Positive: 61.0%, P Negligible: 19.5%, U Negative: 19.5%, U	0.26 (0.75^{L}) {-0.75 to 1.94}	Positive: 79.4%, Li Negligible: 12.7%, U Negative: 7.9%, U
		Left precuneus cortex	0.03 (0.92^{L}) {-0.51 to 2.06}	Positive: 96.8%, VL Negligible: 2.5%, VU Negative: 0.8%, VU	0.47 (0.50^{M}) {-1.18 to 1.60}	Positive: 56.0%, P Negligible: 32.3%, P Negative: 11.7%, U	0.27 (0.71^{M}) {-0.75 to 1.93}	Positive: 77.8%, Li Negligible: 14.4%, U Negative: 7.8%, U
		Right isthmus cingulate cortex	0.01 (1.00^{L}) {-0.50 to 2.01}	Positive: 98.8%, VL Negligible: 1.0%, VU Negative: 0.2%, VU	0.51 (0.24^{S}) {-1.56 to 1.22}	Positive: 11.2%, U Negligible: 40.2%, P Negative: 48.6%, P	0.13 (1.11^{VL}) {-0.52 to 2.23}	Positive: 89.1%, Li Negligible: 7.1%, U Negative: 3.8%, VU

CI, Confidence Intervals; ES, Effect Size; ^{N}Negligible; ^{S}Small; ^{M}Medium; ^{L}Large; ^{VL}Very Large; ^{H}Huge; MBI, Magnitude-based inference; Li, Likely; MU, Most Unlikely; P, Possibly; VL, Very Likely; VU, Very Unlikely; U, Unlikely

Appendix M

Sensory Dependency Calculations

The sensory dependency measures are computed from the sway area measured with APDM's Mobility Lab^{TM} (Portland, Oregon, USA) body-worn inertial sensor.

Sway area: The area of the 95% confidence ellipse encompassing the sway trajectory in the transverse plane.

Sway trajectory: The path of the acceleration signal in the transverse plane (top view looking down) recorded from the lumbar monitor.

Abbreviations:

EO: The sway area for the eyes open, firm surface condition
EC: The sway area for the eyes closed, firm surface condition
EOF: The sway area for the eyes open, foam surface condition
ECF: The sway area for the eyes closed,foam surface condition

1. Visual dependence

Visual dependence = min(((EC-EO)/EO)*100, ((ECF-EOF)/EOF)*100)

This represents a percent change between the eyes closed to the eyes open condition. Both the foam and firm surfaces are independently considered and the minimum of the two is reported.

2. Somatosensory dependence

Somatosensory dependence = min(((EOF-EO)/EO)*100, ((ECF-EC)/EC)*100)

This represents a percent change between the foam to the firm surface condition. Both the eyes open and eyes closed conditions are independently consid-

ered and the minimum of the two is reported.

3. Vestibular loss

Vestibular loss = ((ECF-EO)/EO)*100

This represents the percent change of the sway area of the eyes closed, foam surface condition relative to the eyes open condition.

https://support.apdm.com/hc/en-us/articles/217035886-How-are-the-ICTSIB-composite-scores-computed-

Appendix N

Letter to the Editor

Structural Connectivity Changes within the Basal Ganglia after Eight Weeks of Sensory-Motor Training in Chronic Stroke Survivors: A Randomized Controlled Pilot Study

Dear Editor,

Individuals that have suffered a stroke can present with impaired postural control due to deficits in the different domains and systems responsible for postural stability [27]. Furthermore, stroke survivors struggle with sensory integration of the visual, vestibular and somatosensory systems, i.e. to mobilize available sensory systems when one or more of the other sensory inputs are missing or insufficient [29, 28]. The basal ganglia consist of subcortical nuclei namely the caudate, lentiform (putamen and globus pallidus), substantia nigra and subthalamic nucleus [79]. These have been shown to be key structures in motor learning and postural control, specifically the caudate and lentiform nucleus [150, 79, 81].

