Executive Function and an Eight-week Sensory-motor Training Programme in Independent-living Individuals with Parkinson's Disease.

by
Michelle Puren
(13874322)

Thesis presented in fulfilment of
the requirements for the degree of
MSc Sport Science in the Faculty of Education
at Stellenbosch University

Supervisor: Dr K.E. Welman

March 2016

DECLARATION

By submitting this thesis electronically, I, Michelle Sharon Puren, declare that the entirety of the work contained therein is my own, original work, that I am the sole author thereof (save to the extent explicitly otherwise stated), that reproduction and publication thereof by Stellenbosch University will not infringe any third party rights and that I have not previously, in its entirety or in part, submitted it for obtaining any qualification.

March 2016

ABSTRACT

Introduction: Executive dysfunction is a common non-motor symptom of Parkinson's Disease (PD). However, in individuals with PD, executive function (EF) is also associated with motor functions, i.e. gait and balance (Xu *et al*., 2015) and impaired EF is a predictor of future recurrent falls (Mak *et al*., 2014). Previous research in PD has shown selected improvements in EF through varied exercise interventions, such as aerobic exercise, resistance training and combination exercise (David *et al*., 2015; Duchesne *et al*., 2015; Tanaka *et al*., 2009). Nevertheless, no research to date has investigated the influence of a balance or sensory-motor training (SMT) programme on EF in isolation. Therefore the current study investigated whether an eight-week sensory-motor training programme would alter EF in non-demented individuals with mild to moderate PD.

Methods: A convenience sample of 42 individuals with idiopathic PD was divided into an experimental (EXP) and a placebo (PBO) group. This was a time-series design with an eight-week baseline phase (pre- to mid-intervention), followed by an eight-week treatment phase (mid- to post-intervention) in both groups. The baseline phase was the control period in which the participants continued their normal activities with no intervention. The EXP (n = 25; Age: 66 ± 8years; Hoehn & Yahr (HY) stage: 2.5, 2.0 – 3.0; Movement Disorder Society – Unified Parkinson's Disease Rating Scale (MDS-UPDRS) III rating: 31.9 ± 14.3) participated in an eight-week SMT, while the PBO (n = 17; Age: 71 ± 9years; HY: 2.0, 1.0 – 3.0; MDS-UPDRS III: 22.5 ± 10.0) wore a placebo feedback-wristband over the eight-week treatment phase. The primary outcome measures assessed were Updating (Trail Making Test, TMT), Set shifting (Wisconsin Card Sorting Test; WCST), Inhibition (Adapted Stroop Task), Perceived stability of balance (Activities-Specific Balance Confidence Scale; ABC) and Mobility (Timed Up and Go; TUG). Secondary outcome measures evaluated were Global cognition (Montreal Cognitive Assessment; MoCA), Disease severity (MDS-UPDRS and HY), Quality of life (Parkinson's Disease Questionnaire; PDQ-39) and Depression (Hamilton Rating Scale for Depression; HAM-D). Participants were assessed at pre-, mid- and post-intervention over 16 weeks.

Results: Treatment effects were observed for MDS-UPDRS III ($p<0.01$) and MDS-UPDRS total score ($p=0.02$), TMT A ($p<0.0001$), Global WCST Score ($p<0.0001$), Choice reaction time (CRT) 1: accuracy ($p=0.04$), CRT 2: time ($p=0.007$), Interference: accuracy ($p<0.0001$) and TUG ($p<0.001$). The EXP and PBO differed significantly at post-intervention in PDQ-39

variable Bodily discomfort (p=0.04), TMT A (p=0.03), CRT 2: time (p=0.01), Incongruent 1: time (p=0.04) and TUG (p<0.001).; and the changes over time in EXP, for the treatment phase for UPDRS II (p=0.04), PDQ-39 variable Stigma (p=0.01), CRT 2: time (p=0.048), ABC (p=0.01) and TUG (p<0.001).

Conclusion: The eight-week SMT was beneficial for selected aspects of EF, namely Inhibition, perceived stability of balance, mobility and disease severity. The EF of Updating and Set shifting as well as global cognition, depressive moods, and quality of life, remained unchanged. Thus, a SMT programme has the potential to improve Inhibition and mobility in individuals with mild to moderate PD, which could result in better balance and a reduction in falls.

ABSTRAK

Inleiding: Uitvoerende disfunksie is `n algemene nie-motoriese simptoom van Parkinson se Siekte (PD). In individue met PD, word uitvoerende funksie (EF) egter ook geassosieer met motoriese funksies soos loopgang en balans (Xu *et al*., 2015) en ingekorte EF is `n voorteken van toekomstige herhalende val insidente (Mak *et al*., 2014). Vorige navorsing oor PD het getoon dat sekere verbeteringe in EF gevolg het deur middel van verskeie oefeningintervensies, soos aërobiese-, weerstands- en kombinasie oefeninge (David *et al*., 2015; Duchesne *et al*., 2015; Tanaka *et al*., 2009). Nogtans het geen navorsing tot dusver die invloed van `n balans of sensoriese-motoriese oefenprogram (SMT) op EF in isolasie ondersoek nie. Daarom het die onderhawige studie ondersoek ingestel om te bepaal of `n agt-weke sensoriese-motoriese oefeningsprogram EF sal verbeter in nie-demensie individue met ligte tot matige PD.

Metodes*:* Geriefshalwe is `n steekproef van 42 individue met idiopatiese PD opgedeel in `n eksperimentele (EXP) groep of `n placebo (PBO) groep. Hierdie was `n tyd-reeks ontwerp met `n agt-weke basislyn fase (pre- tot mid-intervensie) gevolg deur `n agt-weke behandelingsfase (mid- tot post-intervensie) in beide groepe. Die basislyn fase was die kontrole periode waartydens die deelnemers voortgegaan het met hul normale aktiwiteite sonder enige intervensie. Die EXP groep (n = 25; Ouderdom: 66 ± 8jaar; Hoehn & Yahr (HY) stadium: 2.5, 2.0 – 3.0; “Movement Disorder Society – Unified Parkinson’s Disease Rating Scale” (MDS-UPDRS) III rating: 31.9 ± 14.3) het deelgeneem aan `n agt-weke SMT, terwyl die PBO groep (n = 17; Oud: 71 ± 9jaar; HY: 2.0, 1.0 – 3.0; MDS-UPDRS III: 22.5 ± 10.0) `n placebo terugvoer-armband oor die agt-weke behandelingsfase gedra het. Die primêre eindresultate wat getoets is was Opdatering (Trail Making Test, TMT), Stel verskuiwing (Wisconsin Card Sorting Test; WCST), Inhibisie (Aangepaste Stroop Task), Waargenome stabiliteit van balans (Activities-Specific Balance Confidence Scale; ABC) en mobiliteit (Timed Up and Go; TUG). Die sekondêre eindresultate wat geëvalueer is was Globale kognisie (Montreal Cognitive Assessment; MoCA), Siekte erns (MDS-UPDRS en HY), Lewenskwaliteit (Parkinson’s Disease Questionnaire; PDQ-39) en Depressie (Hamilton Rating Scale for Depression; HAM-D). Deelnemers is getoets by pre-, mid- en post-intervensie oor 16 weke.

Resultate: Behandelingseffekte is waargeneem vir MDS-UPDRS III ($p<0.01$) en MDS-UPDRS totaal ($p=0.02$), TMT A ($p<0.0001$), Globale WCST Telling ($p<0.0001$), Keuse reaksietyd (CRT) 1: akkuraatheid ($p=0.04$), CRT 2: tyd ($p=0.007$), Interferensie:

akkuraatheid (p<0.0001) en TUG (p<0.001). Die EXP en PBO het statisties betekenisvol verskil tydens post-intervensie in PDQ-39 veranderlike Liggaamlike ongemak (p=0.04), TMT A (p=0.03), CRT 2: tyd (p=0.01), Inkongruent 1: tyd (p=0.04) en TUG (p<0.001).; en die veranderinge met verloop van tyd in EXP, vir die behandelingsfase UPDRS II (p = 0.04), PDQ-39 veranderlike Stigma (p = 0,01), CRT 2: tyd (p = 0,048), ABC (p = 0,01) en TUG (p <0,001).

Gevolgtrekking: Die agt-weke SMT was voordelig vir sekere aspekte van EF, naamlik Inhibisie, persepsie van balans stabiliteit, mobiliteit en die erns van die siekte. Die EF van Opdatering en Stel verskuiwing asook globale kognisie, depressiewe gemoedstoestande en lewenskwaliteit het onveranderd gebly. Dus, `n SMT program het die potensiaal om Inhibisie en mobiliteit te verbeter in individue met lig tot matige PD, wat kan lei tot beter balans en afname in val insidente.

ACKNOWLEDGEMENTS

I would like to acknowledge and thank the following:

- First, and foremost, my heavenly Father for providing me with the opportunity to do this Master's thesis and for carrying me through these two years.
- My wonderful parents, Henry and Anne, for their amazing support, love, prayers and unwavering unbelief in me. Henry was also the actor in our sensory-motor training DVD which was produced for the study.
- My incredible supervisor Dr. Karen Welman. Her wisdom, advice, insight, support, understanding and time have meant so much to me.
- Professor Nel for his statistical analysis work.
- Tania Gregory, for putting together the sensory-motor training programme.
- Elizma Atterbury, Tania Gregory, Aimee Barrett, Claire Walker and Julie Clark for help with testing, conducting of the sensory-motor training programme and other assistance.
- The wonderful PD volunteers who took part in this study. It was a privilege to get to know them and work with them. Without them, this research would not be possible.
- Marie Midcalf for the production and editing of the sensory-motor training DVD and Katie Taylor for assisting with filming and production.
- Bridget Lamont for her editing assistance.
- The National Research Foundation (NRF) for financial assistance. This work is based on the research supported in part by the National Research Foundation of South Africa for the grant no. 87993. Any opinion, finding and conclusion or recommendation expressed in this material is that of the author(s) and the NRF does not accept any liability in this regard.

TABLE OF CONTENTS

Declaration…….. i
Abstract …….. ii
Abstrak …… iv
Acknowledgements…… vi
Table of Contents……... vii
List of Figures……..... xii
List of Tables…….. xiii
Abbreviations…….. xiv
Definitions of Key Terminology.....…….... xv
Overview…….. xvii

Chapter 1: Introduction…….. 1

Chapter 2: Literature Review…… 4
1. Overview of Parkinson's Disease…….. 4
1.1 Introduction ……. 4
1.2 Pathophysiology ……. 6
2. Executive Function …….. 8
2.1 Introduction …… 8
2.2 Exercise and Executive Function …… 12
2.2.1 Possible Mechanisms by which Exercise may Influence Executive Function ……. 13
2.2.2 Aerobic Exercise and Executive Function …… 17
2.2.3 Resistance Training and Executive Function …… 19
2.2.4 Combination Exercise and Executive Function …… 20
2.2.5 Balance Training and Executive Function …… 21
2.3 Exercise and Executive Function in the Parkinson's Disease Population ... 22
2.4 The Relationship between Executive Function and Balance, Mobility and Fall Risk ……. 27
3. Parkinson's Disease and Sensory-motor Training ……. 27
3.1 Benefits of Exercise for Parkinson's Disease ……... 27
3.2 Sensory-motor Training …… 29
3.3 Parkinson's Disease and Sensory-motor Training …….. 30
3.3.1 Balance as Part of a Combination Training Programme …… 30
3.3.2 Balance Training Programme in Isolation …….. 32
4. Conclusion …… 33

Chapter 3: Problem Statement 35
1. Study Purpose 35
2. Research Question 36
2.1 Research Objectives 36
2.2 Variables 37
2.2.1 Independent Variables 37
2.2.2 Dependent Variables 37
2.2.3 Categorical Variables 37
2.2.4 Confounding Variables 37
2.2.5 Assumptions 38
2.2.6 Limitations 38
2.2.7 Delimitations 38

Chapter 4: Methodology 40
1. Study Design 40
1.1 Place of Study 40
2. Participants 41
2.1 Recruitment 41
2.2 Inclusion Criteria 42
2.3 Exclusion Criteria 42
2.4 Sampling Method 43
2.5 Sample Size 43
3. Ethical Approval 43
4. Visits 44
4.1 Pre-intervention Testing: Telephonic Session 44
4.2 Pre-intervention Testing: First and Second Testing Sessions 45
4.3 Mid-intervention Testing: Third and Fourth Testing Sessions 45
4.4 Post-intervention Testing: Fifth and Sixth Testing Sessions 46
5 Phases and Interventions 46
5.1 Baseline Phase 46
5.2 Treatment Phase 46
5.2.1 Eight-week Sensory-motor Training Programme 46
5.2.2 Eight-week Placebo 47
6 Procedures 48
6.1 Anthropometry 48
6.1.1 Height 48
6.1.2 Body Mass 49

6.2 Secondary Outcome Variables 49
6.2.1 Global Cognition: Montreal Cognitive Assessment (MoCA) 49
6.2.2 Parkinson's Disease Severity 49
- Hoehn and Yahr (HY) 49
- Movement Disorder Society – Unified Parkinson's Disease Rating Scale (MDS – UPDRS) 50
6.2.3 Quality of Life: 39-Item Parkinson's Disease Questionnaire (PDQ-39) ... 51
6.2.4 Depression: Hamilton Rating Scale for Depression (HAM-D) 51
6.3 Primary Outcome Variables 52
6.3.1 Executive Function 52
- Updating: Trail Making Test part A and part B 52
- Set shifting: Wisconsin Card Sorting Test (WCST) 53
- Inhibition: Adapted Stroop Task 54
6.3.2 Functional Balance 56
- Perceived Stability of Balance: Activities-specific Balance Confidence Scale (ABC Scale) 56
- Mobility: Timed Up and Go Test (TUG) 56
7. Statistical Analysis 57

Chapter 5: Results 58
1. Participants 58
2. Secondary Outcome Variables 63
2.1 Global Cognition: Montreal Cognitive Assessment (MoCA) 63
2.2 Parkinson's Disease Severity 63
2.2.1 Hoen and Yahr (HY) 63
2.2.2 Movement Disorder Society – Unified Parkinson's Disease Rating Scale (MDS – UPDRS) 64
2.3 Quality of Life: 39-Item Parkinson's Disease Questionnaire (PDQ-39) 68
2.4 Depression: Hamilton Rating Scale for Depression (HAM-D) 70
3. Primary Outcome Variables 70
3.1 Executive Functions (Updating, Set shifting and Inhibition) 70
3.1.1 Updating: Trail Making Test part A (TMT A) and part B (TMT B) 70
3.1.2 Set shifting: Wisconsin Card Sorting Test (WCST) 74
3.1.3 Inhibition: Adapted Stroop Task 76
3.2 Functional Balance 79
3.2.1 Perceived Stability of Balance: Activities-specific Balance Confidence Scale (ABC Scale) 79
3.2.2 Mobility: Timed Up and Go Test (TUG) 80

4. Summary 81

Chapter 6: Discussion 82
1. Introduction 82
2. Participants 82
3. Secondary Outcome Variables 88
3.1 Global Cognition: Montreal Cognitive Assessment (MoCA) 88
3.2 Parkinson's Disease Severity 89
3.2.1 Hoehn and Yahr (HY) 89
3.2.2 Movement Disorder Society – Unified Parkinson's Disease Rating Scale (MDS – UPDRS) 89
3.3 Quality of Life: 39-Item Parkinson's Disease Questionnaire (PDQ-39) 90
3.4 Depression: Hamilton Rating Scale for Depression (HAM-D) 91
4. Primary Outcome Variables 92
4.1 Executive Function (Updating, Set shifting and Inhibition) 92
4.1.1 Updating: Trail Making Test part A (TMT A) and part B (TMT B) 92
4.1.2 Set shifting: Wisconsin Card Sorting Test (WCST) 93
4.1.3 Inhibition: Adapted Stroop Task 94
4.2 Functional Balance 96
4.2.1 Perceived Stability of Balance: Activities-specific Balance Confidence Scale (ABC Scale) 96
4.2.2 Mobility: Timed Up and Go Test (TUG) 97
5. Study Limitations and Future Studies 97
6. Conclusion 100

References 101

Appendices 123
A Ethical Approval Notice – Research Ethics Committee: Human Research (Humanities) 123
B Informed Consent Form (English and Afrikaans) 124
C Newspaper Articles 129
D The Hoehn and Yahr (HY) 130
E Parkinson's Disease Medication and Affected Side 131
F Personal Information Form 132
G Session Information Sheet 134
H General Information and Health Form 135
I 39-Item Parkinson's Disease Questionnaire (PDQ-39) 137

J Activities-specific Balance Confidence Scale (ABC Scale) …….. 139
K The Hamilton Rating Scale for Depression (HAM-D) ……. 141
L Montreal Cognitive Assessment (MoCA) ……. 144
M Trail Making Tests (TMT) part A and B …… 145
N Sensory-motor Training Programme …… 147
O Safety Guidelines …….. 156
P Excessive Depressive Moods (http://www.nhs.uk) ……. 158

LIST OF FIGURES

Figure 2.1 Theoretical Illustration demonstrating the relative impact of exercise on motor (black) and cognitive (red) function on disease progression in PD (Nocera & Hackney, 2015).

Figure 4.1 The study design for both placebo and experimental groups.

Figure 4.2 Placebo wristband worn by placebo group participants.

Figure 4.3 Adapted computer-based Stroop task from Lucas *et al.* (2012).

Figure 5.1 Self-reported activity status (frequencies; *f*).

Figure 5.2 Overall global cognition (MoCA) between EXP and PBO over 16 weeks. * $p \leq 0.05$.

Figure 5.3 Overall Hoehn and Yahr classification between EXP and PBO over 16 weeks. * $p \leq 0.05$.

Figure 5.4 MDS-UPDRS subscale II (M- EDL) between EXP and PBO over 16 weeks ($\bar{x}$ ± SEM). * p = 0.04.

Figure 5.5 MDS-UPDRS III (ME) between EXP and PBO over 16 weeks ($\bar{x}$ ± SEM). *p < 0.05.

Figure 5.6 Total MDS-UPDRS between EXP and PBO over 16 weeks ($\bar{x}$ ± SEM).

Figure 5.7 Hamilton Rating Scale of Depression (HAM-D) between EXP and PBO over 16 weeks ($\bar{x}$ ± SEM). * p < 0.001.

Figure 5.8 TMT A between EXP and PBO over 16 weeks ($\bar{x}$ ± SEM). * p < 0.05.

Figure 5.9 Ratio (a) and difference (b) between TMT B and TMT A between EXP and PBO over 16 weeks ($\bar{x}$ ± SEM).

Figure 5.10 Global WCST Score between TMT B and TMT A between EXP and PBO over 16 weeks ($\bar{x}$ ± SEM).

Figure 5.11 Perceived Stability of Balance (ABC) between EXP and PBO over 16 weeks ($\bar{x}$ ± SEM). * p < 0.05.

Figure 5.12 Timed Up and Go (TUG) between EXP and PBO over 16 weeks. * $p \leq 0.05$.

LIST OF TABLES

Table 2.1. Movement Disorder Society Diagnostic Criteria Framework for MCI in PD (From Litvan *et al*., 2012).

Table 2.2 Principles of Experience-dependent Neuroplasticity (From Kleim & Jones, 2008).

Table 5.1 Pre-intervention descriptive characteristics for the EXP and PBO groups as mean ($\bar{x}$) ± standard deviation (SD).

Table 5.2 Pre-intervention QOL assessment for the EXP and PBO groups as mean ($\bar{x}$) ± standard deviation (SD) and range.

Table 5.3 Pre-intervention EF characteristics for the EXP and PBO groups as mean ($\bar{x}$) ± standard deviation (SD) and range.

Table 5.4 Summary of MDS-UPDRS data reported as mean ($\bar{x}$) ± standard deviation (SD), with (range).

Table 5.5 Summary of PDQ-39 (%) domains reported as mean ($\bar{x}$) ± standard deviation, with (range).

Table 5.6 Summary of Trail Making Test (TMT) Variables reported as mean ($\bar{x}$) ± standard deviation (SD), with (range).

Table 5.7 Summary of WCST variables reported as mean ($\bar{x}$) ± standard deviation (SD), with (range).

Table 5.8 Summary of Stroop variables reported as mean ($\bar{x}$) ± standard deviation (SD), with (range).

ABBREVIATIONS

ABC	Activities-specific Balance Confidence Scale
ADL	Activities of Daily Living
BDNF	Brain-derived Neurotrophic Factor
BMI	Body Mass Index
BOD	Bodily Discomfort
CC	Categories Completed
COG	Cognitions
COM	Communication
CRT	Choice Reaction Time
EF	Executive Function
EMO	Emotional Being
EXP	Experimental Group
FTMS	Failure To Maintain Set
HY	Hoehn and Yahr Scale
KG	Kilogrammes
M	Metres
MCD	Minimal Detectable Change
MCID	Minimal Clinically Important Difference
MDS – UPDRS	Movement Disorder Society – Unified Parkinson's Disease Rating Scale
MED	Median
MOB	Mobility
MoCA	Montreal Cognitive Assessment
PBO	Placebo Group
PD	Parkinson's Disease
PDQ-39	39-Item Parkinson's Disease Questionnaire
PR	Perseverative Responses
QOL	Quality of Life
S	Seconds
SMT	Sensory-motor Training
SOC	Social Support
STI	Stigma
TE	Total Errors
TMT	Trail Making Test
TUG	Timed Up and Go
WCST	Wisconsin Card Sorting Test
WHO	World Health Organization
Y	Years

DEFINITIONS OF KEY TERMINOLOGY

Categories Completed (CC): a Wisconsin Card Sorting Test (WCST) variable referring to the number of categories the individual has correctly sorted, i.e. ten consecutive correctly-sorted cards (maximum = 6) (Strauss *et al*., 2006).

Cognitive Function (CF): includes both basic and higher-level functions. Basic cognitive functions comprise attention, working memory, long-term memory and perception, while higher-level cognitive functions comprise speech and language, decision making and executive functions (Glisky, 2007).

Executive Function (EF): "higher-level" or "meta-cognitive" functioning that manages other more basic cognitive functions as well as the regulation of emotions and attention necessary for goal-directed behaviours (Etnier & Chang, 2009).

Failure To Maintain Set (FTMS): a WCST variable that refers to a situation where an individual correctly sorts five or more consecutive cards, but then makes a mistake and fails to complete the category (Strauss *et al*., 2006).

Independent-living: For the purpose of this study, individuals diagnosed with Parkinson's Disease who are able to lead an independent life without the need for assistance in some ADL and can ambulate on their own or with an assistive device, i.e. a walking stick or crutch. Typically categorized by Hoehn & Yahr stages III and lower, thus excluding stages IV & V.

Inhibition, or Inhibitory Control: involves an individual's ability to intentionally inhibit a response which is dominant, automatic, or prepotent (priority response tendency) (Miyake *et al*., 2000).

Mild to Moderate Parkinson's Disease: refers to those classified as 1, 2 or 3 according to the Hoehn and Yahr Scale (Martínez-Martín *et al.,* 2015).

Neuroplasticity: structural or functional nervous system changes that occur as a result of experience (Nocera & Hackney, 2015).

Perseverative Responses (PR): a WCST variable referring to the number of times an individual continues to (or persists in) responding to an incorrect card characteristic (Strauss *et al*., 2006).

Sensory-motor training: refers to an intervention that focuses on improving postural control, most often through the integration of sensory information and, particularly, through increasing proprioceptive function (Aman *et al*., 2014).

Set shifting: also known as cognitive flexibility, it is the ability to shift back and forth between various tasks or mental sets (Miyake *et al*., 2000).

Total Errors (TE): a WCST variable refers to the total number of errors that the participant makes during the WCST.

Updating, or Working Memory: involves the monitoring of incoming task-relevant information and then appropriately updating the informational content by replacing no-longer relevant information with newer and more appropriate information (Miyake *et al*., 2000).

OVERVIEW

This thesis begins with the first chapter, which provides a general introduction and brief overview of the research topic. This is followed by a more detailed review in Chapter 2 of the available literature on Parkinson's Disease epidemiology and aetiology, cognitive and executive function, exercise and executive function both in the general population as well as the Parkinson's Disease population, the mechanisms at play regarding the effect of exercise on executive function, and sensory-motor training in Parkinson's Disease. Chapter Three outlines the main research question, the objectives and elaborates on variables, assumptions, limitations and delimitations as well as the rationale for the investigation. Thereafter, Chapter Four describes the methodology of the study, expounding on study design, the participants, the timeline and phases of the study, as well as elaborating on the tests and questionnaires which were used. Chapter Five details the results of the study and includes tables and graphs for straightforward reference. Chapter Six expands on and discusses the results of Chapter Five, in addition to providing insight into limitations and recommendations for future studies. The thesis adheres to the Harvard referencing style. Appendices are included at the end of the thesis to expand on or clarify sections which may not be evident in the text and include ethical approval, informed consent forms, tests, questionnaires, sensory-motor training programme lay out and other information pertinent to the study.

CHAPTER ONE

INTRODUCTION

The main purpose of this study was to establish if an eight-week sensory-motor training (SMT) programme with added somatosensory cues could possibly alter executive functioning (EF) in non-demented individuals with mild to moderate Parkinson's Disease (PD). This was to determine whether such an exercise intervention might have a meaningful impact on this important component of cognitive function.

PD is a common, progressive neurodegenerative disease, second only to Alzheimer's disease (Kalia & Lang, 2015; Nocera & Hackney, 2015). It is estimated that between 7 and 10 million individuals worldwide are presently living with PD (Nocera & Hackney, 2015). In addition, PD prevalence rises with increasing age (Taba & Asser, 2004), which is considered the greatest risk factor for the development of PD (Kalia & Lang, 2015). Consequently Dorsey *et al.* (2007) predicted a 50% increase in PD worldwide by 2030. According to Okubadejo *et al.* (2006) Africa is undergoing a demographic transition with a growing number of individuals over the age of 65 years. This statement was supported by Velkoff and Kowal (2007) who predicted that by 2050 there would be an estimated 139 million people in Sub-Saharan African countries older than 60 years. Accordingly, diseases such as PD, which predominantly affect aging populations, are predicted to become more common (Okubaio et al., 2006) and developing countries need to investigate cost-effective interventions to reduce the disease burden. In 2006, Noyes *et al*. considered the progressive nature of PD and estimated that the cost of PD exceeded $100 000 (approximately ZAR 1 382 240) per person.

Individuals with PD are typically affected not only by motor symptoms such as bradykinesia, tremor, rigidity and postural instability but also by non-motor symptoms such as mood disorders, sleep disturbances as well as cognitive and executive dysfunction (Murray *et al*., 2014; Dirnberger & Jahanshahi, 2013). A distinct association has been reported, especially in PD, between motor and cognitive functions (Nocera & Hackney, 2015), which may be attributed to the overlapping neural systems (cortical processing resources) (Domellöf *et al*., 2011). As a result, cognitive impairment may interfere with the motor symptoms (Aarsland *et al*., 2003); for instance, in PD specifically slowness of movement (bradykinesia), mobility

and balance has been associated with executive dysfunction (Kelly *et al*., 2015; McKee & Hackney, 2014; Poletti *et al*., 2012).

Most individuals with PD demonstrate executive dysfunction followed by memory problems (Nocera & Hackney, 2015). Executive Function relates to specific goal-directed behaviours which the brain's frontal lobes process (Murray *et al*., 2014). The three main EF are considered to be Set shifting, Updating and Inhibition (Diamond, 2013; Miyake *et al*., 2000). According to Tanaka *et al.* (2009) these functions assist individuals with judging, planning and executing cognitive tasks, abstract thinking and problem-solving, forming sequential rational actions and approaching strategies, as well as mental or behavioural shifts, flexible attitudes, and monitoring of actions. All of these features are aspects that individuals with PD struggle with (Nocera & Hackney, 2015).

Additionally, basal ganglia dysfunction disrupts automaticity (automated movements) in PD leading to poor motor planning, reduced sensory integration and regulating emotions as well as inadequate EF (Jankovic, 2008, Crossman & Neary 2000). Reduced automaticity contributes to PD mobility being more reliant on conscious processing (cognition) (Wu *et al*., 2014). Consequently, a vicious cycle of impaired mobility and reduced cognition transpires. Furthermore, mild executive dysfunction may progress to mild cognitive impairment in PD, which is a predictor for dementia (Dirnberger & Jahanshahi, 2013). Aarsland *et al*. (2003) reported that only 20% of individuals with PD do not develop cognitive impairment as PD progresses.

Interest in the relationship between motor-cognitive function and ineffectiveness of medication and surgical treatments in treating motor impairments, as well as side effects from pharmacological treatments has resulted in researchers investigating the possible use of exercise as a non-pharmacological treatment. A selection of exercise studies conducted in PD patients have revealed improvements in EF. Duchesne *et al*. (2015) and Rigdel *et al*. (2011) reported improvements following aerobic exercise, while David *et al*. (2015) observed improvements after a resistance training programme. Combination studies of aerobic and resistance training (Cruise *et al*., 2011; Tanaka *et al*., 2009) also reported improvements in EF, with the latter including balance and flexibility exercises as well.

It is believed that individuals with PD have intact motor programs but it is suggested that they have difficulties with accessing these motor programs (Jankovic, 2008). Interestingly,

researchers have found that by adding sensory cues (visual, auditory and somatosensory) these motor programs may be accessed more readily (Abbruzzese *et al*., 2015; Abbruzzese *et al*., 2014; Browner & Giladi, 2010; Jankovic, 2008). The benefits of adding an external cue to activities may be explained by the cues bypassing the defective basal ganglia and stimulating the reticular formation in the brainstem of the amygdala in the limbic system (Crossman & Neary, 2000). Abbruzzese *et al*. (2014) and Rabin *et al.* (2013) specifically highlighted the benefits of somatosensory (proprioceptive and haptic) feedback to improve mobility and balance, and suggest a non-dopaminergic pathway.

It is, thus, important to research EF and investigate which exercise interventions have the potential to improve or maintain EF or delay executive dysfunction. To the researcher's knowledge, this is the first study to specifically investigate the effect of a sensory-motor training programme on the executive function of individuals with mild to moderate PD.

CHAPTER TWO

LITERATURE REVIEW

1. Overview of Parkinson's Disease

1.1 *Introduction*

Parkinson's Disease (PD) was first described by James Parkinson in 1817 where he referred to it as the "shaking palsy" or in Latin, *Paralysis Agitans* (Fahn, 2003). Later, Jean Martin Charcot recommended that the disorder be called Parkinson's Disease (*Maladie de Parkinson*) (Lees *et al*., 2009).

PD is considered to be the most commonly occurring movement disorder apart from essential tremor and, in terms of neurodegenerative diseases, it is the second most common after Alzheimer's disease (Kalia & Lang, 2015; Nocera & Hackney, 2015, Wirdefeldt *et al*., 2011; Alves *et al*., 2008; De Lau & Breteler, 2006). Currently, there is no cure for PD, which is progressive in nature and characterised by motor and non-motor features (Lees *et al*., 2009).

The main or cardinal signs of PD relate to motor problems, such as resting tremor, rigidity, bradykinesia (slowness of movement) and impaired postural reflexes (Wirdefeldt *et al*., 2011; Jankovic, 2008; Gelb *et al.,* 1999). Other secondary motor symptoms are also often observed in PD. These include hypomimia (reduction in facial expressiveness), dysarthria (difficulty in articulating speech), dysphagia (difficulty in swallowing), sialorrhoea (excessive secretion of saliva), micrographia (small handwriting), shuffling gait, festination (galloping forward locomotion), freezing of gait, dystonia (involuntary contractions of muscles) and glabellar reflexes (blinking induced by tapping over the glabella) (Loftus, 2014; Jankovic, 2008; Cutson *et al*., 1995). Some non-motor characteristics include psychiatric symptoms, such as anxiety and depression, as well as a range of dysautonomic symptoms, from hypotension and constipation to seborrheic dermatitis along with sleep disorders and sensory abnormalities like anosmia, paresthesias and pain (Hoang, 2014; Wirdefeldt *et al*., 2011; Jankovic, 2008). Of the varied non-motor symptoms, cognitive dysfunction, which is commonly associated with impaired EF, is particularly widespread in PD (Murray *et al*., 2014; Hely *et al*., 2008; Higginson *et al*., 2003). Furthermore, according to Murray *et al*. (2014), these non-motor symptoms may be just as debilitating as motor symptoms for the

individual's health and general quality of life (QOL). It is this broad spectrum of clinical manifestations of PD which makes this movement disorder heterogeneous.

Parkinson therapies typically prevent neurochemical imbalances or treat symptoms related to the disease severity (Protas *et al.*, 2009). Therapies include pharmacologic and non-pharmacologic treatments such as surgical, physical and psychosocial interventions (Cutson *et al*., 1995). Unfortunately, these therapies are currently inadequate in treating motor impairments such as postural stability, speech and freezing of gait (Bloem *et al*., 2015), and may even result in additional movement disabilities such as dyskinesia, dystonia or motor fluctuations (Protas *et al.*, 2009). Curtze *et al*. (2015) also stated that prolonged use of medication in conjunction with disease progression may bring about unresponsiveness to medication.

The onset of PD usually happens slowly, and since diagnosis generally follows from the onset of motor symptoms, early symptoms can often be mistaken for something else or go unnoticed. According to Lees *et al.* (2009) a delay of two to three years between initial symptoms and diagnosis of PD is not uncommon. In addition, Kalia & Lang (2015) explained that the official PD diagnosis may have been preceded by a premotor phase of about 20 years or more. Symptoms may progress to include dyskinesia (abnormal involuntary movement), retropulsion (falling backwards), propulsion (falling forwards), reduced arm swing and decreased speed of walking (Loftus, 2014; Jones *et al*., 2008). QOL is impacted when decreased mobility and difficulties with balance, posture and walking, result in a loss of independence, lack of activity, social isolation, falls and an increased fear of falling (Loftus, 2014; Jones *et al*., 2008).

The 2006 World Health Organization's (WHO) incidence rate for PD, per 100 000 population per year, is given at 4.5 - 19. The main reasons given for the wide range in incidence include differences in study methodology and the sample population's age distribution. Once age adjustments are applied, the incidence rate, per 100 000 population per year, becomes 9.7 - 13.8 (World Health Organization, 2006). Lees *et al.* (2009) assert a steep increase with age and reported an incidence rate of 17.4 per 100 000 person years between the ages of 50 and 59 years, which then rises sharply to 93.1 per 100 000 for the age group 70 to 79 years. Sixty years of age is given as the median onset age and the mean duration is 15 years from initial diagnosis to eventual mortality (Lees *et al*., 2009). South African epidemiological data for PD is not available (Van der Merwe *et al*., 2012) and there is

inadequate epidemiological data available regarding PD in Sub-Saharan Africa and Africa (Blanckenberg *et al*., 2013; Okubadejo *et al*., 2006). In addition, studies based on clinical data may underreport the incidence of PD as they do not include those who have not sought or do not have access to medical facilities (De Lau & Breteler, 2006; Okubadejo *et al*., 2006). However, according to Blanckenberg *et al*. (2013) PD prevalence in Sub-Saharan Africa may fluctuate between 7 and 20 per 100 000 people, compared to developed countries where the prevalence is estimated to range from 65.6 to 12,500 per 100 000 (Von Campenhausen *et al.*, 2005). This is consistent with Kalia and Lang's (2015) report that PD prevalence is higher in European, North and South American countries compared to African, Asian and Arabic countries.

Few studies have investigated ethnicity or race in relation to PD and these studies differed in terms of their methodology. Although some data may seem to indicate that PD occurs less in Asian and black people, the study methodologies were not the same and the differences seen across ethnic groups may in fact be due to differences in case-ascertainment, survival and response rates (De Lau & Breteler, 2006; McInerney-Leo *et al*., 2004). A recent study by Geldenhuys *et al*. (2014) suggests the possibility of a founder effect for PD in the Afrikaner ethnic group, however, they recommend further genealogical analysis in regard to this (Carr, 2014; Geldenhuys *et al*., 2014).

Despite the variation in methodologies used, most PD epidemiological studies consistently propose that the disease decreases life expectancy. The reduction in life expectancy of PD individuals appears to be mostly due to dementia, as there is only a moderate increase in mortality rate in those PD individuals who do not acquire dementia (De Lau & Breteler, 2006). Identifying cognitive decline in individuals with PD is imperative as dementia increases the burden on health care as well as on patients and their caregivers (Dujardin *et al*., 2010).

1.2 *Pathophysiology*

An important pathological finding relating to the motor and non-motor dysfunction seen in PD patients is the dopaminergic neuron degeneration of the *Substantia Nigra Pars Compacta*. This results in dopamine loss of the striatum. Symptoms do not become evident until there is a loss of roughly 50 to 60% of these *Nigral* neurons and a depletion of 80 to 85% of the striatum's total dopamine. There may also be degeneration of the catecholaminergic and serotonergic neurons of the brainstem. The remaining neurons

exhibit the presence of Lewy-bodies (eosinophilic inclusion bodies which contain a wide variety of proteins) (Wirdefeldt *et al*., 2011). Hoang (2014) explains that the assumption is that this dopamine deficiency, as a result of the loss of dopaminergic neurons, is responsible for the motor and non-motor symptoms of PD. Although dopamine replacement therapy initially provides symptom relief, the disease continues to progress (Hoang, 2014), and individuals with PD may become unresponsive to medication as stated earlier in this chapter.

Current basal ganglia models propose that, within the cerebral cortex, these structures have a minimum of five parallel loops. Two of these loops, frontal eye fields and supplementary motor area, are concerned with motor functioning, while the other three loops, *Anterior Cingulate* circuit, *Dorsolateral Prefrontal* circuit and the *Lateral Orbitofrontal* circuit, are involved in cognition and behaviour (McKinlay, 2013; Taylor & Saint-Cyr, 1995). It is thought that PD-associated deficits result from malfunctioning of these loops which occurs secondary to the dopaminergic neuron depletion in the *Substantia Nigra*. The resultant range of cognitive problems seen in PD individuals relates to this *Fronto-striatal* circuit degeneration (McKinlay, 2013). While the depletion of dopaminergic neurons is thought to be the stand-out characteristic of PD, it is not confined to the dopamine system only and should not be characterized as such. There is evidence of other subcortical structure abnormalities, which includes noradrenergic neuron loss from the nucleus Basalis of Meyner (McKinlay, 2013).

There is also evidence to suggest that cognitive and behavioural functioning deficits stem from the mesocortical dopaminergic system. This system emerges from the ventral segmental area with projections directly to the frontal cortex. These projections have been found to be depleted in PD patients (McKinlay, 2013). Several genes which relate to PD have been identified giving an indication of molecular mechanisms potentially involved in its pathogenesis. It is thought that these could include dysfunction of mitochondria, inflammation, oxidative stress, excitotoxicity and a defect in protein handling (Wirdefeldt *et al*., 2011). These mechanisms are briefly highlighted in the following paragraphs.

A significant discovery in PD is that of a complex 1 deficiency of the mitochondrial respiratory chain. Mitochondria are of utmost importance in the production of cellular energy. This deficiency is PD-specific and is not seen in any other neurodegenerative disorder. Dysfunction of the mitochondria may play a significant role in initiating apoptotic cell death (Zigmond & Smeyne, 2013; Macphee & Stewart, 2012).

Oxidative stress can also increase through mitochondrial dysfunction (Monteiro-Junior *et al*., 2015; Macphee & Stewart, 2012). The cells of the *Substantia Nigra* are susceptible to oxidative stress due to the presence of iron and dopamine. The metabolism of dopamine results in the production of poisonous free radicals and the presence of ferrous iron accelerates this process (Macphee & Stewart, 2012).

The presence of increased levels of inflammatory mediators, TNF-α and interleukins, have also been found in PD. Microglial cells are activated and nitric oxide is produced. This results in more oxidative stress and cellular damage (Zigmond & Smeyne, 2013; Macphee & Stewart, 2012).

Cell damage (excitotoxicity) may occur due to enzyme system activation by excessive glutaminergic stimulation, while calcium ion influx mediates stimulation. A normal membrane potential prevents excessive influx. This is reliant on mitochondrial ATP production which, in PD, may be absent. Consequently, normal physiological glutamate levels in PD may in fact be toxic (Macphee & Stewart, 2012).

Despite these advances, the exact molecular mechanisms involved are still mostly unknown (Murray *et* al., 2014; Macphee & Stewart, 2012; Wirdefeldt *et al*. 2011). Kalia and Lang (2015) discuss a number of risk factors at play in the development of PD. The primary risk factor for the development of PD is age. PD prevalence and incidence rises exponentially with increasing age and reaches its peak after 80 years. Gender is another factor: men are affected more than women at a ratio of 3:2. Ethnicity plays a role in PD risk, with certain races, such as Hispanics more at risk than others (Kalia and Lang, 2015). There are also several environmental factors that are considered risk factors and these include: exposure to pesticides, a previous head trauma, rural living, the use of beta-blocker medications, working in agriculture and consumption of well water. There is also a genetic contribution, with increased risk linked to a family history of PD (Kalia and Lang, 2015).

2. Executive Function

2.1 *Introduction*

Cognitive function (CF) includes both basic and higher-level functions. Basic functions comprise attention, working memory, long-term memory and perception, while higher-level function comprise speech and language, decision making and EF (Glisky, 2007).

The decline of CF is considered a normal part of the aging process. Van Uffelen *et al*. (2008) delineate mild cognitive impairment (MCI) as the intermediate stage in which an individual experiences cognitive deterioration that is more serious than the normal age-related decline but does not meet criteria specific for dementia. Although at an increased risk of progressing to dementia, an individual with MCI may remain in this state or return to a normal cognitive function. Conversely, dementia is associated with an irreversible, progressive decline in cognitive functioning as well as problems with physical and social functioning (Van Uffelen *et al*., 2008).

In 2011 the Movement Disorder Society (MDS) set up a task force to draft the diagnostic criteria for MCI in PD. Table 2.1 summarizes the framework (Litvan *et al*., 2012).

Table 2.1. Movement Disorder Society Diagnostic Criteria Framework for MCI in PD (From Litvan *et al*., 2012).

1. MCI is defined within the context of existing etiology, namely PD;
2. PD-MCI includes not just “memory” complaints, but also other cognitive changes;
3. Cognitive decline can be noted from different sources;
4. PD-MCI must have deficits on either formal neuropsychological testing or a test of global cognitive abilities;
5. Specific level I and II categories are outlined, including the number of domains, tests per domain, and cut-off scores suggested; and
6. Subtyping is recommended only for evaluations in which two neuropsychological tests for each of the five domains are assessed and is strongly suggested for research purposes.

Cognitive dysfunction has a major impact on both the individual and on society as a whole. Firstly, it affects the individual and his or her significant others due to its negative effect on QOL and its potential for increased risk of disability and other limitations. Secondly, cognitive decline affects society by increasing pressure on health care, both financially and in terms of health care workers (Kandiah *et* al., 2009; Van Uffelen *et al*., 2008).

As previously noted, cognitive dysfunction is particularly prevalent in PD and is considered one of its most debilitating aspects (Murray *et al*., 2014; Liu *et* al., 2012; Benito-León *et al*., 2011; Hely *et al*., 2008). Both Liu *et al*. (2012) and Kandiah *et al.* (2009) reported that large

proportions of individuals with PD develop cognitive impairments in the early stages of the disease. As PD progresses, CF deteriorates and many PD patients may develop dementia. According to Dujardin *et al*. (2010) and De Lau and Breteler (2006) roughly 25 to 40% of individuals with PD will develop dementia, whereas Hely *and colleague's* (2008) Sydney Multicentre Study reported the presence of dementia in 83% of individuals with PD after 20 years. The latter study supported the earlier findings by Aarsland *et al*. (2003). The 2006 review by De Lau and Breteler (2006) reported a 1.7 to 5.9 times higher risk of dementia in those with PD compared to healthy individuals. These cognitive dysfunctions are often associated with impaired EF, visuospatial function as well as memory loss (Dujardin *et al*., 2010; Higginson *et al*., 2003).

Halliday & McCann (2010) discussed three cognitive phenotypes in PD. The first phenotype consists of individuals with early-onset (50 to 60 years), longer duration PD (greater than 15 years). This group developed dementia at a much later stage of the disease, often after 10 to 15 years. The second phenotype involves individuals with dementia-dominant syndrome that is early and severe with akinetic-rigid PD and fulfils the requirements for dementia with Lewy bodies (DLB). The third phenotype includes those with an older age of onset (over 70 years), shorter duration of PD (less than 15 years), increased disability and dementia (consistent with PD with Dementia – PDD). There remains much variation in age of onset, symptom onset as well as severity of cognitive impairment.

Executive Function, also known as controlled cognition, resource-demanding cognition or executive control, is predominantly related to goal-directed behaviours which are processed by the brain's prefrontal cortex (Murray *et al*., 2014; Diamond, 2013; Etnier & Chang, 2009; Lezak, 1995). According to Etnier and Chang (2009), EF is a "higher-level" or "meta-cognitive" functioning that manages other more basic cognitive functions as well as the regulation of emotions and attention necessary for goal-directed behaviours (Etnier & Chang, 2009). Dirnberger and Jahanshahi (2013) support this by explaining that EF specifically relates to a group of cognitive processes responsible for goal-directed behaviours. These processes include formulating goals, forming intentions, successfully implementing these goals and outcome processing. Other researchers refer to this as planning, purposive action, effective performance and volition (Murray *et al*., 2014; Tanaka *et al*., 2009). This means that individuals with frontal lobe damage, specifically with EF problems, may exhibit decreased ability to plan and organize functional, goal-oriented behaviour.

There are three main or core EFs, namely Set shifting, Updating and Inhibition. Inhibition, or inhibitory control, involves an individual's ability to intentionally inhibit a response which is dominant, automatic, or prepotent (priority response tendency) (Diamond, 2013; Miyake *et al*., 2000). Inhibition allows one to attend selectively, concentrating on what one chooses to, while suppressing other stimuli. It is also the ability to control one's behaviour, thoughts, attentions, and / or emotions to supersede a strong inclination and rather do what is necessary or required in that situation (Diamond, 2013; Miyake *et al*., 2000).

Updating, or Working Memory, involves the monitoring of incoming task-relevant information and then appropriately updating the informational content by replacing no longer relevant information with newer and more appropriate information (Diamond, 2013; Miyake *et al*., 2000). Updating requires one to hold relevant information in one's mind and work with it when it is no longer present perceptually. Updating is crucial in understanding things that take place over time, where one needs to keep in mind what has occurred previously and then relate it to something in the future. Updating and Inhibition are linked in that you must have in mind what is relevant to the situation and what to inhibit (Diamond, 2013).

