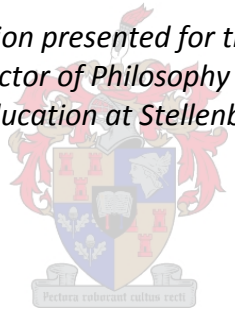
Exploring therapeutic neurogenic tremors with exercise as a treatment for selective motor and non-motor Parkinson's disease symptoms.

by
Elizabeth Maria Atterbury

Dissertation presented for the degree of
Doctor of Philosophy in the
Faculty of Education at Stellenbosch University



Supervisor: Dr Karen Estelle Welman

April 2019

DECLARATION

By submitting this thesis/dissertation electronically, I (Elizabeth Maria Atterbury) 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.

ABSTRACT

Intro: Parkinson's disease (PD) is a chronic neurological progressive disorder accompanied by a wide range of symptoms that affect independence and quality of life (QoL) [1]. Individuals with PD (IwPD) experience motor symptoms, including postural instability and gait disturbances, and non-motor symptoms (NMS), including depressive moods, anxiety and autonomic dysregulation [2]. Daily stress further exacerbates PD symptoms [3]. Therefore stress management is of particular importance for IwPD. Relaxation-based exercises might be a viable option, and recently the addition of therapeutic neurogenic tremors (TNT) to exercise have been shown to aid in the reduction of perceived stress as well as improvement in QoL [4–6]. These tremors are theorised to be a genetically-encoded mechanism part of the stress response [7], and a necessary process for the body to function optimally after stressful and traumatic events [8,9]. Therefore, the current study set out to investigate the effects of relaxation-based exercises with and without TNT on selective motor and non-motor symptoms of IwPD.

Methods: Thirty-six individuals with idiopathic PD participated in this experimental study, with a double-blinded randomised time-series design. Participants were randomly allocated to three groups: 1) Exercises with TNT (TRE), 2) Exercises without TNT (EAR), and 3) a non-exercising waitlist control group (n = 12, 69.6 ± 8.3 years). Group 1 (n = 14, 72.7 ± 7.5 years) participated in a Trauma and Tension Releasing Exercises (TRE) intervention, while Group 2 (n = 10, 70.3 ± 5.7 years) participated in the Exercise and Relaxation (EAR) intervention. Both interventions followed the same protocol except for the addition of TNT in the TRE group, and took place with tapered supervision over nine weeks. Participants, in all three groups, were tested every three weeks (i.e. baseline, 3, 6 and 9 weeks), and after a three week retention period. Primary outcome measures included postural instability, gait disturbances, domains of NMS, depressive moods, general anxiety, and somatisation. Assessments included the Mini Balance Evaluation Systems Test (BESTest), instrumented 2-Minute Walk (2MW), NMS Questionnaire (NMSQuest) and NMS Symptoms Scale (NMSS), as well as the Patient Health Questionnaire for somatic, anxiety and depressive symptoms (PHQ-SADS). Secondary outcome measures included disease severity (assessed with the Movement Disorder Society's – Unified Parkinson's Disease Rating Scale (MDS-UPDRS)), perceived balance confidence (assessed with the Activity-specific Balance Confidence (ABC) scale) and QoL (assessed by the 8-item Parkinson's disease Questionnaire (PDQ-8)).

Results: Groups did not differ in descriptive characteristics or outcome variables at baseline ($p > 0.05$), except for variability of trunk rotation, mood/cognition and attention/memory domains of NMSS between TRE and CON groups ($p < 0.05$). An interaction effect was observed for PDQ-8 ($p = 0.01$) with improvements seen for EAR group ($p = 0.002$, Hedges' $g = 0.45^{M}$) and a tendency for the TRE group to improve ($p = 0.07$, Hedges' $g = 0.35^{S}$) over time. The main findings with practical significance after the intervention period were improvements in gait speed of the EAR group ($p = 0.005$, Hedges' $g = 0.39^{S}$), and variability of trunk rotation during 2MW for TRE group ($p = 0.048$, Hedges' $g = 0.39^{S}$). The EAR and TRE groups showed improvement in gastrointestinal complaints and the severity of stress-related items in the mood/cognition domain of NMSS ($p < 0.03$, Hedges' $g > 0.48^{M}$), while TRE showed additional improvements for frequency stress-related items of NMSS ($p < 0.05$, Hedges' $g > 0.49^{M}$). Additionally significant practical improvements were observed for MDS-UPDRS II (motor experience

of daily living) for TRE ($p = 0.02$, Hedges' $g = 0.29^{S}$) and control group ($p = 0.01$, Hedges' $g = 0.33^{S}$). The retention period showed improvements in Mini BESTest domains for EAR ($p = 0.04$, Hedges' $g = 0.57^{M}$) and control ($p = 0.02$, Hedges' $g = 0.65^{M}$) groups, and improvement in NMSQuest for TRE ($p = 0.04$, Hedges' $g = 0.56^{M}$).

Conclusion: This exploratory study shows promising preliminary results for relaxation-based exercises with TNT. The findings suggest that relaxation-based exercises were beneficial towards improving gait performance, decreasing the severity of selective NMS and possibly improving QoL. The addition of TNT could have the potential of further improvements in the motor experience of daily living, quality of gait, and the frequency of stress-related NMS. Therapies utilizing TNT could be an essential tool for IwPD to reduce the impact of motor and NMS, and manage stress. However, more research is needed to investigate the effects of TNT on populations vulnerable to stress.