To date, only a few studies have shown that balance training focused on sensory manipulation may improve balance ability, functional mobility and muscle activity in chronic stroke survivors [44, 139, 29, 28]. However, neuroimaging studies examining the effect of balance training on structural brain changes in chronic stroke individuals are very limited.

Therefore, this was the first randomized controlled pilot trial set out to investigate whether an eight-week sensory-motor training (SMT) program, focused on balance exercises with sensory system manipulation, could induce any changes in structural connectivity between the two subcortical basal ganglia nuclei, caudate and lentiform nucleus, with other regions of interest (ROI) in chronic stroke survivors. The research hypothesis was that eight-weeks of SMT may improve postural control in chronic stroke survivors due to improved efficiency of the basal ganglia network.

This was a double-blind randomized controlled pilot trial, which included a

magnetic resonance imaging (MRI) scan within one week before and after the interventions. Nine chronic stroke survivors were included in the study and were randomly allocated into the SMT group or attention-matched control (CON) group. Eligibility criteria included individuals 18 years and older, clinically diagnosed with stroke six or more months ago, and no other diagnosed neurological conditions. Both interventions occurred in a group setting, three times a week for 45 to 60-minute sessions over an eight-week period. Written informed consent was received by all participants and the study was approved by the institutional Health Research Ethics Committee (S16/07/128).

The SMT program was built on the principles of Janda's sensory-motor training guides [117] as well as Horak and Nashner's movement strategies [118]. Overall, participants progressed through eight weeks of balance training while the visual, vestibular and somatosensory systems were manipulated. The first three sessions focused on posture and alignment, specifically on providing input to the sensory-motor system from the ground up. According to Janda [117], sensory information being integrated by the central nervous system should be optimum at the foot, sacroiliac joint and cervical spine because of the large amount of proprioceptors in these areas. By increasing somatosensory (proprioceptive and tactile) input, subcortical pathways can be stimulated to facilitate coordinated movements [117]. Session four to nine focused on static balance; therefore, maintaining postural stability while progressing to eyes closed conditions, with head movements as well as on unstable surfaces. Session 10 to 15 progressed to dynamic balance, which added arm and leg movements while maintaining postural stability also while manipulating the three sensory systems as above. The final nine sessions (16-24) executed functional balancing movements, which included activities of everyday life under sensory manipulation and dual tasking conditions. Participants included in the CON group attended educational talks on the importance of living a healthy lifestyle. The use of an attention-matched control group was to control for nonspecific intervention effects (i.e. attention, intervention contact, social support, etc.).

Diffusion tensor imaging data were measured using an echo planar imaging whole brain sequence and FSL software package 5.1 (https://fsl.fmrib.ox.ac.uk/fsl/fslwiki) was used to analyze diffusion-weighted images. A standard freesurfer parcellation scheme and probabilistic whole-brain tractography was used for structural connectome reconstruction. Using the Desikan-Killiany Atlas for automated anatomical segmentation and labelling, 72 ROI (36 in each hemisphere) were created (Table N.1). Data was assessed using normal probability plots and in some cases with outliers, the variables were winsorized which reduced the effects of outliers without having to remove them. The connectivity strength between both the caudate and lentiform with the other ROI, were analyzed between groups (SMT vs. CON) and within groups (pre vs. post) by using a mixed model repeated measures ANOVA with Fisher LSD post-hoc test. Due to the small sample size, Cohen's d effect sizes (ES; i.e. 0.2^{S}: Small, 0.5^{M}: Medium and 0.8^{L}: Large [162]) and magnitude-based inference (MBI;

i.e. substantially positive, trivial and substantially negative [163]) statistics were added to supplement the traditional inferential statistics. Statistical significance was designated by $p \leq 0.05$. All statistical tests involved the use of STATISTICA v13 (StatSoft, Inc., Tulsa, OK, USA).

Table N.1: Cortical parcellation of cortical and subcortical structures using freesurfer software.