Set shifting, also known as Cognitive Flexibility is the ability to shift back and forth between various tasks or mental sets (Diamond, 2013; Miyake *et al*., 2000). An aspect of Updating is the ability to change perspectives spatially (i.e. viewing something from a different direction) or interpersonally (i.e. seeing another person's point of view). In order to do this, one needs to inhibit one's previous perspective and update to a different perspective. In this way, Set shifting is reliant on and contributes to Inhibition and Updating (Diamond, 2013).

Executive functioning, in summary, concerns the things that people do, the way in which they do them and whether they do them in situations that are not routine. It can be described as intentional planning and adjustment that occurs in a situation where previously learned behaviours are inadequate or inaccessible. Executive functioning requires the inhibition of prepotent responses, cognitive flexibility, the ability to plan and monitor, and the ability to not only retrieve from memory but to maintain and manipulate information within memory. Individuals with PD battle with the performance of some or all of these tasks. In addition to this, individuals with PD often display bradyphrenia (decreased psychomotor speed), which may also impact on their executive functioning (Koerts *et al*., 2011).

Impaired cognitive function, more specifically EF in PD, interacts with the affected motor system. Originally, it was thought that distinct cortical regions directed movement and cognition. However, it is now believed that they are supplied by overlapping neural systems. An example of this can be observed in PD, where an increase in bradykinesia is associated with both mild cognitive impairment and impaired executive functioning (Nocera & Hackney, 2015). Every day, individuals (both with and without PD) will encounter situations which require executive functioning. Navigating uneven terrain on a sidewalk, deciding whether there is enough time to cross at a pedestrian crossing before the light changes, remembering an address or the direction to a certain place while walking there are all examples of how executive functioning operates. These events are of particular importance to someone with PD as they are further impacted by their motor dysfunction. Resting tremor, rigidity, bradykinesia and impaired postural stability all play a role in how the individual with PD responds to these situations. Impaired executive functioning makes situations like these seem like large challenges that need to be overcome.

Yogev-Seligmann *et al*. (2008) discussed how impairment in one or more of these elements of EF has the potential to influence a person's ability to walk both efficiently and safely. Walking is a fundamental part of any independently ambulating individual's life. Impaired gait and a loss of automaticity of walking are characteristics of PD and these are accompanied by EF and attention impairments. For instance, when an individual with PD is required to allocate attentional resources to more than one task, an increase in gait abnormalities manifests i.e. shortened stride length, stride variability increases, slower gait speed and double support time increases (Yogev-Seligmann *et al*., 2008).

2.2 *Exercise and Executive Function*

Emerging research increasingly shows that regular physical activity promotes cognitive functioning, especially for age-related neurocognitive decline (Daly *et al*., 2015; Gow, 2013; Ku *et al*., 2012) and for those with neurodegenerative diseases (Nocera & Hackney, 2015; Xu *et al*., 2010; Tanaka *et al*., 2009). The effect of exercise on cognitive and motor function in PD can be seen in Figure 2.1.

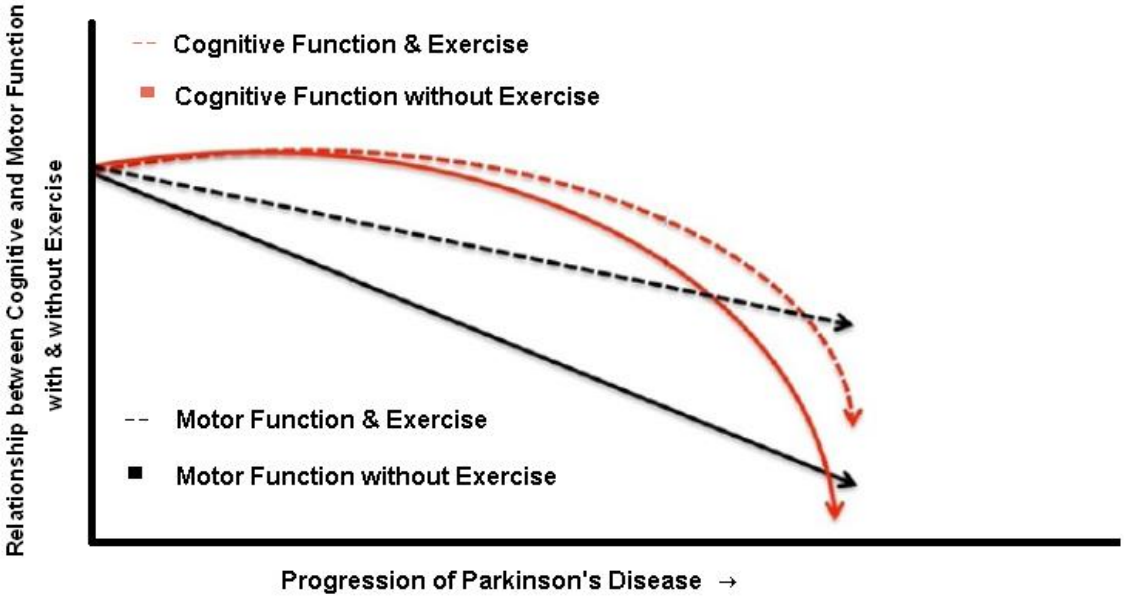


Figure 2.1 Theoretical Illustration demonstrating the relative impact of exercise on motor (black) and cognitive (red) function on disease progression in PD (Nocera & Hackney, 2015).

Evidence suggests that healthy individuals who are physically active tend to demonstrate better executive functioning, as opposed to poor EF observed in individuals with low physical activity levels (Daly *et al*., 2015). The study of Daly *et al*. (2015) suggests a bidirectional relationship between exercise and EF. Subsequent decreases in physical activity participation rates were observed in older individuals with poor EF. In contrast, older individuals who regularly engaged in sports or other physically exerting activities were more likely, over time, to maintain EF at a high level. This adds credence to existing research showing that exercise or physical activity can serve to buffer the aging effects on EF decline.

2.2.1 *Possible mechanisms by which exercise may influence Executive Function*

The possible neural mechanisms for the benefits of exercise on cognitive function relate to neuroplasticity principles. Cotman and Berchtold's (2002) opinion article on exercise and neuroplasticity refers to research that proposes that brain plasticity can be maintained or improved through exercise and behavioural stimulation (modifying behaviour and actions). Petzinger *et al*. (2013) define neuroplasticity as "a process by which the brain encodes experiences and learns new behaviours and is defined as the modification of existing neural networks by addition or modification of synapses in response to changes in behaviour or environment, which can encompass exercise"; or more simply defined as structural or

functional changes to the nervous system that occur as a result of experience (Nocera & Hackney, 2015).

There are two main processes by which neuroplasticity takes place in the damaged or degenerating brain, namely recovery or compensation. Depending on whether the neural or behavioural level is referred to, recovery is loosely defined as the restoration of the original function and compensation as the regaining of function through processes other than the original (Kleim, 2011). The neural strategies of restoration, recruitment and retraining involve either recovery or compensation and take advantage of the brain's functional redundancy. These three neural strategies are not independent of each other and may occur together during rehabilitation, which makes it difficult to distinguish them clearly in research. Hence motor recovery pertains to the ability to execute a previously impaired or lost motor task in precisely the same way as it was performed prior to the injury or degeneration. Whereas neural recovery refers to the reestablishment of motor function, in a region of the motor cortex that was lost (restoration). Motor compensation concerns the ability to carry out a task in a different way using new movements or sequences (recruitment and / or retraining) (Kleim, 2011).

In 2008, based on an extensive review of existing human and animal studies, Kleim and Jones suggested 10 principles which clinical exercise therapists may potentially incorporate in their neurorehabilitation to induce experience-dependent (or exercise-related) neuroplasticity. These 10 principles are summarized in Table 2.2.

Table 2.2 Principles of Experience-dependent Neuroplasticity (From Kleim & Jones, 2008).

Principle	Description
1. Use it or lose it	Failure to drive specific brain functions can lead to functional degradation
2. Use it or improve it	Training that drives a specific brain function can lead to an enhancement of that function.
3. Specificity	The nature of the training experience dictates the nature of the plasticity.
4. Repetition matters	Induction of plasticity requires sufficient repetition.
5. Intensity matters	Induction of plasticity requires sufficient training intensity.

6. Time matters	Different forms of plasticity occur at different times during training.
7. Salience matters	The training experience must be sufficiently salient to induce plasticity. *
8. Age matters	Training-induced plasticity occurs more readily in younger brains.
9. Transference	Plasticity in response to one training experience can enhance the acquisition of similar behaviours.
10. Interference	Plasticity in response to one experience can interfere with the acquisition of other behaviours.

* Salient refers to something important.

Recently Diamond (2015) reiterated the importance of cognitive involvement (attention), similar to Kleim and Jones' (2008) point 7, to improve cognitive functions such as EF in individuals with PD.

Possible mechanisms of neuroplasticity are now briefly discussed.

Brain-derived neurotophic factor (BDNF) plays an important role in the growth and continuity of various neuronal subtypes. When the BDNF gene expression is raised through learning then the resultant BDNF could promote plasticity for learning and memory. The assumption is made that exercise may induce BDNF gene expression, which should then also improve learning (Monteiro-Junior *et al*., 2015; Coelho *et al*., 2013; Ahlskog, 2011; Cotman and Berchtold, 2002). Gene expression of BDNF is controlled in the hippocampus by neurotransmitter interactions and neuronal activity. Modulatory neurotransmitters, such as GABA (Gamma Amino Butyric Acid), ACh (Acetylcholine) and monamines, could affect the expression of BDNF (Xu *et al*., 2010; Cotman and Berchtold, 2002). In addition, peripheral mechanisms play an important role in the BDNF expression and include the effect of corticosteroids, oestrogen and insulin-like growth factor (IGF-I) (Cotman and Berchtold, 2002).

Gene expression, potentially regulated by exercise, also plays a role in neuroplasticity. Synaptic and neurite growth, vesicle recycling and membrane and neurotrophic factor trafficking are associated with these genes (Cotman and Berchtold, 2002). The impact of exercise on genes responsible for encoding neurotrophins and similar proteins reveals

potential for exercise to create a cascade of events resulting in neurogenesis (Cotman and Berchtold, 2002).

Exercise, in animal studies, has been shown to increase blood flow in the brain (Rhyu *et al*., 2010), and similarly, in human studies, regular exercise improves cerebral blood flow (Ainslie *et al*., 2008). In this way, neuroplasticity may be promoted by exercise, by modifying the central nervous system vasculature through angiogenesis and changes in the permeability of the blood-brain barrier (Paillard *et al*., 2015; Petzinger *et al*., 2013).

Another mechanism is a reduction in beta-amyloid protein formation, which is associated with decreased beta-amyloid plaques as seen in Alzheimer's disease (Erickson *et al*., 2014; Coelho *et al*., 2013; Adlard *et al*., 2005).

Zigmond and Smeyne (2013) promote a model for exercise-induced neuroprotection. Their hypothesis is that dopamine signalling is increased by exercise, which increases the availability of neurotrophic factors. These neurotrophic factors are then able to promote energy production of mitochondria, synaptogenesis, angiogenesis, antioxidant defence, reduce inflammation and suppress apoptosis. Animal studies have also documented the protective effect of exercise in models of Parkinsonism by reducing the effects of 6-hydroxydopamine (6-OHDA) and1-methyl,4-phenyl,1,2,3,6-tetrahydropyridine (MPTP) which are dopaminergic neurotoxins (Ahlskog, 2011). However, Ploughman (2008) has pointed out that research on the neuroprotective effects of exercise in humans are limited. These studies reported motor function improvements, dopamine neuron preservation and dopaminergic terminal restoration in the striatum (Petzinger *et al*., 2013).

Furthermore, cognitive differences observed between individuals diagnosed with PD may potentially be clarified by the cognitive reserve theory (Koerts *et al*., 2013). The cognitive reserve theory proposes that the brain actively seeks to deal with brain damage through the utilization of already existing approaches of cognitive processing or by employing compensatory approaches. Thus, individuals possessing greater cognitive reserve would be able to cope better with comparable brain damage. In simple terms, cognitive reserve enables some to better cope with the ramifications of brain pathology and remain mentally intact for a longer duration (Poletti *et al*., 2011). A cognitive impairment buffer is provided by premorbid factors, such as high intellectual capacities or greater levels of education, in the presence of brain pathology (Koerts *et al*., 2013). In PD, individuals with greater cognitive

reserve and intact EF are more likely to enjoy a better QOL and have less difficulty with ADL (Hindle *et al*., 2014). Fratiglioni *et al*. (2004) suggest that neuroplasticity robustly supports the cognitive reserve theory as experience-dependent stimuli are required to elicit plasticity, regardless of the methods or the level at which they occur (cellular, molecular or structural). Becofsky (2014) in addition states that physical activity may protect elderly individuals from cognitive decline by improving their cognitive reserve theory.

Thus, exercise plays an important role in the facilitation of neuroplasticity, via increased neurotrophic factors (BDNF), increased blood flow and angiogenesis, increased gene expression and its impact on neurogenesis and a decrease in beta-amyloid plaques, as well as having potential neuroprotection benefits and improving cognitive reserve.

2.2.2 *Aerobic Exercise and Executive Function*

Aerobic exercise is associated with modest improvements in executive function in individuals of varied ages and in both healthy and clinical populations (Smith *et al*., 2010).

The study of Chang *et al*. (2014) observed the effects of acute aerobic exercise on cognitive performance in healthy, young individuals (n = 36; Age: 21.4 ± 1.6 years) with high, moderate or low fitness levels. They specifically looked at the EF component of Inhibition measured using the Stroop task. All three fitness categories (high, moderate and low) displayed an improvement in EF after a single session of acute aerobic exercise. The session consisted of 20 minutes of moderate intensity cycling with a five-minute warm-up and cool-down. A curvilinear relationship was observed between fitness level and performance on the incongruent condition of the Stroop task. The high fitness group exhibited significantly slower response times compared to the moderate and low fitness groups ($p < 0.02$), with the moderate fitness group producing the fastest response time ($p = 0.06$), suggesting that a moderate fitness level may relate to better EF.

The study of Baker *et al*. (2010) investigated the effects of aerobic exercise on cognition, more specifically executive function, and other Alzheimer's disease biomarkers in a group of older adults (Age: 70.4 ± 8.3 years) diagnosed with MCI. Updating, Inhibition and Set shifting (referred to in this study as Task switching) as well as verbal fluency and processing speed were assessed. The participants (n = 33) were randomized to either an experimental group, which engaged in high-intensity aerobic exercise, or a control group, which participated in stretching exercises, over a six-month period. Participants of both groups

attended four 45-60 minute sessions per week, with the aerobic group exercising at 75-85% of heart rate reserve. Only 28 of the original 33 participants completed the six-month assessment. The experimental group showed improvement in all EF components compared to the control group ($p = 0.04$). However, when broken down by gender, the treatment effect ($p = 0.04$) differed for men ($n = 9$) and women ($n = 10$). Women demonstrated improvements in all of the assessed EF, while men only showed improvement in performance of the Trail Making Test (TMT) B (Updating) ($p = 0.05$). The authors proposed that these differences may be due to metabolic effects of exercise. In response to aerobic exercise, they observed improvements in glucoregulation and insulin sensitivity in women but not men. Furthermore, they found a reduction in cortisol levels for women whilst the levels increased for men. Risk of cognitive decline increases with increasing cortisol levels in women; however in men, cortisol fluctuations appear to have no impact on cognitive performance.

Colcombe *et al.* (2004) looked at the impact of aerobic exercise on executive functioning in aging individuals through both a cross-sectional ($n = 41$; Age = 67.1 ± 8.0 years) and longitudinal study ($n = 29$; Age = 65.6 ± 5.7 years). In the cross-sectional study, participants completed either the Rockport 1-milewalk test or a treadmill-based VO_2 max test to exhaustion. In a separate session, they underwent a functional MRI (fMRI) scan while completing a flanker task (assessing Inhibition). In the longitudinal study, participants were randomized to an aerobic group or a stretch and tone control group. Participants in both groups attended exercise sessions three times per week for six months. Participants in the aerobic group began with 10-minute walking sessions increasing by one minute until they were walking for 45 minutes and they increased their heart rate reserve up to 60-70% over the course of the study. Participants in the control group focused on stretching and toning exercises and followed the same duration of session progression as the aerobic group. Participants in the longitudinal study underwent the same functional MRI (fMRI) scan with flanker task. In the cross-sectional study, participants were rated by a median split as either high fit or low fit in terms of aerobic exercise capacity. Individuals rated as “high fit” performed significantly better on the Inhibition test than those rated as “low fit” ($p = 0.02$). In the longitudinal study, the aerobic group performed significantly better than the control group with regards to the Inhibition test ($p < 0.04$). Both the “high fit” group and aerobic group in these two studies also demonstrated significantly greater cortical activation in regions associated with attentional control compared to the “low fit” and control groups, respectively.

This is in contrast to other studies which investigated the influence of aerobic exercise programmes on EF. These studies compared aerobic exercise to a control group, in elderly individuals (> 60 years) and found no significant improvements in EF (Smiley-Oyen et al., 2008; Fabre *et al*., 2002; Moul *et al*., 1995; Blumenthal *et al*,. 1989) while other meta-analyses of randomized control trials reported minimal improvements (Smith *et al*., 2010; Angevaren *et al*., 2008). The investigations which reported possible benefits suggest that aerobic exercise training programmes of around six month's duration improve inhibition and updating. There may possibly be gender differences involved as seen in the study of Baker *et al*. (2010). The researchers suggest that the following mechanisms may have contributed to the improvements: increased BDNF and other neural growth factors as well as increased blood flow to the brain. However, Diamond (2015) recommends that future studies explore the benefits of other exercise interventions besides aerobic activities which require little thought or attention.

2.2.3 *Resistance training and Executive Function*

Chang and Etnier (2009) examined the dose-response relationship between intensity of acute resistance training and cognitive performance, including EF (Inhibition), in young men and women (n = 68, Age: 26.0 ± 3.2). They looked at three differing resistance training intensities of 40%, 70% and 100% of a 10-repetition maximum together with a control group. Participants in each of the resistance training intensity groups performed two sets of 10 repetitions for six exercises in a single 30-minute session. The control group watched a video on resistance training. The results of this study suggest that 30 minutes of resistance training has a task-related positive influence on Inhibition and information processing. The findings display a significant linear relationship between resistance training intensity and processing speed, and a significant quadratic relationship between resistance training intensity and Inhibition ($p < 0.01$). Thus, high intensity resistance training promotes speed of processing while moderate intensity resistance training is most profitable for EF.

Liu-Ambrose *et al*. (2010) investigated the impact of resistance training on EF in older women, specifically whether there would be a difference between once-weekly (n = 54; Age = 69.5 ± 2.7 years) or twice-weekly (n = 52; Age = 69.4 ± 3.0 years) resistance training sessions compared to a twice-weekly combined balance and tone training control group (n = 49; Age = 70.0 ± 3.3 years). All sessions for all groups were 60 minutes long. Their primary outcome measure of EF was performance on the Stroop task (Inhibition) and their secondary outcome measures of EF were performance on the Trail Making Test, parts A and B (which

they used as a measure of Set shifting), and verbal digit span tests (working memory). At the end of the 12-month period, both resistance training groups ($p \leq 0.03$) demonstrated significant improvements on the Stroop task compared to the balance and tone training group. There were no significant differences observed for the secondary outcome measures between any of the groups ($p > 0.05$). The authors did not elaborate on the results of their secondary outcome measures.

The potential reported benefits from these studies suggest that resistance training may improve selected aspects of EF, most notably Inhibition. In contrast, additional studies which looked at resistance training as an active control condition together with another exercise modality (Moul *et al*., 1995) reported no improvement in EF as a result of resistance training.

2.2.4 *Combination exercise and Executive Function*

Liu-Ambrose *et al*. (2008) used the Otago Exercise Programme (OEP), which incorporated resistance and balance training in a home-based programme, to investigate its effect on older adults with regards to fall risk, functional mobility and EF. Seventy-four participants who had presented at a falls clinic were enrolled in the study, with 36 randomized to the OEP group (Age: 81.4 ± 6.2 years) and 38 to the control group (Age: 83.1 ± 6.3 years). The study was conducted over a six-month period, with those in the OEP encouraged to follow the programme three times per week for roughly 30 minutes, and also to walk a minimum of twice per week. Executive functioning was assessed using the Stroop task, Trail Making Test part B and the verbal digits backwards test. A significant improvement was noted in Inhibition (Stroop task) in the OEP group ($p = 0.05$) compared to the control group. No significant improvements were noted in Set shifting, working memory, physiological falls risk or functional mobility. Interestingly, after one year, the OEP group had reduced their fall incidence by 47% despite showing no significant reduction in falls risk or significant improvement in functional mobility. This is attributed to the significant improvement in Inhibition as a result of the OEP.

These combination studies mainly reported improvements in the EF of Inhibition and Updating (working memory). The reported suggested mechanisms involved are: increased blood flow to the brain and increased neurotrophic or growth factors. In contrast to this, the combination study of Williamson et al. (2009) reported no significant differences between the combination training group and a control group after one year of training.

Langlois *et al.* (2013) looked at a combination exercise training programme on cognition (including EF) and QOL in a sample of frail older adults. The cognitive evaluation comprised six domains which included working memory and one they had termed EF, which referred collectively to the calculated difference score of the TMT and calculated interference score of the Stroop test. The participants were divided into an exercise-training group (n = 36; Age: 71.6 ± 6.3 years) or a waiting listed control group (n = 36; Age: 73.2 ± 5.1 years). The exercise training programme comprised aerobic exercise (main component), resistance exercise, balance and stretching exercises performed three times per week for one hour. At the end of a 12-week period, the exercise training group exhibited significant improvements in cognitive performance, which included EF ($p = 0.04$), working memory ($p = 0.04$) and processing speed ($p = 0.01$) compared to the control group which did not improve.

Pedroso *et* al. (2012) examined the effect of an exercise programme incorporating dual-tasking on older adults with Alzheimer's disease and its impact on falls, balance and EF. Twenty-one individuals with Alzheimer's disease took part in the study with 10 in the training group (Age: 78.3 ± 7.4 years; MMSE (Mini-Mental State Examination): 20.1 ± 4.6) and 11 in the age-matched control group (Age: 77.5 ± 6.9 years; MMSE: 19.0 ± 3.2). Gender was not specified. The study ran over four months, those in the training group attended three 60 minute sessions per week on non-consecutive days. The dual task exercise programme involved performing exercises pertaining to coordination, agility, balance, flexibility, aerobic and resistance exercise while simultaneously performing a cognitive task. The Frontal Assessment Battery (FAB) and Clock Drawing Test (CDT) were used to assess EF. Significant improvements in EF, as seen in the FAB ($p < 0.01$) and CDT ($p = 0.03$) were observed in the training group compared to the control group. This improvement appeared to also be related to improved balance performance and a decreased fall risk.

2.2.5 *Balance training and Executive Function*

The pilot study of Shubert *et al*. (2010) looked at the influence of an exercise-based balance programme on physical and cognitive function, specifically EF (Updating and Set shifting) performance. Of the 76 participants who participated in the 12-week programme, only 52 (Age: 79.6 ± 6.8 years) completed the post-testing. Gender was not specified. Participants attended sessions twice per week for the duration of the study and sessions were roughly 60 minutes long. The programme incorporated balance specific exercises, dual task activities, balance challenges as well as some walking, strength training and flexibility. There was no control group used in this pilot study. Executive function was assessed using the

TMT parts A and B and the Symbol Digit Modality Test (SDMT). At the end of the 12 weeks, participants showed significant improvement in the SDMT ($p < 0.02$), which assesses Set shifting and processing speed, and a tendency towards a significant improvement in TMT part A ($p = 0.03$), which is a measure of visual search. There was no significant improvement in TMT part B.

As can be seen, balance training studies and their impact on EF are sorely lacking. Even in this study by Shubert *et al*. (2010), the balance training programme included small components of resistance and endurance exercise, thus it is questionable whether the observed improvements may be purely attributed to the balance training. This highlights a need and a significant gap in the current literature for an investigation of the impact of a specifically balance-focused exercise intervention on EF, and more specifically in the PD population.

2.3 *Exercise and Executive Function in the Parkinson's Disease population*

The available literature on exercise and the influence on EF in individuals with PD is sadly limited. Nevertheless, the preliminary investigations as well as available animal studies have shown positive influences of exercise on EF in PD (Murray *et al*., 2014).

Only six exercise studies have specifically investigated EF in PD (Tanaka *et al.,* 2009; Rigdel *et al.,* 2011; Cruise *et al.,* 2011; McKee & Hackney, 2013; David *et al*., 2015). All six studies included participants with disease severity rated mild to moderate (Hoehn and Yahr Scale (HY) 1 - 3).

The 2009 study of Tanaka *et al.* looked at 20 older PD participants: there was an equal age-matched split of 10 in the experimental (EXP) group (Age: 64.8 ± 8.5 years; HY: 1.4 ± 0.5; UPDRS Total: 31.0 ± 13.1) and 10 in the control (CON) group (Age: 64.6 ± 6.3 years; HY: 1.8 ± 0.8; UPDRS Total: 39.9 ± 19.7). It is not known whether the participants were tested on or off their medication. The study was conducted over a six-month period with participants attending three 60 minute sessions per week. They used the Wisconsin Card Sorting Test (WCST; Set shifting) and saw significant improvements in the results for "Categories completed" ($p = 0.046$) and "Perseverative errors" ($p = 0.043$) in the EXP. The exercise programme used was a combination of aerobics, flexibility, muscular resistance, motor coordination and balance.

Rigdel *et al.* (2011) observed changes in EF following sessions of acute passive cycling in participants with PD. The study had a total of 19 PD participants (Age: 63.2 ± 8.5 years; HY: 1.9 ± 0.8; UPDRS: not utilized) and used a within-subject design (each participant was also his or her own control). Participants were assessed off their medication (minimum of 10 hours since previous dosage), except for the first session which was a baseline testing session for fitness and measurements. Participants had three sessions, after the initial baseline session, which involved passive for 30 minutes on a motorized bicycle cycling (thus participants did not actively cycle). Each session was one week apart and always on the same day of the week. They made use of the TMT A and B to assess EF (Updating) and they noted significant improvements in the total time to complete TMT B ($p = 0.01$) as well as TMT B-A, the difference score between TMT B and TMT A, ($p = 0.01$).

The study of Cruise *et al.* (2011) investigated the influence of a progressive aerobic and anabolic exercise programme on cognition and QOL in PD. The study included 28 PD participants divided into age-matched experimental (EXP) (Age: 59.5 ± 11.5 years; HY: 1 - 3; UPDRS: not utilized) and control (CON) (Age: 60.6 ± 7.3 years; HY: 1 - 3; UPDRS: not utilized) groups. Participants were tested on medication, 1 to 2 hours after taking it. Participants in the EXP took part in a 12-week progressive programme of strengthening and cardiovascular exercise while those in the CON were asked to maintain their usual activities for the duration. At the end of the study those in the CON were given the opportunity to participate in the 12-week programme that the EXP followed. Those in the EXP had twice weekly 60-minute exercise sessions over the 12-week study period. The authors of the study chose to calculate inferences regarding the true value of the change scores. Their results showed “likely benefit” (>75% confidence interval) for selected frontal lobe-based EF specifically, verbal fluency and spatial working memory. They assessed this using the Cambridge Neuropsychological Test Automated Battery. There was no significant change in QOL or mood ($p > 0.05$).

McKee and Hackney (2013) studied the effects of tango dance classes on the spatial cognition and disease severity of those with PD. A total of 31 PD participants completed the study, 23 in the experimental (EXP) group (Age: 68.4 ± 7.5 years; HY: 2.3 {2.0, 2.6} median {first, third quartiles}; UPDRS III: 28.1 ± 6.9) and eight in the age-matched control (CON) group (Age: 74.4 ± 6.5 years; HY: 2.0 {2.0,2.0} median {first, third quartiles}; UPDRS III: 27.2 ± 7.0). All participants were tested on their medication. The study took place over 12 weeks with each participant attending twenty 90-minute sessions, with tango lessons for the EXP

and educational lessons for the CON. They reported significant improvements in the EXP, compared to the CON, with spatial cognition ($p = 0.021$), measured using the Brooks Spatial Task, and global cognition measured with the MoCA ($p = 0.01$). They also found significant improvements in disease severity ($p = 0.01$) and balance ($p = 0.04$) in the EXP.

David *et al.* (2015) investigated the impact of two different types of exercise programmes on EF in PD. A total of 51 PD participants took part in the study, with 46 and 38 completing the 12- and 24-month follow-ups, respectively. Participants were randomized to a Progressive Resistance Exercise Training (PRET) or modified Fitness Counts (mFC) group. The PRET (Age: 59.0 ± 4.6 years; HY: 2 (range: 2 – 2.5); UPDRS III: 34.5 ± 11.9) followed a progressive resistance training weight-lifting programme while the mFC (Age: 58.6 ± 5.6 years; HY: 2 (range: 2 – 2.5); UPDRS III: 34.7 ± 11.5) followed non-progressive strengthening, balance exercises, stretches and breathing. All results reported were collected off medication. The study was conducted over 24 months, with participants attending twice-weekly sessions of unknown duration. At the 12-month follow-up, they observed improvements in the Digit Span (Updating) in both the PRET ($p < 0.01$) and mFC group ($p = 0.04$) and improvement in the Stroop (Inhibition) in the mFC only ($p = 0.04$). At the 24-month follow-up, improvements were noted in the Digit Span ($p < 0.01$), Stroop ($p = 0.048$) and Brief Test of Attention ($p = 0.048$) for the PRET and in the Digit Span ($p < 0.01$) and Stroop ($p = 0.03$) for the mFC.

The most recent study by Duchesne *et al*. (2015) looked at the effect of aerobic exercise on both motor and cognitive functioning (specifically EF) in PD. For this discussion, we will only focus on the EF component of the study. Nineteen PD participants (Age: 64 ± 8.2 years; HY: 2 ± 0; UPDRS III: 21.8 ± 6.2) and 20 healthy controls (Age: 59 ± 7.1 years) took part in the study. Participants engaged in high intensity aerobic exercise cycling on a recumbent bicycle, three times per week for 12 consecutive weeks. They started at 20 minutes, progressing by 5 minutes per week until they attained 40 minutes. Participants were assessed pre- and post-intervention with the Stroop task and TMT A and B tests. Following 12 weeks of aerobic exercise training, there was a significant improvement in Inhibition ($p = 0.01$) but not in other EF measures ($p > 0.05$).

In contrast to the above mentioned studies, Pierobon *et al.* (2014) decided to investigate whether EF or depression impact on the outcome of a rehabilitation programme. Forty PD participants (Age: 70.1 ± 8.0 years; HY: 3; UPDRS Total: 41.2 ± 10.4; UPDRS III: 21.4 ± 5.3) were enrolled in the study. The participants were subdivided into two groups for two

criteria. Criterion one was impaired or not impaired (EF) and criterion two was depressed or not depressed. Participants were assessed on their medication. The rehabilitation programme was an intensive one for the four-week duration. Participants took part in three daily sessions, for a collective three hours of rehabilitation, five days per week. The authors concluded that neither impaired EF nor moderate-to-severe symptoms of depression impeded the outcome of the rehabilitation programme. PD participants remained on their meds for the duration of the study.

There are other studies which did not specifically investigate EF, but did look at related aspects of cognition in individuals with PD after balance-related interventions (Sehm *et al*., 2014; Dos Santos Mendes *et al*., 2012; Pompeu *et al*., 2012).

Both Pompou *et al*. (2012) and Dos Santos Mendes *et al*. (2012) used the popular Nintendo Wii™ game console in their studies with PD participants. Pompeu *et al.* (2012) studied the effect of motor and cognitive training on the Nintendo Wii™ in PD participants and its impact on their ADL compared to balance exercise therapy. Thirty-two PD participants (HY: 1.7 ± 0.5) were included in the study and split into a Wii™ group (Age: 68.6 ± 8.0 years; UPDRS II: 10.1 ± 3.8) and a Balance group (Age: 66.2 ± 8.3 years; UPDRS II: 8.9 ± 2.9). Participants were assessed on their medication. The participants of both groups participated in 14 twice-weekly individual training sessions over seven weeks. Each session lasted one hour and was composed of two 30 minute components. Both groups performed the same global exercises for 30 minutes which incorporated stretches, resistance and diagonal pattern exercises. The Wii™ group received 30 minutes of motor and cognitive training while the Balance group received 30 minutes of balance exercise therapy. Both groups improved significantly in UPDRS II ($p < 0.01$) and MoCA ($p < 0.01$) scores. The authors concluded that because the improvement seen in cognition, as measured by the MoCA (which also has an EF component), also occurred in the Balance group it could be ascribed to the advantageous effects of physical activity.

Dos Santos Mendes *et al*. (2012) examined the effect of Wii™ training on learning, retention and transfer of improvements in performance in PD and healthy elderly participants. Sixteen PD participants were included in the experimental (EXP) group (Age: 68.6 ± 8.0 years; HY: 1.9 ± 0.3; UPDRS: not utilized) and 11 age-matched healthy elderly in the control (CON) group (Age: 68.7 ± 4.1 years). Both groups took part in twice-weekly sessions conducted over seven weeks. Each session began with 30 minutes of global exercises (same as

Pompeu *et al*., 2012) followed by the Wii™ Fit training. This study suggests that the ability of individuals with PD to learn, retain and transfer this learning, following Wii™ Fit training, depends to a large extant on the cognitive demands of the individual games.

The study of Sehm *et al.* (2014) investigated morphometric changes in the brains of individuals with PD following balance training. Twenty PD participants (Age: 62.9 ± 7.1 years; HY: 2.1 ± 0.4; UPDRS III: 21.9 ± 9.5) and 16 age- and sex-matched healthy volunteers participated in the study. Both groups participated in a whole-body dynamic balancing task (DBT) programme which was run over six consecutive weeks. Each session was 45 minutes long and there was one session per week. Magnetic resonance imaging (MRI) and balance testing were assessed at baseline as well as after 2, 4 and 6 weeks of training. Both groups displayed improvements in performance. The healthy controls exhibited learning-dependant changes in grey matter in the left *hippocampus*, while the PD participants demonstrated changes in grey matter in the right *anterior precuneus*, left *ventral premotor cortex*, left *inferior parietal cortex*, left *middle temporal gyrus* and bilateral *anterior cingulate cortex*. There was also a treatment effect for time-dependant changes in grey matter in the right *cerebellum*. The authors elucidate the ability of the brain to undergo structural plasticity, related to learning, in a degenerative condition such as PD.

The study of Dos Santos Mendes *et al*. (2012) was not able to show that the improvements seen were linked specifically to the balance component of the Wii™ Fit training or whether it was due to the combined balance and cognitive component of this training. The study of Sehm *et al*. (2014), however, revealed the neuroplasticity of the brain that took place in response to balance training.

Comparisons between investigations are challenging for a number of reasons, which are not limited to the studies mentioned. For instance, executive functioning is not defined uniformly, and each of these studies assessed executive functioning with different assessment tools. Similarly, the exercise protocols vary greatly from study to study. This is the variable with the widest range as it can be influenced by type of exercise, duration of session (minutes or hours), exercise sessions per week (or total exercise sessions), duration of exercise period (weeks or months) or intensity of exercise.

2.4 *The relationship between Executive Function and Balance, Mobility and Fall Risk*

Executive dysfunction is common amongst individuals with PD, with impairments reported in Inhibition, Updating and Set shifting (Xu *et al*., 2014; Camicioli & Majumdar, 2010). Impaired EF in older adults has also been shown to have an association with reduced balance performance and gait as well as an increased risk of falling (Xu *et al*., 2014). Camicioli and Majumdar (2010) report that individuals with PD are at a greater risk of falling than age- and sex-matched controls. A study by Xu *et al*. (2014) revealed impairments in EF, cognition, gait and balance in a PD sample. More specifically, they showed that EF, and not general cognition, was linked to poorer gait and balance in individuals with PD. The 2014 study of Gothe *et al*. proposed that the EF components of Inhibition and Set shifting could be potential early indicators of mobility limitations in the future, which could result in difficulty conducting ADL or disability in older adults.

3. Parkinson's Disease and Sensory-motor Training

3.1 *Benefits of Exercise for Parkinson's Disease*

Recent research shows that the early intervention of physical activity or exercise is valuable in improving or maintaining the physical performance of those with mild to moderate PD. This is of particular importance in retaining independence and lessening the load of caregivers (Crizzle & Newhouse, 2006). Physical activity, such as aerobic exercise, resistance training and flexibility exercises, can elicit improvements in general fitness and aerobic capacity as well as improve both motor and non-motor aspects of PD (Van der Kolk & King, 2013; Goodwin *et al*., 2008; Cutson *et al*., 1995). The following section summarizes briefly the benefits of exercise previously reported in the literature.

The types of physical activity or exercise programmes range widely, including but not limited to: aerobic exercise, resistance training, balance and sensory-motor training programmes as well as combination programmes. A variety of benefits of exercise in PD have been reported but more specifically the balance-related improvements include improved balance (King *et al*., 2015; Loftus, 2014; Lauhoff *et al*., 2013; McKee and Hackney, 2013; Smania *et al*., 2010; Hackney and Earhart, 2008; Hirsch *et al*., 2003), increased balance confidence (King *et al*., 2015; Smania *et al*., 2010), a reduction in falls (Loftus, 2014; Smania *et al*., 2010), improved equilibrium (Toole *et al*., 2000) and increased axial mobility and functional reach (Schenkman *et al*., 1998). These balance-related improvements have been reported in varied exercise interventions and not specifically balance interventions.

Increased ambulation or walking speed (Uc *et al*., 2014; Hass *et al*., 2012; Dibble *et al*., 2009; Miyai *et al*., 2002; Scandalis *et al*., 2001), stride length (Scandalis *et al*., 2001) and number of steps (Miyai *et al*., 2002) are reported improvements related to gait and also include positive changes in gait variability (King *et al*., 2015), walking economy (Schenkman *et al*., 2012) and initiation of gait (Hass *et al*., 2012).

Various studies have also documented increased muscular strength (Schilling *et al*., 2010; Hirsch *et al*., 2003; Scandalis *et al*., 2001) as well as enhanced control and coordination of grasping (Rigdel *et al*., 2009). In addition to this, aerobic capacity has been shown to improve (Duchesne *et al*., 2015; Uc *et al*., 2014; Bergen *et al*., 2002), fatigue to decrease (Uc *et al*., 2014) and exercise tolerance to increase (Baatile *et al*., 2000). Another advantage of exercise in PD is an improved functional ability (Lauhoff *et al*., 2013; Dibble *et al*., 2009; Hackney and Earhart, 2008) or physical performance (King *et al*., 2015; Schenkman *et al*., 2012).

Reductions in disease severity of PD have been noted in a decrease in the UPDRS (Unified PD Rating Scale) total score (Lauhoff *et al*., 2013; Baatile *et al*., 2000) as well as in UPDRS I, the mood subscale, (Uc *et al*., 2014), UPDRS II, the ADL (Activities of Daily Living) subscale, (King *et al*., 2015; Schenkman *et al*., 2012) and UPDRS III, the motor subscale, (Carvalho *et al*., 2015; Uc *et al*., 2014; Rigdel *et al*., 2009; Hackney and Earhart, 2008), as well as reductions seen in bradykinesia and tremors (Rigdel *et al*., 2012; Dibble *et al*., 2009).

Decreased depression (King *et al*., 2015; Uc *et al*., 2014; Smania *et al*., 2010) and increased QOL scores (King *et al*., 2015; Uc *et al*., 2014; Dibble *et al*., 2009; Baatile *et al*., 2000), as well as improvements in apathy, self-efficacy (King *et al*., 2015) and subjective well-being (Reuter *et al*., 1999) have been reported as well.

Crizzle and Newhouse (2006) emphasized the importance of designing exercise programmes in a manner that recognize the link between the neurological impairments that pertain specifically to PD (tremor, rigidity, motor planning) and the ensuing musculoskeletal impairments (bent over posture, reduced flexibility of spine and extremities).

In the study of Xu *et al*. (2010) future risk of PD was lowered in those with increased levels of moderate to vigorous exercise between the ages of 35-39 or within the previous 10 years,

again highlighting the importance of exercise with regards to PD. They noted this association in both genders. Thus, it would appear that being moderately to vigorously active, in these age groups, is associated with a decreased PD risk.

There is sufficient evidence to confirm the benefits of exercise for those with PD. These range from physical and motor improvements to those pertaining to mood and QOL. Exercise has the potential to play a significant, and yet relatively inexpensive, role in the nonpharmacological management of PD.

3.2 *Sensory-motor Training*

Somatosensory-, sensory-motor-, neuromuscular- and proprioceptive- training are often used interchangeably since these training modalities refer to interventions that focus on improving postural control, most often through the integration of sensory information and, particularly, through increasing proprioceptive function.

Aman *et al*. (2014) describe proprioception as “the conscious awareness of one’s body and limbs and has several distinct properties: passive motion sense, active motion sense, limb position sense, and the sense of heaviness.” When information from other sensory sources, such as the visual or vestibular systems, is absent, it uses somatosensory signals in the form of proprioception or haptic feedback. The main focus according to Aman *et al*. (2014) is on improving or completely restoring sensory and / or sensory-motor function. Similarly, Riemann and Lephart (2002) referred to the sensory-motor system as encompassing the sensory, motor and central integration as well as processing features involved with joint homeostasis maintenance during movements; in other words, functional joint stability through neuromuscular control.

Aman *et al*. (2014) outlined pertinent features of sensory-motor training in general: sensory-motor training has the potential to improve proprioception and interventions run over a longer period (≥ 6 weeks) appear to show greater improvements; sensory-motor training is relevant and beneficial for a variety of clinical populations, such as those with impaired proprioception (like PD), regardless of whether it is due to a musculoskeletal or neurological problem.

Adults rely predominantly on somatosensory (proprioceptive) information for postural control. As a result, balance activities are often used by clinical exercise therapists as a

means to train proprioception and vice versa. Proprioceptive or neuromuscular activities are often incorporated to improve body control as well as joint control and stability.

Balance (postural control) relies on an ability to maintain centre of mass within the base of support limits, during sitting or standing, and to control it, during walking or running, while changing to a new base of support. Considerable everyday activities are balance-related: walking or getting up off a chair, for example, requires centre of mass control while changing base of support. Most PD individuals will eventually see reductions in their balance, which will further deteriorate as their disease progresses. Poor mobility, falls, disability and a decline in quality of life are associated with reduced balance in individuals with PD. Thus, there is a crucial need to investigate interventions, such as those using sensory-motor training programmes, that could potentially improve balance in this clinical population (Allen *et al*., 2011).

3.3 *Parkinson's Disease and Sensory-motor Training*

Although there have been some sensory-motor training or balance training studies conducted with individuals with PD, most of them tended to look at balance training together with other forms of training (King *et al*. 2015; Schenkman *et al*., 2012; Tanaka *et al*., 2009; Toole *et al*., 2000). Research suggests that external cues (peripheral sensory feedback) can be used to counteract the defective internal signal generation in PD. The provision of external cues can assist with initiating and maintaining continuous motor activities, such as walking (Abbruzzese *et al*., 2015; Abbruzzese *et al*., 2014).

3.3.1 *Balance as Part of a Combination Training Programme*

The research of Hirsch *et al*. (2003) compared a combination group (balance and resistance training) (n = 6; Age: 70.8 ± 2.8 years; HY: 1.8 ± 0.3; UPDRS: not utilized) with a balance only group (n = 9; Age: 75.7 ± 1.8 years; HY: 1.9 ± 0.6; UPDRS: not utilized) in a sample of idiopathic PD participants. The study ran over a 10-week period and participants were assessed pre-, post- and four weeks post-intervention. Both groups received the same balance training three times per week for 30 minutes, while the combination group also participated in 15-minute resistance training sessions three times per week. Both groups significantly improved their balance ($p = 0.06$) with the combination group marginally better than the balance group. Both groups improved their balance time before falling ($p = 0.03$), and this improvement was maintained after four weeks. Strength increased significantly in

both groups ($p < 0.01$) and was maintained at the 4-week follow-up, although this increase was small in the balance group compared to a considerable improvement in the combination group.

Balance and functional training, within a combination programme which included spinal and extremity flexibility, was investigated by Schenkman *et al*. (2012). The balance and flexibility group (n = 39; Age: 64.5 ± 10.0 years; HY: 2.3 ± 0.4; UPDRS III: 24.3 ± 10.5; UPDRS Total: 35.5 ± 13.9) was compared to an aerobic exercise group (n = 41; Age: 63.4 ± 11.2 years; HY: 2.2 ± 0.5; UPDRS III: 24.4 ± 9.1; UPDRS Total: 34.6 ± 13.0) and a home-based exercise group (control) (n = 41; Age: 66.3 ± 10.1 years; HY: 2.3 ± 0.4; UPDRS III: 25.9 ± 8.9; UPDRS Total: 37.5 ± 13.7). The study was conducted over 16 months and all groups exercised 5 to 7 times per week for 45 to 50 mins. The control group exercised at home on their own with one supervised session per month, while the balance and flexibility group and aerobic exercise group had three supervised sessions per week for the first 4 months. Thereafter, the frequency of supervised sessions in the latter two groups tapered down, with the responsibility on themselves to keep up with the frequency of sessions. Overall function (a performance-based physical function measure), measured using the Continuous Scale – Physical Functional Performance Test, was significantly improved in the balance and flexibility group after four months compared to the aerobic exercise group ($p = 0.048$) and control ($p < 0.01$). This was not sustained at the 10- and 16-month follow-ups, possibly due to the fact that supervision tapered down from three times per week to once a month. Interestingly, the balance and flexibility group did not significantly improve their balance over the intervention but neither did it deteriorate. The authors did not elaborate on possible reasons for this result.