OPSOMMING

Inleiding: Parkinson se siekte (PD) is 'n chroniese neurologiese progressiewe versteuring, wat gepaard gaan met 'n wye verskeidenheid simptome wat onafhanklikheid en lewenskwaliteit beïnvloed [1]. Individue met PD (IwPD) ervaar motoriese simptome, insluitende posturale onstabiliteit en loopgangversteurings, en nie-motoriese simptome (NMS), insluitend depressiewe buie, angs en outonomiese-senuweestelsel wanfunksie [2]. Daaglikse stres kan PD-simptome toenemend vererger [3]. Daarom is stresbestuur vir IwPD van besondere belang. Ontspanningsgebaseerde oefeninge kan 'n moontlike opsie van waarde wees, en onlangs het die toevoeging van terapeutiese neurogene bewing (TNT) tot oefeninge getoon dat dit help met die vermindering van waargenome stres asook verbetering in lewenskwaliteit [4–6]. Dit word teoreties voorgestel dat hierdie bewinge 'n geneties-gekodeerde meganisme deel van die stresrespons vorm [7], en 'n noodsaaklike proses van die liggaam is om optimaal te funksioneer na stresvolle en traumatiese gebeure [8,9]. Daarom het die huidige studie ondersoek ingestel na die uitwerking van ontspanninggebaseerde oefeninge met en sonder TNT op selektiewe motoriese en nie-motoriese simptome van IwPD.

Metodes: Ses-en-dertig individue met idiopatiese PD het aan hierdie eksperimentele studie deelgeneem, met 'n dubbelblinde willekeurige tydreeksontwerp. Deelnemers is willekeurig toegewys aan een van drie groepe: 1) Oefeninge met TNT, 2) Oefeninge sonder TNT (EAR), en 3) 'n nie-oefenende waglys kontrole groep (n = 12, 69.6 ± 8.3 jaar). Groep 1 (n = 14, 72.7 ± 7.5 jaar) het deelgeneem aan ’n “Trauma and Tension Releasing Exercises” (TRE) intervensie, terwyl die EAR-groep (n = 10, 70.3 ± 5.7 jaar) aan ’n oefening en ontspanningsintervensie (EAR) deelgeneem het. Beide intervensies het dieselfde protokol gevolg, behalwe vir die byvoeging van TNT in die TRE-groep, en het oor nege weke met afnemende toesig plaasgevind. Deelnemers, in al drie groepe, was elke drie weke getoets (dws basislyn, 3, 6 en 9 weke), en na 'n drie weke retensieperiode. Primêre uitkomsmates het posturale onstabiliteit, loopgangversteurings, areas van NMS, depressiewe buie, angs en somtiese simptome ingesluit. Assesserings het die Minibalansevalueringstoets (Mini BESTest), Instrumentiewe 2-Minute-Stap (2MW), NMS-vraelys (NMSQuest) en NMS-simptoomskaal (NMSS) ingesluit, sowel as die “Patient Health Questionnaire” vir somatiese, angs en depressiewe simptome (PHQ-SADS). Sekondêre uitkomsmates het siekte-erns (gemeet deur die “Movement Disorder Society’s – Unified Parkinson’s Disease Rating Scale” (MDS-UPDRS)), waargeneome balance vertroue (gemeet deur die Aktiwiteits-spesifieke Balansvertroue (ABC) skaal) en lewenskwaliteit (gemeet deur die 8-item Parkinson se siekte vraelys (PDQ-8)) ingesluit.

Resultate: Groepe het nie verskil in beskrywende eienskappe of uitkomsveranderlikes by basislyn nie ($p > 0.05$), behalwe vir variasie van romprotasie, gemoedstoestand/kognitiewe en aandag/geheue areas van die NMSS tussen TRE and CON groepe ($p < 0.05$). ’n Interaksie-effek is waargeneem vir PDQ-8 ($p = 0.01$) met verbeteringe vir die EAR-groep ($p = 0.002$, Hedges’ $g = 0.45^{M}$) en 'n tendens tot verbetering vir die TRE-groep oor die verloop van die intervensie ($p = 0.07$, Hedges’ $g = 0.35^{S}$). Die hoof bevindings wat praktiese betekenisvol was na die intervensieperiode, was die verbeteringe in stapspoed van die EAR-groep ($p = 0.005$, Hedges’ $g = 0.39^{S}$), en variasie van romprotasie gedurende 2MW vir die TRE groep ($p = 0.048$, Hedges’ $g = 0.39^{S}$). Die EAR- en TRE-groepe het verbeterings in gastro-intestinale klagtes getoon asook in die intensiteit van stresverwante items in die gemoedstoestand/kognitiewe-area van die NMSS ($p <0.03$, Hedges’ $g > 0.48^{M}$), terwyl TRE bykomende verbeterings teweeg gebring het vir die frekwensie van stresverwante items van NMSS ($p <0.05$,

Hedges' g > 0.49[M]). Additionele verbeteringe was gevind vir MDS-UPDRS II (motoriese ervaring van daaglikse lewe) vir die TRE (p = 0.02, Hedges' g = 0.29[S]) en kontrole groep (p = 0.01, Hedges' g = 0.33[S]). Die retensieperiode het verbeteringe in Mini BESTest aspekte vir die EAR groep (p = 0.04, Hedges' g = 0.57[M]) en die kontrolegroep (p = 0.02, Hedges' g = 0.65[M]) getoon, asook verbetering in NMSQuest vir die TRE groep (p = 0.04, Hedges' g = 0.56[M]).

Gevolgtrekking: Hierdie verkennende studie toon belowende voorlopige resultate vir ontspanninggebaseerde oefeninge met TNT. Die bevindinge dui daarop dat ontspanningsgebaseerde oefeninge voordelig is vir die verbetering van loopgangprestasie, die vermindering in intensiteit van selektiewe NMS en moontlik verbeterde lewenskwaliteit. Die toevoeging van TNT het moontlik die potensiaal om die motoriese ervaring van die daaglikse lewe, loopangkwaliteit, en die frekwensie van stresverwante NMS te verbeter. Terapieë wat TNT gebruik, kan 'n noodsaaklike hulpmiddel vir IwPD wees om die impak van motoriese simptome en NMS te verminder en stres te bestuur. Meer navorsing is egter nodig om die effekte van TNT op bevolkinggroepe, wat meer vatbaar is vir stres, te ondersoek.

ACKNOWLEDGEMENTS

This research project would not have been possible without the wonderful support at each step along the way. I am very grateful for the help, love, and advice in the completion of this dissertation.