Banks superior temporal sulcus	Parahippocampal gyrus
Caudal anterior-cingulate cortex	Pars opercularis
Caudal middle frontal gyrus	Pars orbitalis
Caudate nucleus	Pars triangularis
Cuneus cortex	Pericalcarine cortex
Frontal pole	Postcentral gyrus
Fusiform gyrus	Posterior-cingulate cortex
Inferior parietal cortex	Precentral gyrus
Inferior temporal gyrus	Precuneus cortex
Insula	Rostral anterior-cingulate cortex
Isthmus-cingulate cortex	Rostral middle frontal gyrus
Lateral occipital cortex	Superior frontal gyrus
Lateral orbital frontal cortex	Superior parietal cortex
Lentiform nucleus	Superior temporal gyrus
Lingual gyrus	Supramarginal gyrus
Medial orbital frontal cortex	Temporal pole
Middle temporal gyrus	Thalamus
Paracentral lobule	Transverse temporal cortex

Out of 15 individuals who met the inclusion criteria, only nine completed the study, five in the SMT group and four in the CON group. No significant differences were found for demographic results between the groups ($p > 0.05$; Table N.2).

After the intervention, the SMT group showed increased structural connectivity between the left caudate and contralateral and ipsilateral caudal anterior cingulate cortex. Increased structural connectivity was also seen between the right caudate with the contralateral paracentral lobule and rostral middle frontal gyrus, as well as with ipsilateral fusiform gyrus, superior frontal gyrus and parahippocampal gyrus. Lastly, increased structural connectivity was observed between the left lentiform and the contralateral and ipsilateral isthmus cingulate cortex, as well as between the right lentiform and contralat-

Table N.2: Demographic characteristics of participants in SMT and CON groups (mean ± SD).

Variable	**SMT group (n = 5)**	**CON group (n = 4)**	**p-value**
Age (years)	68 ± 19	75 ± 10	0.58
Sex: men (%)	60	50	0.80
Body mass (kg)	63.90 ± 21.62	76.30 ± 24.20	0.74
Height (m)	1.72 ± 0.11	1.68 ± 0.18	0.83
Time since stroke (years)	5.92 ± 6.13	6.75 ± 6.29	0.84
Lesion side (R/L)	4/1	3/1	
Lesion type (cortical/subcortical)	2/3	2/2	
MoCA	25.20 ± 1.79	25.25 ± 3.40	0.98

CON, Attention-matched control; L, Left; MoCA, Montral Cognitive Assesment; R, Right; SD, Standard deviation; SMT, Sensory-motor training

eral temporal pole, inferior parietal cortex and precuneus cortex (Table N.3, Appendix L).

The CON group revealed reduced structural connectivity between the left caudate and the ipsilateral parsopercularis and superior frontal gyrus after the intervention. Furthermore, the CON group showed increased structural connectivity between the left caudate with the ipsilateral lingual gyrus and between the right caudate and the contralateral inferior temporal gyrus and cuneus. Lastly, increased connectivity was found between the left lentiform with the ipsilateral rostral anterior cingulate cortex (Table N.3, Appendix L).

This study is the first to assess the effects of eight weeks of SMT on structural brain changes between the basal ganglia nuclei and other ROI in chronic stroke survivors. Results indicated that the SMT group increased their structural connectivity strength between the basal ganglia network and frontoparietal areas (i.e. caudal anterior cingulate cortex, rostral middle frontal gyrus, superior frontal gyrus and isthmus cingulate) after participating in the SMT program. The anterior cingulate cortex forms part of the basal ganglia network and according to previously reported results, activity in the caudal anterior cingulate cortex correlates with sensory-motor regions, and plays an important role in motor control [165, 81]. The frontal lobe can be subdivided into the superior frontal gyrus, middle frontal gyrus and inferior frontal gyrus. The superior frontal gyrus is considered to be comprised of the supplementary motor area (SMA) and is connected with the middle frontal gyrus [73]. According to MRI studies, the SMA plays an important role in postural control [75, 76]. These areas are involved with various brain functions, such as sequencing and initiation of actions, motor learning and motor control [167, 73].

Table N.3: Structural connectivity strength between the caudate and lentiform with other regions of interest for SMT and CON groups.