King *et al*. (2015) observed the effect of a sensory-motor programme on individuals with PD in three different settings, namely, one-on-one individual sessions (n = 21; Age: 64.2 ± 6.7 years; HY: 2.4 ± 0.5; UPDRS III: 39.4 ± 11.1), group sessions (n = 20; Age: 63.9 ± 8.5 years; HY: 2.4 ± 0.5; UPDRS III: 35.4 ± 14.1) or a home programme (n = 17; Age: 64.6 ± 6.8 years; HY: 2.5 ± 0.5; UPDRS III: 35.2 ± 13.7). The programme included various activities, such as Pilates and Tai Chi, to target kinesthesia, stability limits, biomechanical constraints, anticipated adjustments of posture, gait coordination and bradykinesia, and the programme was progressed systematically. The programme took place over a four-week period with individuals attending three one hour sessions per week. The individual group demonstrated the greatest improvements in measures of function, which included the Physical

Performance Test ($p < 0.01$), balance ($p < 0.01$), UPDRS II ($p = 0.01$), depression ($p = 0.01$), self-efficacy ($p = 0.02$) and apathy ($p = 0.048$), while the group sessions group demonstrated the greatest improvements in measures of gait, which included arm swing ($p < 0.01$), stride velocity ($p < 0.01$), gait variability ($p = 0.049$), gait while dual tasking ($p = 0.01$), trunk movement ($p < 0.01$) and freezing of gait ($p < 0.01$). The home programme group showed the least improvement – they only showed improvements in PDQ ($p = 0.02$) and mini-BESTest ($p = 0.01$). They concluded that individual exercise sessions might be most beneficial for improving balance and function while gait might be best improved through group sessions.

The study of Wong-Yu and Mak (2015) examined the effects of an inside and outside multi-dimensional balance training programme in individuals with PD. The programme ran for eight weeks with participants in the exercise group (n = 41; Age: 59.4 ± 9.0 years; HY: 2.5 ± 0.3; UPDRS III: 26.9 ± 10.4) attending a single two-hour session per week. The first four weeks took place indoors and the second four weeks outside. The programme consisted of varied exercises focusing on strengthening, flexibility and balance, among others. A control group (n = 43; Age: 62.6 ± 8.9 years; HY: 2.4 ± 0.3; UPDRS III: 31.3 ± 11.1) performed upper body exercises at the same session frequency. The experimental group showed significant improvements for dual-task TUG ($p < 0.01$) and balance ($p < 0.01$) at post-intervention and these were sustained at six- (balance: $p < 0.01$; dual-task TUG: $p < 0.01$) and twelve-month (balance: $p < 0.01$) follow-up.

3.3.2 *Balance Training Programme in Isolation*

Smania *et al*. (2010) investigated the impact of balance training on postural instability, compared to general physical activity, in individuals with PD. Participants were randomized to the balance training group (n = 28; Age: 67.6 ± 7.4 years; HY: 3.0 ± 0.1; UPDRS Total: 46.1 ± 11.5), which performed balance training exercises aimed at improving feedback and feedforward postural reactions, maintaining balance on uneven surfaces and coordinating limbs during movement, or the physical activity group (n = 27; Age: 67.3 ± 7.2 years; HY: 3.1 ± 0.3; UPDRS Total: 43.0 ± 16.9), which performed muscle stretching, coordination and joint mobilization exercises. Each group participated in sessions three times a week for seven weeks. Balance ($p < 0.01$), balance confidence ($p < 0.01$), postural transfers ($p < 0.01$) and centre of foot pressure self-destabilization ($p < 0.01$) (the latter two both measures of postural instability) had improved statistically significantly after the intervention, and this

was maintained at one-month follow-up. No significant improvement was noted in the control group.

The pilot study of Mirelman *et al*. (2011) looked at the use of an audio-biofeedback system (ABF) in conjunction with a balance training programme in a small group of PD participants (Age: 71.3 ± 8.3 years; HY: 2.5 ± 0.5; UPDRS III: 25.3 ± 11.7). The study was conducted over six weeks and each participant completed 18 45-minute sessions. The ABF provided feedback as a result of the participants' movements and body orientation changes. Balance improved significantly ($p = 0.03$) over the six weeks and there was a trend towards improvement in functional mobility ($p = 0.07$). These changes were maintained at a one-month follow-up. Participants also improved their depressive ($p = 0.05$) and quality of life scores (no reported p value), however, these were not maintained at follow-up.

The study of van den Heuvel *et al*. (2014) investigated the use of augmented visual feedback on balance training compared to conventional balance training (control). Participants took part in twice-weekly sessions over the five-week duration of the study. The visual feedback group (Age: 66.3 ± 6.4 years; HY: 2.5 (2.0, 3.0); UPDRS III: 28 (19.0, 40.5); UPDRS Total: 46.0 (32.3, 63.8)) was exposed to interactive balance games making use of augmented visual feedback, while the control group (Age: 68.8 ± 9.7 years; HY: 2.5 (2.0, 2.5); UPDRS III: 28 (17.8, 35.6); UPDRS Total: 46.0 (32.3, 62.0)) participated in balance training, which included one-leg balancing (eyes open and closed) and dual-task exercises among others. The study found no significant differences between the visual feedback and control groups with regards to functional reach, balance and gait, and health status, level of activity and participation ($p > 0.05$). *HY and UPDRS III and Total were reported as median (first quartile – third quartile).*

Thus balance studies in PD participants tend to improve balance, physical performance or function, functional mobility and aspects of gait.

4. Conclusion

Exercise seems to play an assistive role in the protection of neurons from injury or degeneration. Although the degree to which, and specifically how exercise impacts EF in PD is not clear. To date, the problem with EF research in the PD population is the heterogeneous subject populations, the diverse exercise interventions (in terms of the intensity, mode and duration of the programme) as well as differences in outcome measures.

However, regardless of this, the exercise-based EF interventions conducted in the PD population, have still demonstrated improvement in a range of EF measures. Furthermore, because EF has been linked to poor gait performance and balance in PD, sensory-motor exercise interventions have the potential to improve components of EF as well as aspects of balance and mobility in the PD population.

CHAPTER THREE

PROBLEM STATEMENT

1. Study Purpose

Motor dysfunction, impaired balance and fear of falling are a part of the daily life of an individual with PD. Current therapies, both pharmacologic and non-pharmacologic, remain largely inadequate in successfully treating these daily problems (Cutson *et al*., 1995). Executive Function is important in everyday life and involves setting goals, planning and achieving these goals, even for seemingly simple activities such as walking down stairs (Murray *et al*., 2014). Impairment of EF has been associated with poorer gait and balance in PD (Xu *et al*., 2014) and cognitive impairment has been shown to contribute to QOL scores in this same population (Schrag *et al*., 2000). Impaired EF has an impact on gait efficiency and safety and affects the person with PD's balance in their daily activities (Yogev-Seligmann *et al*., 2008). By investigating the influence of a sensory-motor training program on EF, the findings could be used to enhance clinical practice and neuro-rehabilitation exercise programmes used for treating EF deficits in PD. This is of particular importance in a developing country such as South Africa, where therapists are constantly searching for evidence-based practices that are cost effective to implement.

To date, research which has investigated the influence of various types of exercise on EF in individuals with PD, included sample sizes between 19 and 51 (with an average of 17.0 per group and 28.3 per study) and participants with reported average ages ranging between 58.6 and 74.4 years (average age of 63.2 ± 7.3 years). Participants were at a PD level of mild to moderate based either on the HY scale, with reported average scores ranging from 1.4 to 2.0 (average HY: 1.8 ± 0.5) and/or UPDRS score, with reported average scores ranging from 27.2 to 34.7 for UPDRS III (average UPDRS III: 31.1 ± 9.3) and 21.8 to 39.9 for UPDRS Total (average UPDRS Total: 31.0 ± 13.0). Of the six studies specifically focusing on EF and exercise in PD, four studies included age-matched PD control groups (David *et al*., 2015; McKee & Hackney, 2013; Cruise *et al*., 2011; Tanaka *et al*., 2009), one study included an age-matched healthy control group (Duchesne *et al*., 2015) and another only used an experimental group (Rigdel *et al*., 2011). In all the studies examined, participants continued taking their regularly prescribed medication. Two studies reported testing of participants OFF their medication (David *et al*., 2015; Rigdel *et al*., 2011) and three studies reported testing of participants ON their medication (Duchesne *et al*., 2015; McKee

& Hackney, 2013; Cruise *et al*., 2011). One study was unclear as to whether testing took place while participants were on or off medication (Tanaka *et al*., 2009). These studies assessed global cognitive function, Set shifting (cognitive flexibility), Inhibition, working memory (updating) as well as both spatial working memory and spatial recognition memory, attention, visual search, processing speed and verbal fluency as indictors of EF.

It is still not clearly known how PD drugs affect executive function. Dirnberger and Jahanshahi (2013) discussed the dopamine overdose hypothesis. This hypothesis attempts to explain the varying effects of dopaminergic medication on motor versus certain cognitive functions. Whilst dopaminergic medication raises low levels of dopamine in the putamen and dorsal striatum, the ventral striatum becomes over- stimulated or "overdosed" as it is not seriously depleted of dopamine. This impact on the ventral striatum can affect the limbic and orbitofrontal circuits and influence certain executive function tasks.

It is not ethical to test PD participants off their medication. Some studies have assessed their participants in the morning following an overnight withdrawal or wash-out period. It was beyond the scope of the man-power and resources of this study to do this. With one person assessing the participants, it would have meant testing one person per day which would not have been possible. In this study, participants were tested at the same time (plus or minus an hour) on all three testing occasions – thus consistency was maintained within the study.

To the researcher's knowledge, no studies to date have investigated the influence of sensory-motor or balance training on EF in individuals with mild to moderate PD.

2. Research Question

The main research question was to establish if an eight-week SMT programme could alter EF in individuals with mild to moderate PD.

2.1 *Research Objectives*

To investigate whether an eight-week SMT programme influenced:

I. Executive Function, namely Updating (working memory), Set shifting and Inhibition with TMT A and B, WCST and adapted Stroop task (including selective attention and processing speed), respectively;
II. Global cognitive function, namely Montreal Cognitive Assessment (MoCA), and the cognition component of PDQ-39;

III. Disease severity with HY as well as MDS-UPDRS i.e. subsections II, III and Total.
IV. QOL with the 39-Item PD Questionnaire (PDQ-39);
V. Perception of depressive mood (referred to hereafter as depression: hence it does not refer to the clinical diagnosis of depression) with Hamilton Rating Scale for Depression (HAM-D);
VI. Perceived balance confidence via Activities-specific Balance Confidence (ABC) Scale;
VII. Functional balance and mobility with the Timed Up and Go (TUG) test.

2.2 *Variables*

2.2.1 *Independent Variable*

The independent variable was the eight-week sensory-motor training programme.

2.2.2 *Dependent Variables*

The dependent variables were Set shifting, Updating (Working Memory), Inhibition, processing speed (primary outcome variables). In addition, balance and mobility, as well as QOL and depression, were also assessed (secondary outcome variables).

2.2.3 *Categorical Variables*

- Participant age: 50-85 years of age
- Gender: men and women
- Level of PD: stages 1 - 3 according to the Hoehn and Yahr (HY) Scale and a functional status level of PD less than 59 on subscale III of MDS-UPDRS (Movement Disorder Society – Unified PD Rating Scale).

2.2.4 *Confounding variables*

Mood, medication and education (also relating to socioeconomic status) were considered as variables that may influence executive functioning.

However, individuals with moderate to severe depressive moods (including apathy) on medication which could influence cognition and balance, as well as individuals with moderate to severe/demented global cognition, were excluded. In addition, global cognition was corrected for individuals with < 12 years' education, and the convenience sampling took participants from two areas with a similar socio-economic distribution (Development

Information and GIS Department, 2014; Western Cape Government Provincial Treasury, 2014a, 2014b).

2.2.5 *Assumptions*

Certain assumptions concerning the research participants were made at the start of the study. It was assumed that each participant would answer all questions asked and complete all their forms honestly, and that they would not withhold any information relevant to the study. It was assumed they would attend the exercise sessions and that they would specifically adhere to a 70% attendance rate. It was assumed the participants would perform each test to the best of their ability.

In addition to this, certain assumptions were made regarding the study itself. It was assumed that the sensory-motor training programme would have an effect on executive function and balance.

2.2.6 *Limitations*

A number of limitations were recognized at the beginning of the study. These comprised: the possibility of participants dropping out of the study due to illness or injury, a variety of personal reasons or a lack of interest in continuing with the study; the possibility that participants could be dishonest or not completely truthful when completing forms or answering questions; the possibility that individuals would continue with other activities (although they were asked not to add any additional activities); the possibility of transport issues affecting attendance (especially if the person was reliant on public transport or on another person); and lastly, the possibility that the sample size may be too small and inhibit ability of the research team to conduct a randomized controlled trial.

2.2.7 *Delimitations*

Certain delimitations were set at the beginning of the study. The study was delimited to individuals who presented with a clinical diagnosis of idiopathic PD between stages I and III (mild to moderate), as classified according to the HY scale and a neurologist. Participants with a classification above III were not considered as they would have been unable to participate fully in the sensory-motor training programme. Participants needed to reside within a 70km radius of Stellenbosch in the Western Cape. The research team did not have the resources (manpower or financial) to implement this study further afield at the time.

Participants needed to be between the ages of 50 and 85 years. They were set a minimum attendance requirement of 70% for the sensory-motor training programme sessions and could not miss two consecutive training sessions. Participants unable to meet this requirement were allowed to continue their sessions but their data was excluded from the study. It was accepted that participants who were colour-blind would not be able to complete the WCST or the Stroop Task but would be able to complete all the other tests.

CHAPTER FOUR

METHODOLOGY

1. Study Design

This study was conducted as an interrupted time series (ITS) experimental design with two groups and pre-, mid- and post-data collection. The ITS is considered to be one of the strongest quasi experimental research designs. The two groups (allocation ratio of 18:31, respectively) were a placebo group (PBO) which wore a wristband during the treatment phase and an experimental group (EXP) which participated in the eight-week sensory-motor training programme). Data collection was divided into a 'baseline phase' (pre- to mid-testing) and a 'treatment phase' (mid- to post-testing) for both the EXP and PBO (Figure 4.1).

*SMT: sensory-motor training

Figure 4.1 Illustration of the study design for both placebo and experimental groups.

The baseline phase refers to the eight weeks in which dependent variables were observed and assessed before introduction of the independent variable for eight weeks. The baseline time provided a frame of reference against which the treatment was compared. The treatment phase is when the intervention (independent variable) was introduced and the dependent variables were observed and recorded. In other words, each participant was observed three times and their performance during the intervention (treatment phase) was compared to their own performance prior to this during the baseline phase, hereby making the participant their own control. In addition, to add increased quality to the research design, a placebo group was added. To make the study feasible a sample of convenience was used. This specific placebo-controlled study design was selected as typical exercise-based PD research includes only a few available participants.

1.1 *Place of Study*

The study was conducted in the Cape metropolitan region (Western Cape) of South Africa, specifically in the Southern Suburbs of Cape Town (including Simonstown, Fish Hoek,

Muizenberg; Kirstenhof, Tokai, Claremont, Athlone, Ottery, Sea Point and Hout Bay) as well as the Winelands region (incorporating Stellenbosch, Paarl, Strand and Somerset West) from July 2014 to March 2015.

Participants in the EXP took part in the eight-week sensory-motor training programme at one of two similar venues in the Southern Suburbs of Cape Town. A church hall was used in the Fish Hoek area and a Scout hall in the Bergvliet area. Both halls had comparable wooden flooring. Eleven participants attended the venue in Fish Hoek and the remaining 17 in Bergvliet.

Testing sessions for the EXP took place in their homes. Testing for the PBO took place either in the participant's home or at the Stellenbosch University's Department of Sport Science. Participants were tested at the same location, at the same or similar time of day for all the testing sessions. One participant was an exception as he moved mid-way through the study and thus his subsequent two testing sessions were at different venues.

2. Participants

2.1 *Recruitment*

Ninety-six participants with PD were recruited by way of an invitation to support groups and care facilities in the Western Cape, as well as through newspaper articles which appeared in four local newspapers (Appendix C). However, only those areas which voluntarily responded to the research invitation were contacted for further possible recruitment. These areas were Kenilworth, Noordhoek, Blouberg, Panorama, Stellenbosch, Paarl, Hermanus and Helderberg Basin. The local newspapers were the Plainsman, False Bay Echo, Constantiaberg Bulletin and the Eikestad Nuus. The articles gave a brief introduction to the study as well as the contact details of the researchers for those interested in participating. Participants who showed interest during visits to the support groups were given additional information regarding the study and their contact details were taken.

Of the ninety-six people that responded to the various advertisements, 49 met the criteria for inclusion in the study and completed the informed consent forms (Appendix B). Thirty-one took part in the EXP and 18 in the PBO who wore the wristband. This ratio difference between the two groups was because the EXP and PBO were geographically located in different areas but with a similar socio-economic status (Development Information and GIS Department, 2014; Western Cape Government Provincial Treasury, 2014a, 2014b).

2.2 *Inclusion criteria*

In order to be eligible for inclusion in this study, participants needed to:

- Present with a clinical diagnosis of idiopathic PD. Diagnosis was confirmed by the participants' neurologist or primary care physician.
- Be rated between stages I and III (mild to moderate) as classified according to the Hoehn and Yahr Scale (Hoehn & Yahr, 1967; HY) (Appendix D) and have a functional status level of PD less than 59 on the motor subscale (part III; Martínez-Martín *et al.,* 2015) of the Movement Disorder Society-Unified PD Rating Scale (MDS-UPDRS).
- Be men and women aged between 50 and 85 years.
- Reside within a 70km radius of the Cape Metropole in the Western Cape and be responsible for their own transport to the sensory-motor training programme.
- Be able to stand tandem and perform dynamic balance activities without support for 30 seconds; customary walking aids were permitted such as crutches and walkers.
- Be on a stable medication programme (medication should not have been changed within four weeks of commencing the study). Participants remained on their medication during all testing and during the sensory-motor training programme.
- Have a Montreal Cognitive Assessment (MoCA) score of 18 and above. According to Hoops *et al.* (2009) a score of 27 to 30 is considered normal and 18 to 26 as mild cognitive impairment (MCI) (Hoops *et al*., 2009).

2.3 *Exclusion criteria*

Participants were excluded from this study for the following reasons:

- If they had a PD classification of stage 4 or 5 as classified according to the Hoehn and Yahr Scale (Hoehn & Yahr, 1967).
- If they had any neurological condition (e.g. stroke, diabetes with neuropathy) other than PD or vestibular problems.
- Moderate to severe mental health conditions, with a Montreal Cognitive Assessment (MoCA) score of 17 or less (Hoops *et al*., 2009).
- If they demonstrated moderate to severe depression throughout the study, which is indicated as less than 18 on the Hamilton Rating Scale for Depression questionnaire (Cusin *et al*., 2009).
- If they had any visual problems which could not be corrected through glasses or contact lenses. Participants who were colour blind would not be included for both the Wisconsin Card Sorting Test and the Adapted Stroop Task, since these two tests

require the participant to recognize colour. They were allowed to participate in the other tests.

- If they had sustained any orthopaedic or moderate to severe musculoskeletal injuries (needing the care of a medical practitioner) in the six months prior to the start of the study.
- If they were on any medication with adverse effects such as instability, dizziness and brain fogginess. In addition, individuals specifically on Rasagiline and Selegiline which may affect balance (Pescatello *et al*., 2014) as well as Rivastigmine and Amantadine that affect cognitive function were excluded (Pescatello *et al*., 2014). For the specific list of PD-related medications see Appendix E.
- In the PBO group, participants who did not wear their wristband for 24 hours a day were excluded.
- In the EXP group, participants who did not maintain a minimum attendance of 70% for the sensory-motor training programme sessions and/or missed more than two consecutive training sessions were excluded from the data analysis but were allowed to continue with the programme. A minimum attendance rate of 70% is in line with other studies on PD and EF (Tanaka *et al*., 2009).

2.4 *Sampling method*

Due to the nature of the intervention, the study population consisted of a convenience sample of idiopathic PD patients. However, sampling areas used had the same or similar socioeconomic status (Development Information and GIS Department, 2014; Western Cape Government Provincial Treasury, 2014a, 2014b).

2.5 *Sample size*

The Centre for Statistical Consultation (Stellenbosch University, South Africa) was consulted prior to the start of the research for *a priori* power analysis set at 0.80. The statistician performed a power analysis from pilot study data and determined that at least 14 participants per group would be required. However, the researcher was advised to recruit as many participants as possible because the study design was not randomized and the power analysis was calculated only on one outcome variable.

3. Ethical Approval

Ethical approval (proposal number HS1040/2014) was granted by the Departmental Ethical Screening Committee of the Sport Science Department (Stellenbosch University) as well as

the Research Ethical Committee: Human Research (Humanities) of Stellenbosch University (Appendix A). The *Declaration of Helsinki* was followed as an ethical conduct guide and the researcher and participants were familiarised with this prior to the start of the study.

4. Visits

4.1 *Pre-intervention Testing: Telephonic Session*

During the recruitment phase of the study, participants who indicated their interest were sent an informed consent form, a personal information form (Appendix F) and a session information sheet (Appendix G) via email or post. The personal information form asked for information pertaining to level of PD (if known), when they were diagnosed, medication, daily activities as well as specialist or doctor information. The session information sheet required them to indicate which three days of the week they would be able to attend, which time of the morning would be most suitable as well as the area most convenient for them. They were asked to complete these forms and return them via post or email. The participants using the postal service were sent a self-addressed, stamped envelope in which to return their completed forms.

The researcher telephoned participants who returned their forms and informed them whether they met the study criteria and were able to participate in the study.

During this discussion the researcher introduced herself to participants. The informed consent form was verbally read and explained and participants were given the opportunity to ask questions. Meeting the inclusion criteria and giving their informed consent verbally resulted in their inclusion in the study. During the first face-to-face visit the participants were asked if they had any further questions and to sign the written consent form. Participants were allowed to withdraw at any time and they were informed of this during every testing session. Only after informed consent was given did the researcher complete a brief health questionnaire, the general information and health form (Appendix H) with the participant. The participant was also asked questions about his or her physical activity status according to the General Practice Physical Activity Questionnaire (GPPAQ) and these answers were submitted on an online GPPAQ site and the generated activity status was recorded (Patient, 2011). The testing procedures and nature of the intervention were then explained to the participants in detail.

4.2 *Pre-Intervention Testing: First and Second Testing Sessions*

To avoid participant fatigue each testing session was split into two separate visits due to the number of questionnaires and cognitive tests that needed completion. During the first testing session, the informed consent form was checked to see that it had been completed correctly and that all signatures were in place. The participant was then given an additional opportunity to ask questions. After this, testing began with the recording of the participant's height and body mass. The following questionnaires were then completed with the participant: the 39-Item PD Questionnaire (PDQ-39) (Appendix I), the Activities-specific Balance Confidence Scale (ABC Scale) (Appendix J) and the Movement Disorder Society – Unified PD Rating Scale (MDS – UPDRS) which included the HY scale. The Timed Up and Go test completed the testing for this session. This session took approximately one hour to complete.

During the second testing visit, the Hamilton Rating Scale for Depression (Ham-D) (Appendix K) was completed. Following this, the researcher conducted the cognitive tests, namely the Montreal Cognitive Assessment (MoCA) (Appendix L) and the Trail Making Tests part A and part B (Appendix M) which are paper-based tests. The computer-based Wisconsin Card Sorting Test (WCST) and Adapted Stroop Task completed the testing battery. This session took approximately one hour to complete.

Participants were asked to remain on their medication for the duration of the study for ethical reasons. The logistics of testing everyone at the same time after an overnight withdrawal of medication was also beyond the scope of this study. Time of testing was recorded and re-testing was always performed at the same time or at least within an hour of the initial testing time to ensure consistency. If participants were fatigued or experienced a distressing event (such as a funeral or family-related stress) the testing was rescheduled as this may have influenced the results.

After the second visit participants were assigned to their intervention groups by the main researcher.

4.3 *Mid-intervention Testing: Third and Fourth Testing Sessions*

During this testing session with the participant, all of the questionnaires, cognitive tests and anthropometric tests which were conducted during the pre-intervention testing session were repeated. The tests were again split into two separate visits. The order of the tests remained

the same, and the same researcher collected the same data pre-, mid- and post-intervention.

4.4 *Post-intervention Testing: Fifth and Sixth Testing Sessions*

Again during this testing session with the participant, all of the questionnaires, cognitive tests and anthropometric tests which were conducted during the pre- and mid-intervention testing sessions were repeated. The tests were again split into two separate visits, the order of the tests and researcher collecting the data remained the same as previously noted.

5. Phases and Interventions

5.1 *Baseline Phase*

During the baseline phase, participants (in both the placebo and experimental groups) continued with their usual daily activities without any interference from the researcher for eight weeks. Participants were allowed to continue their normal activities, but were asked to refrain from adding additional structured physical activities (in other words, exercises).

5.2 *Treatment Phase*

The eight-week treatment phase included the sensory-motor training programme and placebo wristband interventions.

5.2.1 *Eight-week Sensory-motor Training Programme*

The sensory-motor training programme took place over eight consecutive weeks. Participants were required to attend morning sessions three times per week for the duration of the study. The duration of the sessions was 60 minutes and included a 10-minute warm-up and 10-minute cool-down period before and after the main sensory-motor training component, respectively. The same warm up and cool down activities were incorporated for all the sessions as a method to familiarise the participants. The focus of the exercise intervention was on neuromotor exercises (postural control and not strength, endurance and/or flexibility).

The sensory-motor training programme was generated using the principles and progressions developed by Janda (Page, 2006). The main sensory-motor focus of the intervention was through somatosensory simulation. Aman *et al.* (2014) explained that somatosensory training included proprioception and haptic feedback while receiving no or limited information from the visual and vestibular system (Aman *et al*., 2015). Aman *et al*.

(2015) also stated that these interventions should mainly focus on the improvement of proprioception and sensory-motor function. Each week of the sensory-motor training programme had a different aim and each session focused on a different objective, from posture, alignment and body awareness, to static, dynamic and functional balance activities (Appendix N). The programme became increasingly more challenging as the weeks progressed. Participants were instructed with verbal cues and allowed to use light touch during the sessions. Each session was led by at least one qualified biokineticist and at least one research assistant. Even though a predetermined programme was followed and completed by all participants, the biokineticist monitored each participant during the sessions and either allowed them to progress to the next activity or repeat if the activities were too difficult. The self-paced activities focused on the quality rather than the quantity for improved motor control. Participants were given a hand-out with safety guidelines (Appendix O) before the start of the sensory-motor training programme.

5.2.2 *Eight-week Placebo*

The placebo group wore an activity monitor (Pivotal Living^{TM}, Pivotal Corporation, U.S.A.) as illustrated in Figure 4.2., referred to as a feedback-wristband (placebo). The placebo was introduced to determine whether the results of the study were due to the exercise intervention itself. It was important to ensure that the results obtained were as a result of the treatment (in this case the sensory-motor training programme) rather than an expectation from the participants that the programme would work. The placebo group was blinded to the fact that the wristband was a placebo. They were informed that they were participating in a sensory-motor intervention, wearing a feedback-wristband and that when they saw the activity monitor they should sit and/or stand up straight, since the purpose of the band was to change their balance behaviour. The wristbands were actual activity monitors which were not activated so they looked authentic. The wristband had to be worn throughout the eight-week duration, including when sleeping or bathing/showering. Participants in the placebo group received a follow-up phone call from the researcher every fortnight and had to keep a weekly diary in which they reported on their mobility and balance. Motivation has been shown to have an influence on cognitive variables such as EF, thus the wristband served to keep them motivated in the same way as the sensory-motor training programme.

Figure 4.2 Placebo wristband worn by placebo group participants (photo by K Welman©)

During the treatment phase, participants continued with their usual daily activities regardless of whether they were in the placebo or experimental group. After the intervention the researcher disclosed to the PBO participants that the wristband was a placebo.

6. Procedures

In addition to collecting medical and personal information the following tests were also assessed at pre, mid and post-intervention, unless otherwise specified.

6.1 *Anthropometry*

6.1.1 *Height*

Stature was measured using the stretch stature method and a measuring tape (Siber-Hegner GPM, Switzerland) attached to the wall. Participants were barefoot and stood erect with their arms at their sides. They were instructed to look straight ahead and inhale deeply. The measurement was recorded as the maximum distance from the ground to the vertex of the head. The vertex of the head is the highest point on the skull when the head is placed in the Frankfort Plane. This position is attained when the imaginary line which joins the *orbitale* to the *tragion* is perpendicular to the body's long axis (De Ridder, 2005). Baseline height was measured in metres and recorded to the nearest 0.01 m.

6.1.2 *Body mass*

Body mass was measured using a portable electronic scale (Safeway® Scale, South Africa). Participants were weighed barefoot and with minimal clothing. They were instructed to stand in the centre of the scale with weight evenly distributed on both feet, and to look straight ahead as their weight was recorded. Before each measurement, the scale was zeroed and baseline body mass was recorded to the nearest 0.1 kg (De Ridder, 2005). Body mass index (BMI) for each participant was determined from their height and body mass measurements.

6.2 ***Secondary Outcome Variables***

6.2.1 *Global Cognition: Montreal Cognitive Assessment (MoCA)*

The Montreal Cognitive Assessment (MoCA) assesses global cognition (Nasreddine *et al*., 2005) and was created to be a more sensitive screening instrument for those presenting with mild cognitive complaints, in particular for those participants who score within the normal range for the Mini Mental State Examination (MMSE) (Nazem *et al*., 2009; Zadikoff *et al*., 2008; Nasreddine *et al*., 2005). Hoops *et al*. (2009) consider it to be a superior screening tool to the MMSE. In particular, the MoCA is considered to be more sensitive in identifying cognitive changes in the early stages of PD, specifically those with impairment of executive function (Chou *et al*., 2014). Dalrymple-Alford *et al*. (2010) concluded that the MoCA is able to successfully differentiate both dementia and MCI in PD (Dalrymple-Alford *et* al., 2010).

The MoCA is a 30 point test conducted on a single page. A result ≥ 26 is considered normal global cognitive ability (Nasreddine *et al*., 2005). Test-retest reliability is high (Pearson correlation coefficient = 0.92). The internal consistency is good (Cronbach α = 0.83 on standardized items). The test was conducted during the study with pen and paper. Each participant was asked to state whether they had completed 12 years of schooling and whether they had any additional training after school, as the MoCA assigns an additional point to those who have completed 12 or less years of education. This is to negate the effect of fewer years of education as a confounding variable. Participants could choose to perform the test in either English or Afrikaans.

6.2.2 *Parkinson's Disease Severity*

Hoehn and Yahr

The Hoehn and Yahr Staging Scale (HY) is the most frequently used global assessment for PD. The basis for this scale is the disability which results from impaired motor and balance

functions; however, it does not provide information on motor features or non-motor symptoms (Martínez- Martín *et al.*, 2015). It was initially designed to be a simple descriptive staging scale that furnished an estimate of PD clinical function, bringing together both deficits in function (disability) and objective signs (impairment). Although it was formulated as a five-point scale (1-5) in 1967 (Hoehn & Yahr, 1967), some studies have added 0.5 increments to a modified scale (Goetz *et al.*, 2004). The HY scale is simple in application, quickly completed, practical in both research and patient care, and it may be used by both specialist as well as those without expertise in movement disorders (Goetz *et al.,* 2004). Inter-rater reliability is documented as moderate to significant ranging from 0.44 to 0.71. Test-retest reliability has not been established (Goetz *et al*., 2004).

The current study made use of the original HY scale and not the modified version. Consequently, parkinsonian motor impairment was rated as unilateral (Stage 1) to bilateral disease (Stage 2) without balance difficulties, to the presence of postural instability (Stage 3), loss of physical independence (Stage 4), and being wheelchair- or bed-bound (Stage 5) (Goetz *et al*., 2004). A HY score < 3.0 is considered to be in the early stages of PD (Martínez-Martín *et al*., 2015; Siderowf *et al*., 2002).

Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS – UPDRS)

The original Unified PD Rating Scale (UPDRS) was created in the 1980s and has since become the most extensively used and tested PD clinical rating scale (Martínez- Martín *et al*., 2015; Goetz *et al*., 2008; Ramaker *et al*., 2002). In 2008, the revised Movement Disorder Society – Unified PD Rating Scale (MDS-UPDRS) was presented. This scale is considered to be more comprehensive than the previous version and devotes several new items to non-motor elements of PD (Goetz *et al*., 2008). The MDS-UPDRS is made up of four parts: Part I relates to the "non-motor experiences of daily living" (nM-EDL) while Part II concerns the "motor experiences of daily living" (M-EDL), Part III is the "motor examination" (ME) and Part IV involves "motor complications" (MC) and specifically assesses complications of therapy for participants treated with dopaminergic medications (Horváth *et al*., 2015). The MDS-UPDRS demonstrated high internal consistency across parts I-IV ranging from 0.79 to 0.93 as well as strong concurrent validity with the original UPDRS with a total score of r = 0.96 and scores ranging from 0.76 to 0.96 across parts I-IV (Goetz *et al*., 2008).

The participants in the study were asked to complete part II on their own or with the help of a caregiver, and for part I and IV they were asked to think back over the past 7 days and

then to answer the specific question. Part III was assessed by a qualified assessor. Harrison *et al*., (2009) suggest that the ADL (ADL) sub score on the UPDRS may be a better indication of disease progression than what is assessed in other sections of the UPDRS.

6.2.3 *Quality of Life: 39-Item Parkinson's Disease Questionnaire (PDQ-39)*

QOL was assessed through the use of the 39-Item PD Questionnaire (PDQ-39), which measures functioning and well-being in those with PD (Hagell *et al.*, 2003; Peto *et al.*, 1998). With regards to disease-specific questionnaires, the PDQ-39 is considered to be the most widely used rating scale in PD (Hagell & Nygren, 2007; Hagell *et al.*, 2003). The PDQ-39 contains 39 items covering eight discrete scales, namely: mobility, emotional well-being, ADL, stigma, social support, cognitions, communication and bodily discomfort. For each item on the scale, there are five possible options: never, occasionally, sometimes, often, always (or cannot do at all).

Participants in the study were asked to think back over the past month and answer each item according to the five possible answers. The higher the score, the lower the QOL. Hagnell and Nygren (2007) reported adequate score reliabilities (Cronbach's α = 0.72-0.95 and test-retest: 0.76-0.93) (Hagell & Nygren, 2007; Peto *et al*., 1998). This questionnaire was included to control for participants' perceived QOL, which may have an impact (confounding variable) on the executive function results.

6.2.4 *Depression: Hamilton Rating Scale for Depression (HAM-D)*

Depression was assessed using the Hamilton Rating Scale for Depression (HAM-D). Leentjens *et al.* (2000) found the Hamilton Rating Scale for Depression to be a good diagnostic instrument to measure depressive symptoms in PD patients. In the current investigation the HAM-D was not used for diagnosing depression but rather determining the feeling or mood of being depressed or disheartened. The HAM-D contains 17 items which consider depressive symptoms that the patient may have experienced over the past week. It was decided beforehand that if the researcher noticed excessive depressive moods and the participant acknowledged that he or she was experiencing some of these excessive depressive symptoms for most of the day, every day for more than two weeks, and/or rated on the HAM-D as severe depression, which is a score of 24 and above (Cusin *et al*., 2009), the researcher would refer the participant to a clinical psychologist. Signs of excessive depressive moods are listed in (Appendix P). Although, the HAM-D was originally meant to be completed after an unstructured interview, it is now usually administered following a semi-

structured interview guide and this is how it was conducted in the current study. Most clinicians accept the following cut-off scores regarding the HAM-D: 0 – 6 as no depression present; 7 to 17 as mild depression; 18 to 24 as moderate depression and any score above 24 as severe depression (Cusin *et al*., 2009). The 2011 meta-analysis of Trajković *et al*. (2011) reported internal consistency at 0.789, inter-rater reliability at 0.937 and test-retest reliability ranging from 0.65 to 0.98. The HAM-D is considered to be both a good screening and diagnostic instrument for depression (Leentjens *et al*., 2000). It was thus included in the study to control for participants' depressive mood which may have an impact (confounding variable) on EF as well as working memory (Harvey *et al*., 2004).

6.3 *Primary Outcome Variables*

6.3.1 *Executive Function*

Updating: Trail Making Test part A and part B

Updating was assessed using the Trail Making Test part B (TMT-B). The TMT comprises two different parts: TMT-A (part A) involves connecting consecutive numbers (1 to 25) by drawing a line. TMT-B (part B) involves connecting numbers and letters in a progressive alternating sequence (1-A-2-B) (Etnier & Chang, 2009). Participants performed one trial of each part, with a shorter sample trial for each part preceding it. Sanchez-Cubillo *et al*. (2009) while investigating the construct validity of the TMT, showed that while TMT-A requires predominantly visuo-perceptual abilities such as visual scanning and visuomotor speed, TMT-B reflects mainly working memory (also known as Updating) and secondly, task-switching ability. However, some researchers see Set shifting as the primary component to this test (Higginson *et al*., 2013; Liu-Ambrose *et al*., 2010; Periáñez *et al*., 2007; Arbuthnott & Frank, 2000).

In the study this test was conducted with pen and paper. Time taken to complete part A and B of the test was recorded separately and to the nearest 0.1 second. Although, errors committed were recorded, they were not reported on in this study. Most studies do not report on errors, as it is felt that the additional time taken to correct these errors is reflected in the overall score. Variables investigated were time to complete TMT A, time to complete TMT B, B-A (the difference score between TMT B and TMT A) and B/A (the ratio score). The difference score (B-A) is believed to minimize both visuo-perceptual abilities and working memory demands resulting in a truer reflection of executive control abilities (Sanchez-Cubillo *et al*., 2009). Test-retest reliability is 0.79 for TMT A and 0.89 for TMT B (Dikmen *et*

al., 1999). Interrater reliability was reported as 0.94 for TMT A and 0.90 for TMT B: both correlation coefficients are considered to be high (Fals-Stewart, 1992).

Set shifting: Wisconsin Card Sorting Test (WCST)

Set shifting was assessed using the Wisconsin Card Sorting Test (WCST) (Albinet *et al*., 2012; Miyake *et al*., 2000). This test was conducted only once on a laptop with a separate mouse (not a laptop mousepad). This test requires the participant to arrange cards based on one of three card characteristics, namely colour, number and form. The participant is reliant on examiner feedback regarding the correct sorting characteristic which is changed every 10 cards. The participant is required to identify the card characteristic and maintain this task set until instructed to change (Etnier & Chang, 2009). The variables investigated were: “categories completed” (CC), “perseverative responses” (PR), “failure to maintain set” (FTMS) and “total errors” (TE). The first two variables are the most commonly used measures of executive control in the WCST (Strauss *et al*., 2006). Categories completed (CC) refers to the number of categories the individual has correctly sorted, namely ten consecutive correctly sorted cards (Strauss *et al*., 2006). Perseverative responses (PR) refers to the number of times an individual continues (or persists) in responding to an incorrect card characteristic (Strauss *et al*., 2006). Failure To Maintain Set (FTMS) refers to a situation where an individual correctly sorts five or more consecutive cards, but then makes a mistake and fails to complete the category (Strauss *et al*., 2006). The FTMS assesses distractibility or the inability to maintain attention (Figueroa & Youmans, 2013; Barceló & Knight, 2002). Total Errors (TE) refers to the total number of errors that the participant makes during the WCST. A global score for the WCST was calculated using a formula proposed by Laiacona *et al.* (2000). This score is representative of overall WCST performance and is calculated as:

Global Score = [number of trials – (number of categories achieved X 10)]

It gives an estimation of the number of cards the participant actually used beyond the necessary minimum to complete the six categories. The score ranges from a theoretical perfect score of 0 to a worse-possible score of 128 (a better performance is indicated by a lower Global Score).

Paolo *et al*. (1995) showed construct validity for the WCST and recommended that it continue to be used as part of a complete neuropsychological evaluation for individuals with PD. This study showed a coefficient of congruence of 0.96 for the first factor, which included the variables number of categories completed, total number of errors, perseverative

responses and errors, and conceptual level response (the latter two were not assessed in the current study) and for the second factor, a coefficient of congruence of 0.71. The second factor comprised the variables number of trials to complete the first category, failure to maintain set and non-perseverative errors (only failure to maintain set was assessed in the current study) (Paolo *et al*., 1995).

Inhibition: Adapted Stroop Task

Inhibition (also known as cognitive inhibition or inhibitory control) was assessed using an adapted Stroop Task as used by Lucas *et al*. (2012). The version of the test used in this study had four conditions instead of the traditional three conditions. The first two conditions related to Choice Reaction Time (CRT), whereas the second two conditions related to interference (Incongruent 1 and Incongruent 2). Finally, an interference score was calculated using the 'new' formula proposed by Chafetz and Matthews (2004), which has been used in PD related studies (Damholdt *et al*., 2012), instead of the original 'Golden' formula proposed by Golden (1978). Chafetz and Matthews (2004) found the new formula to be more sensitive for clinical inferences: the predicted Colour-Word/ Interference Score (items 3 & 4 on adapted Stroop task) in 45 seconds can be calculated with $\frac{((216-W)\times C)}{(216-W)+C)}$; where' W 'represent the word or first congruent task (Reading) and 'C' the Colour or second congruent task (Naming) in the current study's methodology. The predicted interference score is then subtracted from the actual score achieved on the average incongruent trails.

During the test the participant had to complete 4 test conditions and received one practice trial. Participants could choose to perform the test in either English or Afrikaans. In the first condition, CRT 1 (Reading), the participant has to select the word which is the same as the stimulus word, thus reading. In the second condition, CRT 2 (Naming), the participant has to select the colour of a stimulus block, thus naming. In the third condition, Incongruent 1, the participant has to select the colour in which the stimulus word is written (the text is also a colour). Finally, in the fourth condition, Incongruent 2, the participant is again required to select the colour in which the stimulus word is written, but this time all words are in different colours. Cognitive performance was assessed for both speed and accuracy.

Many different versions of the Stroop task have been developed which vary with regard to colour, number of test items, number of subtests as well as administration method; however, the basis of the Stroop task has remained the same. Basic task performance (such as

reading names of colours) is compared to performance of a corresponding task in which a habitual response needs to be inhibited in aid of a different or unusual one (such as naming the text colour of a word rather than the meaning of this “colour” word). The Stroop Interference Effect refers to the increased time taken to do this when compared to the basic task (Van der Elst *et al*., 2006). In this test, the participant is required to inhibit a habitual response (Etnier & Chang, 2009). Interference scores for time and accuracy were calculated according to Chafetz and Matthews (2004).

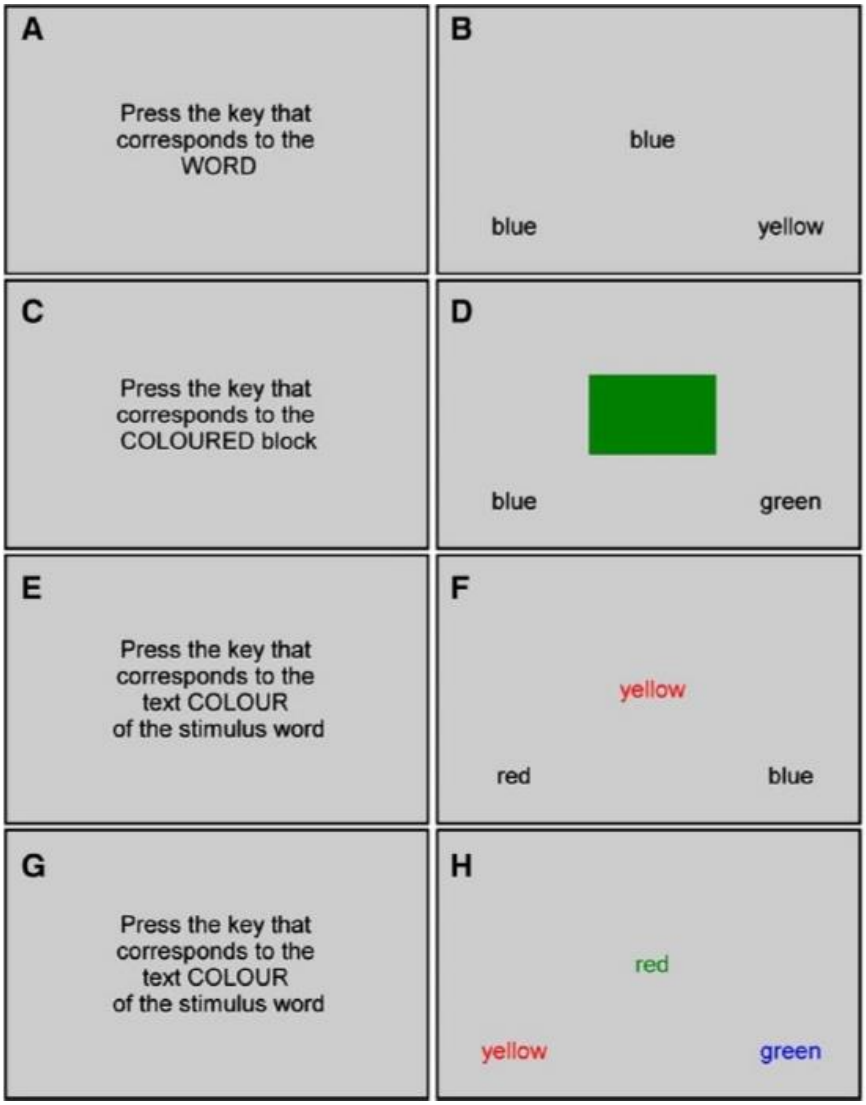


Figure 4.3 Adapted computer-based Stroop task from Lucas *et al.* (2012).

The Stroop task has been used in several studies on executive function (Albinet *et al*., 2012; Hsieh *et al*., 2008). In the current study this test was conducted on a laptop, using left and right arrow keys on the keyboard. Each participant was allowed two trials of the test and the best score was used from each condition. Mean response time and percentage correct responses were recorded. The Stroop Colour-Word Task assessed by Dikmen *et al*. (1999)

reported test-retest reliability as 0.84 for both Stroop I and II (interference) variables (Dikmen *et al*., 1999).

6.3.2 *Functional Balance*

Perceived Stability of Balance: Activities-specific Balance Confidence Scale (ABC Scale)

Perceived stability or balance was assessed using the Activities-specific Balance Confidence Scale (ABC questionnaire). The ABC Scale is used to assess balance confidence, which is particularly relevant in PD with fear of falling. This scale required participants to rate 16 ADLs according to the confidence they had in completing the activity without falling. Designed to detect loss of confidence in balance for individuals of varying functional levels, the scale includes activities that challenge postural control such as walking and reaching activities, as well as indoor and outdoor activities. The scale ranges from 0% (no confidence) to 100% (complete confidence) (Adkin *et al*., 2003). Internal consistency of the ABC has been reported as ranging between 0.80 and 0.98 and test-retest reliability values ranging from 0.70 to 0.92 (Lohnes & Earhart, 2010; Steffen & Seney, 2008). When comparing fallers and non-fallers, Lajoie and Gallagher (2004) showed that the overall ABC score of fallers was significantly lower.