- I would like to express my deepest gratitude towards my supervisor, Dr Karen Welman, for all her support, edits and brainstorming sessions. We have come a long way and I cannot imagine that I would have come this far if it was not for your guidance and enthusiasm. Your wisdom of life and research, and your willingness to help, and encouragement to travel has impacted my life for the better.

- My family have played a major role in keeping me grounded throughout the process. I am very grateful for all the meals, laundry, laughs, and entertainment. I especially want to thank my parents, Leon and Marié Atterbury, for their willingness to check for mistakes my tired eyes have missed; my sister, Laura, for your endless entertainment and silliness to help clear my mind; and my brother, Colin, and his wife, Wilna, and their two wonderful children, Esmé and Aiden, for being a source of playfulness.

- I would like to express my gratitude towards my friends, Charné, Maryke (X2), Rachelle, Thena, Mari, and Carla. Your unwavering faith in my abilities has been a great source of strength. Even though we are scattered around the world, staying in touch is effortless because we share the same heart space. Thank you for your encouragement, no-holds-bar honest chats about life, and belly laughter over a glass of wine.

- A huge thank you to my fellow students at the Movement lab, Tania, Claire, Jeanine, Reghard, and Nadja. I did not expect life-long friendships to be forged in articles and cups of coffee. Each of you has had a major impact on my research and quality of life. It has been such an honour to share a workspace with you, as well as share academic (and non-academic) ideas and random thoughts. The past few years have been filled with adventures such as lunch breaks, overseas conferences trips, road trips, office games, and cocktails.

- I am indebted to the participants and TRE practitioners for their willingness to contribute to the research. I am grateful to each participant who came with an eagerness to help themselves and contribute to knowledge that can help others. I thoroughly enjoyed the process with you. To the keen TRE practitioners who offered up their time and effort to help with the intervention, I am extremely grateful. Your careful care and insights have been a big asset to me and the research.

- I would like to thank Prof Martin Kidd for the Centre for Statistical Consultation at Stellenbosch University. Your help with statistical analyses is much appreciated, as well as your advice, explanations and guidance.

- This research project would not have been possible without the financial support for the National Research Foundation. Disclaimer: *This work is based on the research supported in part by the National Research Foundation of South Africa for the grant no. 102381. 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.*

- Lastly, I would like to thank the Sports Science Department of Stellenbosch University that has been my academic home for the past 9 years for their help and support with equipment, administration and facilities to work. A special thank you to Tannie Mimi and Nico.

DEDICATION

This dissertation is dedicated to my parents, Leon and Marié Atterbury, for their curiosity about life, for showing me the joy of seeking answers, and for teaching me how unconditional love feel. It has granted me the courage to follow my intuition and passions. Thank you for being my lighthouse and safe harbour.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ADDENDUMS

Addendums presented in alphabetical order.

ABBREVIATIONS

2MW	Two minute walk
A.U	Arbitrary units
ABC	Activity-specific Balance Confidence
ADL	Activities of daily living
ANCOVA	Analysis of covariance
ANOVA	Analysis of variance
AR	Akinetic Rigidity
Asym	Asymmetry
BESTest	Balance Evaluation Systems Test
BoS	Base of support
CAM	Complementary and Alternative Medicine
CI	Confidence intervals
CoM	centre of mass
CON	Control group
CoV	Coefficient of variance
DS	Time in Double support
DST	Dynamic Systems Theory
EAR	Exercise and Relaxation group
ES	Effective Size
FoG	Freezing of gait
GAD	General Anxiety Disorder
H&Y	Hoehn & Yahr
HPA	Hypothalamus-Pituitary-Adrenal
IMI	Intrinsic Motivation Inventory
IwPD	Individuals with Parkinson's disease
LEDD	Levodopa Equivalency Daily Dosage
MDS-UPDRS	Movement Disorder Society – Unified Parkinson's disease rating scale
MoCA	Montreal Cognitive Assessment
NMS	Non-motor symptoms

NMSQuest	Non-motor symptoms questionnaire
NMSS	Non-motor symptoms scale
PCI	Phase coordination index
PCI	Phase coordination index
PD	Parkinson's disease
PDQ	Parkinson's disease questionnaire
PHQ	Patient Health Questionnaire
PHQ-SADS	Patient Health Questionnaire – Somatization Anxiety Depression Symptoms
PIGD	Postural Instability and Gait Disturbances
PTSD	Post Traumatic Stress Disorder
QoL	Quality of Life
RBD	REM behaviour disorder
REM	Rapid eye movement
RoM	Range of Movement
RPE	Rate of Perceived Exertion
SADS	Somatic, anxiety and depressive symptoms
SD	Standard Deviation
SEM	Standard Error of Measurement
SL	Stride length
SNc	Substania nigra pars compacta
SSA	Sub-Saharan Africa
STN	Subthalamic nucleus
SV	Stride velocity
TD	Tremor dominant
TNT	Therapeutic Neurogenic Tremors
TRE	Trauma and Tension Releasing Exercises
VTA	Ventral tegmental area

DEFINITION OF KEY TERMINOLOGY

- **Activities of Daily Living** - umbrella term for Routine activities and tasks that individuals that perform during their everyday life without needing assistance [10]

- **Anxiety** - An emotional state characterized by feelings of displeasure, angst, apprehension and dread associated with the physiological changes that occur in the body during stress[11]

- **Autonomic dysregulation** - condition in which the autonomic nervous system does not regulate the systems of the body fully, affecting the functioning of the heart, bladder, intestines, sweat glands, pupils, and blood vessels [12]

- **Balance control –** can also be referred to as postural control. Defined as a multisystem function that strives to keep the body upright while sitting or standing and while changing posture [13]

- **Complementary and alternative medicine** - Complementary and alternative medicine (CAM) is a broad term that describes a multitude of unrelated treatments and practices but are globally connected with a holistic approach to health and wellness [14]