			Sensory-motor training group (n = 5)			**Attention-matched control group (n = 4)**			**Group differences**		**Interaction effect**
	Lobes	Region of interest	Pre-test mean (SD) {95% CI}	Post-test mean (SD) {95% CI}	p-value (ES) {ES 95% CI}	Pre-test mean (SD) {95% CI}	Post-test mean (SD) {95% CI}	p-value (ES) {ES 95% CI}	Pre-test p-value (ES) {ES 95% CI}	Post-test p-value (ES) {ES 95% CI}	p-value
Left caudate	Frontal	Left caudal cingulate cortex, anterior	0.67 (0.26) {0.38 to 0.95}	1.05 (0.24) {0.77 to 1.33}	0.05 (1.7^{H}) {-0.1 to 2.75}	0.63 (0.25) {0.31 to 0.94}	0.53 (0.32) {0.21 to 0.85}	0.60 (0.39^{S}) {-1.09 to 1.70}	0.82 (0.19^{S}) {-1.18 to 1.46}	0.02 (2.11^{H}) {0.14 to 3.19}	0.08
		Right caudal cingulate cortex, anterior	0.62 (0.38) {0.25 to 0.98}	1.15 (0.22) {0.79 to 1.52}	0.01 (1.92^{H}) {0.13 to 2.95}	0.54 (0.32) {0.13 to 1.94}	0.48 (0.44) {0.08 to 0.89}	0.74 (0.16^{S}) {-1.25 to 1.52}	0.74 (0.26^{S}) {-1.12 to 1.52}	0.02 (2.3^{H}) {0.24 to 3.34}	**0.02**
		Left pars opercularis	0.10 (0.12) {-0.06 to 0.26}	0.15 (0.22) {-0.01 to 0.31}	0.47 (0.33^{S}) {-0.99 to 1.50}	0.32 (0.15) {0.14 to 0.50}	0.11 (0.09) {-0.07 to 0.29}	0.03 (2.04^{H}) {-0.09 to 3.04}	0.07 (1.93^{H}) {-0.02 to 2.94}	0.70 (0.27^{S}) {-1.12 to 1.52}	**0.03**
		Left superior frontal gyrus	0.48 (0.17) {0.21 to 0.74}	0.55 (0.29) {0.29 to 0.82}	0.32 (0.37^{S}) {-0.98 to 1.51}	0.56 (0.32) {0.26 to 0.85}	0.37 (0.21) (0.07 to 0.66)	0.05 (0.81^{L}) {-0.81 to 2.03}	0.65 (0.36^{S}) {-1.03 to 1.61}	0.30 (0.83^{L}) {-0.73 to 1.96}	**0.04**
	Occipital	Left lingual gyrus	0.007 (0.006) {-0.001 to 0.015}	0.005 (0.004) {-0.003 to 0.013}	0.41 (0.50^{M}) {-0.90 to 1.60}	0.005 (0.006) {-0.004 to 0.014}	0.013 (0.013) {0.003 to 0.022}	0.05 (0.82^{L}) {-0.74 to 2.11}	0.72 (0.37^{S}) {-1.03 to 1.62}	0.19 (0.94^{L}) {-0.58 to 2.15}	**0.05**
Right caudate	Frontal	Left paracentral lobule	0.02 (0.02) {-0.01 to 0.05}	0.05 (0.04) {0.02 to 0.08}	0.008 (1.05^{L}) {-0.44 to 2.15}	0.01 (0.003) {-0.02 to 0.04}	0.012 (0.01) {-0.02 to 0.04}	0.68 (0.59^{M}) {-0.93 to 1.88}	0.51 (0.85^{L}) {-0.65 to 2.05}	0.06 (1.36^{VL}) {-0.32 to 2.50}	0.09
		Left rostral middle frontal gyrus	0.006 (0.005) {-0.002 to 0.014}	0.017 (0.011) {0.01 to 0.025}	0.01 (1.51^{H}) {-0.18 to 2.50}	0.005 (0.007) {-0.003 to 0.014}	0.006 (0.004) {-0.003 to 0.014}	0.92 (0.07^{N}) {-1.24 to 1.54}	0.90 (0.13^{N}) {-1.17 to 1.47}	0.05 (1.53^{H}) {-0.29 to 2.53}	**0.05**
		Right superior frontal gyrus	0.08 (0.09) {0.0004 to 0.15}	0.14 (0.09) {0.06 to 0.21}	0.02 (0.75^{L}) {-0.76 to 1.87}	0.07 (0.04) {-0.015 to 0.16}	0.05 (0.01) {-0.03 to 0.14}	0.48 (0.67^{M}) {-0.82 to 2.01}	0.90 (0.1^{N}) {-1.19 to 1.44}	0.12 (1.34^{VL}) {-0.25 to 2.59}	**0.04**