Mobility: Timed Up and Go Test (TUG)

Mobility was assessed using the Timed Up and Go Test (TUG). The TUG test is used to assess lower extremity function and mobility in older adults, specifically balance, walking ability and fall risk (Donoghue *et al*., 2012; Herman *et al*., 2011). In addition, Donoghue *et al.* (2012) reported that a slower TUG time is associated with poorer memory, EF and processing speed. Other researchers have also shown a relationship between TUG and cognitive performance in PD (Stegemöller *et al*., 2014).

The TUG test requires a participant to stand up from a seated position on a standard chair, walk 3 metres at a comfortable pace, turn around and return to a seated position in the chair. Time taken is measured in seconds and recorded to the 0.01 s (Donoghue *et al*., 2012, Herman *et al*., 2011, Morris *et al*., 2001). Interrater reliability for the TUG is high with intraclass correlation coefficients (ICC) ≥ to 0.80 (Huang *et* al., 2011; Morris *et al*., 2001). Pearson correlation coefficients for retest reliability range from 0.73 to 0.99 (Huang *et al*., 2011; Morris *et al*., 2001).

7. Statistical Analysis

Descriptive statistics are reported as percentages, frequencies, mean ($\bar{x}$) and standard deviation (SD), unless otherwise specified. For all primary and secondary outcome variables, if normality was demonstrated with a Shipiro-Wilks test, a multi-factorial ANOVA (3 x 2) was conducted to compare the group, time and treatment effect. Non-normally distributed data was log transformed, and again assessed for normality, before a multi-factorial ANOVA was also performed. For a post-hoc analysis the Fisher Exact LSD test was used at individual time points. Ordinal data which did not satisfy parametric assumptions was assessed with the Mann–Whitney U-test (between groups) and Wilcoxon signed rank test (over time in a group). For categorical data the Fisher Exact test was used. The alpha level was set as 5%.

CHAPTER FIVE

RESULTS

1. Participants

In total ninety-six people responded to the newspaper articles, support group talks and information left at medical practices. These prospects were sent additional information regarding the study including a personal information form. Sixty-seven participants completed and returned this form.

In the EXP group, 46 participants were allocated to take part in the sensory-motor training programme. Three did not meet the inclusion criteria for the study, seven had problems with transportation (lived too far away or were reliant on others for transport, for example), three were going away on holiday or for business during the testing and / or treatment phase and two did not proceed due to personal reasons. Of the remaining 31, only 25 (16 men, 9 women) were included in the final data analysis. Three participants fell below the required 70% attendance, one participant had a bad fall prior to beginning the intervention (which was unrelated to the research), another participant stopped coming and was uncontactable and the sixth participant could not keep up with his session attendance due to clashes with his work.

Twenty-one participants were allocated to the PBO group, three of whom did not meet the inclusion criteria: one presented with moderate cognitive impairment (MoCA score of 14) and could not complete the cognitive component of testing (this participant also scored 4 on the Hoehn and Yahr scale) and the other two both scored 4 on the Hoehn and Yahr scale. Out of the remaining 18, only 17 (8 men, 9 women) were included in the final data analysis as one participant felt unmotivated to complete the last 3 weeks of the study and withdrew. This participant also indicated severe depression on the Hamilton Rating Scale for Depression (HAM-D) and was referred to a clinical psychologist as well as her neurologist for assessment and treatment. Two of the included participants were colour blind, and could not complete the Stroop and Wisconsin Card Sorting (WCST) tests. They were able to complete the other cognitive tests, however, and were included for statistical analysis.
Eighty-four percent (n = 21) of participants in the EXP (14 men, 7 women) and 88% (n = 15) of participants in the PBO (7 men, 8 women) had more than 12 years of education.

The results of the General Practice Physical Activity Questionnaire (GPPAQ; Figure 5.1) revealed that half of the participants in the EXP group indicated that they were inactive, 21% indicated that they were moderately active, 17% said that they were moderately inactive and just 13% of the EXP indicated that they were active, with one participant not completing the section on activity status. In the PBO group, none of the participants indicated that they were active. Sixty-five percent rated themselves as inactive, 24% as moderately active and 12% as moderately inactive. There was no significant difference between the two groups in terms of physical activity status ($p = 0.53$).

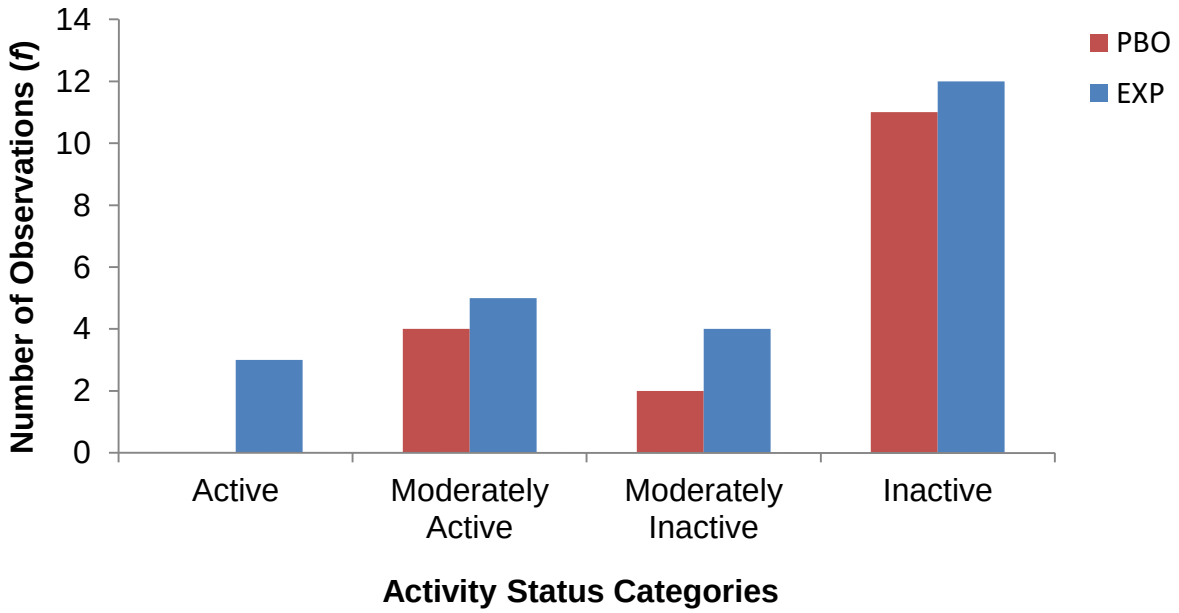


Figure 5.1 Self-reported activity status (frequencies; *f*).

Tables 5.1 – 5.3 summarize the descriptive and baseline characteristics of all the participants at pre-intervention.

At pre-assessment the baseline descriptive characteristics (Table 5.1) for HY, MDS-UPDRS I, III & IV and HAM-D, differed significantly between the two groups ($p \leq 0.05$).

The two groups showed no statistically significant difference for the 39-Item Parkinson's Disease Questionnaire at the pre-intervention assessment for QOL (Table 5.2).

Table 3 summarises the EF variables between the two groups at pre-intervention, with the EXP showing significantly worse WCST PR scores as well as faster reaction time during Incongruent 2 trials and in the Interference score ($p < 0.05$).

Table 5.1 Pre-intervention descriptive characteristics for the EXP and PBO groups as mean ($\bar{x}$) ± standard deviation (SD) and range.

Characteristics	EXP (n=25)	Range	PBO (n=17)	Range	p value
Age (y)	66 ± 8	50 – 79	71 ± 9	49 – 83	p = 0.057
Height (m)	1.67 ± 0.1	1.50 – 1.89	1.67 ± 0.1	1.48 – 1.79	p = 0.97
Body mass (kg)	80.8 ± 17.2	52.0 – 126.7	79.0 ± 17.6	47.0 – 106.3	p = 0.75
BMI ($kg.m^{-2}$)	28.8 ± 6.0	21.1 – 43.6	28.1 ± 5.8	19.7 – 40.0	p = 1.00
MoCA	24 ± 3	19 – 30	24 ± 3	17 – 30	p = 0.89
HY	2.3 ± 0.6 (Med = 2.5)	2.0 – 3.0	1.9 ± 0.7 (Med = 2)	1.0 – 3.0	p = 0.01*
MDS-UPDRS I	3.4 ± 2.3	0 – 9	11.4 ± 5.0	3 – 19	p < 0.001*
MDS-UPDRS II	13.0 ± 6.0	2 – 28	10.2 ± 5.6	2 – 23	p = 0.22
MDS-UPDRS III	31.9 ± 14.3	6 – 53	22.5 ± 10.0	7 – 45	p = 0.02*
MDS-UPDRS IV	4.5 ± 3.9	0 – 17	1.9 ± 2.1	0 – 7	p = 0.003*
MDS-UPDRS Total	52.1 ± 22.1	17 – 88	45.9 ± 18.6	16 – 85	p = 0.41
HAM-D	5 ± 3	0 – 13	8 ± 4	2 – 14	p < 0.001*
ABC	74.1 ± 19.9	41.5 – 100	65.6 ± 23.9	20.6 – 93.1	p = 0.07
TUG (s)	11.3 ± 3.4	5.8 – 18.3	11.7 ± 4.9	8.0 – 26.9	p = 0.71

BMI: Body Mass Index; MoCA: Montreal Cognitive Assessment; HY: Hoehn and Yahr Scale; Med: Median; MDS-UPDRS: Movement Disorder Society – Unified Parkinson's Disease Rating Scale; HAM-D: Hamilton Rating Scale for Depression; ABC: Activities-specific Balance Confidence Scale; TUG: Timed Up and Go; y: years; m: metres; kg: kilogrammes; s: seconds; * $p \leq 0.05$

Table 5.2 Pre-intervention QOL assessment for the EXP and PBO groups as mean ($\bar{x}$) ± standard deviation (SD) and range.

Domains	EXP (n=25)	Range	PBO (n=17)	Range	p value
PDQ MOB (%)	21.3 ± 21.8	0 – 75	27.8 ± 27.0	3 – 93	p = 0.23
PDQ ADL (%)	25.0 ± 21.1	0 – 79	20.8 ± 18.9	0 – 67	p = 0.74
PDQ EMO (%)	25.3 ± 16.6	4 – 63	23.5 ± 22.5	0 – 67	p = 0.59
PDQ STI (%)	14.3 ± 13.7	0 – 44	12.1 ± 20.8	0 – 75	p = 0.39
PDQ SOC (%)	10.8 ± 14.0	0 – 50	9.8 ± 18.0	0 – 58	p = 0.49
PDQ COG (%)	22.7 ± 17.2	0 – 63	21.3 ± 18.1	0 – 63	p = 0.71
PDQ COM (%)	28.8 ± 21.4	0 – 83	19.1 ± 16.1	0 – 67	p = 0.22
PDQ BOD (%)	34.7 ± 22.5	0 – 92	35.8 ± 26.6	8 – 83	p = 0.69

PDQ: 39-Item Parkinson's Disease Questionnaire; MOB: Mobility; ADL: Activities of Daily Living; EMO: Emotional being; STI: Stigma; SOC: Social support; COG: Cognitions; COM: Communication; BOD: Bodily discomfort; * $p < 0.05$

Table 5.3 Pre-intervention EF characteristics for the EXP and PBO groups as mean ($\bar{x}$) ± standard deviation (SD) and range.

Variables	EXP (n=25)	Range	PBO (n=17)	Range	p value
TMT A (s)	55.6 ± 21.2	26.3 – 97.7	52.7 ± 32.5	24.2 – 143.3	p = 0.83
TMT B (s)	145.5 ± 77.1	64.3 – 345.5	169.0 ± 151.5	51.6 – 677.0	p = 0.93
TMT B / TMT A	2.6 ± 1.0	1.6 – 5.7	3.3 ± 2.4	1.6 – 9.7	p = 0.30
TMT B – TMT A	89.8 ± 63.3	24.0 – 285.2	116.2 ± 138.6	23.7 – 601.2	p = 0.82
WCST Global Score	106 ± 16	68 - 128	98 ± 78	10 - 118	p = 0.11
WCST CC	2.2 ± 1.6	0 – 6	3.0 ± 1.0	1 – 5	p = 0.18
WCST PR	9.4 ± 8.3	0 – 31	17.5 ± 6.5	6 – 25	p = 0.004*
WCST FTMS	1.4 ± 1.6	0 – 5	0.5 ± 0.7	0 – 2	p = 0.38
WCST TE	60.0 ± 16.2	13 – 87	66.3 ± 9.4	43 – 76	p = 0.22
CRT 1: Reading Time (s)	1.5 ± 0.3	1.1 – 2.1	2.2 ± 2.2	0.9 – 10.2	p = 0.16
CRT 1: Reading Accuracy (%)	99.5 ± 1.8	91.7 – 100	99.3 ± 2.2	91.7 – 100	p = 0.82
CRT 2: Naming Time (s)	1.5 ± 0.3	1.2 – 2.1	2.1 ± 2.3	0.9 – 10.3	p = 0.26
CRT 2: Naming Accuracy (%)	99.2 ± 2.1	91.7 – 100	98.1 ± 4.1	87.5 – 100	p = 0.29
Incongruent 1: Time (s)	2.7 ± 0.9	1.7 – 4.8	3.6 ± 3.1	1.6 – 14.1	p = 0.31
Incongruent 1: Accuracy (%)	93.8 ± 7.0	79.2 – 100	92.5 ± 11.4	58.3 – 100	p = 0.48
Incongruent 2: Time (s)	2.8 ± 0.9	1.9 – 5.1	4.5 ± 3.4	2.1 – 15.3	p = 0.005*
Incongruent 2: Accuracy (%)	90.8 ± 11.5	54.2 – 100	86.4 ± 14.9	58.3 – 100	p = 0.13
Interference Score: Time (s)	1.3 ± 0.7	0.5 – 2.9	1.9 ± 1.1	1.0 – 4.8	p = 0.003*
Interference Score: Accuracy (%)	38.7 ± 8.5	13.0 – 47.5	36.2 ± 11.0	11.1 – 46.3	p = 0.26

TMT: Trail Making Test; WCST: Wisconsin Card Sorting Test; CC: Categories Completed; PR: Perseverative Responses; FTMS: Failure To Maintain Set; TE: Total Errors; CRT: Choice Reaction Time; s: seconds; * $p < 0.05$

2. Secondary Outcome Variables

2.1 *Global Cognition: Montreal Cognitive Assessment (MoCA)*

There was no significant treatment effect (Assessment x Group) (p = 0.10), nor difference between EXP and PBO over the time points – pre- (p = 0.89) and mid-intervention (p = 0.49) for the MoCA. However, there was a weak tendency for EXP and PBO to differ at post-intervention (p = 0.09). There was a significant difference from pre- to mid-intervention (p = 0.001) and pre- to post-intervention (p < 0.001) in EXP, which can be seen in Figure 5.2. There was no significant difference from pre- to mid-intervention (p = 0.12) and mid-to post-intervention in PBO (p = 0.82). Both EXP and PBO did not change significantly from mid- to post-intervention (p > 0.05).

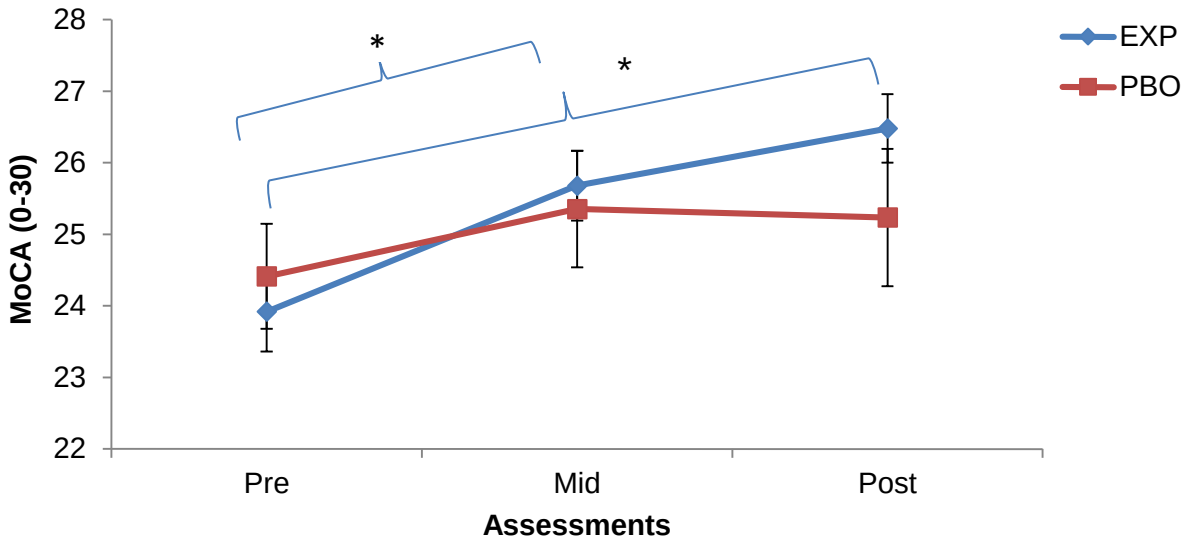


Figure 5.2 Overall global cognition (MoCA) between EXP and PBO over 16 weeks ($\bar{x}$ ± SEM). * p ≤ 0.05

2.2 *Parkinson's Disease Severity*

2.2.1 *Hoehn and Yahr (HY)*

No treatment effect (Assessment x Group) was observed for HY for the EXP (p = 0.65) nor PBO (p = 0.43). In addition, there was a significant difference between EXP and PBO at pre- (p = 0.01) and mid-intervention (p = 0.002). There was no significant difference observed at post-intervention between EXP and PBO (p = 0.18). There was no significant change over time in EXP (pre- to mid-, mid- to post- or pre- to post-intervention, p > 0.05) or in PBO (pre- to mid-, mid- to post- or pre- to post-intervention, p > 0.05). Although not significant, PBO severity deteriorated by 15% from mid- to post-intervention (p < 0.01) and overall by 15% from pre- to post-intervention (p < 0.01) as shown in Figure 5.3.

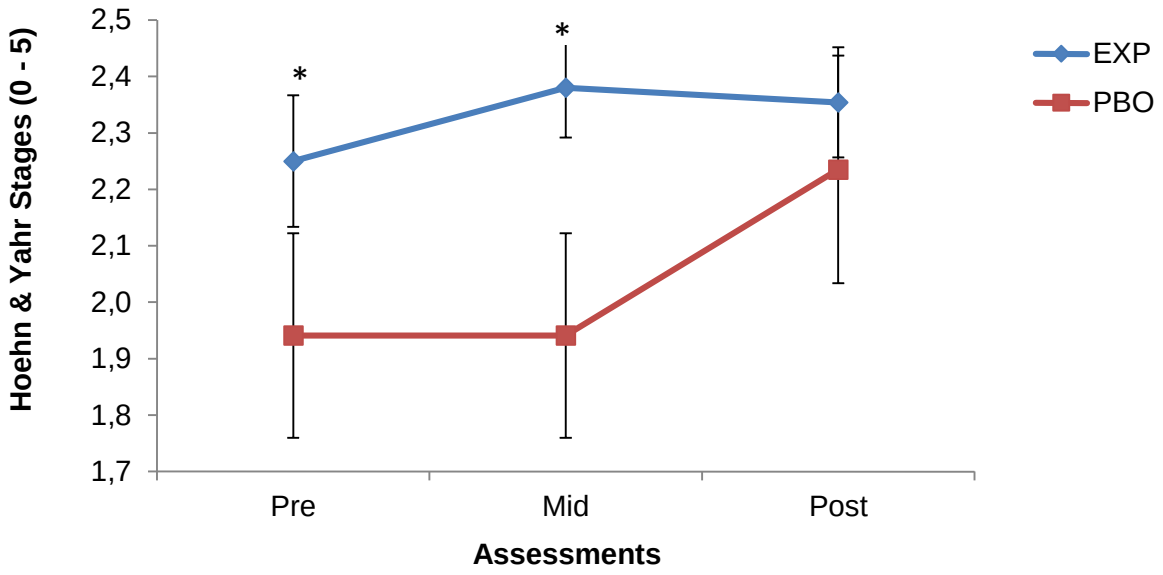


Figure 5.3 Overall Hoehn and Yahr (HY) classification between EXP and PBO over 16 weeks ($\bar{x}$ ± SEM). * $p \leq 0.05$

2.2.2 *Movement Disorder Society – Unified Parkinson's Disease Rating Scale (MDS – UPDRS)*

There was no significant treatment effect (Assessment x Group) for MDS-UPDRS I ($p = 0.31$), MDS-UPDRS II ($p = 0.22$) or MDS-UPDRS IV ($p = 0.94$). There was, however, a significant treatment effect (Assessment x Group) for MDS-UPDRS III ($p < 0.01$) as well as for the total MDS-UPDRS score ($p = 0.02$). Table 5.4 summarizes the MDS-UPDRS data for MDS-UPDRS I to IV and Total. Figure 5.4 illustrates the change over time for MDS-UPDRS II. There was no significant difference between EXP and PBO at pre-, mid- or post-intervention ($p > 0.05$). There was, however, a significant change in EXP from mid- to post-intervention ($p = 0.04$), indicating an improvement in motor experiences of daily living (M-EDLs) for the EXP. There was no significant change in EXP, from pre- to mid- or pre- to post- intervention ($p > 0.05$), or in PBO, from pre- to mid-, mid- to post- and pre- to post-intervention ($p > 0.05$).

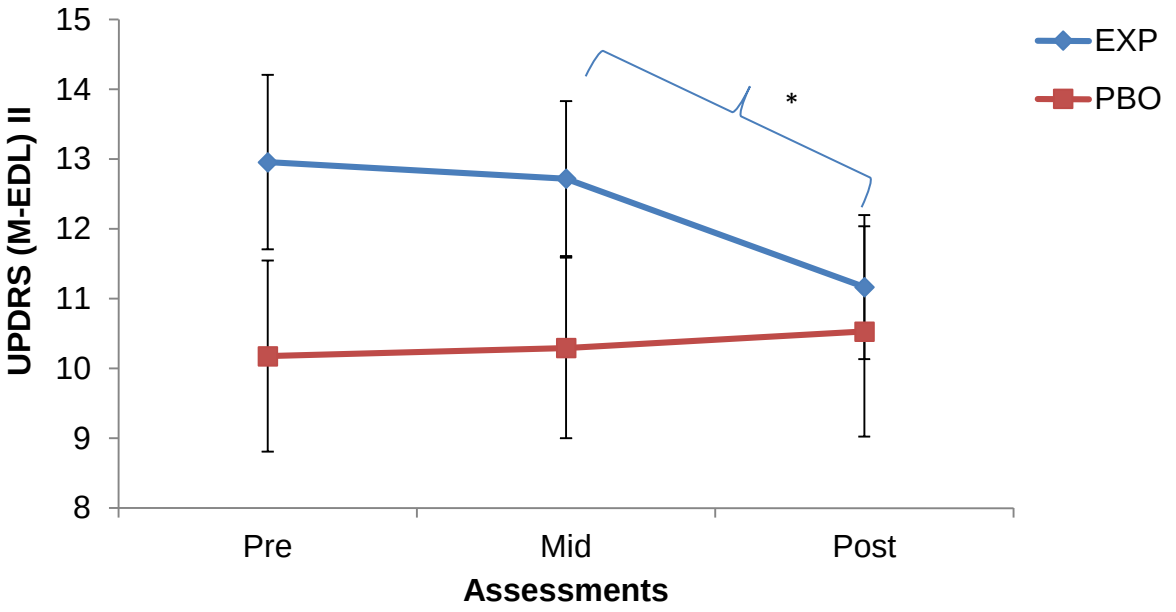


Figure 5.4 MDS-UPDRS subscale II (M- EDL) between EXP and PBO over 16 weeks ($\bar{x}$ ± SEM). * p = 0.04

There was a significant difference between EXP and PBO at pre-intervention (p = 0.02), but no significant difference between EXP and PBO at mid- (p = 0.09) or post-intervention (p = 0.50) for MDS-UPDRS III motor subscale. There was no significant change over time in EXP (pre- to mid-, mid- to post- and pre- to post-intervention EXP, p > 0.05).

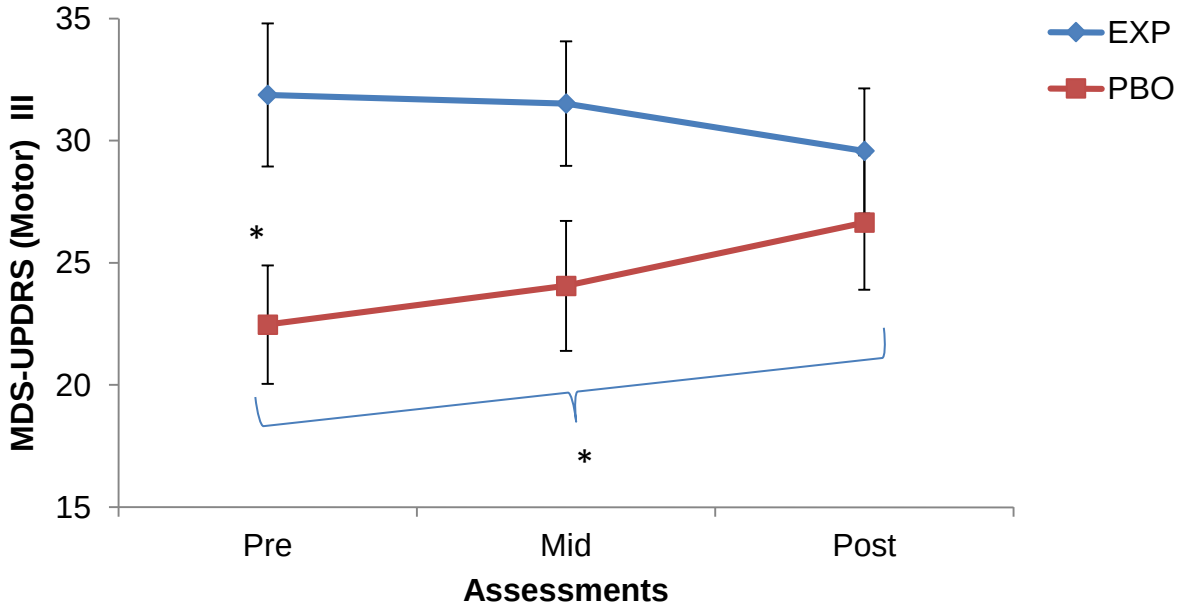


Figure 5.5 MDS-UPDRS III (ME) between EXP and PBO over 16 weeks ($\bar{x}$ ± SEM). *p < 0.05

There was no change in the PBO group from pre to mid-intervention (p = 0.29), however, Figure 5.5 reveals a significant deterioration from pre- to post-intervention in PBO (p = 0.007), as well as a tendency from mid- to post-intervention (p = 0.09) in the direction of increased PD severity for motor functioning.

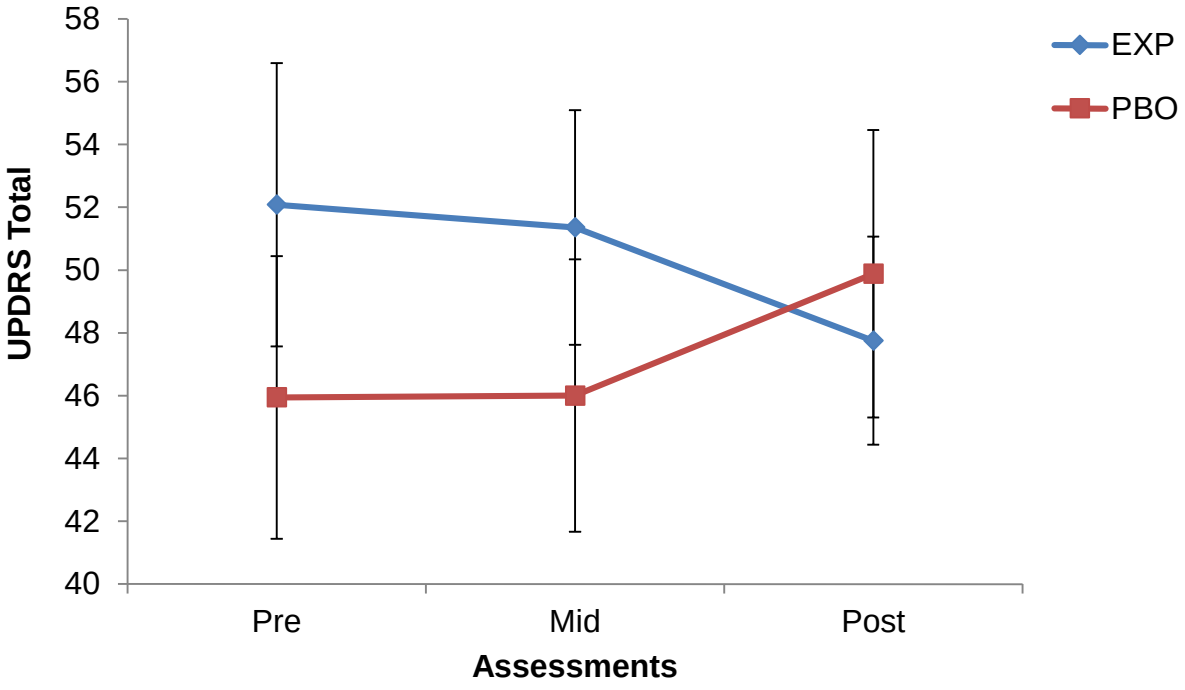


Figure 5.6 Total MDS-UPDRS between EXP and PBO over 16 weeks ($\bar{x}$ ± SEM).

For the Total MDS-UPDRS score there was no significant difference between EXP and PBO over any of the time points – pre- (p = 0.41), mid- (p = 0.42) or post-intervention (p = 0.71). There was no significant change over time in EXP (pre- to mid-, mid- to post- and pre- to post-intervention EXP, p > 0.05). Although PBO did not change from pre- to mid-intervention (p = 0.97), there was a non-significant 8% and 9% deterioration from mid- to post- (p = 0.07) and pre- to post-intervention (p = 0.07), respectively. This change in PBO is depicted in Figure 5.6. Additional post-hoc analysis revealed a 4% difference only at post-intervention between the groups (p = 0.71).

Table 5.4 Summary of MDS-UPDRS data over 16 weeks reported as mean ($\bar{x}$) ± standard deviation (SD), with (range).

Variable	EXP (n = 25)[a]			PBO (n = 17)[b]			p value
Assessments	**Pre[1]**	**Mid[2]**	**Post[3]**	**Pre[1]**	**Mid[2]**	**Post[3]**	
MDS-UPDRS I	3.4 ± 2.3 (0 – 9)	3.5 ± 2.4 (0 – 9)	3.8 ± 1.7 (1 – 7)	11.4 ± 5.0 (3 – 19)	10.5 ± 4.6 (4 – 19)	11.4 ± 5.1 (4 – 22)	$p < 0.001^{a1 \text{ vs } b1}$ $p < 0.001^{a2 \text{ vs } b2}$ $p < 0.001^{a3 \text{ vs } b3}$
MDS-UPDRS II	13.0 ± 6.0 (2 – 28)	12.7 ± 5.5 (3 – 22)	11.2 ± 5.1 (2 – 20)	10.2 ± 5.6 (2 – 23)	10.3 ± 5.3 (2 – 19)	10.5 ± 6.2 (2 – 24)	$p = 0.04^{a2 \text{ vs } a3}$
MDS-UPDRS III	31.9 ± 14.3 (6 – 53)	31.5 ± 12.7 (10 – 56)	29.6 ± 12.5 (6 – 54)	22.5 ± 10.0 (7 – 45)	24.1 ± 11.0 (6 – 50)	26.6 ± 11.3 (10 – 56)	$p = 0.007^{b1 \text{ vs } b3}$
MDS-UPDRS IV	4.5 ± 3.9 (0 – 17)	3.6 ± 3.5 (0 – 17)	3.3 ± 1.7 (1 – 7)	1.9 ± 2.1 (0 – 7)	1.1 ± 1.7 (0 – 7)	1.4 ± 1.4 (0 – 5)	$p = 0.003^{a1 \text{ vs } b1}$ $p = 0.003^{a3 \text{ vs } b3}$
MDS-UPDRS Total	52.1 ± 22.1 (17 – 88)	51.4 ± 18.7 (19 – 80)	47.8 ± 16.2 (18 – 71)	45.9 ± 18.6 (16 – 85)	46.0 ± 17.9 (18 – 84)	49.9 ± 18.9 (16 – 97)	$p > 0.05$

MDS-UPDRS: Movement Disorder Society – Unified Parkinson's Disease Rating Scale; [a] EXP (Experimental group); [b] PBO (Placebo group); [1] Pre-testing; [2] Mid-testing; [3] Post-testing

2.3 *Quality of Life: 39-Item Parkinson's Disease Questionnaire (PDQ-39)*

There was no significant treatment effect (Assessment x Group) for any of the PDQ-39 domains ($p > 0.05$), although there was a tendency for a treatment effect ($p = 0.07$) with Mobility (MOB). Table 5.5 summarizes the variables for the PDQ-39. Mobility (MOB) changed by 13% from pre- to mid-intervention PBO and demonstrated a tendency for significance ($p = 0.053$). Emotional Being (EMO) showed a significant 21% decrease from pre- to post-intervention EXP ($p = 0.04$) and a 31% decrease from pre- to mid-intervention PBO ($p = 0.03$). Stigma (STI) was significant from mid- to post-intervention EXP ($p = 0.01$) demonstrating a 35% reduction between the two time points. Communication (COM) was significant between EXP and PBO at mid-intervention ($p = 0.047$) where the two groups differed by 50%. Bodily Discomfort (BOD) was significant between EXP and PBO at post-intervention ($p = 0.04$) with a 49% difference between the two groups.

Table 5.5 Summary of PDQ-39 (%) domains over 16 weeks reported as mean ($\bar{x}$) ± standard deviation, with (range).

Variable	EXP (n = 25)[a]			PBO (n = 17)[b]			p value
Assessments	**Pre[1]**	**Mid[2]**	**Post[3]**	**Pre[1]**	**Mid[2]**	**Post[3]**	
MOB	21.3 ± 21.8 (0 – 75)	21.4 ± 24.4 (0 – 75)	18.5 ± 22.5 (0 – 75)	27.8 ± 27.0 (3 – 93)	24.1 ± 24.7 (0 – 93)	23.1 ± 20.3 (0 – 60)	p = 0.053[b1 vs b2]
ADL	25.0 ± 21.1 (0 – 79)	20.0 ± 18.2 (0 – 58)	16.8 ± 13.7 (0 – 46)	20.8 ± 18.9 (0 – 67)	17.9 ± 25.3 (0 – 100)	21.9 ± 15.7 (4 – 54)	p > 0.05
EMO	25.3 ± 16.6 (4 – 63)	25.3 ± 20.0 (0 – 83)	20.0 ± 18.3 (0 – 63)	23.5 ± 22.5 (0 – 67)	16.2 ± 16.2 (0 – 58)	17.7 ± 19.4 (0 – 63)	p = 0.04[a1 vs a3] p = 0.03[b1 vs b2]
STI	14.3 ± 13.7 (0 – 44)	17.2 ± 5.6 (0 – 69)	11.2 ± 13.7 (0 – 50)	12.1 ± 20.8 (0 – 75)	14.7 ± 22.4 (0 – 63)	11.3 ± 17.6 (0 – 69)	p = 0.01[a2 vs a3]
SOC	10.8 ± 14.0 (0 – 50)	10.4 ± 15.4 (0 – 50)	8.3 ± 13.7 (0 – 50)	9.8 ± 18.0 (0 – 58)	9.3 ± 17.4 (0 – 67)	7.3 ± 12.9 (0 – 42)	p > 0.05
COG	22.7 ± 17.2 (0 – 63)	23.2 ± 16.5 (0 – 69)	23.7 ± 14.0 (0 – 44)	21.3 ± 18.1 (0 – 63)	19.5 ± 17.2 (0 – 63)	20.7 ± 14.6 (6 – 50)	p > 0.05
COM	28.8 ± 21.4 (0 – 83)	26.0 ± 17.1 (0 – 58)	21.5 ± 14.3 (0 – 50)	19.1 ± 16.1 (0 – 67)	15.7 ± 17.6 (0 – 58)	17.7 ± 18.0 (0 – 58)	p = 0.047[a2 vs b2]
BOD	34.7 ± 22.5 (0 – 92)	26.4 ± 20.4 (0 – 67)	25.0 ± 18.6 (0 – 83)	35.8 ± 26.6 (8 – 83)	35.3 ± 24.4 (0 – 83)	41.1 ± 25.2 (8 – 92)	p = 0.04[a3v s b3]

ADL: Activities of Daily Living; BOD: Bodily Discomfort; EMO: Emotional being; STI: Stigma; SOC: Social support; COG: Cognitions; COM: Communication; BOD: Bodily discomfort. [a] EXP (Experimental group); [b] PBO (Placebo group); [1] Pre-testing; [2] Mid-testing; [3] Post-testing

2.4 *Depression: Hamilton Rating Scale for Depression (HAM-D)*

There was no significant treatment effect (Assessment x Group) for HAM-D ($p = 0.42$). The two groups, EXP and PBO, were significantly different at each of the three time points: pre- ($p < 0.001$), mid- ($p < 0.001$) and post-intervention ($p < 0.001$) as is illustrated in Figure 5.7 Additional analysis revealed the two groups differed from each other at each time point by 52% at pre-, 69% at mid- and 77% at post-intervention. Over the 16 weeks the EXP group reported an average rating of 5 ± 3 and the PBO of 9 ± 4 for depressive mood ($p < 0.01$). There was no significant change in time over EXP (pre- to mid-, mid- to post- and pre- to post-intervention EXP, $p > 0.05$) or PBO (pre- to mid-, mid- to post- and pre- to post-intervention PBO, $p > 0.05$).

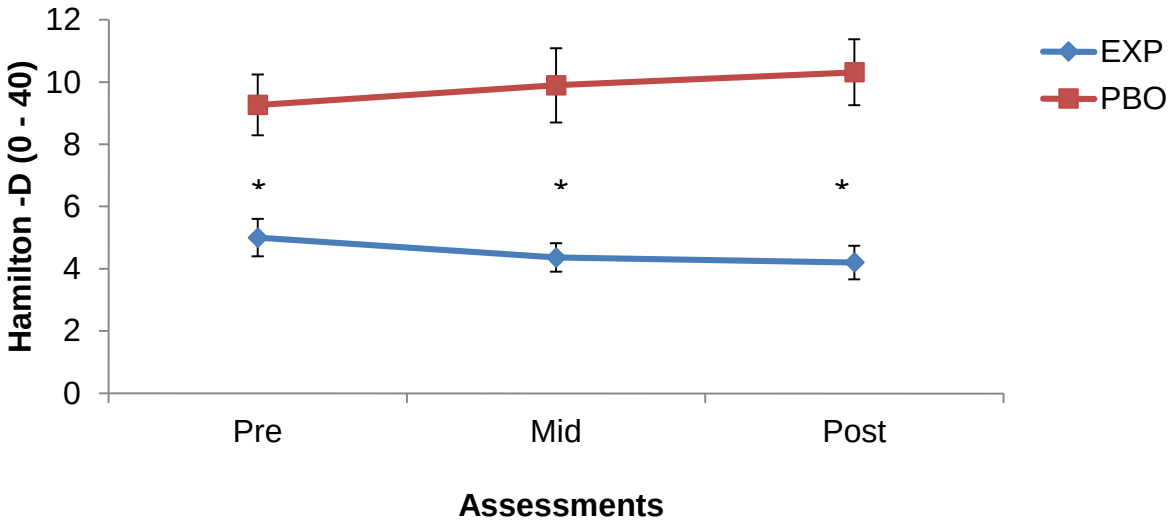


Figure 5.7 Hamilton Rating Scale of Depression (HAM-D) between EXP and PBO over 16 weeks ($\bar{x}$ ± SEM). * $p < 0.001$.

3. Primary Outcome Variables

3.1 *Executive Function*

3.1.1 *Updating: Trail Making Test (TMT) part A (TMT A) and part B (TMT B)*

A significant treatment effect (Assessment x Group) was observed for TMT A ($p < 0.0001$) but not for TMT B, TMT B / TMT A or TMT B – TMT A ($p > 0.05$). At post intervention PBO and EXP differed significantly ($p = 0.03$) as can be seen in Figure 5.8. The PBO showed a significant increase in time to complete TMT A from pre- to post-intervention ($p = 0.02$), while EXP remained constant in their times.

*

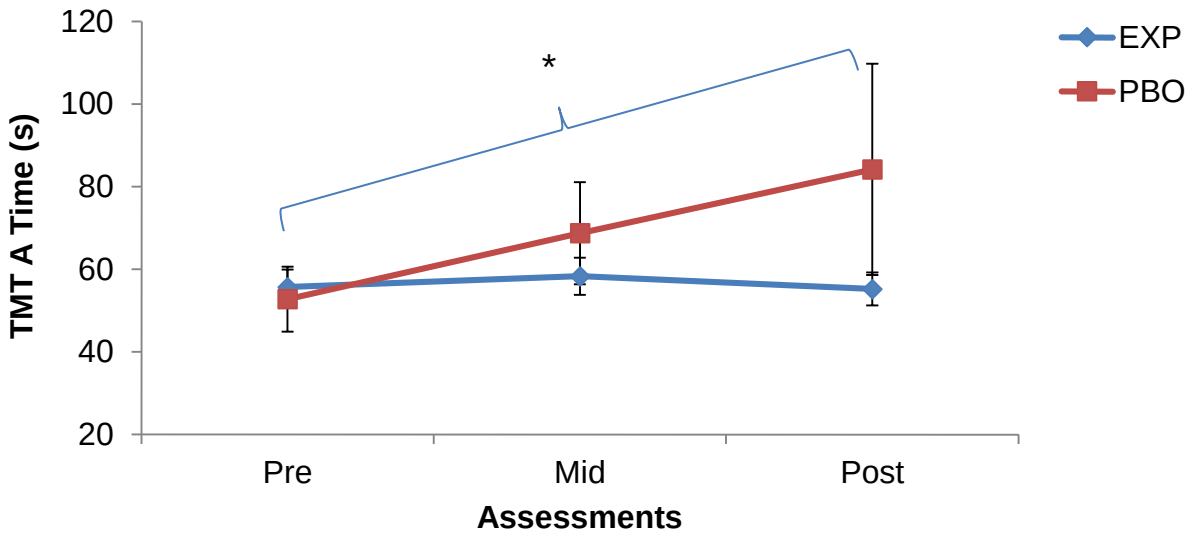
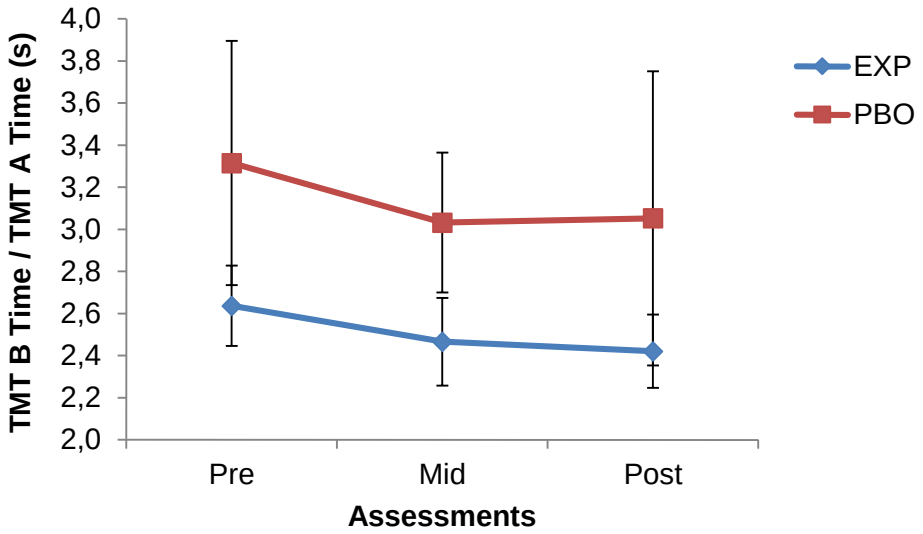


Figure 5.8 TMT A between EXP and PBO over 16 weeks ($\bar{x}$ ± SEM). * p < 0.05.

Figure 5.9 depicts the ratio (TMT B / TMT A; treatment effect = 0.97) and difference (TMT B – TMT A; treatment effect = 0.54) between TMT B and TMT A and Table 5.6 summarizes the absolute values for the TMT variables. Although there was no significant difference between the two groups for TMT B / TMT A, over the three time points, pre- (p = 0.30), mid- (p = 0.24) and post-intervention (p = 0.38), additional analysis revealed that the two groups differed from each other at each time point by 23% at pre-, 21% at mid- and 23% at post-intervention. Similarly, TMT B – TMT A showed no significant difference between the two groups at pre- (p = 0.82), mid- (p = 0.32) and post-intervention (p = 0.31) although the two groups differed at these time points by 26%, 53% and 55%, respectively.

a)



b)

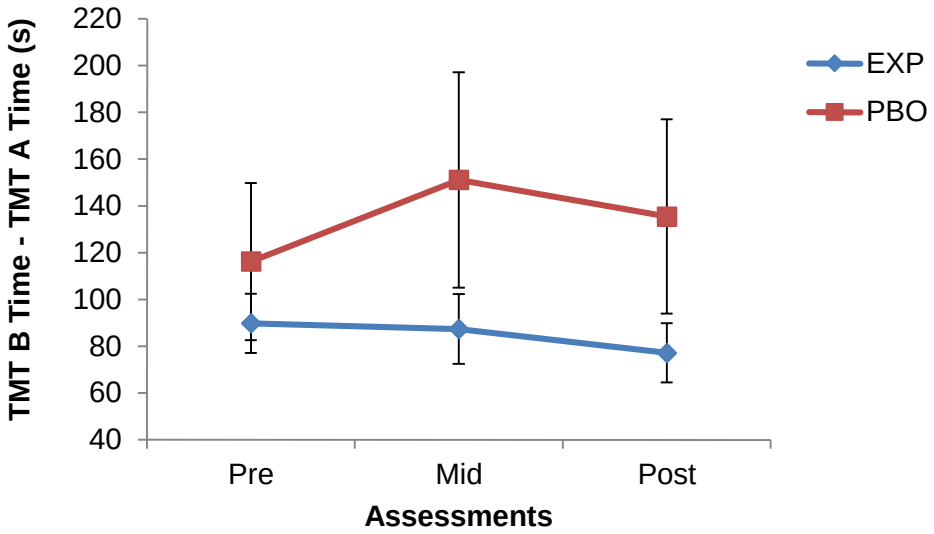


Figure 5.9 Ratio (a) and difference (b) between TMT B and TMT A between EXP and PBO over 16 weeks ($\bar{x}$ ± SEM).