- **Depressive moods** - Feelings of prolonged sadness and/or a loss of interest in activities once enjoyed; feeling “blue” [15]

- **Dynamic systems theory** – The theory states that human movement is propagated through the self-organization of ever-changing complex interactions amongst different systems in the body, environment/context and task; and is formulated to achieve a movement or behavioural goal [16]

- **Freezing of Gait** - a transient halt in walking ability described as the sensation of your feet being ‘glued to the floor’ resulting in the inability to complete effective stepping [17]

- **Gait -** refers to the act and manner of walking or running

- **Gait asymmetry -** in the lower extremities is defined as the bilateral coordination of the timing of swing durations during gait, i.e. the swing times of one leg compared to the swing time of the contra-lateral leg [18]

- **Gait variability** refers to the variability seen in spatiotemporal gait parameters and is presented as the coefficient of variation of a specific parameter [19]

- **Mobility** - Defined as the ability to move about in an environment, where the outcome is determined by the dynamic interplay between capabilities and the demands of the environment [20]

- **Mood –** temporary state of mind or feeling, often used as an umbrella term for general anxiety, apathy, depressive moods [21]

- **Neurogenic tremors -** the central nervous system's innate way of discharging excessive tension through the rapid muscle contraction and relaxation of the tremors to calm the body down from an over excited adrenal state [22]

- **Non-linear** - a non-linear system is a system in which the change of the output is not proportional to the change of the input

- **OFF phase** - Refers to period when medication is wearing off and motor fluctuations become more apparent [23]

- **ON phase** - Refers to period when medication is controlling motor symptoms, or when their symptoms are most under control, in individuals with Parkinson's disease [23]

- **Perceived Stress** - The degree to which situations in one's life are appraised as stressful. The perception of stress involves an evaluation of events as threatening, and a lack of confidence in one's ability to cope [24]

- **Postural instability -** Refers to alterations in postural control strategies during standing tasks when responding to perturbations or when performing voluntary movements and leads to impaired balance [25]

- **Quality of life -** Multidisciplinary concept that reflects the perception of position in life, is influenced by cultural and value systems and specifically relates to standards, expectations, concerns and goals by combining physical, psychological and social aspects with personal experiences and opinions about well-being and satisfaction with health [26]

- **Shuffling gait -** A walking pattern where the feet hardly leave the ground and is often combined with short steps [27]

- **Somatization -** Individual tendency to experience and communicate somatic symptoms in response to psychological distress and to seek medical help for it [28]

- **Somatic Symptoms** - Physical, bodily complaints such as pain, numbness, dizziness, etc. caused by psychological stress or worry [29]

- **Stooped posture -** An abnormal forward flexed trunk during normal stance [30]

- **Stress** - Described as a physiological change in the body chemicals [31]

- **Trauma** - A shocking or stressful experience that occurs in a state of helplessness" [32]

OVERVIEW

This dissertation is divided into six distinct chapters. The first chapter provides a general introduction and a brief overview of the research topic. The relevant literature pertaining to the researcher topic is reviewed and discussed in more detail in the second chapter. This chapter contains three sections namely Parkinson's disease (including prevalence, aetiology, pathophysiology, motor and non-motor symptoms); exercise as a treatment for Parkinson's disease, with special focus on complementary and alternative medicine therapies utilizing vibrational or tremoring modalities; and lastly therapeutic neurogenic tremors are discussed. This last section details aspects of Trauma and tension releasing exercises (which is the therapy in questions for this research) and how it relates to stress, and possible theories of this tremoring mechanism, ending the chapter with a review of the current research available on Trauma and tension releasing exercises. Chapter three outlines the motivation and rationale for the investigation, followed by the main research question, hypothesis, aims, objectives, limitations and assumptions. Thereafter the fourth chapter describes the methodology of the study, expanding on the study design, recruitment, intervention and outcome measures. Chapter five details the results of the study, including the consort flow-diagram of participant inclusion, baseline characteristics of the participants, tabulated results and figures. In the following chapter, the results are discussed and explanations are theorized, in addition, the limitations and recommendations are highlighted and a conclusion brings Chapter six to a close. This dissertation follows the Vancouver referencing format style, with a reference list at the end of the dissertation. Addendums are provided at the end of the dissertation to give clarity or additional details regarding the study and includes the Turnitin report (Addendum P), ethical approval letter, informed consent forms, tests, questionnaires, summary intervention programme and other information pertinent to the study.

CHAPTER 1 - INTRODUCTION

Stress has become a worldwide challenge resulting in a quarter to a third of the European population suffering from mental health disorders [33], such as anxiety, depression, attention deficiency, bi-polar and other mood-related disorders. In addition, daily stress might accelerate or contribute to the increase prevalence in diseases or conditions such as strokes, obesity, and high blood pressure [34,35]. Stress has been linked to other health problems, including pain, gastrointestinal complaints, etc. [36,37]. Serious stress-related disorders, such as posttraumatic stress disorder (PTSD), chronically present with overlapping symptoms of depressive moods, anxiety and somatisation [9,38]. Moreover, chronic stress and trauma have been postulated to influence auto-immune diseases (including diabetes, rheumatoid arthritis and multiple sclerosis) [39] and neurological disorders, such as Alzheimer's, Dementia and Parkinson's disease (PD) [40]. In light of this, it is vital to find more effective ways to relieve and manage stress to promote overall health and improve quality of life (QoL).