	Temporal	Left inferior temporal gyrus	0.003 (0.003) {0.001 to 0.006}	0.003 (0.002) {0.001 to 0.006}	0.46 (0.15^{S}) {-1.11 to 1.37}	0.001 (0.001) {-0.002 to 0.004}	0.002 (0.002) {-0.0003 to 0.005}	0.05 (0.96^{L}) {-0.86 to 1.96}	0.20 (1.04^{L}) {-0.50 to 2.25}	0.74 (0.28^{S}) {-0.93 to 1.73}	**0.05**
		Right fusiform gyrus	0.005 (0.004) {0.001 to 0.009}	0.01 (0.005) {0.006 to 0.014}	0.05 (1.1^{L}) {-0.32 to 2.31}	0.002 (0.001) { -0.002 to 0.007}	0.004 (0.003) {-0.0005 to 0.009}	0.45 (0.79^{L}) {-0.66 to 2.21}	0.29 (1.17^{VL}) {-0.51 to 2.23}	0.06 (1.4^{VL}) {-0.18 to 2.69}	0.37
		Right parahippocampal gyrus	0.0004 (0.0004) {-0.0004 to 0.0012}	0.002 (0.001) {0.0008 to 0.002}	0.03 (1.37^{VL}) {-0.76 to 1.75}	0.0002 (0.0001) {-0.0007 to 0.001}	0.0005 (0.0004) {-0.0004 to 0.001}	0.50 (1.21^{VL}) {-0.56 to 2.35}	0.63 (0.98^{L}) {-1.26 to 1.37}	0.07 (1.2^{VL}) {0.14 to 3.19}	0.23
	Occipital	Left cuneus cortex	0.0007 (0.0007) {-0.0002 to 0.0015}	0.0007 (0.0008) {-0.0002 to 0.0015}	0.94 (0.04^{N}) {-1.11 to 1.37}	0.0003 (0.0003) {-0.0007 to 0.0012}	0.0014 (0.0012) {0.0005 to 0.0024}	0.03 (1.54^{H}) {-0.39 to 2.58}	0.50 (0.81^{L}) {-0.64 to 2.07}	0.23 (0.81^{L}) {-0.64 to 2.07}	0.09
Left lentiform	Frontal	Left rostral cingulate cortex, anterior	0.7 (0.46) {0.25 to 1.14}	0.46 (0.44) {0.01 to 0.91}	0.17 (0.58^{M}) {-0.76 to 1.76}	0.32 (0.34) {-0.18 to 0.82}	0.79 (0.43) {0.29 to 1.29}	0.03 (1.4^{VL}) {-0.43 to 2.53}	0.23 (1.02^{L}) {-0.55 to 2.19}	0.29 (0.86^{L}) {-0.66 to 2.05}	**0.02**
	Parietal	Right isthmus cingulate cortex	0.12 (0.05) {0.04 to 0.2}	0.18 (0.11) {0.1 to 0.26}	0.04 (0.83^{L}) {-0.64 to 1.90}	0.09 (0.05) {-0.01 to 0.18}	0.12 (0.08) {0.03 to 0.22}	0.20 (0.68^{M}) {-1.01 to 1.79}	0.54 (0.75^{L}) {-0.81 to 1.87}	0.30 (0.68^{M}) {-0.80 to 1.88}	0.53
Right lentiform	Temporal	Left temporal pole	0.006 (0.005) {-0.001 to 0.01}	0.014 (0.008) {0.007 to 0.02}	0.02 (1.31^{VL}) {-0.25 to 2.4}	0.006 (0.007) {-0.002 to 0.01}	0.008 (0.008) {0.00004 to 0.02}	0.48 (0.32^{S}) {-1.16 to 1.62}	0.94 (0.07^{N}) {-1.26 to 1.38}	0.25 (0.86^{L}) {-0.68 to 2.02}	0.19
	Parietal	Left inferior parietal cortex	0.005 (0.003) {-0.004 to 0.014}	0.016 (0.012) {0.007 to 0.025}	0.02 (1.43^{VL}) {-0.20 to 2.47}	0.006 (0.008) {-0.004 to 0.016}	0.009 (0.008) {-0.001 to 0.019}	0.56 (0.38^{S}) {-1.07 to 1.72}	0.80 (0.31^{S}) {-1.16 to 1.47}	0.26 (0.75^{L}) {-0.75 to 1.94}	0.19
		Left precuneus cortex	0.06 (0.04) {0.001 to 0.13}	0.12 (0.09) {0.06 to 0.19}	0.03 (0.92^{L}) {-0.51 to 2.06}	0.06 (0.03) {-0.01 to 0.13}	0.07 (0.05) {0.004 to 0.15}	0.47 (0.50^{M}) {-1.18 to 1.60}	0.85 (0.25^{S}) {-1.12 to 1.52}	0.27 (0.71^{M}) {-0.75 to 1.93}	0.24
		Right isthmus cingulate cortex	0.27 (0.15) {0.04 to 0.5}	0.47 (0.29) {0.24 to 0.7}	0.01 (1.00^{L}) {-0.50 to 2.01}	0.26 (0.2) {0.004 to 0.52}	0.22 (0.21) {-0.04 to 0.48}	0.51 (0.24^{S}) {-1.56 to 1.22}	0.98 (0.03^{N}) {-1.26 to 1.37}	0.13 (1.11^{VL}) {-0.52 to 2.23}	**0.02**