Table 5.6 Summary of Trail Making Test (TMT) variables over the 16 weeks reported as mean ($\bar{x}$) ± standard deviation (SD), with (range).

TMT Variable	EXP (n = 25)[a]			PBO (n = 17)[b]			p value
Assessments	**Pre[1]**	**Mid[2]**	**Post[3]**	**Pre[1]**	**Mid[2]**	**Post[3]**	
TMT A (s)	55.6 ± 21.2 (26.3 – 97.7)	58.3 ± 22.4 (24.0 – 114.0)	55.2 ± 20.0 (28.5 – 108.5)	52.7 ± 32.5 (24.2 – 143.3)	68.7 ± 51.0 (22.5 – 171.8)	84.2 ± 105.4 (17.6 – 437.6)	$p = 0.02^{b1 \text{ vs } b3}$ $p = 0.03^{a3 \text{ vs } b3}$
TMT B Time (s)	145.5 ± 77.1 (64.3 – 345.5)	145.6 ± 87.8 (57.7 – 401.3)	132.3 ± 75.0 (62.8 – 393.2)	169.0 ± 151.5 (51.6 – 677.0)	219.8 ± 226.5 (53.1 – 916.8)	219.7 ± 232.1 (46.6 – 657.4)	$p > 0.05$
TMT B / TMT A	2.6 ± 1.0 (1.6 – 5.7)	2.5 ± 1.0 (1.4 – 5.5)	2.4 ± 0.9 (1.3 – 4.8)	3.3 ± 2.4 (1.6 – 9.7)	3.0 ± 1.4 (1.4 – 5.4)	3.1 ± 2.9 (1.2 – 14.0)	$p > 0.05$
TMT B – TMT A (s)	89.8 ± 63.3 (24.0 – 285.2)	87.3 ± 74.8 (16.1 – 327.5)	77.1 ± 63.2 (20.6 – 310.9)	116.2 ± 138.6 (23.7 – 601.2)	151.1 ± 189.9 (17.7 – 745.0)	135.5 ± 171.5 (22.9 – 610.4)	$p > 0.05$

TMT: Trail Making Test; s: seconds; [a] EXP (Experimental group); [b] PBO (Placebo group); [1] Pre-testing; [2] Mid-testing; [3] Post-testing

3.1.2 *Set shifting: Wisconsin Card Sorting Test: (WCST)*

Table 5.7 summarizes all of the variables for the WCST. There was no significant treatment effect (Assessment x Group) for any of the WCST variables i.e. Perseverative responses (PR), Categories completed (CC), Failure to maintain set (FTMS) and Total Errors (TE) ($p > 0.05$). The PR was significantly different between EXP and PBO at pre-, mid- and post-intervention ($p < 0.01$), as well as from pre- to mid-intervention EXP ($p = 0.04$). There were no changes from mid- to post-intervention for either PBO or EXP ($p > 0.05$). Failure to maintain set (FTMS) showed no significant differences between EXP and PBO, however there was a tendency for the two groups to differ by 56% at mid-intervention ($p = 0.07$). Total errors (TE) was statistically significant from pre- to mid-intervention EXP ($p = 0.050$).

Table 5.7 Summary of WCST variables over the 16 weeks reported as mean ($\bar{x}$) ± standard deviation (SD), with (range).

WCST Variable	EXP (n = 25)[a]			PBO (n = 15)[b]			p value
Assessments	**Pre[1]**	**Mid[2]**	**Post[3]**	**Pre[1]**	**Mid[2]**	**Post[3]**	
CC	2.2 ± 1.6 (0 – 6)	1.7 ± 1.8 (0 – 6)	2.0 ± 2.1 (0 – 6)	3.0 ± 1.0 (1 – 5)	2.6 ± 1.1 (1 – 4)	2.7 ± 0.6 (1 – 3)	p > 0.05
PR	9.4 ± 8.3 (0 – 31)	6.2 ± 7.7 (0 – 25)	6.4 ± 8.4 (0 – 34)	17.5 ± 6.5 (6 – 25)	10.5 ± 3.0 (6 – 18)	15.1 ± 6.3 (7 – 31)	p = 0.004[a1 vs b1] p = 0.004[a2 vs b2] p = 0.003[a3 vs b3] p = 0.04[a1 vs a2]
FTMS	1.4 ± 1.6 (0 – 5)	2.2 ± 2.1 (0 – 8)	1.8 ± 1.3 (0 – 4)	0.5 ± 0.7 (0 – 2)	1.3 ± 0.8 (0 – 2)	1.6 ± 1.8 (0 – 7)	p > 0.05
TE	60.0 ± 16.2 (13 – 87)	55.2 ± 18.9 (15 – 88)	56.9 ± 17.8 (20 – 93)	66.3 ± 9.4 (43 – 76)	61.1 ± 7.9 (41 – 69)	62.5 ± 10.8 (35 – 77)	p = 0.050[a1 vs a2]

WCST: Wisconsin Card Sorting Test; CC: Categories Completed; PR: Perseverative Responses; FTMS: Failure To Maintain Set; TE: Total Errors; [a] EXP (Experimental group); [b] PBO (Placebo group); [1] Pre-testing; [2] Mid-testing; [3] Post-testing

Two participants in PBO were colour blind and could not perform the WCST therefore the results are reported as n = 15 in PBO group.

Additional analysis was performed concerning the Global Wisconsin Card Sorting Test (WCST) Score, which indicates the participant's overall efficiency in the WCST (Figure 5.10). A score closer to zero is better. A statistically significant treatment effect (Assessment x Group) ($p < 0.0001$) was found. No significant differences were found specifically between groups and over time ($p > 0.05$), however on average the PBO group scored better (group effect; $p < 0.0001$).

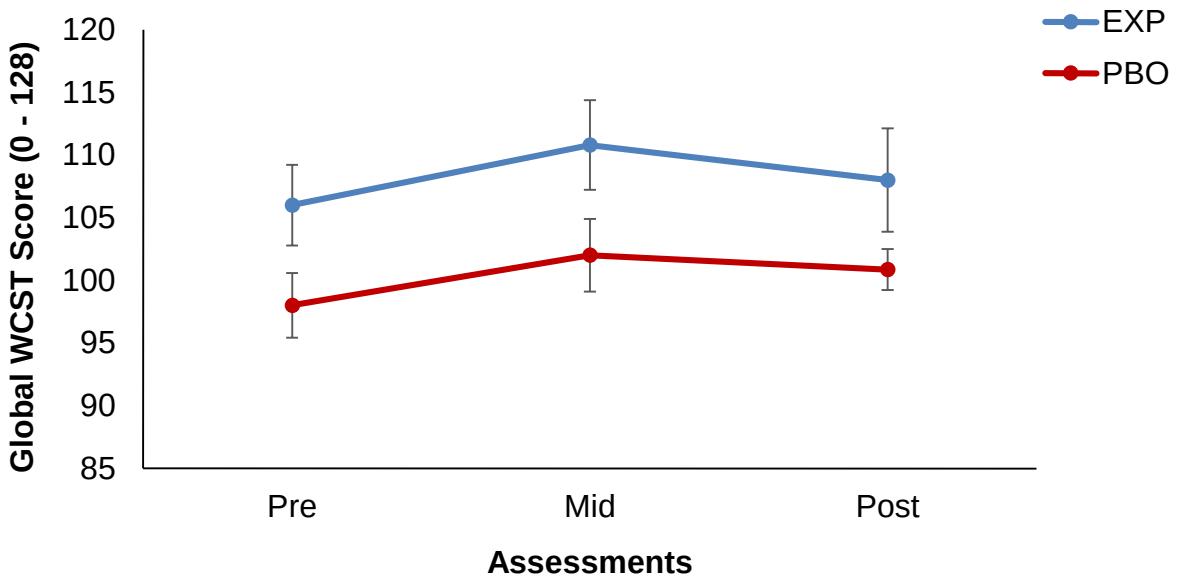


Figure 5.10 Global WCST Score between TMT B and TMT A between EXP and PBO over 16 weeks ($\bar{x}$ ± SEM).

3.1.3 *Inhibition: Adapted Stroop Task*

Table 5.8 summarizes all of the variables for the Adapted Stroop task. There was a weak tendency for a treatment effect (Assessment x Group) for time, for Choice Reaction Time for Reading (CRT 1) ($p = 0.08$) and a significant treatment effect for time, for Choice Reaction Time for Naming (CRT 2) ($p = 0.007$). However only CRT 1 showed a significant treatment effect for accuracy ($p = 0.04$). The Stroop variables for Incongruent exhibited no significant treatment effect for time or accuracy ($p > 0.05$).

The congruent trials include the CRT 1 and 2 trials. In CRT 1: time there was a significant difference between EXP and PBO at mid- ($p = 0.03$) and post-intervention ($p = 0.01$). No significant change over time was found in EXP from pre- to mid-intervention ($p = 0.13$).

Nonetheless, there was a significant change in EXP from pre- to post-intervention ($p < 0.01$), as well as a tendency to differ from mid- to post-intervention ($p = 0.06$). The PBO showed no change over the 16 weeks ($p > 0.05$) in CRT 1: time. The CRT 1: accuracy for PBO and EXP groups differed at mid-intervention ($p = 0.02$). For CRT 2: time the two groups differed by 42% ($p = 0.01$) at post-intervention. While PBO's reaction time was maintained over the 16 weeks, EXP's did not change from pre- to mid-intervention ($p = 0.18$), but improved by 7% from mid- to post-intervention ($p = 0.048$). In addition, EXP also improved over the 16 weeks by 10% ($p = 0.01$).

Table 5.8 Summary of Adapted Stroop task variables over the 16 weeks reported as mean ($\bar{x}$) ± standard deviation (SD), with (range).

Variable	EXP (n = 24)[a]			PBO (n = 15)[b]			p value
Assessments	**Pre[1]**	**Mid[2]**	**Post[3]**	**Pre[1]**	**Mid[2]**	**Post[3]**	
CRT 1: Reading							
Time (s)	1.5 ± 0.3 (1.1 – 2.1)	1.5 ± 0.5 (1.0 – 2.7)	1.4 ± 0.5 (1.0 – 2.8)	2.2 ± 2.2 (0.9 – 10.2)	2.2 ± 2.2 (1.0 – 10.2)	2.2 ± 2.0 (1.0 – 9.3)	$p = 0.03^{a2 \text{ vs } b2}$ $p = 0.01^{a3 \text{ vs } b3}$ $p < 0.001^{a1 \text{ vs } a3}$
Accuracy (%)	99.5 ± 1.8 (91.7 – 100)	99.8 ± 0.8 (95.8 – 100)	99.5 ± 1.4 (95.8 – 100)	99.3 ± 2.2 (91.7 – 100)	97.5 ± 4.9 (83.3 – 100)	98.6 ± 3.5 (88.0 – 100)	$p = 0.002^{a2 \text{ vs } b2}$
CRT 2: Naming							
Time (s)	1.5 ± 0.3 (1.2 – 2.1)	1.5 ± 0.3 (1.1 – 2.2)	1.4 ± 0.3 (0.9 – 2.0)	2.1 ± 2.3 (0.9 – 10.3)	2.0 ± 2.0 (1.0 – 8.8)	2.1 ± 1.6 (1.0 – 7.1)	$p = 0.01^{a3 \text{ vs } b3}$ $p = 0.048^{a2 \text{ vs } a3}$ $p = 0.001^{a1 \text{ vs } a3}$
Accuracy (%)	99.2 ± 2.1 (91.7 – 100)	99.7 ± 1.2 (95.8 – 100)	99.0 ± 2.2 (91.7 – 100)	98.1 ± 4.1 (87.5 – 100)	98.6 ± 3.0 (91.7 – 100)	98.3 ± 5.4 (79.2 – 100)	$p > 0.05$
Incongruent 1							
Time (s)	2.7 ± 0.9 (1.7 – 4.8)	2.5 ± 0.9 (1.6 – 5.0)	2.3 ± 1.0 (1.3 – 5.1)	3.6 ± 3.1 (1.6 – 14.1)	3.7 ± 3.9 (1.4 – 17.2)	3.4 ± 2.9 (1.3 – 11.7)	$p = 0.04^{a3 \text{ vs } b3}$ $p = 0.02^{a1 \text{ vs } a2}$ $p = 0.053^{a2 \text{ vs } a3}$ $p < 0.001^{a1 \text{ vs } a3}$
Accuracy (%)	93.8 ± 7.0 (79.2 – 100)	96.4 ± 4.3 (83.3 – 100)	97.2 ± 3.6 (87.5 – 100)	92.5 ± 11.4 (58.3 – 100)	92.8 ± 11.1 (62.5 – 100)	94.2 ± 9.1 (67.0 – 100)	$p = 0.05^{a1 \text{ vs } a3}$
Incongruent 2							
Time (s)	2.8 ± 0.9 (1.9 – 5.1)	2.6 ± 0.9 (1.6 – 4.7)	2.6 ± 1.1 (1.5 – 5.3)	4.5 ± 3.4 (2.1 – 15.3)	4.2 ± 3.0 (1.6 – 14.2)	4.2 ± 3.5 (1.5 – 15.3)	$p = 0.005^{a1 \text{ vs } b1}$ $p = 0.005^{a2 \text{ vs } b2}$ $p = 0.008^{a3 \text{ vs } b3}$
Accuracy (%)	90.8 ± 11.5 (54.2 – 100)	93.9 ± 7.2 (75.0 – 100)	95.3 ± 6.4 (79.2 – 100)	86.4 ± 14.9 (58.3 – 100)	89.2 ± 11.4 (62.5 – 100)	89.2 ± 14.5 (54.0 – 100)	$p = 0.053^{a3 \text{ vs } b3}$
Interference Score							
Time (s)	1.3 ± 0.7 (0.5 – 2.9)	1.1 ± 0.7 (0.3 – 2.9)	1.1 ± 0.8 (0.4 – 3.6)	1.9 ± 1.1 (1.0 – 4.8)	1.9 ± 1.7 (0.4 – 7.2)	1.7 ± 1.6 (0.3 – 6.6)	$p = 0.003^{a1 \text{ vs } b1}$ $p < 0.001^{a2 \text{ vs } b2}$
Accuracy (%)	38.7 ± 8.5 (13.0 – 47.5)	41.5 ± 5.3 (27.6 – 47.5)	42.7 ± 4.0 (32.9 – 46.3)	36.2 ± 11.0 (11.1 – 46.3)	37.2 ± 10.4 (11.1 – 46.3)	38.2 ± 11.0 (5.6 – 46.3)	$p = 0.05^{a2 \text{ vs } b2}$ $p = 0.04^{a3 \text{ vs } b3}$

CRT: Choice Reaction Time; s: seconds; [a] EXP (Experimental group); [b] PBO (Placebo group); [1] Pre-testing; [2] Mid-testing; [3] Post-testing

For Incongruent trials, the reaction time for Incongruent 1 differed by 41% at post-intervention ($p = 0.04$), EXP improved from pre to mid-intervention ($p = 0.02$), as well as from mid to post-intervention ($p = 0.053$) and over the 16 weeks in total ($p < 0.01$), whereas PBO demonstrated no change over time ($p > 0.05$). The accuracy during this trial only improved from pre- to post-intervention in EXP ($p = 0.048$). For the second, more distractive trial (Incongruent 2) EXP and PBO differed significantly at pre-, mid- and post-intervention ($p < 0.01$) by 45%, 44% and 45% respectively. Both EXP and PBO's reaction times tended to slow over the 16 weeks ($p = 0.06$), but no differences were noted from pre- to mid-intervention or from mid- to post-intervention ($p > 0.05$). Only EXP tended to improve their accuracy (less errors) over the 16 weeks ($p = 0.06$) while EXP and PBO tended to differ by 7% at post-intervention ($p = 0.053$).

A treatment effect was observed for Interference: score accuracy ($p < 0.0001$) but not for Interference: score time ($p > 0.05$). The EXP and PBO differed significantly at all three time points: pre- ($p = 0.003$); mid- ($p < 0.0001$) and post-intervention ($p = 0.006$) for Interference: time and at mid- ($p = 0.050$) and post-intervention ($p = 0.04$) for Interference: accuracy. A tendency for significant change was observed from pre- to post-intervention ($p = 0.07$) in EXP.

Two participants in PBO were colour blind and could not perform the Stroop test. The results are reported as n = 15 in PBO. One participant in EXP was unable to read words in the colour yellow for the conditions of Incongruent 1 and 2 and his results were excluded for these two conditions. The results for these two conditions are reported as n = 24 in EXP.

3.2 *Functional Balance*

3.2.1 *Perceived Stability of Balance: Activities-specific Balance Confidence Scale (ABC Scale)*

There was no significant treatment effect for ABC ($p = 0.54$). Post-hoc analysis found a 14% difference between EXP and PBO at post-intervention ($p = 0.051$), however the two groups did tend to differ at pre-intervention ($p = 0.07$) by 12%. Closer investigation showed that there was a significant difference from mid- to post-intervention ($p = 0.02$) and pre- to post-intervention for the EXP ($p = 0.01$), but not from pre- to mid-intervention for the EXP ($p = 0.87$). The PBO showed no change from pre- to mid-intervention or from mid- to post-intervention ($p > 0.05$), but tended to improve over the 16 weeks ($p = 0.06$) in general as can be seen in Figure 5.11.

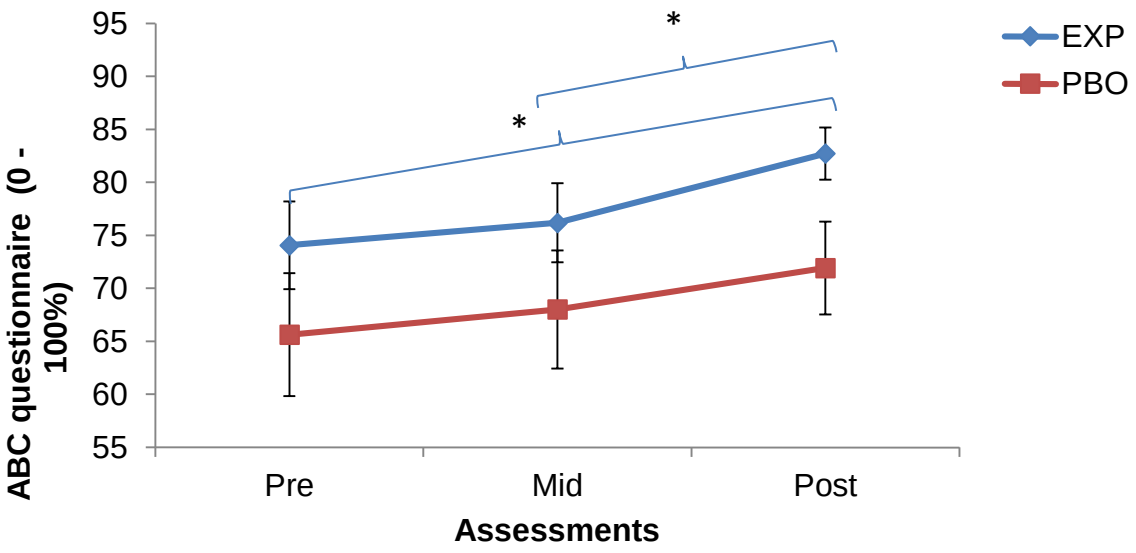


Figure 5.11 Perceived Stability of Balance (ABC) between EXP and PBO over 16 weeks ($\bar{x}$ ± SEM). * p < 0.05

3.2.2 *Mobility: Timed Up and Go Test (TUG)*

There was a significant treatment effect for TUG (p < 0.01; Figure 5.12). In addition, EXP and PBO differed by 28% at post-intervention (p < 0.01). There was a significant difference from pre- to mid- (p = 0.001), mid- to post- (p < 0.01) and pre- to post-intervention (p < 0.01) in EXP. Additional analysis revealed a 14% improvement by EXP compared to a 3% change by PBO from mid- to post-intervention).

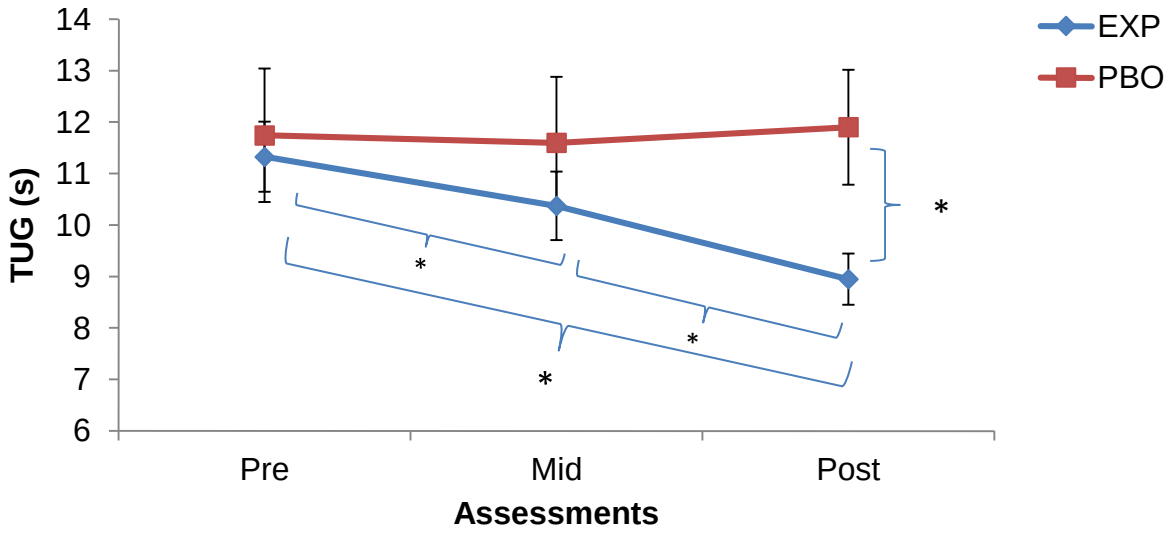


Figure 5.12 Timed Up and Go (TUG) between EXP and PBO over 16 weeks ($\bar{x}$ ± SEM). * p < 0.05

4. Summary

In summary, there were significant treatment effects observed for MDS-UPDRS III and MDS-UPDRS total score, TMT A, Global WCST Score, CRT 1: accuracy, CRT 2: time, Interference Score: accuracy and the TUG.

Between-groups differences were observed for EXP and PBO at pre-intervention in HY, MDS-UPDRS III, HAM-D, WCST: PR, Incongruent 2: time and Interference: accuracy; at mid-intervention in HY, PDQ-39 variable COM, HAM-D, WCST: PR, CRT 1: time, CRT 1: accuracy, Incongruent 2: time, Interference: time and Interference: accuracy; and at post-intervention in PDQ-39 variable BOD, HAM-D, TMT A, WCST: PR, CRT 1: time, CRT 2: time, Incongruent 1: time, Incongruent 2: time, Incongruent 2: accuracy, Interference: time, Interference: accuracy, ABC and TUG.

Within-group changes over time in EXP were seen from pre- to mid-intervention in MoCA, WCST PR, WCST TE, Incongruent 1: time and TUG; from mid- to post-intervention in MDS-UPDRS II, PDQ-39 variable STI, CRT 2: time, Incongruent 1: time, ABC and TUG; and from pre- to post-intervention in MoCA, PDQ-39 variable EMO, CRT 1: time, CRT 2: time, Incongruent 1: time, Incongruent 1: accuracy, ABC and TUG. Within-group changes over time in PBO were seen from pre- to mid-intervention in PDQ-39 variables MOB and EMO; and from pre- to post-intervention in MDS-UPDRS III and TMT A. The following chapter will discuss these findings.

CHAPTER SIX

DISCUSSION

1. Introduction

The current study set out to determine if an eight-week SMT programme could influence executive functioning, namely Inhibition, Set shifting and Updating in non-demented individuals with mild to moderate PD. The main findings of the study suggest that participants with PD who engaged in this exercise intervention in comparison to those who received a placebo, showed a slowing in disease progression, a reduction in perceived body discomfort, improvement in dynamic balance, mobility and confidence, as well as maintaining visuomotor abilities, and possibly an improvement in inhibitory control. Even though there is some evidence suggesting that sensory-integration and processing may have improved with the SMT, this programme had no significant benefit on Updating and Set shifting. These findings will be discussed in more detail in the following section. The chapter starts with a basic discussion about the participants' descriptive characteristics, as well as secondary outcomes, and identifies possible confounding factors; this is followed by a discussion about the primary outcome variables.

2. Participants

The participants differed significantly, before the start of the baseline phase, regarding disease severity (HY and MDS-UPDRS I, III & IV), depressive moods (HAM-D) and some EF, namely Set shifting and Inhibition (WCST PR and Incongruent 2: time and Interference Score: accuracy). In addition, even though age differences were not statistically significant (the PBO was older), there was a tendency for the two groups to differ. These factors may have contributed to the specific reaction of each group to their intervention. Both EXP and PBO had similar activity status profiles, with most participants indicating that they were inactive.

The descriptive variables of Depression (HAM-D) and Disease Severity (MDS-UPDRS I, III, IV and HY) differed significantly between the two groups at baseline. At mid-intervention (before the start of the treatment phase), only depressive mood and HY differed. Consequently, an ANCOVA was run and the analysis showed that only depression had an influence on the PDQ variables of perceived emotional well-being, cognitions and bodily discomfort. HY had no statistically significant difference and neither did gender or education.

Thus, depression may have influenced participants' perceived wellbeing, cognitive abilities and bodily discomfort. Additional statistical analysis (ANOVA) was done, dividing the groups into men and women to see if gender, as an independent variable, had an influence: there were no statistically significant differences regarding any of the dependent variables.

Participants in EXP were on average five years younger than those in PBO. The study of Allain *et al.* (2005) revealed that apparently healthy older adults (80.3 ± 5.9 years) typically demonstrate impairments in planning, which relate to executive functions. In other words, elderly individuals have greater difficulty in deciding upon a complex course of action which will result in a specific goal, than they do in actually performing and successfully completing this course of action. This suggests that normal aging has an effect on the ability to formulate complex plans more than it impacts on the ability to execute the task (Allain *et al.,* 2005). The 5-year difference between groups in the current study, therefore, may have had an influence on the lower Set shifting (WCST: PR) and Inhibition (Incongruent 2 & Interference Scores) results, even though no group differences were noted in global cognition (MoCA) or in mobility (TUG). Previous research has also shown that a large inter-individual variability exists in age-related changes in cognition (Gilsoul *et al.*, 2015) which has also been reported in individuals with PD (Hindle *et al.*, 2014; Koerts *et al.*, 2013). However, as discussed later in this chapter, these differences may be attributed more to the cognitive reserve differences found between individuals with PD (Hindle *et al.*, 2014; Koerts *et al.*, 201).

Furthermore, a reduction in postural control in the elderly, is accompanied by an increase in the prevalence of falls and poor mobility (Kanekar & Aruin, 2014). Likewise, there is a tendency for TUG performance times to decrease with increasing age in both men and women (Steffen *et al.*, 2002). For individuals aged 65 years and older, falls are the chief cause of injury-related fatalities and falling is also the third highest cause of reduced or poor health (Scheffer *et al.*, 2008). Roughly 30% of this age category will fall once per year and at least half of these will fall again (Scheffer *et al.*, 2008; Stel *et al.*, 2004; Moreland *et al.*, 2003). Once individuals reach 80 years and above, 50% will fall once per year (Hartholt *et al.*, 2011). Correspondingly, both groups on average, fell in an age bracket associated with a higher risk for falls. However, even though the two groups seem to differ in age, there was little indication that this age difference directly influenced the mobility performance between the two groups, as seen in the TUG, particularly as there was no significant difference at baseline between EXP and PBO for the TUG. On the other hand, as noted before, the age bracket in which the two groups fell would have influenced their mobility and balance.

PD severity was worse in EXP compared to PBO as determined by the MDS-UPDRS and Hoehn and Yahr scales. The only exception was the MDS-UPDRS I scale, in which the PBO scored worse. Nevertheless, the total MDS-UPDRS and MDS-UPDRS II scores did not differ significantly when compared to the PBO. Part I of the MDS-UPDRS gives an indication of the non-motor experiences of daily living such as cognitive impairment, hallucinations, depressive and anxious mood, apathy and dopamine dysregulation. This part was assessed by the researcher, except for the final 7 questions, which were completed by the participant or caregiver and included questions on sleep, staying awake, pain, abnormal sensory sensations, urinary functions, constipation, light-headedness when standing and fatigue. The possible differences between the two groups in part I could, therefore, be attributed to non-motor experiences seven days prior to the testing day. This is partially supported by the HAM-D, as the two groups differed significantly from the start. A score between 0 and 6 indicates no depression, between 7 and 17 indicates mild depression, between 18 and 24 indicates moderate depression and any score above 24 indicates severe depression (Cusin *et al.*, 2009). Hence the PBO were classified as having mild depressive moods and the EXP classified as having no depressive moods. Consequently, depression (with HAM-D) was considered a confounding variable in this study. One possible explanation for these significant differences observed (MDS-UPDRS I and HAM-D) during the pre-testing is that the start of the study for the two groups was staggered (due to practical constraints). The EXP group started first with their intervention, followed by the PBO. The time during which the PBO was assessed for their pre-intervention (and for some mid-intervention) data coincided with the largest religious and family holiday of the year. Even though this is merely speculative, the time of the year may have contributed to the PBO group possibly experiencing depressive emotions. Carr *et al.* (2014) found that older bereaved individuals experience psychological distress at times of special significance like Christmas or times usually spent with loved ones. Similar results have recently been reported in individuals who have suffered an injury or disability (Deegan *et al.*, 2015). Therefore, individuals who are disabled (chronic or acute injury) may experience feelings of loneliness, isolation, absence from loved ones, and depression (Deegan *et al.*, 2015).

Part IV of the MDS-UPDRS discloses motor complications typically associated with medication such as dyskinesia and motor fluctuations (Goetz *et al.*, 2007) whereas most PD studies use the UPDRS II and/or III in their investigations (Harrison *et al.*, 2009) for reasons which will be highlighted later in this chapter. Hence part II and III, which report the

participants' motor experiences of daily living (self-reported) and the motor examination by the researcher, respectively, may be considered the most relevant subscales of the current study.

The two groups differed at pre-intervention for part III: in particular, the EXP performed worse than PBO, which was supported by the HY staging in which the PBO's disease severity was better compared to EXP. An increase in HY staging has been associated with dopaminergic loss, increased motor impairment, disability and reduced quality of life (Goetz *et al.*, 2004). Typically, the HY only takes into consideration postural instability (balance and gait problems) and bilateral involvement, and no other motor or non-complications, which may explain why the results on the HY of this study relates to the motor subscale (part III) of the MDS-UPDRS.

In this study, the EXP (Med: 2.5) predominantly consisted of participants between stage 2 (bilateral involvement without balance difficulties) and stage 3 (bilateral disease with balance difficulties), whereas the PBO (Med: 2.0) was predominantly composed of stage 2 participants (bilateral involvement without balance difficulties). Stages 1 and 2 are considered as mild or early PD, whereas stage 3 is seen as moderate PD (Goetz *et al.*, 2004). Consequently, both groups could be considered to include mild to moderate PD. Goetz *et al.* (2004) further explains how participants in stage 2 may demonstrate a stable disease severity rating (as reported by MDS-UPDRS) even with an increase in medication, whereas stage 3 disease severity fluctuates with changes in medications and places the participant at a higher risk for dementia, balance problems and a decreased survival rate. Hence the EXP participants may not have differed clinically from the PBO but were progressing towards stage 3, suggesting that they may have had slightly poorer disease severity than the PBO.

The MoCA is considered to be a more sensitive test for the detection of mild cognitive impairment (MCI) than the Mini-Mental State Exam (MMSE) and is an indication of global cognition (Nazem *et al.*, 2009; Zadikoff *et al.*, 2008; Nasreddine *et al.*, 2005). A score below 26 is considered the optimal cut-off for cognitive impairment (Nasreddine *et al.*, 2005). Thus, both groups were classified as having mild cognitive impairment (MCI) and did not seem to differ in global cognition. Harkness *et al.* (2011) found that elderly individuals (> 65 years) who scored lower than 26 on the MoCA (suggesting MCI), had significant deficits in the delayed recall, language and visuospatial/executive function compared with individuals who

scored more than 26. Nevertheless, Harkness *et al.* (2011) did not assess individuals with PD. However executive functioning is a subdomain of the MoCA, in addition to attention, concentration, memory, language, visuospatial skills, abstraction, calculation and orientation, which may suggest that both groups in the current study had some executive dysfunction, which is reflected in the MoCA score of less than 26. This is supported by Dalrymple- Alford *et al.* (2010) who reported cut-off scores of 20/21 for PD with dementia, and 25/26 for PD with MCI.

Baseline differences between EXP and PBO were also evident for some aspects of EF, namely Set shifting as seen in PR and Inhibition as seen in Incongruent 2: Time and Interference: time. The PBO group seems to have had more problems with 'thinking outside the box', adjusting to shifting priorities and reacting to impulsive, unexpected opportunities or problems (Diamond, 2015). They also struggled more at the start of the study with inhibiting automatic responses (habits) or resisting temptations and distractions (Diamond, 2015). One possible contributing factor that may have influenced the PBO group negatively is depressive mood (referring to MDS-UPDRS I and HAM-D). Uekermann *et al.* (2003) suggest that even mild depressive symptoms are likely to worsen cognitive impairment in early PD. However, Uekermann *et al.* (2003) used different tests of EF as well as a different rating scale of depression compared to the current study. It is possible that the mild depressive moods seen in the PBO had an impact on these two EF variables, although one would expect to also see this for all or at least more of the variables (CC, FTMS, TE, CRT 1: time and accuracy; CRT 2: time and accuracy; Incongruent 1: time and accuracy and Incongruent 2: accuracy). Both of the tests used for these two variables, namely the WCST and the adapted Stroop task, made use of a laptop computer. It is possible that the older age profile of the PBO relative to the EXP had an impact in terms of computer use. It was informally noted that some older participants in both groups were less comfortable using a computer and mouse than some of the younger participants.

Hu *et al.* (2006) stated that Body Mass Index (BMI) ≥ 23 kg/m^2 is associated with an increased risk of PD among middle-aged men and women, yet individuals with PD have typically been reported to have a lower BMI than healthy age-match controls (van der Marck *et al.*, 2012). Consequently, one may think that BMI should be considered when making inferences. Both groups in the current study were classified as overweight (defined as a BMI between 25.0 kg/m^2 and 29.9 kg/m^2). Interestingly, Gunstad *et al*. (2007) previously found that regardless of age, elevated body mass index (BMI) is associated with executive

dysfunction in healthy individuals. Conversely, it is undetermined whether this same relationship is also true for PD specific populations, although lower BMI has been found to be associated with cognitive decline in PD (Kim *et al*., 2012).

The two groups were conveniently recruited from two different areas in the Cape metropolitan and Winelands district of the Western Cape. More specifically the EXP group was from the Cape metropole (southern suburb areas), whereas the PBO was from the Cape metropole (Strand and Somerset West) and Winelands districts (Stellenbosch and Paarl). The socioeconomic status of the two areas was similar. Socioeconomic status may have indirectly influenced global cognition and, as a result, also EF. However, based on the MoCA, both groups had similar education levels with only 4 (EXP group) and 2 participants (PBO group) having less than 12 years of education. Both groups also achieved an average global cognition score of 24 which is indicative of mild cognitive impairment (Nasreddine *et al.*, 2005). Hackman *et al*. (2015) suggested that the association between socioeconomic status and EF has its roots in early childhood, a factor that the study could not have controlled.

When looking at the various baseline differences between the two groups (disease severity, depressive mood and some EF) one may expect the mobility test (TUG) to also differ between groups, as previous researchers have shown that these descriptive specific variables have an influence on balance. For instance, Donoghue *et al*. (2012) showed that poorer performance on TUG for mobility is independently associated with reduced global cognition, EF, memory and processing speed. As pointed out earlier, balance impairment is the critical criteria between stages of disease severity on HY specifically (Goetz *et al.*, 2004). Whereas Cubo *et al.* (2000) found that lower global cognition, axial bradykinesia, as well as gait and balance impairment were significant predictors of depression. Consequently, one may ask why the two groups would have similar TUG scores at baseline assessments. A possible reason is the heterogeneity found between the two groups, and that the combinations of these descriptive characteristics of each group, may have influenced their balance performance differently, resulting in similar TUG scores. For instance, EXP had poorer disease severity scores yet better EF, whereas the PBO had experienced higher depressive scores but lower EF. This may have contributed to similar mobility capabilities in both groups, though they were influenced differently.

The participants of the EXP group maintained a high session attendance rate throughout the intervention. All 25 participants maintained an attendance rate of 70% and above for the duration of the intervention which is similar to the study of Tanaka *et al.* (2009). Only one participant had an attendance rate less than 75%. Eleven participants had attendance rates above 90%. Three participants were excluded from the study for an attendance rate less than 70%. Although they were allowed to continue with the intervention their results were not included in the study. This is considered a good attendance rate compared to studies such as Shubert *et al.* (2010) who reported an attendance rate ranging from 40 to 100%.

The attrition rate (study drop-outs) of the current study was low. In the EXP, of the 30 participants who started the eight-week balance training programme, only two dropped out. Three were not included in the data analysis as they did not meet the required 70% attendance criteria. In the PBO, four participants dropped out of the original 21. This leaves a 6.7% attrition rate in the EXP, 19% in the PBO and 11.8% if EXP and PBO are combined. Compared to studies such as Shubert *et al.* (2010) who reported an attrition rate of 33%, this is much lower. Although participants attended these classes over a 12-week period, they attended only twice a week whereas the current study had classes three times a week over an eight-week period.

3. Secondary Outcome Variables

3.1 *Global Cognition: Montreal Cognitive Assessment (MoCA)*

The scores between EXP and PBO were similar for the pre- and mid-interventions. The scores for PBO at pre-, mid- and post-intervention all fell below the cut-off of 26, as did the scores for EXP at pre- and mid-intervention. Although not significant, the post-intervention score (26.5 ± 2.4) for EXP was above the cut-off score, which is classified as normal cognition. To date no minimal detectable change (MDC) has been reported for the MoCA, however considering that the individuals in the EXP improved from MCI to no cognitive impairment classification after the treatment phase, this may be considered as clinically significant instead, albeit not statistically significant. The only significant change over time was observed in the EXP group over the baseline phase as well as from pre- to post-intervention. Considering that there was no significant change over the treatment phase, this overall change may be attributed to a learning or demand effect and not necessarily to the intervention. In other words, participants may have become accustomed to the assessment questions. Similarly, MacKee and Hackney (2013) found a main effect of time for the MoCA, in their study on adapted tango in PD, but no treatment effect.

3.2 *Parkinson's Disease Severity*

3.2.1 *Hoehn and Yahr Scale (HY)*

In the current study, the EXP group maintained their HY stage rating and thus did not show any further disease progression. In contrast, the PBO group did show some deterioration in their disease severity over time: this change was not significant, however, nor can it be considered a clinically significant change as some clinicians have suggested that only a change from one stage to another is clinically significant (Goetz *et al.*, 2004). Furthermore, for disease severity it is best to refer to the MDS-UPDRS II and III data, since the wide difference between stages in the original HY is not sensitive enough to determine treatment-related changes especially in the lower PD stages (< 3). Therefore, the HY is mostly recommended for inclusion and exclusion criteria and for descriptive purposes in research (Goetz *et al.*, 2004).

3.2.2 *Movement Disorder Society – Unified Parkinson's Disease Rating Scale (MDS – UPDRS):*

The MDS-UPDRS was designed to detect both disease progression and changes associated with therapeutic interventions such as this study's exercise intervention (Horváth *et al.,* 2015). Previous researchers have found that subscale II of the UPDRS is a better indicator of disease progression compared to other subscales (Harrison *et al.*, 2011). These researchers suggested that subscale II is more sensitive to functional change and is less affected by motor fluctuations like part III (the motor examination subscale). In addition, subscale III was found to be influenced by placebo-related improvements, whereas subscale II was not. Other researchers, however, have suggested that both subscales II and III should be considered when assessing disease progression, especially in early PD (Parashos *et al.*, 2014; Tomlinson *et al.*, 2013). These are observations made concerning the original UPDRS whereas the newer MDS-UPDRS is considered to be more comprehensive and consistent than the original (Goetz *et al.*, 2008). Moreover, Lang *et al.* (2013) report subscale II to be even more sensitive to change over time than the original UPDRS subscale II in individuals with early- to mild-stage PD. Subscales I and IV of the original and new versions differ quite considerably while parts II and III remain similar and have been calibrated (Goetz *et al.*, 2012). Subscale II assesses motor features of experiences of daily living (M-EDL) and is able to identify problems with daily activities. Higher subscale II scores are linked with increasing severity of disease and its duration (Rodriguez-Blazquez *et al.*, 2013). In the

current study, the EXP improved their MDS-UPDRS subscale II over the treatment phase, while there was no improvement in the score of the PBO.

Subscale III is able to evaluate the severity of motor symptoms reliably. The recent study of Horváth *et al.* (2015) estimated minimal clinically important differences (MCID) in part III of the MDS-UPDRS as -3.25 points for improvement and +4.63 points for deterioration. In the current study, there was a treatment effect for part III, and the PBO showed deterioration from pre- to post-intervention as well as a tendency to deteriorate from mid- to post-intervention, which indicates an increase in PD severity. However, although this deterioration over the whole 16 weeks is considered significant, it falls slightly below the cut-off for MCID (change of 4.1). Although there was no improvement in the EXP, neither was there any deterioration. Thus, it is possible that the exercise may have acted to prevent possible progression of the disease.

There was also a treatment effect seen for Total MDS-UPDRS. The study of Pierobon *et al.* (2014) saw a similar improvement in MDS-UPDRS III and MDS-UPDRS Total following an intensive rehabilitation programme. Although they did not include a control group in their study, they distinguished between “impaired” and “not impaired” and “depressed” vs “non-depressed” individuals with PD. Regardless of the grouping, they saw the same trend and significant improvement ($p < 0.0001$) in MDS-UPDRS III and MDS-UPDRS Total as was seen in the current study.

3.3 *Quality of Life: 39-Item Parkinson’s Disease Questionnaire (PDQ-39)*

Schrag et al. (2000) did a stepwise multiple regression analysis on 92 individuals with PD and found that depression, disability, postural instability, and cognitive impairment have the greatest influence on QOL in PD. Due to the nature of the intervention, the current study wanted to determine the impact of the SMT programme on specific aspects of functioning and wellbeing in PD. Therefore, the PDQ-39 profile form was assessed instead of the summary index, which determines the impact of the illness on functioning and well-being (Jenkinson *et al*., 1997). The tendency in the PDQ-39 variable MOB (mobility) complements and compares to the treatment effect observed for the TUG. Both of these assessments evaluate functional mobility and balance. The EXP and PBO differed significantly at mid-intervention for COM (communication) and at post-intervention for BOD (bodily discomfort). Although the two groups were significantly different at these time points, there was no

significant improvement or deterioration in either group during the lead up to these points and thus they would not appear to be of great relevance.

There was a significant reduction in STI (stigma) in the EXP, perhaps as a result of the SMT or from being around other individuals with PD. An informal observation of the EXP was that hardly any of the participants had met each other before and apart from a few who attended a once-monthly PD support group, they did not interact with other PD individuals. It is not known what accounted for the improvement over the baseline phase in MOB (mobility) in the PBO.

Both the EXP and PBO showed improvements in EMO (emotional wellbeing). The PBO had an initial decrease over the baseline phase and the EXP decreased from pre- to post-intervention; however, closer inspection shows that the EXP improvement took place primarily over the treatment phase. This predominantly mid- to post-intervention improvement in the EXP may have been as a result of the SMT or increased social interaction of the SMT or a combination of the two.

3.4 *Depression: Hamilton Rating Scale for Depression (HAM-D)*

The two groups differed significantly from each other throughout the baseline and treatment phases. The EXP were classified as being without depression and they stayed this way throughout the study (pre: 5; mid: 4; post: 4). The PBO were classified as having mild depression and they, too, stayed in this classification for the duration of the study (pre: 8; mid: 9; post: 9). Although the differences between the two groups remained significant throughout (pre: $p < 0.001$; mid: $p < 0.001$; post: $p < 0.001$) and the two groups were in different categories throughout, there is only a small difference between the two categories of no depression (0-6) and mild depression (7-17). A possible reason for the discrepancy between the two groups could be the timing of their interventions. The EXP ran from late July to early December, while the PBO ran from late October to early March. As mentioned earlier, the PBO group ran over the year-end holiday time which is considered to be a stressful and often depressing time of the year, particularly for those who have lost loved ones or whose family do not live close by. Furthermore, three participants in the PBO lost a close family member or friend in the duration of the study. The 2005 study by Prado and Barbosa investigated the presence of depression in 60 individuals with PD and reported a frequency of depression of 38.33%. Of those found to be depressed, 82.60% had mild depression, 8.69% had moderate depression and 8.69% had severe depression. Thus, the

finding of the control group falling into the mild depression category is not out of the ordinary. Uekermann *et al*. (2003) suggest that depressed mood in PD has the potential to aggravate cognitive impairments, including EF. Thus depression could potentially have influenced the EF of the PBO group in this study.

4. Primary Outcome Variables

4.1 *Executive Function (Updating, Set shifting and Inhibition)*

4.1.1 *Updating: Trail Making Test (TMT) part A (TMT A) and part B (TMT B)*

The Trail Making Test (TMT) was included in this study to assess Updating (also known as working memory). Trail Making Test part A was the only TMT variable to demonstrate a treatment effect or any significant changes over time. The PBO's time to complete the TMT A deteriorated over the 16-week period of the study, while the EXP maintained their times. At the end of the treatment phase the PBO and EXP were significantly different. The TMT A requires the use of visual scanning and visuomotor speed and is not generally considered to assess pure EF, while the more challenging TMT B reflects Updating. The difference (TMT B – TMT A) and ratio (TMT B / TMT A) scores were developed to provide a more distinct measure of the executive components that distinguish the two parts of the test (Drane *et al.*, 2002). However, no differences were observed in these variables, indicating that the SMT programme did not benefit working memory/updating.