Stress management might be of particular importance for individuals with Parkinson's disease (IwPD), who are possibly more vulnerable to the effects of stress [41]. Parkinson's disease is defined as a chronic, progressive neurological disorder and is the second most common neurodegenerative disorder after Alzheimer's disease [1,42–44]. The main pathophysiology is a reduced production of the neurotransmitter, dopamine, in the substantia nigra, which results in associated dysfunction of the basal ganglia. However, the cause of PD remains unknown [41]. Some researchers hypothesize that chronic stress or trauma might increase the risk of developing PD [45–50]. The risk of developing PD, for instance, have been found to be four times higher in individuals who have been diagnosed with PTSD [46]. According to Hemmerle et al. (2012), IwPD might be at risk of experiencing more chronic stress due to the disease itself and/or might not be able to cope with stress effectively [49]. Furthermore, the symptoms experienced by IwPD are influenced by daily stress, and it is interesting to observe how many general stress symptoms overlap with symptoms of PD [40,51–54], most probably adding to the decrease in QoL. The reasons why they might be more vulnerable to stress symptoms, is that stress places greater demand on the neurotransmitters, endocrinology and skeletal muscles as well as further inhibits systems IwPD already struggle with, such as sleep cycles, digestion, reproduction, mental health and immune system [55].

Parkinson's disease is marked by a wide range of motor and non-motor symptoms that influences IwPD's independence and QoL. The main motor symptoms include rigidity, slowness of movement, postural instability, gait dysfunctions, and resting tremors [2]. While the non-motor symptoms include depressive moods, sleep disorders, apathy, anxiety, cognitive decline, autonomic dysfunction, pain and fatigue [56]. These symptoms are usually managed by medications to address the dysfunctional dopaminergic and non-dopaminergic pathways involved in PD [57,58]. However, medications often do not address all the motor and non-motor symptoms, nor do some symptoms respond well to medication, most notable is postural instability [59]. Moreover, long-term use of medication can worsen symptoms or result in additional movements disorders, such as dyskinesia [2,59]. Several motor and non-motor symptoms are exaggerated by stress [3,60,61], resulting in greater severity and frequency of freezing of gait, cognitive impairment, anxiety and pain. The dysfunctional balance and impaired ambulation resulting from postural instability have been linked to the risk of falling [13] and is also affected by perceived stress and anxiety. In recent studies, the link between anxiety and postural instability have been highlighted in IwPD [62,63]. Non-pharmacological interventions, such as exercise, have been used to successfully address motor or non-motor symptoms

of PD [64]. However, an intervention that can address motor and non-motor simultaneously, as well as incorporate stress management, could be a cost-effective, highly beneficial treatment for IwPD.

Trauma and Tension Releasing Exercises (TRE) is a new body-based stress-relief therapy that has attracted some interest in the past decade as a treatment modality for stress and related disorders. This therapy was designed to evoke neurogenic tremors; believed to be a genetically-encoded mechanism in all animals as part of the stress response [65]. Trauma and Tension Releasing Exercises are a series of simple exercises that stretch and fatigue specific muscle patterns throughout the body evoking neurogenic tremors in a controlled and sustained manner [66]. Neurogenic tremors are hypothesised to be an innate adaptive mechanism by which the human organism can restore homeostasis, possibly through calming down a hyper-aroused nervous sytem [66]. Researchers in stress and trauma and its role in neurogenic tremors note that these tremors are spontaneous and theorized to be part of the recovery process after a stressful event; thereby returning the body to full functional mobility [8,66]. The notion that tremors can be therapeutic is not new; with “shake it off” often referring to rid or free oneself from something that one finds aggravating, upsetting, or annoying. Furthermore, this body tremor has been part of various cultures as a healing ritual all over the world for centuries [67,68].

Research into the potential beneficial properties of tremoring or vibrational therapies for IwPD have also been postulated as early as 1892. Where a researcher [69] noticed improvements in the symptoms of IwPD after a train ride and attributed this to the vibrations. Whole body vibrational (WBV) therapy, where individuals receive a vibrational stimulus from an oscillating machine, have been researched extensively in the general population, elderly and even PD [70,71]. However, research into IwPD offers mixed results with inconclusive evidence that WBV might promote postural control or mobility [71–73]. Recently, new therapies have focussed on inducing a tremoring response in the body. It is suggested that these self-initiated neurogenic tremors can be activated therapeutically to discharge an incomplete stress response or possibly enables the body and nervous system to re-organize itself into more coherent states [74]. These therapeutic tremors are spontaneous, chaotic and non-linear and can be activated voluntarily through different therapies, often demanding a low physical and cognitive load. Therapies that utilize this tremoring mechanism include Somatic Experiencing (to some extent), Neurophysics therapy, and TRE. Often these tremors are called by different names, but for the purpose of this study, any natural chaotic tremoring induced through therapy modalities will be referred to as therapeutic neurogenic tremors (TNT). Research into self-induced TNT on IwPD could be of value since it is a more individualistic approach than WBV, and the TNT may help the body improve symptoms through reducing perceived stress and anxiety, releasing chronic muscle tension and possibly through somatosensory stimulation of the body [8,65,71,74]. The above mentioned benefits might improve postural instability and resultant gait disturbances either through the lessening the impact of motor symptoms or through impacting on non-motor symptoms, thereby utilizing the mind-body connection within the human organism.

The therapeutic value of neurogenic tremors is an emerging concept, in its research infancy, with very little research conducted internationally or in South Africa. The utilization of TNT as an intervention have shown to have promising results in performance, pain, stress, sleep, health complaints, depression, anxiety and QoL in a variety of populations presenting with high distress or physical impairments [6,22,66,74–76]. Very few studies have investigated TRE specifically, and none to date has explored its effect on Parkinsonian symptoms or any motor symptoms. There are currently

six experimental studies on the effects of TRE [4–6,77–79]. The studies were performed on a large variety of populations either suffering from stress-related problems and health complaints, including non-professional caregivers of orphans, teachers at high-risk secondary schools, psychotherapists, adolescents with mental health concerns and their parents, and lastly individuals suffering from restless legs syndrome. The current available research on TRE is inadequate, with small sample sizes, no controls groups and limited quantitative data. Furthermore, anecdotal evidence suggests that TRE might be able to help IwPD manage stress symptoms better and improve their QoL via a reduction in non-motor symptoms, such as anxiety, depression, pain, autonomic dysfunction, etc., as well as possibly improving postural instability.