CI, Confidence Intervals; ES, Effect Size; ^{N}Negligible; ^{S}Small; ^{M}Medium; ^{L}Large; ^{VL}Very Large; ^{H}Huge; SD, Standard Deviation

Lastly, the isthmus cingulate includes involvement of the medial and inferior lateral parietal areas and has been used to study the default mode network (DMN) as it shows characteristic features of the DMN [168, 64]. Connectivity within the DMN is associated with various functions such as monitoring the world around us and can be modulated by the basal ganglia through the dopamine system [81].

In contrast, the CON group showed increased connectivity strength between the basal ganglia network with the orbito-temporal and frontal lobe areas (i.e. lingual gyrus, inferior temporal gyrus and rostral anterior cingulate cortex) after the educational talks. The lingual gyrus comprises of the primary visual cortex which plays an important role in visual processing [67]. Additionally, the inferior temporal gyrus is connected behind the inferior occipital gyrus and also plays a role in the higher levels of visual processing [172]. Therefore, increases within these areas in the CON group could be due to the nature of the intervention, which solely consisted of educational talks using presentations. A relationship has been shown to exist between the basal ganglia and visual processing, as the output of the basal ganglia targets the occipitotemporal processing pathways within the inferiortemporal cortex [173]. Lastly, the rostral anterior cingulate cortex correlates with prefrontal regions, which are responsible for higher mental functions [63]. Consequently, the educational talks could have contributed to improved cognitive functioning in the CON group.

Taken together, there seems to be potential for increased connectivity strength between the basal ganglia nuclei and fronto-parietal areas after participating in a SMT program, as well as increased structural connectivity in visual processing and higher cognitive orbito-temporal and frontal lobe areas after listening to educational talks. The results from both groups are representative of the type of intervention executed. The findings suggest that SMT could have postural control-related restorative effects on structural connectivity and support causal changes in activity-dependent neuroplasticity in chronic stroke survivors. Nevertheless, this was the first preliminary study regarding this topic and results should be interpreted with caution. The clinical implications of the changes in structural connectivity have across-the-board applications and show that it is possible to produce postural control improvements long after stroke by means of SMT. As such, it is a topic that should be researched further.

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Appendix O

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