This is similar to the PD study of Duchesne *et al.* (2015) and non-Parkinson's disease studies of Shubert *et al.* (2010) and Liu-Ambrose *et al.* (2008) who also found no significant improvements in these variables. The exercise interventions used in these three studies were an aerobic exercise training programme, an exercise-based balance programme and a strength and balance training programme, respectively. Liu-Ambrose *et al.* (2008) used TMT B as a measure of Set shifting. Although there was no statistically significant improvement in Set shifting (TMT B), the EXP group improved by 8.7% compared to the control group who deteriorated by 3.6%. The current study also showed no statistically significant improvement in TMT B of EXP yet they also improved by 9% (over the 16 weeks) compared to the 30% deterioration of PBO (30% deterioration over baseline phase, plateauing over treatment phase). Although Shubert *et al.* (2010) found a tendency to improve in TMT A time ($p = 0.03$), there was no improvement in TMT B. Their study reported great variation in the results of this test, particularly in TMT B (> 218 seconds variation), which is comparable to the current study. The EXP variation in the TMT B ranged from 281 to 330 seconds over the 16 weeks, while the PBO variation ranged from 625 to 863 seconds.

One must bear in mind that the studies of Shubert *et al.* (2010) and Liu-Ambrose *et al.* (2008) were not conducted in a PD population. Duchesne *et al.* (2015) suggest that the motor element of the TMT could increase the difficulty of completing this task in those with PD.

Interestingly, in an unrelated study, Engel-Yeger *et al*. (2012) reported that deterioration in sensory-processing abilities can lead to inefficiencies in visuomotor performance. This may indirectly suggest that the SMT programme improved sensory-processing abilities in individuals with PD. Individuals with PD typically have deficits in sensory processing and integration, which is not improved, and may be aggravated, by dopaminergic medication (Mongeon *et al*., 2009). The basal ganglia (which are defective in PD) play a critical role in proprioceptive integration with visual information which is provided simultaneously during the action or recalled from memory. This interaction between the visual and proprioceptive information assists individuals with PD by guiding their movements. This is also one of the reasons why individuals with PD are predominantly visually dependent for accuracy in targeted movements (Adamovich *et al*., 2001).

4.1.2 *Set shifting: Wisconsin Card Sorting Test (WCST)*

The WCST test was used to assess Set shifting in the PD participants of the current study. In the variable Perseverative Responses (PR), significant differences were observed between EXP and PBO at all three time points. This variable refers to the number of times an individual continues (or persists) in responding to an incorrect card characteristic (Strauss *et al.*, 2006), as well as an inability to use feedback to modify response patterns (Moore *et al*., 2000). It may indicate an inability to surrender the old sorting category in favour of a different one. It is unclear why the two groups should have differed from the start and maintained the difference throughout. The PBO did tend to improve at the mid-intervention point but deteriorated again to post-intervention. The EXP improved in WCST: PR and WCST: TE over the baseline phase, which may suggest that a learning effect took place for this test. This is likely confirmed by the tendency of the PBO to improve in the WCST: PR for this same period. Global WCST Score did not differ between the two groups at any time point but the PBO scored lower on average than the EXP. One might assume that this conflicts with the PR scores where EXP did better. However, this score does not just depend on right and wrong answers, but also the number of attempts. Over time there was no difference in Global WCST Score, thus there was no difference in Set shifting. Miyake *et al.* (2000) discussed the strength of involvement of EF when a task or test is novel or new. Repeated attempts at the task may reduce its efficacy in assessing the target EF, resulting

in low correlations between EF performance at the task when it was novel and later when it becomes familiar. David *et al.* (2015) also touched on the known practice effects of repeated cognitive or EF testing. Lemay *et al*. (2010) looked at practice effect and test-retest reliability of EF tests in middle-aged to elderly subjects and Burke *et al*. (2015) looked at practice effects on repeated neuropsychological measures of executive functioning. Lemay *et al*. (2010) did three assessments with each assessment 14 days apart and they found practice effects for all tests except those that utilized a different format for subsequent tests. On the other hand, Burke *et al*. (2015) also did three assessments with each assessment six months apart and found no practice effects. However, these studies were conducted in a normal population. My assessments were conducted between eight and nine weeks apart. I believe that the baseline phase would have helped with this as the practice effect would have been evident over the baseline phase. Reinforcing this, none of the EF variables in this study showed a statistically significant practice effect.

Alevriadou *et al.* (1999) reported a significant correlation between the WCST variables PR, percent PR (not used in this study) and FTMS and UPDRS part III (motor score). In addition to this, a significant correlation was observed between PR and percent PR and the PD symptom rigidity.

Tanaka *et al.* (2009) used the WCST test in their study which examined the impact of a multi-modal exercise programme on executive function in older people with PD. They chose to only use the WCST to assess EF in terms of mental flexibility (also known as Set shifting), attention and abstraction. Their results showed a significant improvement in the treatment group in the CC and “Perseverative errors” variables compared to the control group; however, they did not note any significant improvement in the variable FTMS. This is similar to the current study which also demonstrated no improvement in this variable. The current study, did not see the same significant improvements regarding CC and PR (very similar to “Perseverative errors”) that Tanaka *et al.* (2009) observed.

4.1.3 *Inhibition: Adapted Stroop Task*

Treatment effects were observed for CRT 1: accuracy, CRT 2: time and Interference score: accuracy, as well as a tendency for a treatment effect for CRT 1: time. The CRT 1 and CRT 2 are considered the easiest two conditions of the adapted Stroop task and measure response to identify the colour name of a word in a neutral text colour (CRT 1: Reading) and block colour without colour-word information (CRT 2: Naming), respectively. They do not

assess Inhibition but reaction time to a stimulus. CRT 1 is considered the easier of the two. The treatment effect observed in CRT 2: time and tendency in CRT 1: time may be due to an improvement in response time as a result of the SMT programme and the two groups differed significantly at post-intervention. The improvement in CRT 1: accuracy reveals that the participants were able to perform the test more accuracy.

Incongruent 1 and Incongruent 2 are the more difficult components of the adapted Stroop task and specifically assess the ability to respond on the basis of text colour while inhibiting the prepotent reaction to the word name. At all three time points, the EXP and PBO differed with regards to Inhibition 2: time. Although this was the only response time of the four that showed significance, closer inspection of the other three revealed consistent (although not significant) differences between EXP and PBO at all three time points (pre-, mid- and post-intervention). It is possible that the age difference and the depressive moods of the PBO could have played a role as both age (Allain *et al.,* 2005) and depressed moods (Uekermann *et al*., 2003) are known to be linked with EF. At post-intervention, the two groups also differed significantly regarding Incongruent 1: time and Incongruent 2: accuracy.

Both Interference: time and Interference: accuracy demonstrated differences between the EXP and PBO over the duration of the study. Interference: time was significantly different at all three time points and Interference: accuracy at mid- and post-intervention. The treatment effect and difference between the two groups suggest that the EXP were better able to inhibit their prepotent responses, which manifested as an improvement in their accuracy. The significant differences between the two groups over the study duration with regards to Interference Score: time suggest that the PBO battled with regards to the aspect of time. Interestingly, if one refers back to Figure 5.8, one can clearly observe the progressive deterioration of the time to complete TMT A (the easier of the two parts).

Changes over time in EXP were seen in several variables. Improvement in Incongruent 1: time is unlikely to be too meaningful as changes took place over the baseline phase, treatment phase as well as the duration of the study (baseline and treatment phases). CRT 1: time and Incongruent 1: time were significant over the duration of the study but not for the treatment phase, and thus the improvement is unlikely to have occurred as a result of the SMT. Improvement in CRT 2: time was significant over the treatment phase as well as the duration of the study. This could be indicative of a learning effect for the test. However, both groups underwent a baseline or control phase first, thus the practice effect would have been

added to the experimental and placebo groups' treatment phase. Consequently, when the different scores are averaged over the treatment phase, the practice effect disappears leaving the treatment effect (provided the two groups have the same number of subjects). The only variable to show a significant practice effect over baseline was the TUG and none of the other dependent variables. Hence, when the treatment phase improved significantly the treatment effect was greater than the practice effect.

Poor performance on the Incongruent component of the Stroop task is considered a strong predictor of executive dysfunction. Individuals are required to ignore insignificant stimuli or inhibit their natural response. Impaired Stroop task performance in non-demented PD patients predicted future dementia development (David *et al.*, 2015; Janvin *et al.*, 2005). Impaired Inhibition is associated with poorer gait performance and balance in the elderly (Xu *et al*., 2014).

In contrast to the current study, David *et al.* (2015), Duchesne *et al.* (2015), Baker *et al.* (2010) and Liu-Ambrose *et al.* (2008) all reported improvements in Inhibition as a result of their exercise interventions. In the current study only Interference 1: accuracy (measure of Inhibition) demonstrated a treatment effect. An observation regarding these studies is that they were conducted over three months to one year. Perhaps significant changes might have been observed if the SMT was conducted over a longer period.

4.2 *Functional Balance*

4.2.1 *Perceived Stability of Balance: Activities-specific Balance Confidence Scale (ABC)*

The Activities-specific Balance Confidence Scale (ABC) was designed to measure the confidence of individuals in their ability to perform activities of daily living without falling. Both groups tended to show a learning effect over the baseline phase. Only the EXP improved, however, over the treatment phase and overall from pre- to post-intervention. It would appear that as their functional mobility and balance improved so, too, did their confidence in their balance. This is also reflected in the TUG results. At post-intervention, the two groups differed significantly, suggesting that even without seeing a treatment effect for this variable, ABC probably improved as a result of the improved functional mobility via the SMT. A similar improvement in ABC was seen in the balance training study of Smania *et al*. (2010) in individuals with PD. In contrast, the Wii Fit balance training programme of Esculier *et al*. (2012) saw no improvement in ABC. Neither group attained the minimal detectable change MDC of 11.12 (Dal Bello-Haas *et al*., 2011).

Mak *et al.* (2009) showed that over a 12-month period balance confidence can predict fear of falling in individuals with PD: a score lower than 69% was associated with an increased risk for recurrent falls and a cut-off score has been determined as ≤ 46% (Almeida *et al*., 2014). The EXP was above the 69% cut-off for the duration of the study, while the PBO was below this at both the pre- and mid-intervention time points. At post-intervention, the PBO improved to move above the cut-off to 71.9%.

4.2.2 *Mobility: Timed Up and Go Test (TUG)*

The Timed Up and Go (TUG) Test is considered a simple test requiring an individual to stand up from a chair, walk 3 metres, turn around, walk back to the chair and sit down. It is considered a good test of functional mobility and balance. Although this appears easy, the TUG actually assesses multiple balance and mobility components (Herman *et al.*, 2010). The TUG is considered to be associated with cognitive function, including EF, as well as motor performance. This is seen in the planning and organization needed to perform this movement (Stegemöller *et al.*, 2014; McGough *et al.*, 2011; Herman *et al.*, 2010).

A treatment effect was demonstrated for the TUG and the two groups differed significantly at post-intervention. The EXP improved over the baseline phase, treatment phase, as well as over the 16-week duration of the study. In contrast, the PBO plateaued and no improvement was seen. Thus, although the EXP's improved ABC score mirrored their improved TUG score, this was not the case for the PBO. Thus, it would appear that the PBO perceived an improvement in their balance due to the feedback-wristband but this did not translate into an actual improvement in functional mobility and balance (TUG). No MCD or MCID have been determined for the TUG.

The improvement in TUG seen in the current study, in contrast to the study of Shubert *et al.* (2010) who saw no improvement in TUG in their EXP as a result of an exercise-based balance intervention, is similar to other studies which also saw a significant improvement in TUG times in response to exercise interventions (Sage & Almeida, 2010; Sage & Almeida, 2009; Hackney & Earhart 2008).

5. Study Limitations and Future Studies

Some limitations were noted during the course of this study and will now be briefly discussed. The participants were selected using a sample of convenience. Unfortunately, it

was not practical to randomize participants for this study. This would have meant having more, smaller groups spread over the Western Cape, making holding and travelling to and from the exercise groups impossible. Insufficient resources (manpower and financial) made it impossible to implement this study further afield during the study period. Thus, participants had to reside within a 70km radius of Stellenbosch in the Western Cape and be responsible for their own transport to the SMT programme. Future studies would be enhanced by targeting a wider area and having more groups available. Consequently, one understandable limitation of convenience sampling is that it may not be representative of the population. The sample size was also small and, thus, it may not be appropriate to extrapolate these finding to the greater PD population. Research in the future would be improved by having a larger sample size. This may also explain the observed differences between the two groups at baseline.

Participants were tested on their medication for this study. Future research should also attempt to assess participants off their medication (after a wash-out period). Unfortunately, it was not possible to do this in the current study due to limited man-power and resources. However, participants were tested at the same time (plus or minus one hour) at each testing session in order to maintain consistency during the study.

The current study was conducted over an eight-week period and it is possible that this was not long enough to see changes in EF. Other studies investigated the effect of their exercise intervention on EF over a minimum 12-week period (Duchesne *et al.*, 2015; David *et al.*, 2015; McKee & Hackney, 2013; Cruise *et al.*, 2010; Tanaka *et al.*, 2009).

This study only made use of one version of the MoCA in English and Afrikaans, and therefore did not randomize the use of the MoCa. This was because there was only one Afrikaans version available at the time of the study. In future studies it may be beneficial to use one or more of the other MoCA versions as well.

Another limitation to this study was the increase in social and cognitive interaction as a result of participating in this study. Participants attended sessions three times a week for eight weeks where they met and engaged with other PD participants going through similar experiences and difficulties and interacted with the biokineticists and research assistants. The placebo group did not receive this same social or group interaction. This was also

mentioned in the study of David *et al.* (2015). A potential way to improve on this in future studies would be to organize PD-relevant talks or educational classes for participants.

As noted earlier in the chapter, some of the older participants were not completely confident using a computer and/or a computer mouse. It may be worthwhile developing a system that requires participants to press only two individual buttons rather than specific keys on a keyboard. An alternative option may be to focus only on non-computerized tests.

The beginning stages of the programme were highly repetitive which was positive in terms of emphasizing posture and practicing balance but at times it was a little too drawn out and perhaps boring. Most of the participants enjoyed the latter parts of the study with the increasing challenges and this should perhaps have begun earlier. The research of Abbruzzese *et al*. (2016) emphasize the importance of intensive challenging rehabilitation for those with PD to induce neuroplasticity. In addition, Allen *et al*. (2011) also recommend that highly challenging balance exercises be incorporated into PD rehabilitation programmes. Future studies should consider increasing the intensity and challenge of the balance exercises as this could have a different outcome on the EF variables.

The three tests which were used in this study – the WCST, the adapted Stroop task and the TMT – are standardized and commonly used neuropsychological tests for the assessment of EF in PD (Dirnberger & Jahanshahi, 2013). They are objective tests and can be easily compared. The WCST and adapted Stroop task were computer based and the TMT conducted with pen and paper. During the study it became apparent that they were possibly not functional enough. In other words, the tests differed in comparison to activities or tasks encountered in daily living.

Every attempt was made to make this study enjoyable and convenient for the participants, such as assessing them in their homes where possible and phoning the PBO group every two weeks to follow up with them. This study also appears to be the first to investigate the impact of an SMT programme on the EF of individuals with PD. As can be seen in the available literature, studies addressing the effects of exercise on EF in PD are scarce.

Reflecting back on the study, I believe the sensory-motor training programme was successful. The participants really seemed to enjoy it and the attendance for classes was

mostly very high. Informal feedback from the participants, as well as their caregivers, was very positive.

6. Conclusion

In conclusion, the SMT programme conducted three times per week over eight weeks, in a sample of participants with mild to moderate PD, had an influence on selected aspects of EF. The neuroplasticity mechanisms pertaining to the results of this study are likely to include an increase in BDNF and in cerebral blood flow, as well as the cognitive reserve theory. The SMT programme did not have a significant effect on the ability to shift back and forth between different choices (Set shifting) nor on the ability to hold and work with information in one's mind (Updating). However, an improvement relating to the ability to inhibit prepotent responses (Inhibition) was noted but further research is needed to confirm this. Impaired Inhibition has been associated with poorer balance and gait so an intervention that can maintain or improve Inhibition will be of significant benefit. An interesting finding from the study was the improvement in visuomotor abilities. There is a link between visuomotor ability and sensory integration, which people with PD battle with and a SMT programme is able to assist this. General cognition, perception of depressive moods, and quality of life in general, remained unchanged as a result of the eight-week SMT. However, significant improvements in balance confidence and functional mobility were observed. These can have a direct impact on the life of individuals with PD in terms of improved balance and a reduction in fall risk. In addition to this, significant improvements were noted in MDS-UPDRS II, III and Total which relate to a reduction in PD severity.

REFERENCES

Aarsland, D., Andersen, K., Larsen, J.P., Lolk, A. & Kragh-Sørensen, P. (2003). Prevalence and Characteristics of Dementia in Parkinson's Disease: An 8-Year Prospective Study. *Archives of Neurology*, 60:387-392.

Abbruzzese, G., Trompetto, C., Mori, L. & Pelosin, E. (2014). Proprioceptive Rehabilitation of Upper Limb Dysfunction in Movement Disorders: a Clinical Perspective. *Frontiers in Human Neuroscience*, 8: Article 961.

Abbruzzese, G., Marchese, R., Avanzino, L. & Pelosin, E. (2015). Rehabilitation for Parkinson's Disease: Current outlook and future challenges. *Parkinsonism and Related Disorders*, http://dx.doi.org/10.1016/j.parkreldis.2015.09.005.

Adkin, A.L., Frank, J.S. & Jog, M.S. (2003). Fear of Falling and Postural Control in Parkinson's Disease. *Movement Disorders*, 18(5):496-502.

Adlard, P.A., Perreau, V.M., Pop, V. & Cotman, C.W. (2005). Voluntary Exercise Decreases Amyloid Load in a Transgenic Model of Alzheimer's Disease. *The Journal of Neuroscience*, 25(17):4217-4221.

Adamovich, S.V., Berkinblit, M.B., Hening, W., Sage, J. & Poizner, H. (2001). The interaction of visual and proprioceptive inputs in pointing to actual and remembered targets in Parkinson's Disease. *Neuroscience*, 104(4):1027-1041.

Ahlskog, J.E. (2011). Does vigorous exercise have a neuroprotective effect in Parkinson Disease? *Neurology*, 77:288-294.

Ainslie, P.N., Cotter, J.D., George, K.P., Lucas, S., Murrell, C., Shave, R., Thomas, K.N., Williams, M.J.A. & Atkinson, G. (2008). Elevation in cerebral blood flow velocity with aerobic fitness throughout healthy human aging. *The Journal of Physiology*, 586 (16):4005-4010.

Albinet, C.T., Boucard, G., Bouquet, C.A. & Audiffren, M. (2012) Processing speed and executive functions in cognitive aging: How to disentangle their mutual relationship? *Brain and Cognition*, 79:1-11.

Alevriadou, A., Katsarou, Z., Bostantjopoulou, S., Kiosseoglou, G. & Mentenopoulos, G. (1999). Wisconsin Card Sorting Test Variables in Relation to Motor Symptoms in Parkinson's Disease. *Perceptual and Motor Skills*, 89:824-830.

Allain, P., Nicoleau, S., Pinon, K., Etcharry-Bouyx, F., Barré, J., Berrut, G., Dubas, F. & Le Gall, D. (2005). *Executive functioning in normal aging: a study of action planning using the Zoo Map Test.*

Almeida, L.R.S., Valença, G.T., Negreiros, N.N., Pinto, E.B. & Oliveira-Filho, J. (2014) Recurrent Falls in People with Parkinson's Disease without Cognitive Impairment: Focusing on Modifiable Risk Factors. *Parkinson's Disease*, 2014:432924.

Alves, G., Forsaa, E.B., Pedersen, K.F., Gjerstad, M.D. & Larsen, J.P. (2008). Epidemiology of Parkinson's Disease. *Journal of Neurology*, 255(5):18-32.

Allen, N.E., Sherrington, C., Paul, S.S. & Ganning, C.G. (2011). Balance and Falls in Parkinson's Disease: A Meta-analysis of the Effect of Exercise and Motor Training. *Movement Disorders*, 26 (9):1605-1615.

Aman, J.E., Elangovan, N., Yeh, I.L., Konczak, J. (2014). The effectiveness of proprioceptive training for improving motor function: a systematic review. *Frontiers in Human Neuroscience*, 8:1075.

Angevaren, M., Aufdemkampe, G., Verhaar, H.J.J., Aleman, A. & Vanhees, L. (2008). Physical Activity and Enhanced Fitness to Improve Cognitive Function in Older People without Known Cognitive Impairment (Review). *Cochrane Database of Systematic Reviews*, Issue 3. Art. No.: CD005381. DOI: 10.1002/14651858.CD005381.pub3.

Arbuthnott & Frank. (2000). Trail Making Test, Part B as a Measure of Executive Control: Validation Using a Set-Switching Paradigm. *Journal of Clinical and Experimental Neuropsychology*, 22(4):518-528.

Baatile, J., Langbein, W.E., Weaver, F., Maloney, C. & Jost, M.B. (2000). Effect of exercise on perceived quality of life of individuals with Parkinson's Disease. *Journal of Rehabilitation Research and Development*, 37(5):529-534.

Baker, L.D., Frank, L.L., Foster-Schubert, K., Green, P.S., Wilkinson, C.W., McTiernan, A., Plymate, S.R., Fischel, M.A., Watson, G.S., Cholerton, B.A., Duncan, G.E., Mehta, P.D. & Craft, S. (2010). Effects of Aerobic Exercise on Mild Cognitive Impairment: A Controlled Trial. *Archives of Neurology*, 67(1):71-9.

Barceló & Knight. (2002). Both random and perseverative errors underlie WCST deficits in prefrontal patients. *Neuropsychologia*, 40:349-356.

Becofsky, K.M. (2014). The effects of exercise training on cognitive reserve and cognitive function in healthy older women. (Doctoral dissertation). Retrieved from http://scholarcommons.sc.edu/edt/2795.

Benito-León, J., Louis, E.D., Posada, I.J., Sanchez-Ferro, A., Trincado, R., Villarejo, A., Mitchell, A.J. & Bermejo-Pareja, F. (2011). Population-based case-control study of cognitive function in early Parkinson's Disease (NEDICES). *Journal of the Neurological Sciences*, 310:176-182.

Bergen, J.L., Toole, T., Elliott III, R.G., Wallace, B., Robinson, K. & Maitland, C.G. (2002). Aerobic exercise intervention improves aerobic capacity and movement initiation in Parkinson's Disease patients. *NeuroRehabilitation*, 17:161-168.

Blanckenberg, J., Bardien, S., Glanzmann, B., Okubadejo, N.U. & Carr, J.A. (2013). The prevalence and genetics of Parkinson's Disease in Sub-Saharan Africans. *Journal of the Neurological Sciences*, 335:22-25.

Bloem, B.R., de Vries, N.M. & Ebersbach, G. (2015). Nonpharmalogical Treatments for Patients with Parkinson's Disease. *Movement Disorders*, 30(11):1504-1520.

Blumenthal, J.A., Emery, C.F., Madden, D.J., George, L.K., Coleman, R.E., Riddle, M.W., McKee, D.C., Reasoner, J. & Williams, R.S. (1989). Cardiovascular and behavioural effects of aerobic exercise training in healthy men and women. *The Journals of Gerontology*, 44(5):M147-157.

Browner, N. & Giladi, N. (2010). What Can We Learn from Freezing of Gait in Parkinson's Disease. *Current Neurology and Neuroscience Reports*, 10:345-351.

Burke, T., Wynne, B., O'Brien, C., Elamin, M., Bede, P., Hardiman, O. & Pender, N. (2015). Retrospective investigations of practice effects on repeated neuropsychological measures of executive functioning. *The Irish Journal of Psychology*, 35(4):178-187.

Camicioli, R. & Majumdar, S.R. (2010). Relationship between mild cognitive impairment and falls in older people with and without Parkinson's Disease: 1-Year Prospective Cohort Study. *Gait & Posture*, 32:87-91.

Carr, J. (2014). A putative founder effect for Parkinson's Disease in South African Afrikaners. *South African Medical Journal*, 104(6):411-412.

Carr, D., Sonnega, J., Nesse, R.M. & House, J.S. (2014). Do Special Occasions Trigger Psychological Distress Among Older Bereaved Spouses? An Empirical Assessment of Clinical Wisdom. *Journals of Gerontology, Series B: Psychological Sciences and Social Sciences*, 69(1):113-122.

Carvalho, A., Barbirato, D., Araujo, N., Martins, J.V., Cavalcanti, J.L.S., Santos, T.M., Coutinho, E.S., Laks, J. & Deslandes, A.C. (2015). Comparison of strength training, aerobic training and additional physical therapy as supplementary treatments for Parkinson's Disease: pilot study. *Clinical Interventions in Aging*, 10:183-191.

Chafetz, M.D. & Matthews, L.H. (2004). A New Interference Score for the Stroop test. *Archives of Clinical Neurology*, 19:555-567.

Chang, Y.K. & Etnier, J.L. (2009). Exploring the Dose-Response Relationship between Resistance Exercise Intensity and Cognitive Function. *Journal of Sport and Exercise Psychology*, 31:640-656.

Chang, Y.K., Chi, L., Etnier, J.L., Wang, C.C., Chu, C.H. & Zhou, C. (2014). Effect of acute aerobic exercise on cognitive performance: Role of cardiovascular fitness. *Psychology of Sport and Exercise*, 15(5):464-470.

Chou, K.L., Lenhart, A., Koeppe, R.A., Bohnen, N.I. (2014). Abnormal MoCA and normal range MMSE scores in Parkinson Disease without dementia: Cognitive and neurochemical correlates. *Parkinsonism and Related Disorders*, 20:1076-1080.

Coelho, F.G., Gobbi, S., Andreatto, C.A., Corazza, D.I., Pedroso, R.V. & Santos-Galduróz, R.F. (2013). Physical exercise modulates peripheral levels of brain-derive neurotrophic factor (BDNF): A systematic review of experimental studies in the elderly. *Archives of Gerontology and Geriatrics*, 56:10-15.

Colcombe, S.J., Kramer, A.F., Erickson, K.I., Scalf, P., McAuley, E., Cohen, N.J., Webb, A., Jerome, G.J., Marquez, D.X. & Elavsky, S. (2004). Cardiovascular fitness, cortical plasticity, and aging. *Proceedings of the National Academy of Sciences*, 101(9):3316-3321.

Cotman, C.W. & Berchtold, N.C. (2002). Exercise: A Behavioral Intervention to Enhance Brain Health and Plasticity. *Trends in Neurosciences,* 25(6):295.

Crizzle, A.M. & Newhouse, I.J. (2006). Is Physical Exercise Beneficial for Person's with Parkinson's Disease? *Clinical Journal of Sport Medicine*, 16(5):422-425.

Crossman, A.R. & Neary, D. (2000). *Neuroanatomy: An Illustrated Colour Text*, 2nd edn., Churchill Livingstone, London.

Cruise, K.E., Bucks, R.S., Loftus, A.M., Newton, R.U., Pegoraro, R. & Thomas, M.G. (2011). Exercise and Parkinson's: benefits for cognition and quality of life. *Acta Neurologica Scandinavica*, 123:13-19.

Cubo, E., Bernard, B., Leurgans, S. & Raman, R. (2000). Cognitive and Motor Function in Patients with Parkinson's Disease with and without Depression. *Clinical Neuropharmacology*, 23(6):331-334.

Curtze, C., Nutt, J.G., Carlson-Kuhta, P., Mancini, M. & Horak, F.B. (2015). Levodopa Is a Double-Edged Sword for Balance and Gait in People with Parkinson's Disease. *Movement Disorders*, 30(10):1361-1370.

Cusin, C., Yang, H., Yeung, A. & Fava, M. (2009). Rating Scales for Depression. In: Baer, L. and Blais, M.A. *Handbook of Clinical rating Scales and Assessment in Psychiatry and Mental Health*. New York: Humana Press. p7-35.

Cutson, T.M., Lamb, K.C. & Schenkman, M. (1995). Pharmacological and Nonpharmacological Interventions in the Treatment of Parkinson's Disease. *Physical Therapy*, 75(5):363-373.

Dal Bello-Haas, V., Klassen, L., Sheppard, M.S. & Metcalfe, A. (2011). Psychometric Properties of Activity, Self-Efficacy, and Quality-of-Life Measures in Individuals with Parkinson Disease. *Physiotherapy Canada*, 63(1):47-57.

Dalrymple-Alford, J.C., MacAskill, M.R., Nakas, C.T., Livingston, L., Graham, C., Crucian, G.P., Melzer, T.R., Kirwan, J., Keenan, R., Wells, S., Porter, R.J., Watts, R. & Anderson, T.J. (2010). The MoCA: Well-suited screen for cognitive impairment in Parkinson Disease. *Neurology*, 75:1717-1725.

David, F.J., Robichaud, J.A., Leurgans, S.E., Poon, C., Kohrt, W.M., Goldman, J.G., Comella, C.L., Vaillancourt, D.E. & Corcos, D.M. (2015). Exercise Improves Cognition in Parkinson's Disease: The PRET-PD Randomized, Clinical Trial. *Movement Disorders*, DOI: 10.1002/mds.26291.

Deegan, M.J. (2015). Holidays as Multiple Realities: Experiencing Good Times and Bad Times after a Disabling Injury. *The Journal of Sociology & Social Welfare*, 13(4):7.

De Lau, L.M.L. & Breteler, M.M.B. (2006). Epidemiology of Parkinson's Disease. *The Lancet Neurology*, 5:525-535.

De Ridder, J.H. (2005). *Kinanthropometry in exercise and sport: A textbook for students.* Potchefstroom.

Development Information and GIS Department. (2014). *Cape Town Census 2011 Socio-Economic Index*. Development Information and GIS Department, City of Cape Town.

Diamond, A. (2013). Executive Functions. *Annual Review Psychology*, 64:135-168.

Diamond, A. (2015). Effects of Physical Exercise on Executive Functions: Going beyond Simply Moving to Moving with Thought. *Annals of Sports Medicine and Research*, 2(1):1011.

Dibble, L.E., Hale, T.F., Marcus, R.L., Gerber, J.P. & LaStayo, P.C. (2009). High intensity eccentric resistance training decreases bradykinesia and improves quality of life in persons with Parkinson's Disease: A preliminary study. *Parkinsonism and Related Disorders*, 15:752-757.

Dikmen, S.S., Heaton, R.K., Grant, I. & Temkin, N.R. (1999). Test-retest reliability and practice effects of Expanded Halstead-Reitan Neuropsychological Test Battery. *Journal of International Neuropsychological Society*, 5:346-356.

Dirnberger, G. & Jahanshahi, M. (2013). Executive dysfunction in Parkinson's Disease. A review. *Journal of Neuropsychology*, 7:193-224.

Domellöf, M.E., Elgh, E. & Forsgren, L. (2011). The Relationship Between Cognition and Motor Dysfunction in Drug-Naïve Newly Diagnosed Patients with Parkinson's Disease. *Movement Disorders*, 26(12):2183-2189.

Donoghue, O.A., Horgan, N.F., Savva, G.M., Cronin, H., O'Regan, C. & Kenny, R.A. (2012). Association between Timed Up-and-Go and Memory, Executive Function and Processing Speed. *Journal of the American Geriatrics Society*, 60:1681-1686.

Dorsey, E.R., Constantinescu, R., Thompson, J.P., Biglan, K.M., Holloway, R.G., Kieburtz, K., Marshall, F.J., Ravina, B.M., Schifitto, G., Siderowf, A. & Tanner, C.M. (2007). Projected Number of People with Parkinson Disease in the most Populous Nations, 2005 through 2030. *Neurology*, 68:384-386.

Dos Santos Mendes, F.A., Pompeu, J.E., Lobo, A.M., Da Silva, K.G., Oliveira, T.D.P., Zomignami, A.P. & Piemonte, M.E.P. (2012). Motor learning, retention and transfer after virtual-reality-based training in Parkinson's Disease – effect of motor and cognitive demands of games: a longitudinal, controlled clinical study. *Physiotherapy*, 98: 217-223.

Drane, D.L., Yuspeh, R.L., Huthwaite, J.S. & Klingler, L.K. (2002). Demographic Characteristics and Normative Observations for Derived-Trail Making Test Indices. *Neuropsychiatry, Neuropsychology and Behavioral Neurology*, 15(1):39-43.

Duchesne, C., Lungu, O., Nadeau, A., Robillard, M.E., Boré, A., Bobeuf, F., Lafontaine, A.L., Gheysen, F., Bherer, L. & Doyon, J. (2015). Enhancing both motor and cognitive functioning in Parkinson's Disease: Aerobic exercise as a rehabilitative intervention. *Brain and Cognition*, 99:68-77.

Dujardin, K., Duhamel, A., Delliaux, M., Thomas-Antérion, C., Destée, A. & Defebvre, L. (2010). Cognitive complaints in Parkinson's Disease: its relationship with objective cognitive decline. *Journal of Neurology*, 257:79-84.

Emre, M. (2003). Dementia associated with Parkinson's Disease. *The Lancet Neurology*, 2:229-237.

Engel-Yeger, B., Hus, S. & Rosenblum, S. (2012). Age effects on sensory-processing abilities and their impact on handwriting. *Canadian Journal of Occupational Therapy*, 79:264-274.

Erickson, K.I., Oberlin, L., Gujral, S., Leckie, R.L., Weinstein, A.M., Hodzic, J.C., Dabbagh, A., Whitmoyer, P.R. & Wollam, M.E. (2014). Exercise as a Way of Capitalizing on Neuroplasticity in Late Adulthood. *Topics in Geriatric Rehabilitation*, 30(1):8-14.

Esculier, J-F., Vaudrin, J., Bériault, P., Gagnon, K. & Tremblay, L.E. (2012). Home-based balance training programme using Wii Fit with balance board for Parkinson's Disease: a pilot study. *Journal of Rehabilitation Medicine*, 44:144-150.

Etnier, J.L. & Yu-Kai Chang. (2009). The Effect of Physical Activity on Executive Function: A Brief Commentary on Definitions, Measurement Issues, and the Current State of the Literature (Report). *Journal of Sport & Exercise Psychology,* 31(4):469-83.

Fabre, C., Chamari, K., Mucci, P., Massé-Biron, J. & Préfaut, C. (2002). Improvement of Cognitive Function by Mental and / or Individualized Aerobic Training in Healthy Elderly Subjects. *International Journal of Sports Medicine*, 23(6):415-421.

Fahn, S. (2003). Description of Parkinson's Disease as a Clinical Syndrome. *Annals New York Academy of Sciences*, 991:1-14.

Fals-Stewart, W. (1992). An Interrater Reliability Study of the Trail Making Test (Parts A and B). *Perceptual and Motor Skills*, 74:39-42.

Figueroa, I.J. & Youmans, R.J. (2013). Failure to Maintain Set: A Measure of Distractibility or Cognitive Flexibility. In *Proceedings of the Human Factors and Ergonomics Society 57th Annual Meeting – 2013*:828-832.

Flensborg Damholdt, M., Shevlin, M., Borghammer, P., Larsen, L. & Østergaard, K. (2012). Clinical Heterogeneity in Parkinson's Disease Revisited: A Latent Profile Analysis. *Acta Neurologica Scandinavica*, 125:311-318.

Fratiglioni, L., Paillard-Borg, S. & Winblad, B. (2004). An Active and Socially Integrated Lifestyle in Late Life Might Protect Against Dementia. *Lancet Neurology*, 3:343-353.

Gelb, D.J., Oliver, E. & Gilman, S. (1999). Diagnostic Criteria for Parkinson's Disease. *Archives of Neurology*, 56(1):33-39.

Geldenhuys, G., Glanzmann, B., Lombard, D., Boolay, S., Carr, J. & Bardien, S. (2014). Identification of a common founder couple for 40 South African Afrikaner families with Parkinson's Disease. *South African Medical Journal*, 104(6):413-419.

Gilsoul, J., Simon, J. & Fabienne, C. (2015). Executive functions in normal aging: Impact of cognitive reserve and objective physical activity. http://hdl.handle.net/2268/182197

Glisky, E.L. (2007). Changes in cognitive function in human aging, in Riddle, D.R.(ed.). *Brain aging: Models, methods, and mechanisms.* Boca Raton: CRC Press. Pages 4-15.

Gothe, N.P., Fanning, J., Awick, E., Chung, D., Wójcicki, T.R., Olson, E.A., Mullen, S.P., Voss, M., Erickson, K.I., Kramer, A.F. & McAuley, E. (2014). Executive Function Processes Predict Mobility Outcomes in Older Adults. *Journal of the American Geriatrics Society*, 62(2):285-290.

Goetz, C.G., Poewe, W., Rascol, O., Sampaio, C., Stebbins, G.T., Counsell, C., Giladi, N., Holloway, R.G., Moore, C.G., Wenning, G.K., Yahr, M.D. & Seidl, L. (2004). Movement Disorder Society Task Force Report on the Hoehn and Yahr Staging Scale: Status and Recommendations. *Movement Disorders*, 19(9):1020-1028.

Goetz, C.G., Tilley, B.C., Shaftman, S.R., Stebbins, G.T., Fahn, S., Martínez-Martín, P., Poewe, W., Sampaio, C., Stern, M.B., Dodel, R., Dubois, B., Holloway, R., Jankovic, J., Kulisevsky, J., Lang, E.A., Lees, A., Leurgans, S., LeWitt, P.A., Nyenhuis, D., Olanow,

C.W., Rascol, O., Schrag, A., Teresi, J.A., van Hilten, J.J. & LaPelle, N. (2008). *Movement* Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale Presentation and Clinimetric Testing Results. *Movement Disorders*, 23(15):2129-2170.

Goetz, C.G., Stebbins, G.T. & Tilley, B.C. (2012). Calibration of Unified Parkinson's Disease Rating Scale Scores to *Movement* Disorder Society-Unified Parkinson's Disease Rating Scale Scores. *Movement Disorders*, 27(10):1239-1242.

Golden, C.J. (1978). *Stroop Color and Word Test*. Wood Dale, IL: Stoelting.

Goodwin, V.A., Richards, S.H., Taylor, R.S., Taylor, A.H. & Campbell, J.L. (2008). The Effectiveness of Exercise Interventions for People with Parkinson's Disease: A Systematic Review and Meta-Analysis. *Movement Disorders*, 23(5):631-640.

Gow, A.J. (2013). Enhancing brain health: 10,000 steps at a time? *Aging Health*, 3(3):239-241.

Gunstad, J., Paul, R.H., Cohen, R.A., Tate, D.F., Spitznagel, M.B. & Gordon, E. (2007). Elevated body mass index is associated with executive dysfunction in otherwise healthy adults. *Comprehensive Psychiatry*, 48:57-61.

Hackman, D.A., Gallop, R., Evans, G.W. & Farah, M.J. (2015). Socioeconomic status and executive function: developmental trajectories and mediation. *Developmental Science*, 18(5):686-702.

Hackney, M.E. & Earhart, G.M. (2008). Tai Chi Improves Balance and Mobility in People with Parkinson Disease. *Gait Posture*, 28(3):456-460.

Hagell, P. & Nygren, C. (2007). The 39 item Parkinson's Disease questionnaire (PDQ-39) revisited: implications for evidence-based medicine. *Journal of Neurology, Neurosurgery & Psychiatry*, 78:1191-1198.

Hagell, P., Whalley, D., McKenna, S.P. & Lindvall, O. (2003). Health Status Measurement in Parkinson's Disease: Validity of the PDQ-39 and Nottingham Health Profile. *Movement Disorders*, 18(7):773-783.

Halliday, G.M. & McCann, H. (2010). The Progression of Pathology in Parkinson's Disease. *Annals of the New York Academy of Sciences*, 1184:188-195.

Harkness, K., Demers, C., Heckman, G.A. & McKelvie, R.S. (2011). Screening for Cognitive Deficits using the Montreal Cognitive Assessment Tool in Outpatients ≥65 years of age with Heart Failure. *American Journal of Cardiology*, 107:1203-1207.

Harrison, M.B., Wylie, S.A., Frysinger, R.C., Patrie, J.T., Huss, D.S., Currie, L.J. & Wooten, G.F. (2009). UPDRS Activity of Daily Living Score as a Marker of Parkinson's Disease Progression. *Movement Disorders*, 24(2):224-230.

Hartholt, K.A., Van Beeck, E.F., Polinder, S., Van der Velde, N., Van Lieshout, E.M.M., Panneman, M.J.M., Van der Cammen, T.J.M. & Patka, P. (2011). Societal Consequences of Falls in the Older Population: Injuries, Healthcare Costs, and Long-Term Reduced Quality of Life. *The Journal of Trauma*, 71:748-753.

Harvey. P.O., Le Bastard, G., Pochon, J.B., Levy, R., Allilaire, J.F., Dubois, B. & Fossati, P. (2004). Executive functions and updating of contents of working memory in unipolar depression. *Journal of Psychiatric Research*, 38:567-576.

Hass, C.J., Buckley, T.A., Pitsikoulis, C. & Barthelemy, E.J. (2012). Progressive resistance training improves gait initiation in individuals with Parkinson's Disease. *Gait & Posture*, 35:669-673.

Hely, M.A., Reid, W.G.J., Adena, M.A., Halliday, G.M. & Morris, J.G.L. (2008). The Sydney Multicenter Study of Parkinson's Disease: The Inevitability of Dementia at 20 years. *Movement Disorders*, 23(6):837-844.

Herman, T., Giladi, N. & Hausdorff, J.M. (2011). Properties of the 'Timed Up and Go' Test: More than Meets the Eye. *Gerontology*, 57: 203-210.

Higginson, C.I., King, D.S., Levine, D., Wheelock, V.L., Khamphay, N.O. & Sigvardt, K.A. (2003). The relationship between executive function and verbal memory in Parkinson's Disease. *Brain and Cognition*, 52:343-352.

Higginson, C.I., Lanni, K., Sigvardt, K.A. & Disbrow, E.A. (2013). The contribution of trail making to the prediction of performance-based instrumental activities of daily living in Parkinson's Disease without dementia. *Journal of Clinical and Experimental Neuropsychology*, 35(5):530-539.

Hindle, J.V., Martyr, A. & Clare, L. (2014). Cognitive reserve in Parkinson's Disease: A systematic review. *Parkinsonism and Related Disorders*, 20(1):1-7.

Hirsch, M.A., Toole, T., Maitland, C.G. & Rider, R.A. (2003). The Effects of Balance Training and High-Intensity Resistance Training on Persons with Idiopathic Parkinson's Disease. *Archives of Physical Medicine and Rehabilitation*, 84:1109-1117.

Hoang, Q.Q. (2014). Pathway for Parkinson's Disease. *Proceedings of the National Academy of Sciences*, 111(7):2402-2403.

Hoehn, M.M. & Yahr, M.D. (1967). Parkinsonism: onset, progression, and mortality. *Neurology*, 17(5): 427-442.

Hoops, S., Nazem, S., Siderowf, A.D., Duda, J.E., Xic, S.X., Stern, M.B. & Weintraub, D. (2009). Validity of the MoCA and MMSE in the detection of MCI and dementia in Parkinson Disease. *Neurology*, 73:1738-1745.

Horváth, K., Aschermann, Z., Ács, P., Deli, G., Janszky, J., Komoly, S., Balázs, É., Takács, K., Karádi, K. & Kovács, N. (2015). Minimal Clinically Important Difference on the Motor Examination Part of MDS-UPDRS. *Parkinsonism and Related Disorders*, doi: 10.1016/j.parkreldis.2015.10.006.

Hsieh, Y., Chen, K., Wang, C. & Lai, C. (2008). Cognitive and Motor Components of Response Speed in the Stroop Test in Parkinson's Disease Patients. *Kaohsiung Journal of Medical Sciences*, 24:197-203.

Huang, S-L., Hsieh, C-L., Wu, R-M., Tai, C-H., Lin, C-H. & Lu, W-S. (2011). Minimal Detectable Change of the Timed "Up & Go" Test and the Dynamic Gait Index in People with Parkinson Disease. *Physical Therapy*, 91(1): 114-121.

Hu, G., Jousilahti, P., Nissinen, A., Antikainen, R., Kivipelto, M. & Tuomilehto, J. (2006). Body mass index and the risk of Parkinson disease. *Neurology*, 67:1955-1959.

Jankovic, J. (2008). Parkinson's disease: clinical features and diagnosis. *Journal of Neurology, Neurosurgery and Psychiatry*, 79:368-376.

Janvin, C.C., Aarsland, D. & Larsen, J.P. (2005). Cognitive Predictors of Dementia in Parkinson's Disease: A Community-Based, 4-Year Longitudinal Study. *Journal of Geriatric Psychiatry and Neurology*, 18:149-154.

Jenkinson, C., Fitzpatrick, R., Peto, V., Greenhall, R. & Hyman, N. (1997). The Parkinson's Disease Questionnaire (PDQ-39): development and validation of a Parkinson's Disease summary index score. *Age and Ageing*, 26:353-357.

Jones. D., Rochester, L., Birleson, A., Hetherington, V., Nieuwboer, A., Willems, A.M., Van Wegen, E. & Kwakkel, G. (2008). Everyday Walking with Parkinson's Disease: Understanding Personal Challenges and Strategies. *Disability and Rehabilitation*, 30(16):1213-1221.

Kalia, L.V. & Lang, A.E. (2015). Parkinson's Disease. *Lancet*, 386:896-912.

Kanekar, N. & Aruin, A.S. (2014). The effect of aging on anticipatory postural control. *Experimental Brain Research*, 232:1127-1136.

Kandiah, N., Narasimhalu, K., Lau, P-N., Seah, S-H., Au, W.L. & Tan, L.C.S. (2009). Cognitive Decline in Early Parkinson's Disease. *Movement Disorders*, 24(4):605-616.

Kelly, V.E., Johnson, C.O., McGough, E.L., Shumway-Cook, A., Horak, F.B., Chung, K.A., Espay, A.J., Revilla, F.J., Devoto, J., Wood-Siverio, C., Factor, S.A., Cholerton, B., Edwards, K.L., Peterson, A.L., Quinn, J.F., Montine, T.J., Zabetian, C.P. & Leverenz, J.B. (2015). Association of Cognitive Domains with Postural Instability / Gait Disturbance in Parkinson's Disease. *Parkinsonism and Related Disorders*, 21:692-697.

Kim, H.J., Oh, E.S., Lee, J.H., Moon, J.S., Oh, J.E., Shin, J.W., Lee, K.J., Baek, I.C., Jeong, S.H., Song, H.J., Sohn, E.H. & Lee, A.Y. (2012). Relationship between changes of body mass index (BMI) and cognitive decline in Parkinson's Disease (PD). *Archives of Gerontology and Geriatrics*, 55:70-72.