Therefore, the current exploratory study set out to investigate the effect of exercises with TNT on selective motor and non-motor symptoms of IwPD. The use of TRE as a treatment for IwPD to reduce their perceived stress and thereby improving their motor and non-motor symptoms is a worthwhile exploration. To date, no other studies have investigated the effects of TNT on the symptoms of IwPD and additionally no research to date have explored the effects of TNT with relaxation-based exercises on postural instability and gait disturbances in general. This exploratory study do not have a singular primary outcome due to the heterogeneity of PD symptoms and the individualized effects of stress and/or relaxation, and thus the study set out to investigate global scores, and specific symptoms where possible, to establish a general idea of the effectiveness of this novel intervention. It is vital to find an effective therapy to aid IwPD to reduce the impact of motor and non-motor symptoms, and manage stress, to enhance their QoL, and thereby lessen the burden on their caregivers and possibly the greater community. Should relaxation-based exercises with TNT prove to be beneficial, it could inform healthcare practitioners of a more holistic and comprehensive rehabilitation programme for IwPD.

CHAPTER 2 - LITERATURE REVIEW

In this chapter, three main concepts will be discussed across three sections. Firstly Parkinson's disease will be briefly discussed, followed by exercise interventions for Parkinson's disease, specifically focussed on complementary and alternative therapies utilizing therapeutic neurogenic tremors (TNT). Lastly TNT will be discussed in further detail as it relates to stress and trauma, and the therapy of this research study will be elaborated on in the light of this.

2.1 PARKINSON'S DISEASE

In 1817, James Parkinson first described a neurological disorder as the "shaking palsy" or in Latin, *Paralysis Agitans* [80]. Later, Jean-Martin Charcot recommended that the disorder is referred to as Parkinson's disease (PD) [81]. Today, PD is defined as a chronic, progressive neurological disorder marked by several cardinal signs including resting tremor, rigidity, bradykinesia (i.e. slowness of movement), and impaired postural control [1]. The main pathophysiology is a reduction in dopamine production in the substantia nigra, which results in associated dysfunction of the basal ganglia; however, the cause of PD remains unknown [43]. A wide variety of motor and non-motor signs and symptoms manifests in individuals with PD (IwPD) [2] which reduces independence and quality of life (QoL). The main risk factor for PD is increasing age [43]. It influences about 1%-2% of the population aged over 65 years [42] and this prevalence increases to 4% in individuals aged over 80 years [82]. No cure has yet been found [81] and the management plan currently being prescribed to IwPD is a combination of pharmacological treatments (for instance dopaminergic medications) and non-pharmacological interventions, such as physical exercise, nutrition, speech therapy, to name a few [83].

In this section of the chapter, the prevalence, possible aetiology and known pathophysiology of PD will be discussed. The motor and non-motor symptoms that occur in PD will be highlighted in part 2.1.4 as well as appropriate outcome measures for specific symptoms relevant to this study.

2.1.1 PREVALENCE

Parkinson's disease is the second most common neurodegenerative disorder with unknown aetiology after Alzheimer's disease, [42,43]. It is estimated that there are currently between 7 to 16.1 million individuals living with PD worldwide [84,85]. The World Health Organization (2006) reported an annual PD incidence of 4.5-19 cases per 100 000 individuals [85]. Men generally have a 1.5 times higher incidence rate than women [86,87]. Generally, women with PD reach the Hoehn & Yahr (H&Y) stage III (refers to IwPD demonstrating mild to moderate bilateral disease with impaired balance but still independent) sooner and experience motor fluctuations earlier than men [42]. However the reason for these observed differences between the sexes are not fully known or understood yet.

There is sufficient evidence that shows age is the strongest risk factor for PD [88]. According to Lees and colleagues (2009) [81], the age of sixty is given as the median onset age and the mean duration from initial diagnosis to eventual mortality is 15 years. Interestingly disease onset before the age of 60 years shows no difference between sexes. The PD incidence starts to increase sharply after 60 years of

age [89]. Dorsey et al. (2007) [90] predicts that by 2030 the worldwide PD population would double due to an increase in life expectancy; together with early detection and rate of diagnosis also becoming more accurate [91]. However, researchers have found that PD incidence peaks in the age-range from 70– 79 years and then decline in very old patients [86]. This phenomenon might be explained by the difficulty in distinguishing between typical ageing-related signs and PD-related signs [86].

Europe and North America have a higher reported prevalence of PD (>200 per 100 000 people) compared to Asia (up to 32 per 100 000 people) and Africa (up to 20 per 100 000 people) [87]. There is inadequate epidemiological data available regarding PD in Africa and Sub-Saharan Africa (SSA) [92,93]. According to Blanckenberg et al. (2013) [92] PD prevalence in SSA may fluctuate between 7 and 20 per 100 000 people, however, studies may underreport the incidence of PD as they do not include those who do not have access to medical facilities or those who sought medical treatment [93]. Sub-Sahara African countries have a multitude of factors that hamper, and often take priority above, the diagnoses and management of neurological conditions. Factors include unaffordable medications; a shortage of health workers, neurologists and resources; and international aid is often more focussed on infectious diseases and malnutrition than on neurological disorders [89,92]. These factors may partially contribute to the decreased prevalence in SSA compared to developed countries as life expectancy can sometimes be as low as 46.5 years due to the collective factors in these countries; which is substantially lower than the general age of PD diagnosis [87]. On the other hand, some SSA, such as Tanzania, mostly consist of rural areas, where there are fewer potential harmful factors (to be discussed in the aetiology section below) that may increase the risk of developing PD [88]. In 2006, Okubadejo and colleagues [93] noted that Africa and SSA countries are experiencing a demographic transition and thus many of the above-mentioned factors might be minimized. Velkoff and Kowal (2007) [94] predict that by 2050 there will be an estimated 139 million people in SSA countries older than 60 years. As a result, diseases predominantly affecting older individuals, such as PD, are expected to become more common in SSA countries like South Africa [90,93]. Unfortunately, there are no epidemiological data available for South Africa to date.

2.1.2 AETIOLOGY

The aetiology of PD is largely unknown and possible causes are complex [2]. Factors most likely involved in PD pathogenesis include ageing, environmental factors, oxidative stress, mitochondrial dysfunction, inflammation, genetic factors and other pathological mechanisms [2,43,95]. Several genetic and environmental factors have been identified as risk factors for the development of PD [44], and recently researchers have hypothesized that chronic stress or trauma might trigger, contribute or accelerate PD [46–48,50,96]. In the following section, these possible causes will be briefly discussed with a specific focus on trauma/stress as this pertains to the motivation for researching neurogenic tremor exercises for IwPD.

The identification of several genes related to the development of PD has provided clues about the molecular mechanisms involved in its pathogenesis. Faulty mechanisms expressed by genes may include defective handling of proteins, mitochondrial dysfunction, oxidative stress, and inflammation [97], which can also be aggregated by acute and chronic stress. Genetic variants are considered to be the most likely aetiological factor for PD incidence in patients under 40 years of age [87]. Specific genes possibly responsible for PD have been identified, although those genes are not found in all IwPD and similarly not all individuals with the specific genes have developed PD. Investigations into why some individuals' PD-related genes "turn on" or why others' genes undergo mutations leading to PD are still underway [97].

Epigenetics (the study of how the environment effect and changes genetics) might provide possible explanations [98].

The environment we are exposed to as children, working adults and elderly individuals might have a significant effect on how our bodies deteriorate, adapt and compensate. Certain occupational and environmental factors add additional risk to the incidence of PD [2]. Several studies showed that people with agricultural occupations, such as farmers in rural areas, have higher incidence rates of PD, which could be associated with their increased exposure to herbicides/pesticides relative to the general population [43]. Other studies reported the higher incidence rates of PD in urban than in rural areas, suggesting the possible links of PD with higher levels of pollutants/oxidative stress in cities or construction site chemicals [88]. Some researchers suggest that the environment parents (particularly mothers) are exposed to could impact the development of children possibly pre-disposing them to certain illnesses [98]. Driederich (2012) [98] argues that PD might be caused by damage to the archaic neural networks, which might occur due to a detrimental environment (either a physically toxic environment or a psychosocial traumatic event).

Chronic stress or trauma, whether physical or psychological, has a considerable burden on the human body (as will be explained in section 3 in this chapter). The idea that neurological diseases can be triggered by a single traumatic event or chronic stress is not new; in 1974 research have linked increased stress to the development of illness and diseases [99]. A multitude of diseases have been linked to trauma or chronic distress, such as diabetes type 1; rheumatoid arthritis, fibromyalgia, chronic fatigue, inflammatory bowel disease such as Crohn's and Ulcerative Colitis, and multiple sclerosis [39]. The majority of diseases mentioned are autoimmune diseases where they have found strong correlations between increased stress and the resultant disease [39], and some might even argue that PD is a form of autoimmune disease [100] although more conclusive research is needed. In a recent study by Chan (2017) [46] they theorized that individuals who have been diagnosed with post-traumatic stress disorder (PTSD) could have a higher risk of developing PD, and their results concluded that PTSD individuals had a four times higher risk of developing PD than their age-matched controls. The reasons supporting stress as a trigger for PD are varied, complex and sometimes speculative, however, it offers a new approach to the treatment of PD symptoms. Part of the reasoning for this study is that if IwPD are more vulnerable to chronic or perceived stress. Not only do several stress symptoms overlap with PD symptoms, but there is also evidence linking increases stress and anxiety to declines in postural control [61–63]. Thus finding interventions to improve stress management might be of great value to the PD community.

2.1.3 PATHOPHYSIOLOGY

The motor, as well as certain non-motor dysfunctions, are due to a variety of cortical and sub-cortical miscommunications in IwPD. The basal ganglia operate as a "control master" for movement planning, control, execution and automation [101]; and helps regulate emotions, motivation and executive functions [102,103]. In PD, dopamine production in the basal ganglia becomes dysfunctional, resulting in decreased efficiency with which neural messages are conducted [104]. In this section the basic pathology of PD will be briefly discussed, especially looking at the importance and function of the basal ganglia and dopamine.

The basal ganglia designate the areas of the basal forebrain and midbrain known to be involved in the control of movement (Figure 2.1). The basal ganglia comprise of several subcortical areas, which

mainly included (but are not limited to) the striatum (caudate, putamen & nucleus accumbens), globus pallidus, subthalamic nucleus (STN), substania nigra pars compacta (SNc), and ventral tegmental area (VTA) [105]. The basal ganglia are closely related to the thalamus and the limbic system in the midbrain and connect the cerebellum and cortex [102,106]. Specialized neurons in the SNc, and to a lesser extent the VTA, produce an important neurotransmitter, dopamine, which is critical for the communication, synchronization and modulation of circuits and loops between and within brain structures [107]. With PD, more than 50% of dopamine production is already lost by the time of initial diagnosis [108]. This phase of early neurodegeneration is often called the preclinical, prodromal or premotor phase of PD. This prodromal phase is characterized by the occurrence of non-motor and/or slight motor features [108] (which often overlap with general stress symptoms) and is also a testimony to how the body is capable of adapting before motor behaviour is impacted.

Basic motor behaviour can either occur due to activation of central pattern generators in the brainstem and spinal cord, or it can be produced by neural pathways to produce selective and voluntary movements. Dopamine and the associated basal ganglia parts play a crucial part in many pathways, most importantly the motor and limbic loop. In the motor loop (Figure 2.2A), healthy individuals' movements are propagated by sensory input to the cerebral cortex, and via the basal ganglia and two different antagonistic dopamine pathways, movements are coordinated [101,102]. Dopamine has a simultaneous excitatory and inhibitory effect on the thalamus that relays signals to the motor cortex via direct and indirect pathways. The resultant motor output of this "go-no-go" or "prepare-and-select" [109] system is maintained muscle tone, proprioception, appropriate scaling and control of muscle movements [105]. In PD, the degenerated SNc cannot produce sufficient dopamine causing the pathways to become dysfunctional (Figure 2.2B) - the excitatory (direct) pathway become much less active and the inhibitory (indirect) pathway is favoured [105,109]. This disproportionate "go-no-go" or "prepare-and-select" system in PD leads to, amongst other things, inappropriate muscle tone, reduced proprioception, and difficulty initiating movements with appropriate timing and amplitude [110]. This intermittent or insufficient availability of dopamine can explain cardinal motor symptoms such as rigidity and bradykinesia.