King, L.A., Wilhelm, J., Chen, Y., Blehm, R., Nutt, J., Chen, Z., Serdar, A. & Horak, F.B. (2015). Effects of Group, Individual, and Home Exercise in Person's With Parkinson's Disease: A Randomized Clinical Trial. *Journal of Neurologic Physical Therapy*, 39:204-212.

Kleim, J.A. & Jones, T.A. (2008). Principles of Exercise-Dependent Neural Plasticity: Implications for Rehabilitation After Brain Damage. *Journal of Speech, Language and Hearing Research*, 5:S225-S239.

Kleim, J.A. (2011). Neural plasticity and neurorehabilitation: Teaching the new brain old tricks. *Journal of Communication Disorders*, 44:521-528.

Koerts, J., Van Beilen, M., Tucha, O., Leenders, K.L. & Brouwer, W.H. (2011). Executive Functioning in Daily Life in Parkinson's Disease: Initiative, Planning and Multi-Task Performance. *PLOS ONE*, 6(12):1-8.

Koerts, J., Tucha, L., Lange, K.W. & Tucha, O. (2013). The influence of cognitive reserve on cognition in Parkinson's Disease. *Journal of Neural Transmission*, 120:593-596.

Ku, P-W., Stevinson, C. & Chen, L-J. (2012). Prospective Associations Between Leisure-Time Physical Activity and Cognitive Performance Among Older Adults Across an 11-Year Period. *Journal of Epidemiology*, 22(3):230-237.

Laiacona, M., Inzaghi, M.G., De Tanti, A. & Capitani, E. (2000). Wisconsin card sorting test: a new global score, with Italian norms, and its relationship with the Weigl sorting test. *Neurological Sciences*, 21(5):279-291.

Lajoie, Y. & Gallagher, S.P. (2004). Predicting falls within the elderly community: comparison of postural sway, reaction time, the Berg balance scale and the Activities-specific Balance Confidence (ABC) scale for comparing fallers and non-fallers. *Archives of Gerontology and Geriatrics*, 38:11-26.

Lang, A.E., Eberly, S., Goetz, C.G., Stebbins, G., Oakes, D., Marek, K., Ravina, B., Tanner, C.M. & Shoulson, I. (2013). *Movement* Disorder Society Unified Parkinson Disease Rating Scale Experiences in Daily Living: Longitudinal Changes and Correlation With Other Assessments. *Movement Disorders*, 28(14):1980-1986.

Langlois, F., Vu, T.T., Chassé, K., Dupuis, G., Kergoat, M.J. & Bherer, L. (2013). Benefits of Physical Exercise Training on Cognition and Quality of Life in Frail Older Adults. *The*

Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 68(3)400-404.

Lauhoff, P., Murphy, N., Doherty, C. & Horgan, N.F. (2013). A controlled clinical trial investigating the effects of cycle ergometer training on exercise tolerance, balance and quality of life in patients with Parkinson's Disease. *Disability & Rehabilitation*, 35(5):382-387.

Leentjens, A.F.G., Verhey, F.R.J., Lousberg, R., Spitsbergen, H. & Wilmink, F.W. (2000). The Validity of the Hamilton and Montgomery-Asberg Depression Rating Scales as screening and Diagnostic Tools for Depression in Parkinson's Disease. *International Journal of Geriatric Psychiatry*, 15: 644-649.

Lees, A.J, Hardy, J. & Revesz, T. (2009). Parkinson's Disease. *Lancet*, 373:2055-2066.

Lemay, S., Bédard, M.A., Rouleau, I. & Tremblay, P.L. (2004). Practice Effect and Test-Retest Reliability of Attentional and Executive Tests in Middle-Aged to Elderly Subjects. *The Clinical Neuropsychologist*, 18(2):284-302.

Lezak, M.D. (1995). *Neuropsychological assessment.* 3rd edition. New York: Oxford University Press.

Litvan, I., Goldman, J.G., Troster, A.I., Schmand, B.A., Weintraub, D., Petersen, R.C., Mollenhauer, B., Adler, C.H., Marder, K., Williams-Gray, C.H., Aarsland, D., Kulisevsky, J., Rodriguez-Oroz, M.C., Burn, D.J., Barker, R.A. & Emre, M. (2012). Diagnostic Criteria for Mild Cognitive Impairment in Parkinson's Disease: Movement Disorder Society Task Force Guidelines. *Movement Disorders*, 27(3):349-356.

Liu, J.H., Li, X.S., Ye, J., Gao, L.H., Zhang, Z.P., Wu, W., Yao, L. & Zhang, J. (2012). Cognitive impairments in Parkinson's Disease. *Aging & Mental Health*, 16(4): 529-536.

Liu-Ambrose, T., Donaldson, M.G., Ahamed, Y., Graf, P., Cook, W.L., Close, J., Lord, S.R. & Khan, K.M. (2008). Otago Home-Based Strength and Balance Retraining Improves Executive Functioning in Older Fallers: A Randomized Controlled Trial. *Journal of the American Geriatrics Society*, 56:1821-1830.

Liu-Ambrose, T., Nagamatsu, L.S., Graf, P., Beattie, B.L., Ashe, M. & Handy, T.C. (2010). Resistance Training and Executive Functions: A 12-Month Randomized Controlled Trial. *Archive of Internal Medicine*, 170(2):170-178.

Loftus, S.L. (2014). Qi Gong to Improve Postural Stability (QTIPS) for Parkinson Fall Prevention: A Neuroplasticity Approach. *Topics in Geriatric Rehabilitation*, 30(1):58-69.

Lohnes, C. A., & Earhart, G. M. (2010). External validation of abbreviated versions of the activities-specific balance confidence scale in Parkinson's Disease. *Movement Disorders*, 25(4): 485-489.

Lucas, S.J.E., Ainslie, P.N., Murrell, C,J,, Thomas, K.N., Franz, E.A. & Cotter, J.D. (2012). Effect of age on exercise-induced alterations in cognitive executive function: Relationship to cerebral perfusion. *Experimental Gerontology*, 47:541-551.

Macphee, G.J.A. & Stewart, D.A. (2012). Parkinson's Disease – pathology, aetiology and diagnosis. *Reviews in Clinical Gerontology*, 22:165-178.

Mak, M.K.Y. & Pang, M.Y.C. (2009). Balance confidence and functional mobility are independently associated with falls in people with Parkinson's Disease. *Journal of Neurology*, 256:742-749.

Mak, M.K., Wong, A., & Pang, M.Y. (2014). Impaired Executive Function Can Predict Recurrent Falls in Parkinson's Disease. *Archives of Physical Medicine and Rehabilitation*, 95:2390-2395.

Martínez-Martín, P., Rodríguez-Blázquez, C., Alvarez, M., Arakaki, T., Arillo, V.C., Chaná, P., Fernández, W., Garretto, N., Martínez-Castrillo, J.C., Rodríguez-Violante, M., Serrano-Dueñas, M., Ballesteror, D., Rojo-Abuin, J.M., Chaudhuri, K.R. & Merello, M. (2015). Parkinson's Disease severity levels and MDS-Unified Parkinson's Disease Rating Scale. *Parkinsonism and Related Disorders,* 21:50-54.

McGough, E.L., Kelly, V.E., Logsdon, R.G., McCurry, S.M., Cochrane, B.B., Engel, J.M. & Teri, L. (2011). Associations between Physical Performance and Executive Function in Older Adults with Mild Cognitive Impairment: Gait Speed and the Timed "up & Go" Test. *Physical Therapy*, 91(8):1198-1210.

McInerney-Leo, A., Gwinn-Hardy, K. & Nussbaum, R.L. (2004). Prevalence of Parkinson's Disease in Populations of African Ancestry: A Review. *Journal of the National Medical Association*, 96(7):974-979.

McKee, K.E. & Hackney, M.E. (2013). The Effects of Adapted Tango on Spatial Cognition and Disease Severity in Parkinson's Disease. *Journal of Motor Behaviour*, 45(6):519-529.

McKee, K.E. & Hackney, M.E. (2014). The Four Square Step Test in Individuals with Parkinson's Disease: Association with Executive Function and Comparison with Older Adults. *NeuroRehabilitation*, 35:279-289.

McKinlay, A. (2013). A review of cognitive and other non-motor problems in Parkinson's Disease. *Aging Health*, 9(1):89-102.

Mirelman, A., Herman, T., Nicolai, S., Zijlstra, A., Zijlstra, W., Becker, C., Chiari, L. & Hausdorff, J.M. (2011). Audio-Biofeedback training for posture and balance in Patients with Parkinson's Disease. *Journal of Neuroengineering and Rehabilitation*, 8:35.

Miyai, I., Fujimoto, Y., Yamamoto, H., Ueda, Y., Saito, T., Nozaki, S. & Kang, J. (2002). Long-Term Effect of Body Weight-Supported Treadmill Training in Parkinson's Disease: A Randomized Controlled Trial. *Archives of Physical Medicine and Rehabilitation*, 83:1370-1373.

Miyake, A., Emerson, M.J. & Friedman, N.P. (2000). Assessment of executive functions in clinical settings: Problems and Recommendations. *Seminars in Speech and Language*, 21(2):169-183.

Mongeon, D., Blanchet, P. & Messier, J. (2009). Impact of Parkinson's Disease and dopaminergic medication on proprioceptive processing. *Neuroscience*, 158:426-440.

Monteiro-Junior, R.S., Cevada, T., Oliveira, B.R.R., Lattari, E., Portugal, E.M.M., Carvalho, A. & Deslandes, A.C. (2015). We need to move more: Neurobiological hypotheses of physical exercise as a treatment for Parkinson's Disease. *Medical Hypotheses*, http://dx.doi.org/10.1016/j.mehy.2015.07.011.

Moore, T.L., Schettler, S.P., Killiany, R.J., Rosene, D.L. & Moss, M.B. (2009). Effects on Executive Function following damage to the Prefrontal Cortex in the Rhesus Monkey (*Macaca mulatta*). *Behavioural Neuroscience*, 123(2):231-241.

Moreland, J., Richardson, J., Chan, D.H., O'Neill, J., Bellissimo, A., Grum, R.M. & Shanks, L. (2003). Evidence-Based Guidelines for the Secondary Prevention of Falls in Older Adults. *Gerontology*, 49:93-116.

Morris, S., Morris, M.E. & Iansek, R. (2001). Reliability of Measurements Obtained with the Timed "Up & Go" Test in People with Parkinson's Disease. *Physical Therapy*, 81(2):810-818.

Moul, J.L., Goldman, B. & Warren, B. (1995). Physical activity and cognitive performance in the older population. *Journal of Aging & Physical Activity*, 3:135-145.

Murray, D.K., Sacheli, M.A., Eng, J.J. & Stoessl, A.J. (2014). The effects of exercise on cognition in Parkinson's Disease: a systematic review. *Translational Neurodegeneration*, 3(5):1-13.

Nasreddine, Z.S., Phillips, N.A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., Cummings, J.L. & Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: A Brief Screening Tool for Mild Cognitive Impairment. *Journal of the American Geriatrics Society*, 53(4):695-699.

Nazem, S., Siderowf, A.D., Duda, J.E., Have, T.T., Colcher, A., Horn, S.S., Moberg, P.J., Wilkinson, J.R., Hurtig, H.I., Stern, M.B. & Weintraub, D. (2009). Montreal Cognitive Assessment Performance in Patients with "Normal" Global Cognition According to Mini-

Mental State Examination Score. *Journal of the American Geriatrics Society*, 57(2):304-308.

Nocera, J.R. & Hackney, M.E. (2015). The Cognition-exercise Interaction in Parkinson's Disease: A Perspective on Current Rehabilitative Approaches with Promise to Impact the Whole Disease Sequelae. *Journal of Gerontology & Geriatric Medicine*, 1(1):1-4.

Noyes, K., Liu, H., Li, Y., Holloway, R. & Dick, A.W. (2006). Economic Burden Associated with Parkinson's Disease on Elderly Medicare Beneficiaries. *Movement Disorders*, 21(3):362-372.

Okubadejo, N.U., Bower, J.H., Rocca, W.A. & Maraganore, D.M. (2006).Parkinson's Disease in Africa: A Systematic Review of Epidemiologic and Genetic Studies. *Movement Disorders*, 21(12):2150-2156.

Page, P. (2006). Sensorimotor training: A "global" approach for balance training. *Journal of Bodywork and Movement Therapies*, 10:77-84.

Paillard, T., Rolland, Y. & de Souto Barreto, P. (2015). Protective Effects of Physical Exercise in Alzheimer's Disease and Parkinson's Disease: A Narrative Review. *Journal of Clinical Neurology*, 11(3):212-219.

Paolo, A.M., Troster, A.I., Axelrod, B.N. and Koller, W.C. (1995). Construct Validity of the WCST in Normal Elderly and Person's with Parkinson's Disease. *Archives of Clinical Neuropsychology*, 10(5):463-473.

Parashos, S.A., Luo, S., Biglan, K.M., Bodis-Wollner, I., He, B., Liang, G.S., Ross, G.W., Tilley, B.C. & Shulman, L.M. (2014). Measuring Disease Progression in Early Parkinson's Disease: the National Institutes of Health Exploratory Trials in Parkinson Disease (NET-PD) Experience. *Journal of the American Medical Association*, 71(6):710-716.

Patient. (2011). *General Practice Physical Activity Questionnaire (GPPAQ).* [Online] Available from: http://patient.info/doctor/general-practice-physical-activity-questionnaire-gppaq [Accessed: 24 July 2014].

Pedroso, R.V., Coelho, F.G., Santos-Galduróz, R.F., Costa, J.L., Gobbi, S. & Stella, F. (2012). Balance, executive functions and falls in elderly with Alzheimer's Disease (AD): A longitudinal study. *Archives of Gerontology and Geriatrics*, 54:348-351.

Periáñez, J.A., Ríos-Lago, M., Rodríguez-Sánchez, J.M., Adrover-Roig, D., Sánchez-Cubillo, I., Crespo-Facorro, B., Quemada, J.I. & Barceló, F. (2007). Trail Making Test in traumatic brain injury, schizophrenia, and normal ageing: Sample comparisons and normative data, *Archives of Clinical Neuropsychology*, 22:433-447.

Pescatello, L.S. (ed.) (2014). *ACSM's Guidelines for Exercise Testing and Prescription.* 9th edn., Philadelphia, Wolters Kluwer / Lippincott Williams & Wilkins.

Peto, V, Jenkinson, C, Fitzpatrick, R. (1998). PDQ-39: A review of the development, validation and application of a Parkinson's Disease quality of life questionnaire and its associated measures. *Journal of Neurology,* 245 (Supplement 1): S10-S14.

Petzinger, G.M., Fisher, B.E., McEwen, S., Beeler, J.A., Walsh, J.P. & Jakowec, M.W. (2013). Exercise-enhanced neuroplasticity targeting motor and cognitive circuitry in Parkinson's Disease. *Lancet Neurology*, 12:716-726.

Pierobon, A., Giardini, A., Maestri, R., Farina, C., Callegari, S., Torlasch, V., Bertotti, G., Majani, G. & Frazzitta, G. (2014). Disexecutive Functions and Depression in Patients with Parkinson Disease. *American Journal of Physical Medicine and Rehabilitation*, 93(9): 764-773.

Ploughman, M. (2008). Exercise is brain food: The effects of physical activity on cognitive function. *Developmental Neurorehabilitation*, 11(3):236-240.

Poletti, M., Emre, M. & Bonuccelli, U. (2011). Mild Cognitive Impairment and Cognitive Reserve in Parkinson's Disease. *Parkinsonism and Related Disorders*, 17:579-586.

Poletti, M., Frosini, D., Pagni, C., Baldacci, F., Nicoletti, V., Tognoni, G., Lucetti, C., Del Dotto, P., Ceravolo, R. & Bonuccelli, U. (2012). Mild Cognitive Impairment and Cognitive-Motor Relationships in Newly Diagnosed Drug-Naïve Patients with Parkinson's Disease. *Journal of Neurology, Neurosurgery and Psychiatry*, 83:601-606.

Pompeu, J.E., Dos Santos Mendes, F.A., Da Silva, K.G., Lobo, A.M., Oliveira, T.D.P., Zomignami, A.P. & Piemonte, M.E.P. (2012). Effect of Nintendo Wii™-based motor and cognitive training on activities of daily living in patients with Parkinson's Disease: a randomised clinical trial. *Physiotherapy*, 98: 196-204.

Prado, R.C. & Barbosa, E.R. (2005). Depression in Parkinson's Disease. *Arquivos de neuro-psiquiatria*, 63(3B):766-771.

Protas, E.J., Stanley, R.K. & Jankovic, J. (2009). 'Parkinson's Disease', in Durstine, J.L., Moore, G.E., Painter, P.L. & Roberts, S.O. (eds), *ACSM's Exercise Management for Person's With Chronic Diseases and Disabilities*, 3rd edn, Human Kinetics, Champaign, IL.

Rabin, E., Chen, J., Muratori, L., DiFrancisco-Donoghue, J. & Werner, W.G. (2013). Haptic Feedback from Manual Contact Improves Balance Control in People with Parkinson's Disease. *Gait & Posture*, 38:373-379.

Ramaker, C., Marinus, J., Stiggelbout, A.M. & van Hilten, B.J. (2002). Systematic Evaluation of Rating Scales for Impairment and Disability in Parkinson's Disease. *Movement Disorders*, 17(5):867-876.

Reuter, I., Engelhardt, M., Stecker, K. & Horst, B. (1999). Therapeutic value of exercise training in Parkinson's Disease. *Medicine & Science in Sports & Exercise*, 31(11):1544-1549.

Rhyu, I.J., Bytheway, J.A., Kohler, S.J., Lange, H., Lee, K.J., Boklewski, J., McCormick, K., Williams, N.I., Stanton, G.B., Greenough, W.T. & Cameron, J.L. (2010). Effects of Aerobic Exercise Training on Cognitive Function and Cortical Vascularity in Monkeys. *Neuroscience, 167(4):1239-1248.*

Riemann, B.L. & Lephart, S.M. (2002). The Sensorimotor System, Part I: The Physiologic Basis of Functional Joint Stability. *Journal of Athletic Training*, 37(1):71-79.

Rigdel, A.L., Vitek, J.L. & Alberts, J.L. (2009). Forced, Not Voluntary, Exercise Improves Motor Function in Parkinson's Disease Patients. *Neurorehabilitation and Neural Repair*, 23(6):600-608.

Rigdel, A.L., Kim, C-H., Fickes, E.J., Muller, M.D. & Alberts, J.L. (2011). Changes in Executive Function After Bouts of Passive Cycling in Parkinson's Disease. *Journal of Aging and Physical Activity*, 19(2):87-98.

Rigdel, A.L., Peacock, C.A., Fickes, E.J. & Kim, C.H. (2012). Active-Assisted Cycling Improves Tremor and Bradykinesia in Parkinson's Disease. *Archives of Physical Medicine and Rehabilitation*, 93:2049-2054.

Rodriguez-Blazquez, C., Rojo-Abuin, J.M., Alvarez-Sanchez, M., Arakaki, T., Bergareche-Yarza, A., Chade, A., Garretto, N., Gershanik, O., Kurtis, M.M., Martinez-Castrillo, J.C., Mendoza-Rodriguez, A., Moore, H.P., Rodriguez-Violante, M., Singer, C., Tilley, B.C., Huang, J., Stebbins, G.T., Goetz, C.G. & Martinez-Martin, P. (2013). The MDS-UPDRS Part II (motor experiences of daily living) results useful for assessment of disability in Parkinson's Disease. *Parkinsonism and Related Disorders*, 19:889-893.

Sage, M.D. & Almeida, Q.J. (2009). Symptom and Gait Changes After Sensory Attention Focused Exercise vs Aerobic Training in Parkinson's Disease. *Movement Disorders*, 24(8):1132-1138.

Sage, M.D. & Almeida, Q.J. (2010). A Positive Influence of Vision on Motor Symptoms During Sensory Attention Focused Exercise for Parkinson's Disease. *Movement Disorders*, 25(1):64-69.

Sánchez-Cubillo, I., Perianez, J.A., Adrover-Roig, D., Rodriguez-Sanchez, J.M., Rios-Lago, M., Tirapu, J. & Barcelo, F. (2009). Construct validity of the Trail Making Test: Role of

task-switching, working memory, inhibition/interference control and visuomotor abilities. *Journal of the International Neuropsychological Society*, 15:438-450.

Scandalis, T.A., Bosak, A., Berliner, J.C., Helman, L.L. & Wells, M.R. (2001). Resistance Training and Gait Function in Parkinson's Disease. *American Journal of Physical Medicine & Rehabilitation*, 80:38-43.

Scheffer, A.C., Schuurmans, M.J., Van Dijk, N., Van der Hooft, T. & De Rooij, S.E. (2008). Fear of falling: measurement strategy, prevalence, risk factors and consequences among older persons. *Age and Ageing*, 37:19-24.

Schenkman, M., Cutson, T.M., Kuchibhatla, M., Chandler, J., Pieper, C.F., Ray, L. & Laub, K.C. (1998). Exercise to improve spinal flexibility and function for people with Parkinson's Disease: a randomized, controlled trial. *Journal of the American Geriatrics Society*, 46(10):1207-1216.

Schenkman, M., Hall, D.A., Barón, A.E., Schwartz, R.S., Mettler, P. & Kohrt, W.M. (2012). Exercise for People in Early- or Mid-Stage Parkinson's Disease: A 16-Month Randomized Controlled Trial. *Physical Therapy*, 92:1395-1410.

Schilling, B.K., Pfeiffer, R.F., LeDoux, M.S., Karlage, R.E., Bloomer, R.J. & Falvo, M.J. (2010). Effects of Moderate-Volume, High-Load Lower-Body Resistance Training on Strength and Function in Person's with Parkinson's Disease: A Pilot Study. *Parkinson's Disease*, 2010:824734.

Schrag, A., Jahanshahi, M & Quinn, N. (2000). What contributes to quality of life in patients with Parkinson's Disease? *Journal of Neurology, Neurosurgery & Psychiatry*, 69:308-312.

Sehm, B., Taubert, M., Conde, V., Weise, D., Classen, J., Dukart, J., Draganski, B., Villringer, A. & Ragert, P. (2014). Structural brain plasticity in Parkinosn's disease uinduced by balance training. *Neurobiology of Aging*, 35:232-239.

Shubert, T.E., McCulloch, K., Hartman, M. & Giuliani, C.A. (2010). The Effect of an Exercise-Based Balance Intervention on Physical and Cognitive Performance for Older Adults: A Pilot Study. *Journal of Geriatric Physical Therapy*, 33:157-164.

Siderowf, A., McDermott, M., Kieburtz, K., Blindauer, K., Plumb, S., Shoulson, I. & the Parkinson Study Group. (2002). Test-Retest Reliability of the Unified Parkinon's Disease Rating Scale in Patients with Early Parkinson's Disease: Results from a Multicenter Clinical Trial. *Movement Disorders*, 17(4):758-763.

Smania, N., Corato, E., Tinazzi, M., Stanzani, C., Fiaschi, A., Girardi, P. & Gandolfi, M. (2010). Effect of Balance Training on Postural Instability in Patients With Idiopathic Parkinson's Disease. *Neurorehabilitation and Neural Repair*, 24(9):826-834.

Smith, P.J., Blumenthal, J.A., Hoffman, B.M., Cooper, H., Strauman, T.A., Welsh-Bohmer, K., Browndyke, J.N. & Sherwood, A. (2010). Aerobic Exercise and Neurocognitive Performance: A Meta-Analytic Review of Randomized Controlled Trials. *Psychosomatic Medicine*, 72(3):239-252.

Smiley-Oyen, A.L., Lowry, K.A., Francois, S.J., Kohut, M.L. & Ekkekakis, P. (2008). Exercise, Fitness and Neurocognitive Function in Older Adults: The "Selective Improvement" and "Cardiovascula Fitness" Hypotheses. *Annals Of Behavioral Medicine*, 36(3):280-291.

Steffen, T.M., Hacker, T.A. & Mollinger, L. (2002). Age- and Gender-Related Test Performance in Community-Dwelling Elderly People: Six-Minute Walk Test, Berg Balance Scale, Timed Up & Go Test, and Gait Speeds. *Physical Therapy*, 82:128-137.

Steffen, T. & Seney, M. (2008). Test-Retest Reliability and Minimal Detectable Change on Balance and Ambulation Tests, the 36-Item Short-Form Health Survey, and the Unified Parkinson Disease Rating Scale in People with Parkinsonism. *Physical Therapy*, 88(6):733-746.

Stegemöller, E.L., Nocera, J., Malaty, I., Shelley, M., Okun, M.S., Hass,C.J. & the NPF Quality Improvement Initiative Investifgators. (2014). Timed Up and Go, Cognitive, and Quality-of-Life Correlates in Parkinson's Disease. *Archives of Physical Medicine and Rehabilitation*, 95:649-655.

Stel, V.S., Smit, J.H., Pluijm, S.M.F. & Lips, P. (2004). Consequences of falling in older men and women and risk factors for health service use and functional decline. *Age and Ageing*, 33:58-65.

Strauss, E., Sherman, E.M.S., & Spreen, O. (2006). *A compendium of Neuropsychological Tests: Administration, Norms and Commentary.* Third Edition. New York: Oxford University Press.

Taba, P. & Asser, T. (2004). Epidemiology of Parkinson's Disease. *Reviews in Clinical Gerontology*, 14:211-228.

Tanaka, K., de Quadros Jr., A.C., Santos, R.F, Stella, F., Gobbi, L.T.B. & Gobbi, S. (2009). Benefits of physical activity on executive functions in older people with Parkinson's Disease. *Brain and cognition*, 69:435-441.

Taylor, A.E. & Saint-Cyr, J.A. (1995). The Neuropsychology of Parkinson's Disease. *Brain and Cognition*, 28:281-296.

Tomlinson, C.L., Patel, S., Meek, C., Herd, C.P., Clarke, C.E., Stowe, R., Shah, L., Sackley, C.M., Deane, K.H.O., Wheatley, K. & Ives, N. (2013). Physiotherapy versus

placebo or no intervention in Parkinson's Disease. *Cochrane Database of Systematic Reviews* 2013, 9: CD002817. DOI:10.1002/14651858.CD002817.pub4.

Toole, T., Hirsch, M.A., Forkink, A., Lehman, D.A. & Maitland, C.G. (2000). The effects of a balance and strength training programme on equilibrium in Parkinsonism: A preliminary study. *NeuroRehabilitation*, 14(3):165-174.

Trajković, G., Starčević, V., Latas, M., Leštarević, M., Ille, T., Bukumirić, Z. & Marinković, J. (2011). Reliability of the Hamilton Rating Scale for Depression: A meta-analysis over a period of 49 years. *Psychiatry Research*, 189:1-9.

Uc, E.Y., Doerschug, K.C., Magnotta, V., Dawson, J.D., Thomsen, T.R., Kline, J.N., Rizzo, M., Newman, S.R., Mehta, S., Grabowski, T.J., Bruss, J., Blanchette, D.R., Anderson, S.W., Voss, M.W., Kramer, A.F. & Darling, W.G. (2014). Phase I/II randomized trial of aerobic exercise in Parkinson Disease in a community setting. *Neurology*, 83:413-425.

Uekermann, J., Daum, I., Peters, S., Wiebel, B., Przuntek, H & Müller, T. (2003). Depressed mood and executive dysfunction in early Parkinson's Disease. *Acta Neurologica Scandinavica*, 107:341-348.

Van der Marck, M.A., Dicke, H.C., Uc, E.Y., Kentin, Z.H.A., Borm, G.F., Bloem, B.R., Overeem, S. & Munneke, M. (2012). Body mass index in Parkinson's Disease: A meta-analysis. *Parkinsonism and Related Disorders*, 18:263-267.

Van der Elst, W., Van Boxtel, M.P.J., Van Breukelen, G.J.P. & Jolles, J. (2006). The Stroop Color-Word Test: Influence of Age, Sex, and Eduaction, and Normative Data for a Large Sample Across the Adult Age Range. *Assessment*, 13(1):62-79.

Van den Heuvel, M.R.C., Kwakkel, G., Beek, P.J., Berendse, H.W., Daffertshofer, A. & van Wegen, E.E.H. (2014). Effects of augmented visual feedback during balance training in Parkinson's Disease: A pilot randomized clinical trial. *Parkinsonism and Related Disorders*, 20:1352-1358.

Van der Kolk, N.M. & King, L.A. (2013). Effects of Exercise on Mobility in People with Parkinson's Disease. *Movement Disorders*, 28(11):1587-1596.

Van der Merwe, C., Haylett, W., Harvey, J., Lombard, D., Bardien, S. & Carr, J. (2012). Factors influencing the development of early- or late-onset Parkinson's Disease in a cohort of South African patients. *South African Medical Journal,* 102(11):848-851.

Van Uffelen, J.G.Z., Chin, A., Paw, M.J.M., Hopman-Rock, M. & Van Mechelen, W. (2008). The Effects of Exercise on Cognition in Older Adults with and Without Cognitive Decline: A Systematic Review. *Clinical Journal of Sport Medicine*, 18:486-500.

Velkoff, V.A. & Kowal, P.R. (2007). Population Aging in Sub-Saharan Africa: Demographic Dimensions 2006. U.S. Department of Commerce, Economics and Statistics Administration, U.S. Census Bureau.

Von Campenhausen, S., Bornschein, B., Wick, R., Bötzel, K., Sampaio, C., Poewe, W., Oertel, W., Siebert, U., Berger, K. & Dodel, R. (2005). Prevalence and Incidence of Parkinson's Disease in Europe. *European Neuropsychopharmacology*, 15:473-490.

Western Cape Government Provincial Treasury. (2014a). *Socio-economic Profile: Cape Winelands District 2014*. Western Cape Government Provincial Treasury, Cape Town.

Western Cape Government Provincial Treasury. (2014b). *Socio-economic Profile: City of Cape Town 2014*. Western Cape Government Provincial Treasury, Cape Town.

Williamson, J.D., Espeland, M., Kritchevsky, S.B., Newman, A.B., King, A.C., Pahor, M., Guralnik, J.M., Pruitt, L.A. & Miller, M.E. (2009). Changes in Cognitive Function in a Randomized Trial of Physical Activity: Results of the Lifestyle Interventions and Independence for Elders Pilot Study. *Journal of Gerontology*, 64A(6):688-694.

Wirdefeldt, K., Adami, H., Cole, P., Trichopoulos, D. & Mandel, J. (2011). Epidemiology and etiology of Parkinson's Disease: a review of the evidence. *European Journal of Epidemiology*, 26:S1-S58.

Wong-Yu, I.S.K. & Mak, M.K.Y. (2015). Multi-dimensional balance training programme improves balance and gait performance in people with Parkinson's Disease: A pragmatic randomized controlled trial with 12-month follow-up. *Parkinsonism and Related Disorders*, 21:615-621.

World Health Organization (2006). *Neurological Disorders: public health challenges.* (p141). Geneva: WHO Press.

Wu, T. & Hallett, M. (2013). The Cerebellum in Parkinson's Disease. *Brain*, 136:696-709.

Wu, T., Liu, J., Zhang, H., Hallett, M., Zheng, Z. & Chan, P. (2014). Attention to Automatic Movements in Parkinson's Disease: Modified Automatic Mode in the Striatum. *Cerebral Cortex*, 25(10):3330-3342.

Xu, Q., Park, Y., Huang, X., Hollenbeck, A., Blair, A., Schatzkin, A. & Chen, H. (2010). Physical activities and future risk of Parkinson Disease. *Neurology*, 75:341-348.

Xu, D., Cole, M.H., Mengersen, K., Silburn, P.A., Qiu, F., Graepel, C. & Kerr, G.K. (2014). Executive Function and Postural Instability in People with Parkinson's Disease. *Parkinson's Disease*, Article ID 684758, 8 pages.

Yogev-Seligmann, G., Hausdorff, J.M. & Giladi, N. (2008). The Role of Executive Function and Attention in Gait. *Movement Disorders*, 23(3):329-342.

Zadikoff, C., Fox, S.H., Tang-Wai, D.F., Thomsen, T., De Bie, R.M.A., Wadia, P., Miyasaki, J., Duff-Canning, S., Lang, A.E. & Marras, C. (2008). A comparison of the Mini Mental State Exam to the Montreal Cognitive Assessment in Identifying Cognitive Deficits in Parkinson's Disease. *Movement Disorders*, 23(2):297-299.

Zigmond, M.J. & Smeyne, R.J. (2013). Exercise: Is it neuroprotective and if so, how does it work? *Parkinsonism and Related Disorders*, 00S0:S205-S209.

APPENDICES

Appendix A

Ethical Approval Notice – Research Ethics Committee: Human Research (Humanities)

UNIVERSITEIT·STELLENBOSCH·UNIVERSITY
jou kennisvennoot • your knowledge partner

Approval Notice
Stipulated documents/requirements

14-Aug-2014
Puren, Michelle M

Proposal #: HS1040/2014

Title: **The influence of an eight-week Sensory-motor Training programme on the Executive function of independent-living individuals with Parkinson's Disease.**

Dear Ms Michelle Puren,

Your **Stipulated documents/requirements** received on **13-Aug-2014**, was reviewed by members of the **Research Ethics Committee: Human Research (Humanities)** via Expedited review procedures on **14-Aug-2014** and was approved.
Sincerely,

Clarissa Graham
REC Coordinator
Research Ethics Committee: Human Research (Humanities)

Appendix B

Informed Consent Form

UNIVERSITEIT•STELLENBOSCH•UNIVERSITY
jou kennisvennoot • your knowledge partner

STELLENBOSCH UNIVERSITY

INFORMED CONSENT TO PARTICIPATE IN RESEARCH

The Influence of an Eight-week Sensory-motor Training Intervention on the Executive Function of Independent-living Individuals with Parkinson's Disease.

You are invited to participate in a research study conducted by Michelle Puren (Main researcher, biokineticist and MSc Student) and Dr Karen Welman (Study Leader and biokineticist), through the Department of Sport Science at Stellenbosch University. The data generated from the study will be utilized in an MSc thesis and in research articles which will assist in increasing the existing knowledge in the field of Parkinson's Disease and exercise.

1. PURPOSE OF THE STUDY

The main objectives of the study are:

1. To investigate whether eight weeks of a specific sensory-motor intervention will have a significant effect on brain function (executive function).
2. To determine whether eight weeks of a specific sensory-motor intervention will have a significant effect on quality of life, depression and perceived stability or balance

2. PROCEDURES

We will begin with a telephone call (the first contact session) and then six testing sessions conducted at Stellenbosch University's Sport Science Department or at your home (for your convenience). The telephone call should take approximately 15-30 minutes to complete. Each appointment for testing should take approximately 60-90 minutes. Testing sessions 1 and 2 will take place within a few days of each other and will then be followed by an eight-week baseline period. After this eight-week period,

you will be re-tested with testing sessions 3 and 4 again taking place within a few days of each other. You will be asked to complete the same tests and questionnaires that you completed the first time around. After this, you will be participating in one of two sensory-motor interventions over an eight week period. After this eight-week period, you will again be re-tested with testing sessions 5 and 6 again taking place within a few days of each other. These will be the last testing sessions and you will be asked to complete the same tests and questionnaires that you completed previously.

Phone call Session: at the beginning of the telephone call, you will be introduced to the researcher. This informed consent form will be explained to you and you will be given the opportunity to ask questions. Once you have given your consent (permission to participate) and provided you meet all the inclusion requirements, you will be included in the study.

First Testing Session: during this session, your completed informed consent form will be collected. You will have additional opportunity to ask questions. Your body measurements will be recorded and a short functional test will be conducted. Three questionnaires concerning quality of life, balance confidence and a Parkinson's Disease rating scale will be completed with you

Second Testing Session: during this second testing session, two additional questionnaires will be completed with you to assess cognitive status and your mood. Following this, tests of brain function (executive function) will be conducted, using pen and paper as well as a computer, and you will be given clear instruction regarding what you need to do for each test.

Resting Phase: We will then have an eight-week baseline period (also known as a control phase) where you will continue with your normal activities of daily living. There should be no changes to your activity levels during this time period.

Third and Fourth Testing Sessions: during these testing sessions, all the questionnaires and tests that were conducted at the first and second testing sessions will be repeated.

Sensory-motor Intervention: We will then have an eight week sensory-motor intervention period and you will be in one of two sensory-motor groups:
Feedback-wristband: if you are in this group, you will be required to wear a feedback-wristband for the eight-week duration. The feedback-wristband needs to be worn at all times. The feedback-wristband will give you sensory feedback through the sensation of touch (tactile stimulation). There should be no changes to your activity levels during this time period.
Sensory-motor training programme: if you are in this group, you will be required to participate in a structured sensory-motor training programme. You will need to attend three sessions per week over the eight-week period. Each session will be led by a qualified biokineticist and one or two

research assistants. A biokineticist is a clinical exercise specialist who is registered with the Health Professions Council of South Africa (HPCSA). The research assistants will be there to help you if you feel a bit unstable or if you are anxious about attempting an activity on your own. Each week of the balance training programme will have a different aim and each session will focus on a different objective. The programme will become increasingly more challenging as the weeks progress. Each session will begin with a 10-minute warm-up, followed by 15-40 minutes of balance training and ended with a 10-minute cool-down and relaxation technique session. Other than the sensory-motor training programme, there should be no changes to your activity levels during this time period.

Fifth and Sixth Testing Sessions: during these testing sessions, all the questionnaires and tests that were conducted at the previous testing sessions will be repeated.

3. DOCTOR / SPECIALIST COMMUNICATION

We would like to have your doctor / specialist's contact details so that we can contact them telephonically or via email to inform them of your intent to participate in the research. They will also get a summary of the proposed research protocol. If you have not seen your doctor / specialist in the six months prior to the start of the research study, the department of Sport Science will pay for this appointment.

4. PARTICIPATION

You will need to have a minimum attendance of 70% for the balance training sessions. You will not be able to continue if you miss more than 30% of the sessions (in total) or if you miss two consecutive sessions.

You will also be responsible for your own transport to the venue for the balance training sessions.

5. POTENTIAL RISKS

The sensory-motor training programme and the testing used during this intervention are scientific and evidence-based and should not pose any serious risk. The potential for balance loss and / or falling is a possibility but we will do our best to minimise these risks. We will have chairs and mats available during the sensory-motor training programme in an attempt to avoid this. You will be permitted to stop at any stage if you do not feel you are able to continue with a particular exercise. We will also be on hand to assist you. Safety procedures will be in place in case of any emergencies that may arise during testing or the balance training programme. The biokineticists are qualified in basic life support and emergency contact numbers will be on hand (Netcare 082 911, Constantiaberg MediClinic 021 799 2196, Cape Medical Response 082 782 444). The University of Stellenbosch is insured for emergencies during research interventions. The Sport Science department will cover costs if Netcare (private ambulance service) is required and the person does not have their own medical aid.

6. POTENTIAL BENEFITS

As a participant, you will not directly benefit from your involvement in the study (you will not receive payment for participating in the study), however, your balance might improve as a result of your involvement in one of the sensory-motor interventions.

Upon completion of the study, you will also receive a DVD of the exercises which will be used in the sensory-motor training programme. There is also the **potential** benefit of improved brain function (executive function) as a result of your participation in the study (this is not guaranteed as this is what is being investigated).

7. PARTICIPATION COSTS

Participation in this study is strictly voluntary. There will be no financial remuneration for participation in the study nor will there be any cost to you to participate in the study.

8. CONFIDENTIALITY

Your information will be protected and remain anonymous in this study. All participants' names will be coded in order to ensure anonymity. Your data will be stored on a password protected computer accessible by the researchers alone. Questionnaires, informed consent forms and any other hard copy information will be stored in a locked filing system in the Motor Learning Laboratory at Stellenbosch University's Department of Sport Science. No participant names will be given in the MSc thesis or in any research articles.

9. PARTICIPATION, WITHDRAWAL & RIGHTS OF RESEARCH SUBJECTS

Your participation in this study is voluntary and you are free to withdraw at any time without reason. You also have the right to decline to answer any questions which you do not wish to answer. The researcher reserves the right to withdraw your participation from this study should a situation arise where this is warranted. If you have questions concerning research subject rights, please contact Ms **Maléne Fouché (mfouche@sun.ac.za; 021 808 4622)** at Stellenbosch University's Division for Research Development.

All efforts are made to ensure your safety during the balance exercises and testing. However, if you obtain a research-related injury the researcher is trained in first aid and able to assist you. You can 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.

10. **RESEARCHERS**

The two main researchers for this study are Dr **Karen Welman** (Study leader; **welman@sun.ac.za; 021 808 4733 or 082 098 5387**) and **Michelle Puren** (MSc Student; 13874322@sun.ac.za**; 084 246 7870**). Please direct any queries or concerns regarding this study to them.

SIGNATURE OF RESEARCH SUBJECT OR LEGAL REPRESENTATIVE

The information above was explained to _____ (*me/the subject/the participant)* by _____ _____ (*name of relevant person)* in _____ (*English /Afrikaans /Xhosa /other)* and _____ (*I am/the subject is/the participant is)* in command of this language or it was satisfactorily translated to _____ (*me/him/her*). _____ (*I/the participant/the subject)* was given the opportunity to ask questions and these questions were answered to _____ *(my/his/her)* satisfaction.

(I hereby consent to voluntarily participate in this study/I hereby consent that the subject/participant may participate in this study.) I have been given a copy of this form.

_____

Name of Subject/Participant

_____

Name of Legal Representative (if applicable)

_____ _____

Signature of Subject/Participant or Legal Representative Date

SIGNATURE OF INVESTIGATOR

I declare that I explained the information given in this document to _____ (*name of the subject/participant)* and/or (his/her) representative _____ (*name of the representative). (H*e/she) was encouraged and given sufficient time to ask additional questions. This conversation was conducted in (*Afrikaans/*English/*Xhosa/*Other*) and (*no translator was used/this conversation was translated into* _____ by _____*).*

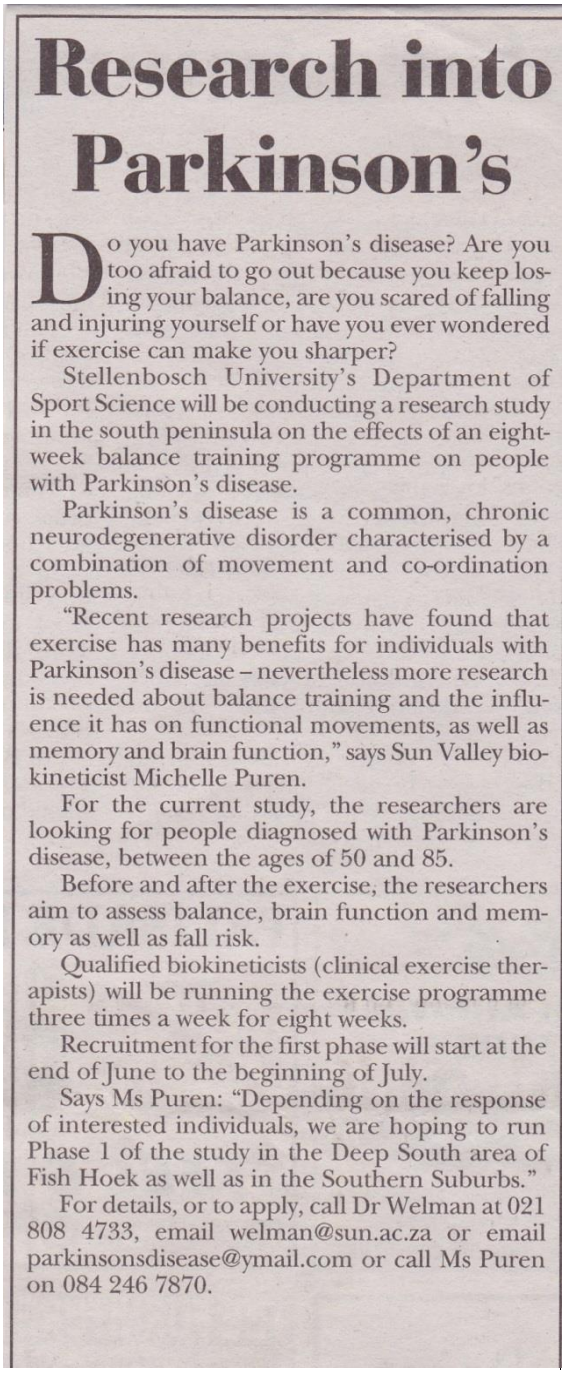
_____ _____

Signature of Investigator Date

Appendix C

Newspaper Articles

Article 1: False Bay Echo. Article 2: Constantiaberg Bulletin.



Research into Parkinson's

Do you have Parkinson's disease? Are you too afraid to go out because you keep losing your balance, are you scared of falling and injuring yourself or have you ever wondered if exercise can make you sharper?

Stellenbosch University's Department of Sport Science will be conducting a research study in the south peninsula on the effects of an eight-week balance training programme on people with Parkinson's disease.

Parkinson's disease is a common, chronic neurodegenerative disorder characterised by a combination of movement and co-ordination problems.

"Recent research projects have found that exercise has many benefits for individuals with Parkinson's disease – nevertheless more research is needed about balance training and the influence it has on functional movements, as well as memory and brain function," says Sun Valley biokineticist Michelle Puren.

For the current study, the researchers are looking for people diagnosed with Parkinson's disease, between the ages of 50 and 85.

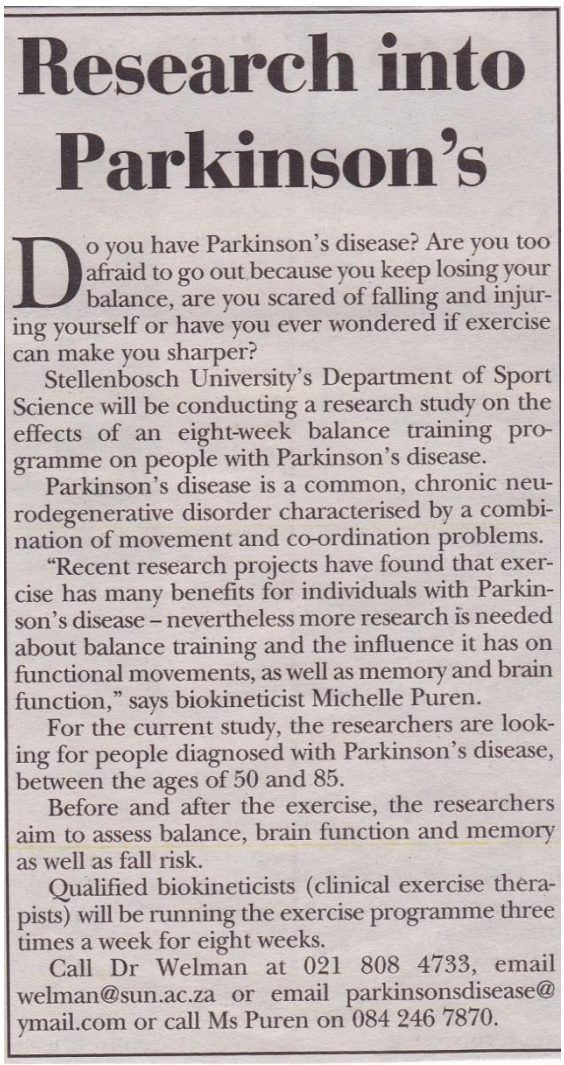
Before and after the exercise, the researchers aim to assess balance, brain function and memory as well as fall risk.

Qualified biokineticists (clinical exercise therapists) will be running the exercise programme three times a week for eight weeks.

Recruitment for the first phase will start at the end of June to the beginning of July.

Says Ms Puren: "Depending on the response of interested individuals, we are hoping to run Phase 1 of the study in the Deep South area of Fish Hoek as well as in the Southern Suburbs."

For details, or to apply, call Dr Welman at 021 808 4733, email welman@sun.ac.za or email parkinsonsdisease@ymail.com or call Ms Puren on 084 246 7870.



Research into Parkinson's

Do you have Parkinson's disease? Are you too afraid to go out because you keep losing your balance, are you scared of falling and injuring yourself or have you ever wondered if exercise can make you sharper?

Stellenbosch University's Department of Sport Science will be conducting a research study on the effects of an eight-week balance training programme on people with Parkinson's disease.

Parkinson's disease is a common, chronic neurodegenerative disorder characterised by a combination of movement and co-ordination problems.

"Recent research projects have found that exercise has many benefits for individuals with Parkinson's disease – nevertheless more research is needed about balance training and the influence it has on functional movements, as well as memory and brain function," says biokineticist Michelle Puren.

For the current study, the researchers are looking for people diagnosed with Parkinson's disease, between the ages of 50 and 85.

Before and after the exercise, the researchers aim to assess balance, brain function and memory as well as fall risk.

Qualified biokineticists (clinical exercise therapists) will be running the exercise programme three times a week for eight weeks.

Call Dr Welman at 021 808 4733, email welman@sun.ac.za or email parkinsonsdisease@ymail.com or call Ms Puren on 084 246 7870.

Appendix D

The Hoehn and Yahr Scale

The Hoehn and Yahr scale (HY) is a clinical rating scale that describes broad categories of motor function in PD. This scale is widely used because it is simple and easily applied. Since it captures typical patterns of progressive motor impairment, which is apparent in PD subjects, it can be applied whether they are receiving dopaminergic therapy or not. It has been found that progression in HY stages correlate with motor decline, decline in quality of life, and neuroimaging and studies of dopaminergic loss (Hoehn & Yahr, 1967).

Table 1. The Hoehn and Yahr Scale which is used to categorize motor function in PD (Hoehn & Yahr, 1967).

Stage	**Description**
Stage 1	Only unilateral involvement, usually with minimal or no functional disability
Stage 2	Bilateral or midline involvement without impairment of balance
Stage 3	Bilateral disease: mild to moderate disability with impaired postural reflexes; physically independent
Stage 4	Severely disabling disease; still able to walk or stand unassisted
Stage 5	Confinement to bed or wheelchair unless aided

Appendix E

PD-related Medication and Affected Side

Table .1: List of Medication and Affected Side of Sample

EXP	Medication	AS	PBO	Medication	AS
1	Carbilev	Right	**1**	Sinemet	Left
2	Carbilev	Left	**2**	Requip; Carbilev	Both
3	Carbilev; Serdep	Right	**3**	Carbilev	Right
4	Carbilev	Left	**4**	Madopar	Right
5	Carbilev	Right	**5**	Carbilev	Both
6	Azilect	Left	**6**	Carbilev	Both
7	Carbilev; Dissipal	Right	**7**	Pexola; Carbilev; Azilect; Sinemet	Both
8	Carbilev; Parkilyne	Right	**8**	Medopar; Pexola	Right
9	Pexola; Akineton	Right	**9**	Medopar	Left
10	Carbilev; Trepline	Right	**10**	Medopar	Both
11	Stalevo; Requip; Parkilyne	Both	**11**	Carbilev	Both
12	Carbilev	Left	**12**	Carbilev; Pexola; Sinmet	Left
13	None	Right	**13**	Carbilev; Migroben; Zuvamor	Both
14	Parkilyne; Carbilev	Right	**14**	Carbilev	Left
15	Cyprolex; Carbilev	Left	**15**	Carbilev	Left
16	Carbilev	Right	**16**	Pexola; Azilect	Both
17	Carbilev; Pexola	Right	**17**	Pexola; Carbilev; Sinmet	Both
18	Carbilev; Trepiline	Right			
19	Carbilev; Azilect	Both			
20	Carbilev; Azilect	Both			
21	Dissipal	Both			
22	Carbilev	Left			
23	None	Left			
24	Carbilev; Topiramat; Solain; Dissipal; Pexola	Left			
25	Madopar; Requip	Both			

Abbreviations: EXP Experimental group; PBO Placebo group; AS Affected side

Appendix F

Personal Information Form

Personal Information Form:
Name:
Surname:
Age:
Gender:
Contact number (please indicate your preferred contact method):
Level of Parkinson's (Hoehn &Yahr Scale), if known
When were you diagnosed with PD?
Most affected side: (Left, right, both)
Occupation (if retired, state previous):
Current medication; and duration of use:
Any adverse effects of medication:

Who is your caregiver:

Relationship of caregiver:

Time spent without caregiver:

Would your caregiver like to attend the exercises as well?

Household chores:

Leisure time activities:

Has your doctor given you approval to participate in this study?

Who is your doctor?

Would you mind if we contact him/her?
If not please provide us with his/her contact no.

Are you going away anytime between August and November 2014? If yes, please state dates.

***** Afrikaanse vorms is ook beskikbaar.

Appendix G

Session Information Sheet

Session Information Sheet

Please tick ✓ which **dates, time and area** would suit you best to come for exercises:

Days: Please select a minimum of 3 possible days

Mondays	Tuesdays	Wednesday	Thursdays	Fridays

Times:

9:00 – 10:00	10:00 – 11:00	11:00 – 12:00

Area:

Fishhoek	Kenilworth/ Kirstenhof	Stellenbosc	Paarl	Strand

Appendix H

General Information and Health Form

General Information and Health Form

Patient Name: _____ Patient Surname: _____

Assessment date: _____ Date of Birth: _____

Level of Parkinson's disease (if known): _____

Complete the following questions as accurately as possible. Tick the appropriate block (☐).

1. Has your doctor given you permission to participate in this study? ☐ Yes ☐ No
   Doctor's name and contact details _____

2. Are you on regular medication? ☐ Yes ☐ No
   If yes, please indicate name, dosage and purpose _____
   _____

3. Most affected side: ☐ Left ☐ Right ☐ Both

4. Occupation (if you are retired, please indicate this and what you did before you retired:
   _____

5. Do you do housework and / or gardening? ☐ Yes ☐ No
   If yes, please indicate what chores you do_____

6. How often do you participate in physical activity or exercise?
   Times per week: _____ Duration: _____ Type: _____

7. Do you have a history of any of the following?

☐ Heart attack	☐ Coronary thrombosis	☐ Narrowing arteries
☐ High cholesterol	☐ High blood pressure	☐ Leaking valve
☐ Stroke	☐ Angina /Chest pains	☐ Other heart condition or disease
☐ Rheumatic fever	☐ Known heart murmur	☐ Palpitations
☐ Recent operation	☐ Aedema / swelling of ankles	☐ Breathing problems / difficulties
☐ Low blood pressure	☐ Seizures	☐ Lung disease
☐ Fainting or dizziness	☐ Cancer	☐ Diabetes
☐ Intermittent claudication	☐ Unusual fatigue / shortness of breath	☐ Pain/ discomfort in chest, neck, jaw, arms

   ☐ Other (please indicate): _____

8. Do you have a recent history of, or currently have, any joint / muscle injuries or pain?

☐ Neck ☐ Upper back ☐ Lower back ☐ Hip

☐ Thigh ☐ Knee ☐ Lower leg ☐ Ankle

☐ Foot ☐ Shoulder ☐ Elbow ☐ Wrist or hand

☐ Other (please specify: _____)

9. Has your doctor previously indicated any other conditions that we should know of?

_____

10. Are you colour blind? ☐ Yes ☐ No

Appendix I

39-Item Parkinson's Disease Questionnaire (PDQ-39)

Please complete the following:

Please tick one box for each question **Due to having Parkinson's Disease, how often <u>during the last month</u> have you…**					
	Never	**Occasion-ally**	**Sometimes**	**Often**	**Always** (Or cannot do at all)
1. Had difficulty doing the leisure activities which you would like to do?					
2. Had difficulty looking after your home, e.g. DIY, housework, cooking?					
3. Had difficulty carrying bags of shopping?					
4. Had problems walking half a mile?					
5. Had problems walking 100 yards?					
6. Had problems getting around the house as easily as you would like?					
7. Had difficulty getting around in public?					
8. Needed someone else to accompany you when you went out?					
9. Felt frightened or worried about falling over in public?					
10. Been confined to the house more than you would like?					
11. Had difficulty washing yourself?					
12. Had difficulty dressing yourself?					
13. Had problems doing up your shoe laces?					
14. Had problems writing clearly?					
15. Had difficulty cutting up your food?					
16. Had difficulty holding a drink without spilling it?					
17. Felt depressed?					
18. Felt isolated and lonely?					

19. Felt weepy or tearful?					
20. Felt angry or bitter?					
21. Felt anxious?					
22. Felt worried about your future?					
23. Felt you had to conceal your Parkinson's from people?					
24. Avoided situations which involve eating or drinking in public?					
25. Felt embarrassed in public due to having Parkinson’s Disease?					
26. Felt worried by other people's reaction to you?					
27. Had problems with your close personal relationships?					
28. Lacked support in the ways you need from your spouse or partner? (If you do not have a spouse or partner tick here)					
29. Lacked support in the ways you need from your family or close friends?					
30. Unexpectedly fallen asleep during the day?					
31. Had problems with your concentration, e.g. when reading or watching TV?					
32. Felt your memory was bad?					
33. Had distressing dreams or hallucinations?					
34. Had difficulty with your speech?					
35. Felt unable to communicate with people properly?					
36. Felt ignored by people?					
37. Had painful muscle cramps or spasms?					
38. Had aches and pains in your joints or body?					
39. Felt unpleasantly hot or cold?					

Appendix J

Activities-specific Balance Confidence Scale (ABC)

0%	10	20	30	40	50	60	70	80	90	100%

How confident are you that you will not lose your balance or become unsteady when you…

1. Walk around the house?

0%	10	20	30	40	50	60	70	80	90	100%

2. Walk up or down stairs?

0%	10	20	30	40	50	60	70	80	90	100%

3. Bend over and pick up a slipper from the front of a closet floor

0%	10	20	30	40	50	60	70	80	90	100%

4. Reach for a small can off a shelf at eye level?

0%	10	20	30	40	50	60	70	80	90	100%

5. Stand on your tiptoes and reach for something above your head?

0%	10	20	30	40	50	60	70	80	90	100%

6. Stand on a chair and reach for something?

0%	10	20	30	40	50	60	70	80	90	100%

7. Sweep the floor?

0%	10	20	30	40	50	60	70	80	90	100%

8. Walk outside the house to a car parked in the driveway?

0%	10	20	30	40	50	60	70	80	90	100%

9. Get into or out of a car?

0%	10	20	30	40	50	60	70	80	90	100%

10. Walk across a parking lot to the mall?

0%	10	20	30	40	50	60	70	80	90	100%

11. Walk up or down a ramp?

0%	10	20	30	40	50	60	70	80	90	100%

12. Walk in a crowded mall where people rapidly walk past you?

0%	10	20	30	40	50	60	70	80	90	100%

13. Are bumped into by people as you walk through the mall?

0%	10	20	30	40	50	60	70	80	90	100%

14. Step onto or off an escalator while you are holding onto a railing?

0%	10	20	30	40	50	60	70	80	90	100%

15. Step onto or off an escalator while holding onto parcels such that you cannot hold onto the railing?

0%	10	20	30	40	50	60	70	80	90	100%

16. Walk outside on icy sidewalks?

0%	10	20	30	40	50	60	70	80	90	100%

Appendix K

The Hamilton Rating Scale for Depression (HAM-D)

Patient Name: _____

Assessment date: _____

Instructions:
Complete the scale based on a structured interview. For each item, select the one "cue" which best characterizes the patient. Be sure to record the answers in the appropriate spaces (positions 0 through 4).

1) Depressed mood (sadness, hopeless, helpless, worthless)

☐ Absent;

☐ These feeling states indicated only on questioning;

☐ These feeling states spontaneously reported verbally;

☐ Communicates feeling states non-verbally, i.e. through facial expression, posture, voice and tendency to weep;

☐ Patient reports virtually only these feeling states in his/her spontaneous verbal and non-verbal communication

2) Feelings of guilt

☐ Absent;

☐ Self-reproach, feels he/she has let people down;

☐ Ideas of guilt or rumination over past errors or sinful deeds;

☐ Present illness is a punishment. Delusions of guilt;

☐ Hears accusatory or denunciatory voices and/or experiences threatening visual hallucinations

3) Suicide

☐ Absent;

☐ Feels life is not worth living;

☐ Wishes he/she were dead or any thoughts of possible death to self;

☐ Ideas or gestures of suicide;

☐ Attempts at suicide (any serious attempt rate 4)

4) Insomnia: Early in the night

☐ No difficulty falling asleep;

☐ Complains of occasional difficulty falling asleep, i.e. more than 1/2 hour;

☐ Complains of nightly difficulty falling asleep

5) Insomnia: Middle of the night

☐ No difficulty;

☐ Complains of being restless and disturbed during the night;

☐ Waking during the night - any getting out of bed rates 2 (except for purposes of voiding)

6) Insomnia: Early hours of the morning

☐ No difficulty;

☐ Waking in early hours of the morning but goes back to sleep;

☐ Unable to fall asleep again if he/she gets out of bed

7) Work and Activities

☐ No difficulty;

☐ Thoughts and feelings of incapacity, fatigue or weakness related to activities, work or hobbies;

☐ Loss of interest in activity, hobbies, or work - either directly reported by the patient or indirect in listlessness, indecision and vacillation (feels he/she has to push self to work or activities);

☐ Decrease in actual time spent in activities or decrease in productivity. Rate 3 if the patient does not spend at least three hours a day in activities (job or hobbies) excluding routine chores;

☐ Stopped working because of present illness. Rate 4 if patient engages in no activities except routine chores, or if patient fails to perform routine chores unassisted.

8) Retardation

☐ Normal speech and thought;

☐ Slight retardation during interview;

☐ Obvious retardation during interview;

☐ Interview difficult;

☐ Complete stupor

9) Agitation

☐ None;

☐ Fidgetiness;

☐ Playing with hands, hair, etc;

☐ Moving about, can't sit still;

☐ Hand wringing, nail biting, hair-pulling, biting of lips

10) Anxiety Psychic

☐ No difficulty;

☐ Subjective tension and irritability;

☐ Worrying about minor matters;

☐ Apprehensive attitude apparent in face or speech;

☐ Fears expressed without questioning

11) Anxiety Somatic (physiological concomitants of anxiety) such as:
Gastro-intestinal - dry mouth, wind, indigestion, diarrhoea, cramps, belching; Cardiovascular - palpitations, headaches; Respiratory - hyperventilation, sighing; Urinary frequency; Sweating

☐ Absent;

☐ Mild;

☐ Moderate;

☐ Severe;

☐ Incapacitating

12) Somatic symptoms gastro-intestinal

☐ None;

☐ Loss of appetite but eating without staff encouragement. Heavy feelings in abdomen;

☐ Difficulty eating without staff urging. Requests or requires laxatives or medication for bowels or medication for
gastro-intestinal symptoms

13) General somatic symptoms

☐ None;

☐ Heaviness in limbs, back, or head. Backaches, headaches, muscle aches. Loss of energy and fatigability;

☐ Any clear-cut symptom rates 2

14) Genital symptoms (symptoms such as loss of libido, menstrual disturbances)

☐ Absent;

☐ Mild;

☐ Severe

15) Hypochondriasis

☐ Not present;

☐ Self-absorption (bodily);

☐ Preoccupation with health;

☐ Frequent complaints, requests for help, etc;

☐ Hypochondriacal delusions

16) Loss of weight (Rate either A or B)

A) According to the patient: ☐ No weight loss; ☐ Probable weight loss associated with present illness; ☐ Definite (according to patient) weight loss; ☐ Not assessed	**B)** According to weekly measurements: ☐ Less than 1lb weight loss in week; ☐ Greater than 1lb weight loss in week; ☐ Greater than 2lb weight loss in week; ☐ Not assessed

17) Insight

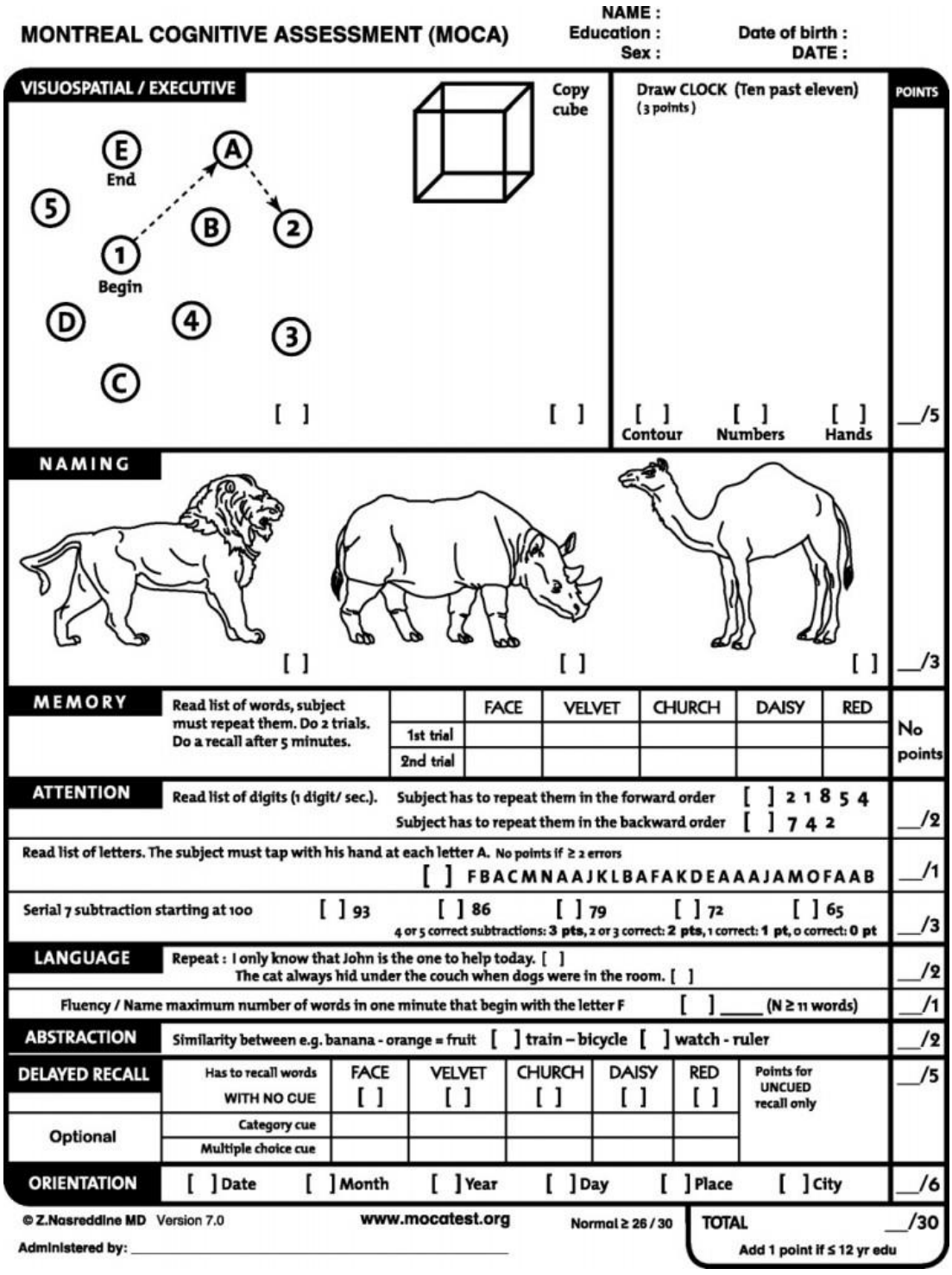
☐ Acknowledges being depressed and ill;

☐ Acknowledges illness but attributes cause to bad food, climate, overwork, virus, need for rest, etc;

☐ Denies being ill at all

Appendix L

Montreal Cognitive Assessment (MoCA)



MONTREAL COGNITIVE ASSESSMENT (MOCA)

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

VISUOSPATIAL / EXECUTIVE — POINTS

Copy cube

Draw CLOCK (Ten past eleven) (3 points)

E End, A, 5, B, 2, 1 Begin, D, 4, 3, C

[ ] [ ]

[ ] Contour [ ] Numbers [ ] Hands

__/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

© Z.Nasreddine MD Version 7.0 www.mocatest.org Normal ≥ 26 / 30

TOTAL __/30

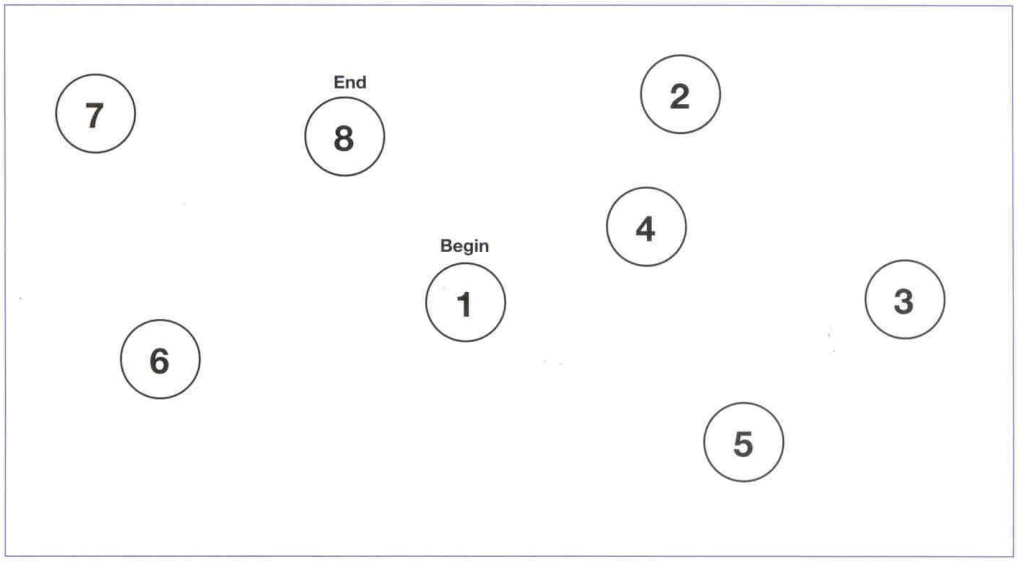
Add 1 point if ≤ 12 yr edu

Administered by: _____

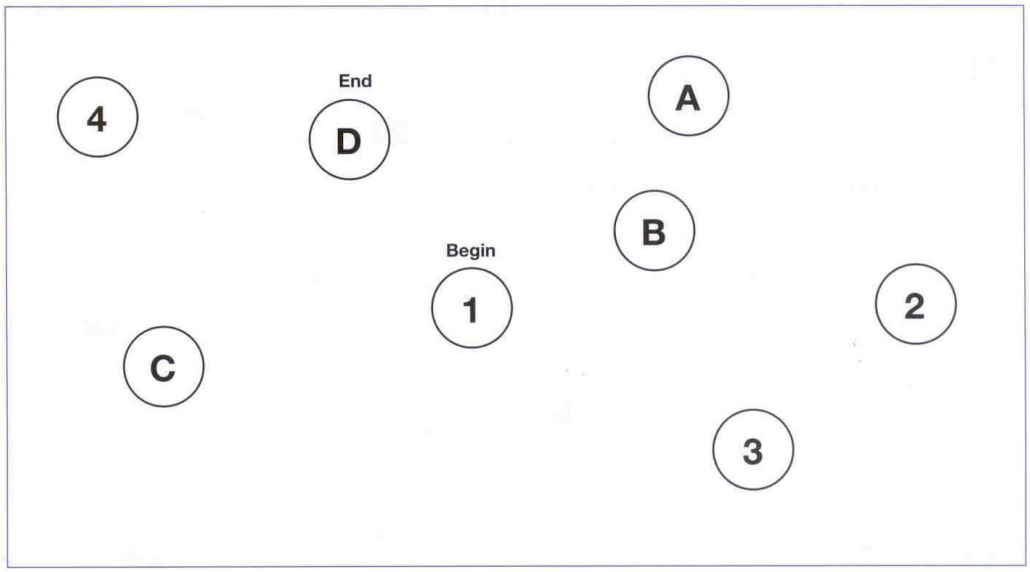
Appendix M

Trail Making Tests (TMT) parts A and B

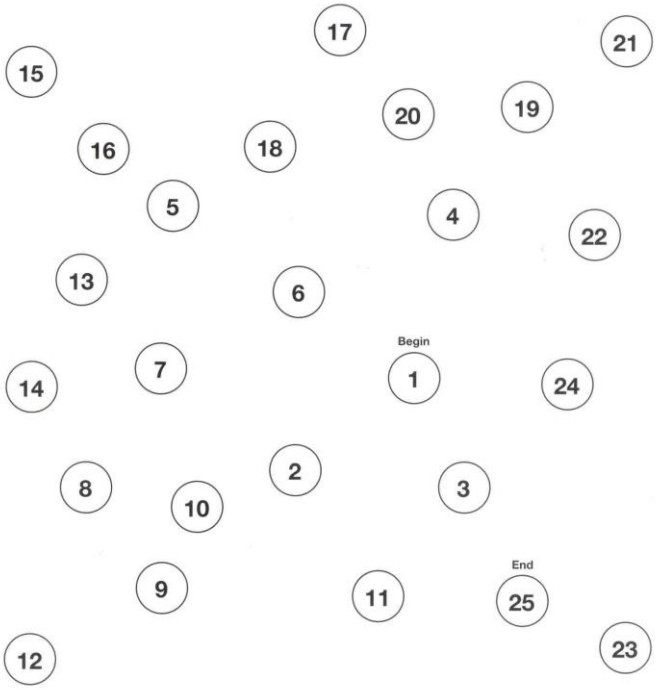
Trails A: Sample



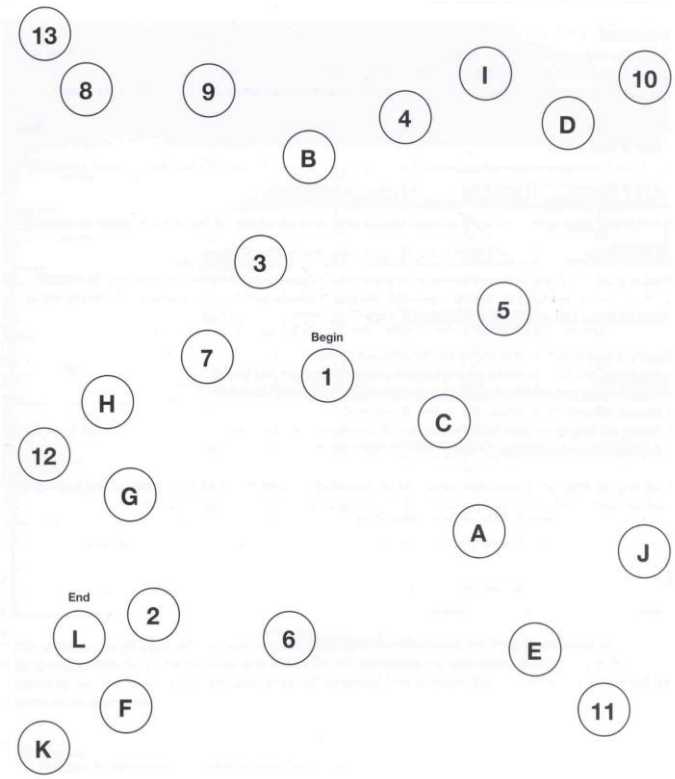
Trails B: Sample



Trails A:



Trails B:



Appendix N

Sensory-motor Training Programme with Aims and Objectives

<table>
<tr><td colspan="3"><u>Week 1</u>
<u>Aim:</u> Familiarization and alignment
1. To increase proprioceptive input to foot, sacro-iliac joint (SIJ) and cervical spine to ensure proper positioning during exercise sessions.</td></tr>
<tr><td><u>Session 1</u>
Objective: Foot proprioception</td><td><u>Session 2</u>
Objective: SIJ proprioception</td><td><u>Session 3</u>
Objective: Cervical spine proprioception</td></tr>
<tr><td>• Cue Posture
• Short foot training
▪ Sitting: Passive modelling or hand positioning
▪ Standing:
- try to 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
▪ Inversion
▪ Eversion
▪ Plantar flexion
• Marble pick ups
• Weight shifts</td><td>• Cue posture - close zip for TA activation
• Short foot training (recap) – 10min
• SIJ training
▪ Seated:
- Pelvic tilt
▪ Standing:
- Pelvic tilt
- try to maintain short foot (SF)
- one leg balance with SF
- modified tandem stance with SF
• Weight shifts with TA activation</td><td>• 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)</td></tr>
<tr><td colspan="3"><u>Week 2</u>
<u>Aim:</u> Static balance
1. To maintain postural control on unstable surfaces and progress to weight shifting, eliminating vision or adding head movements.
2. Focus on using the ankle strategy during exercise sessions.</td></tr>
<tr><td><u>Session 1</u>
Objective: Posture</td><td><u>Session 2</u>
Objective: Base of support</td><td><u>Session 3</u>
Objective: Centre of gravity</td></tr>
<tr><td>• Cue Posture</td><td>• Cue posture</td><td>• Cue posture</td></tr>
</table>

• Balance exercises ▪ **Sitting with feet on firm surface:** - trunk leans in different directions - Reaching for objects - Catching and throwing objects (group) ▪ **Standing with feet on firm surface:** - Eyes open - Trunk leans in different directions - Reaching for objects - Catching and throwing objects (group) ▪ Modified Tandem stance: - Eyes open • Somatosensory activity ▪ The ball game ▪ Over the moon ▪ Over the moon – rock forward, step up	• Balance exercises ▪ Standing with feet on firm surface: - Eyes open - Trunk leans in different directions - Reaching for objects - Catching and throwing objects (group) ▪ **Modified Tandem stance:** - Eyes open - Trunk leans in different directions - Reaching for objects - Catching and throwing objects (group) ▪ Single leg stance: - Eyes open • Somatosensory activity ▪ Belly button training ▪ Standing weight shifts	• Balance exercises ▪ Standing with feet on firm surface: - Eyes open - Trunk leans in different directions - Reaching for objects - Catching and throwing objects (group) ▪ Modified Tandem stance: - Eyes open - Dim room lights - Dark glasses ▪ **Single leg stance:** - Eyes open - Dim room lights - Dark glasses • Somatosensory activity ▪ Standing weight shifts ▪ Making waves

Week 3

Aim: Static balance

1. To maintain postural control on unstable surfaces and progress to weight shifting, eliminating vision or adding head movements.
2. 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
• Cue Posture • Balance exercises ▪ **Sitting with feet on firm surface:** - trunk leans in different directions - Reaching for objects - Catching and throwing objects (group) ▪ **Standing with feet on firm surface:** - trunk leans in different directions	• Cue posture • Balance exercises ▪ Standing with feet on firm surface: - trunk leans in different directions - Reaching for objects - Catching and throwing objects (group) ▪ **Modified Tandem stance on firm surface:** - Eyes open	• Cue posture • Balance exercises ▪ Standing with feet on firm surface: - trunk leans in different directions - Reaching for objects - Catching and throwing objects (group) ▪ Modified Tandem stance on firm surface: - Eyes open

- Reaching for objects - Catching and throwing objects (group) ▪ Modified Tandem stance on firm surface: - Eyes open - Dark glasses - One eye closed - Both eyes closed • Somatosensory activity ▪ Standing weight shifts ▪ Making waves	- Dark glasses - One eye closed - Both eyes closed ▪ Single leg stance on firm surface: - Eyes open - Dark glasses - One eye closed - Both eyes closed • Somatosensory activity ▪ Keeping you on your toes	- Dark glasses - One eye closed - Both eyes closed ▪ **Single leg stance on firm surface:** - Eyes open - Dark glasses - One eye closed - Both eyes closed • Somatosensory activity ▪ Rock and walk
Week 4 *Aim:* Dynamic balance 1. To maintain postural control on progressively unstable surfaces while adding upper- and lower extremity movement. 2. Maintain ankle strategy during exercise sessions and focus hip strategy.		
Session 1 *Objective:* Posture	**Session 2** *Objective:* Base of support	**Session 3** *Objective:* Centre of gravity
• Cue Posture • Balance exercises ▪ Modified Tandem stance on firm surface: - Eyes open - Dark glasses - One eye closed - Both eyes closed ▪ Single leg stance on firm surface: - Eyes open - Dark glasses - One eye closed - Both eyes closed ▪ **Walking** (15m) - normal walking - high knees walking	• Cue posture • Balance exercises ▪ Modified Tandem stance on firm surface: - Eyes open - Dark glasses - One eye closed - Both eyes closed ▪ Single leg stance on firm surface: - Eyes open - Dark glasses - One eye closed - Both eyes closed ▪ Walking (15m) - normal walking - high knees walking	• Cue posture • Balance exercises ▪ Single leg stance on firm surface: - Eyes open - Dark glasses - One eye closed - Both eyes closed ▪ Walking (15m) - normal walking - high knees walking - butt kicks walking - sideways walking ▪ Tandem Walking ▪ Weight shifts with stepping strategy ▪ **Walking with reduced vision** (15m)

- butt kicks walking - sideways walking • Somatosensory activity ▪ Opposing circles and high fives	- butt kicks walking - sideways walking ▪ **Tandem Walking** ▪ **Weight shifts with stepping strategy** • Somatosensory activity ▪ Follow the light	- normal walking - high knees walking - butt kicks walking - sideways walking • Somatosensory activity ▪ Agility ladders
Week 5 *Aim:* Dynamic balance 1. To maintain postural control on progressively unstable surfaces while adding upper- and lower extremity movement. 2. Maintain ankle strategy, focus on hip strategy and start introducing stepping strategy in exercise sessions		
Session 1 *Objective:* Posture	**Session 2** *Objective:* Base of support	**Session 3** *Objective:* Centre of gravity
• Cue Posture • Balance exercises ▪ Single leg stance on compliant surface: - Eyes open - Dark glasses - One eye closed - Both eyes closed ▪ Walking (15m) - normal walking - high knees walking - butt kicks walking - sideways walking ▪ Tandem Walking ▪ Weight shifts with stepping strategy ▪ **Walking with reduced vision** (15m) - normal walking - high knees walking - butt kicks walking - sideways walking	• Cue posture • Balance exercises ▪ Walking (15m) - normal walking - high knees walking - butt kicks walking - sideways walking ▪ Tandem Walking ▪ Weight shifts with stepping strategy ▪ Walking with reduced vision (15m) - normal walking - high knees walking - butt kicks walking - sideways walking ▪ **Tandem Walking with reduced vision** ▪ **Weight shifts with stepping strategy with reduced vision** • Somatosensory activity ▪ Follow the light	• Cue posture • Balance exercises ▪ Walking (15m) - normal walking - high knees walking - butt kicks walking - sideways walking ▪ Tandem Walking ▪ Weight shifts with stepping strategy ▪ Walking with reduced vision (15m) - normal walking - high knees walking - butt kicks walking - sideways walking ▪ **Tandem Walking with reduced vision** ▪ **Weight shifts with stepping strategy with reduced vision** • Somatosensory activity ▪ Agility ladders

<table>
<tr><td>• Somatosensory activity
▪ Opposing circles and high fives</td><td></td><td></td></tr>
<tr><td colspan="3"><u>Week 6</u>
<u>Aim:</u> Functional balance
1. To perform functional movements of everyday life on progressively unstable surfaces.
2. Maintain ankle and hip strategy and focus on stepping strategy in exercise sessions</td></tr>
<tr><td><u>Session 1</u>
Objective: Posture</td><td><u>Session 2</u>
Objective: Base of support</td><td><u>Session 3</u>
Objective: Centre of gravity</td></tr>
<tr><td>• Cue posture
• Balance exercises
▪ Recap Modified Tandem stance on firm
▪ Recap Single leg stance on firm surface:
▪ Walking (15m)
- normal walking
- high knees walking
- butt kicks walking
- sideways walking
▪ Tandem Walking
▪ Weight shifts with stepping strategy
▪ Walking with reduced vision (15m)
- normal walking
- high knees walking
- butt kicks walking
- sideways walking
▪ Tandem Walking with reduced vision
▪ Weight shifts with stepping strategy with reduced vision
▪ Walking with reduced vision & head movements (15m)
- normal walking
- high knees walking</td><td>• Cue posture
• Balance exercises
▪ Walking (15m)
- normal walking
- high knees walking
- butt kicks walking
- sideways walking
▪ Tandem Walking
▪ Weight shifts with stepping strategy
▪ Walking with reduced vision (15m)
- normal walking
- high knees walking
- butt kicks walking
- sideways walking
▪ Tandem Walking with reduced vision
▪ Weight shifts with stepping strategy with reduced vision
▪ Walking with reduced vision & head movements (15m)
- normal walking
- high knees walking
- butt kicks walking
- sideways walking</td><td>• Cue posture
• Balance exercises
▪ Walking (15m) with added obstacles
- normal walking
- high knees walking
- butt kicks walking
- sideways walking
▪ Tandem Walking
▪ Weight shifts with stepping strategy
▪ Walking with reduced vision (15m)
- normal walking
- high knees walking
- butt kicks walking
- sideways walking
▪ Tandem Walking with reduced vision
▪ Weight shifts with stepping strategy with reduced vision
▪ Walking with reduced vision & head movements (15m)
- normal walking
- high knees walking
- butt kicks walking
- sideways walking</td></tr>
</table>

- butt kicks walking - sideways walking • Somatosensory activity ▪ Agility ladders	• Somatosensory activity ▪ Agility ladders	• Somatosensory activity ▪ Agility ladders
Week 7 *Aim:* Functional balance 1. To perform functional movements of everyday life on progressively unstable surfaces. 2. Maintain ankle and hip strategy and focus on stepping strategy in exercise sessions		
Session 1 *Objective:* Posture	**Session 2** *Objective:* Base of support	**Session 3** *Objective:* Centre of gravity
• Cue posture • Balance exercises ▪ Recap Modified Tandem stance on firm ▪ Recap Single leg stance on firm surface: ▪ Walking (15m) with added obstacles - normal walking - high knees walking - butt kicks walking - sideways walking ▪ Tandem Walking ▪ Reaching exercises - Reaching high on shelf - Reaching shoulder height - Reaching down to ground ▪ Weight shifts with stepping strategy ▪ Walking with direction change *(t-test)* - normal walking - high knees walking - butt kicks walking - sideways walking ▪ Tandem Walking with reduced vision	• Cue posture • Balance exercises ▪ Recap Modified Tandem stance on firm ▪ Recap Single leg stance on firm surface: ▪ Walking (15m) with added obstacles - normal walking - high knees walking - butt kicks walking - sideways walking ▪ Tandem Walking ▪ Reaching exercises - Reaching high on shelf - Reaching shoulder height - Reaching down to ground ▪ Weight shifts with stepping strategy ▪ Walking with direction change *(t-test)* - normal walking - high knees walking - butt kicks walking - sideways walking ▪ Tandem Walking with reduced vision	• Cue posture • Balance exercises ▪ Recap Modified Tandem stance on firm ▪ Recap Single leg stance on firm surface: ▪ Walking (15m) with added obstacles - normal walking - high knees walking - butt kicks walking - sideways walking ▪ Tandem Walking ▪ Reaching exercises - Reaching high on shelf - Reaching shoulder height - Reaching down to ground ▪ Weight shifts with stepping strategy ▪ Walking with direction change *(t-test)* - normal walking - high knees walking - butt kicks walking - sideways walking ▪ Tandem Walking with reduced vision

▪ Weight shifts with stepping strategy with reduced vision ▪ Walking and counting (15m) - normal walking - high knees walking - butt kicks walking - sideways walking - backwards walking ▪ Group Sit-to-stands in circle (move from chair 1 to chair 2)	▪ Weight shifts with stepping strategy with reduced vision ▪ Walking and counting (15m) - normal walking - high knees walking - butt kicks walking - sideways walking - backwards walking ▪ Group Sit-to-stands in circle (move from chair 1 to chair 2)	▪ Weight shifts with stepping strategy with reduced vision ▪ Walking and counting (15m) - normal walking - high knees walking - butt kicks walking - sideways walking - backwards walking ▪ Group Sit-to-stands in circle (move from chair 1 to chair 2)
Week 8 *Aim:* Functional balance 1. To perform functional movements of everyday life on progressively unstable surfaces. 2. Maintain ankle and hip strategy and focus on stepping strategy in exercise sessions		
Session 1 *Objective:* Posture	**Session 2** *Objective:* Base of support	**Session 3** *Objective:* Centre of gravity
• Cue posture • Balance exercises ▪ Recap Modified Tandem stance on firm ▪ Recap Single leg stance on firm surface: ▪ Walking with added obstacles and music - normal walking - high knees walking - butt kicks walking - sideways walking ▪ Tandem Walking ▪ Reaching exercises with reduced vision - Reaching high on shelf - Reaching shoulder height - Reaching down to ground	• Cue posture • Balance exercises ▪ Walking with added obstacles and music - normal walking - high knees walking - butt kicks walking - sideways walking ▪ Tandem Walking ▪ Weight shifts with stepping strategy ▪ Walking with direction change and obstacles (t-test) - normal walking - high knees walking - butt kicks walking	• Cue posture • Balance exercises ▪ Walking with added obstacles and music - normal walking - high knees walking - butt kicks walking - sideways walking ▪ Tandem Walking ▪ Weight shifts with stepping strategy ▪ Walking with direction change and obstacles (t-test) - normal walking - high knees walking - butt kicks walking - sideways walking

▪ Weight shifts with stepping strategy ▪ Walking with direction change and obstacles (t-test) - normal walking - high knees walking - butt kicks walking - sideways walking ▪ Tandem Walking with reduced vision ▪ Walking and counting backwards (15m) - normal walking - high knees walking - butt kicks walking - sideways walking - backwards walking ▪ Group Sit-to-stands in circle (move from chair 1 to chair 2) ▪ 360° turns	- sideways walking ▪ Tandem Walking with reduced vision ▪ Walking and counting backwards (15m) - normal walking - high knees walking - butt kicks walking - sideways walking - backwards walking ▪ Group Sit-to-stands in circle (move from chair 1 to chair 2) ▪ 360° turns ▪ Sitting on Swiss Ball ▪ Sitting on Swiss Ball + Reaching exercises - Reaching high on shelf - Reaching shoulder height - Reaching down to ground	▪ Tandem Walking with reduced vision ▪ Walking and counting backwards (15m) - normal walking - high knees walking - butt kicks walking - sideways walking - backwards walking ▪ Group Sit-to-stands in circle (move from chair 1 to chair 2) ▪ 360° turns ▪ Sitting on Swiss Ball ▪ Sitting on Swiss Ball + Reaching exercises - Reaching high on shelf - Reaching shoulder height - Reaching down to ground

<u>Warm-up and Cool-Down</u> at the beginning and end of every session.

<u>Aim:</u> To provide an opportunity to warm up and prepare for the session ahead, at the beginning, and to cool down and relax, at the end.

<u>Warm Up</u> *Objective:* Preparation for session (10 minutes)	**<u>Cool Down</u>** *Objective:* Relaxation at end of session (10 minutes)
• Warm-up game: Balloon Volleyball / Circle Soccer / Shift Around The Clock / Line passing • Whole body stretches ▪ Shoulder circles ▪ Neck stretch ▪ Arm stretch ▪ Arm pushes and circles ▪ Back squeezes ▪ Hugs	• Deep breathing • Muscular relaxation ▪ Hands ▪ Arms ▪ Neck ▪ Face ▪ Chest ▪ Stomach ▪ Buttocks

▪ Wrist circles ▪ Thumb to finger ▪ Quadriceps stretch ▪ Hamstrings stretch ▪ Calf stretch ▪ Deep breathing	▪ Legs • Deep breathing ▪ Chin-to-chest ▪ Chin-to-shoulder ▪ Trunk rotation ▪ Close eyes

Appendix O
Safety guidelines

The following booklet contains tips to keep in mind while doing balance training. Please make yourself familiar with its contents before you start the 8-week intervention program.

- **Nothing should hurt.** This is a simple rule, if it hurts inform the instructor. 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 instructor'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 instructor 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 instructor 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 instructor if necessary
    - Any participants standing should sit down
    - Clear the area around the injured participant
    - Make the participant as comfortable as possible

Appendix P

Excessive depressive moods (http://www.nhs.uk)

If the participant experiences some of these signs listed below for most of the day, every day **for more than two weeks**, you should advise them to seek help from their general physician.

Psychological signs include:

- continuous low mood or sadness
- feeling hopeless and helpless
- having low self-esteem
- feeling tearful
- feeling guilt-ridden
- feeling irritable and intolerant of others
- having no motivation or interest in things
- finding it difficult to make decisions
- not getting any enjoyment out of life
- feeling anxious or worried
- having suicidal thoughts or thoughts of harming yourself

Physical signs include:

- moving or speaking more slowly than usual
- change in appetite or weight (usually decreased, but sometimes increased)
- constipation
- unexplained aches and pains
- lack of energy or lack of interest in sex (loss of libido)
- changes to your menstrual cycle
- disturbed sleep (for example, finding it hard to fall asleep at night or waking up very early in the morning)

Social signs include:

- not doing well at work
- taking part in fewer social activities and avoiding contact with friends
- neglecting your hobbies and interests
- having difficulties in your home and family life