Motor programmes are not lost in PD, but rather are difficult to access and execute. This is supported by the phenomenon called kinesia paradoxical, where an IwPD can sometimes move quickly and efficiently when startled or the situation necessitates it for survival [110]. This suggests that IwPD have intact motor programmes but have difficulties accessing them without an external cue such as a loud noise, music or visual feedback guiding them [111]. External cues might bypass the defective basal ganglia by stimulating the brainstem or amygdala in the limbic system, both of which are connected to fear or reaction upon danger [103]. This also shows a link between the movement quality of IwPD and the influence of their emotional state.

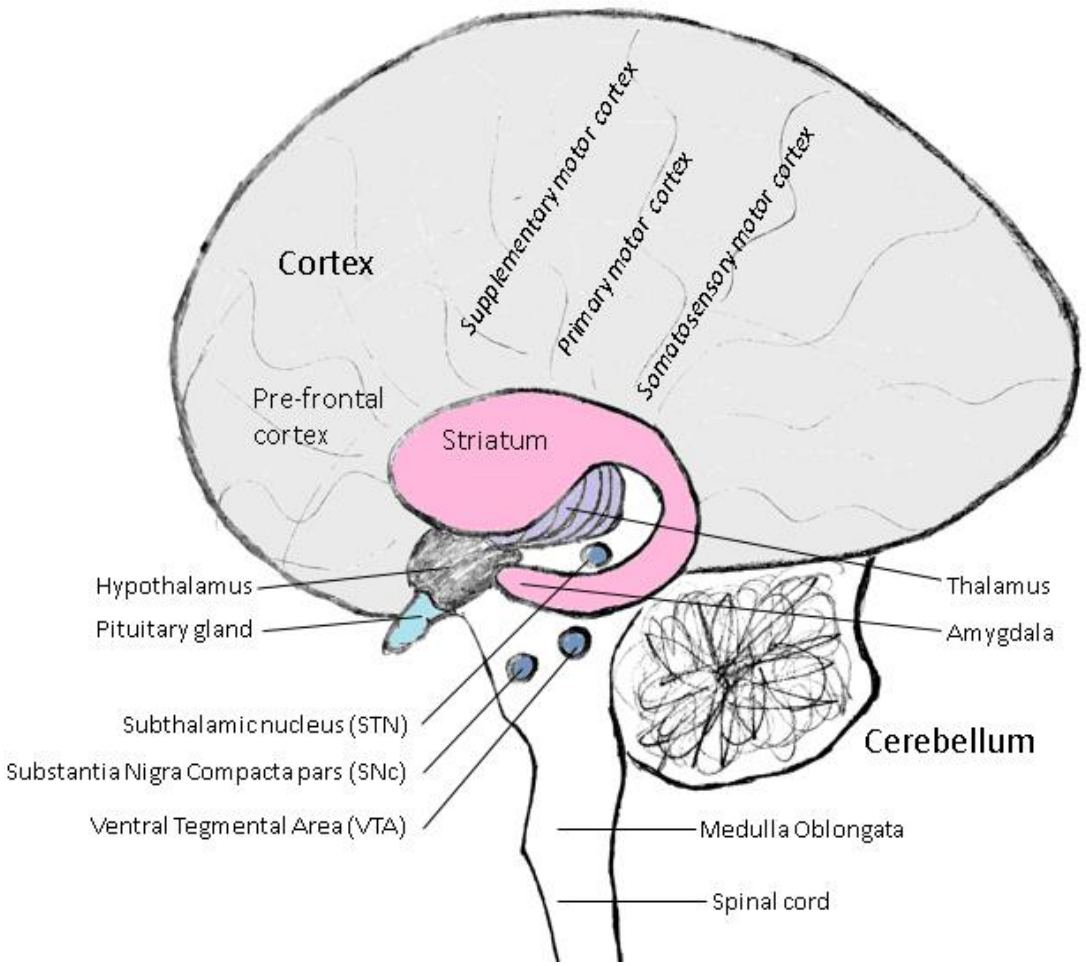


Figure 2.1: *Representation of the brain important to understand PD pathology*
(Source: Personal collection of EM Atterbury©)

Dopamine is required for other pathways to run smoothly as well. The VTA (located in the basal ganglia) also produces dopamine and projects to the forebrain and limbic regions, where it is more involved in executive function, reward-seeking behaviour, emotion regulation and expression [102,112]. Dopamine reduction is also involved in the expression of various non-motor symptoms, such as depressive moods, pain, anxiety, sleep disturbances, and early cognitive decline [113]. The limbic loop of the basal ganglia is rich in dopaminergic nerve endings and passes from the inferior pre-frontal cortex, through the anterior striatum and returns to the prefrontal cortex via the thalamus (Figure 2.1; pathways not indicated). This loop is likely to be involved in giving motor expression to emotions, such as through smiling or gesturing or through the adoption of aggressive or submissive postures [101,105]. A decline in dopamine production in this loop may account for the mask-like face and absence of spontaneous gesturing that are characteristic of PD. Interestingly Balaban and colleagues (2001 & 2013) postulates that anxiety and postural control shares a neural pathway, namely the Parabrachial nucleus network, which might provide a mechanistic link to the phenomenon observed where more anxious individuals display less postural control [114,115]. Dopamine and the thalamus is closely intertwined in the Parabrachial nucleus network which might also give insight into the comorbidity of postural instability and anxiety found in IwPD.

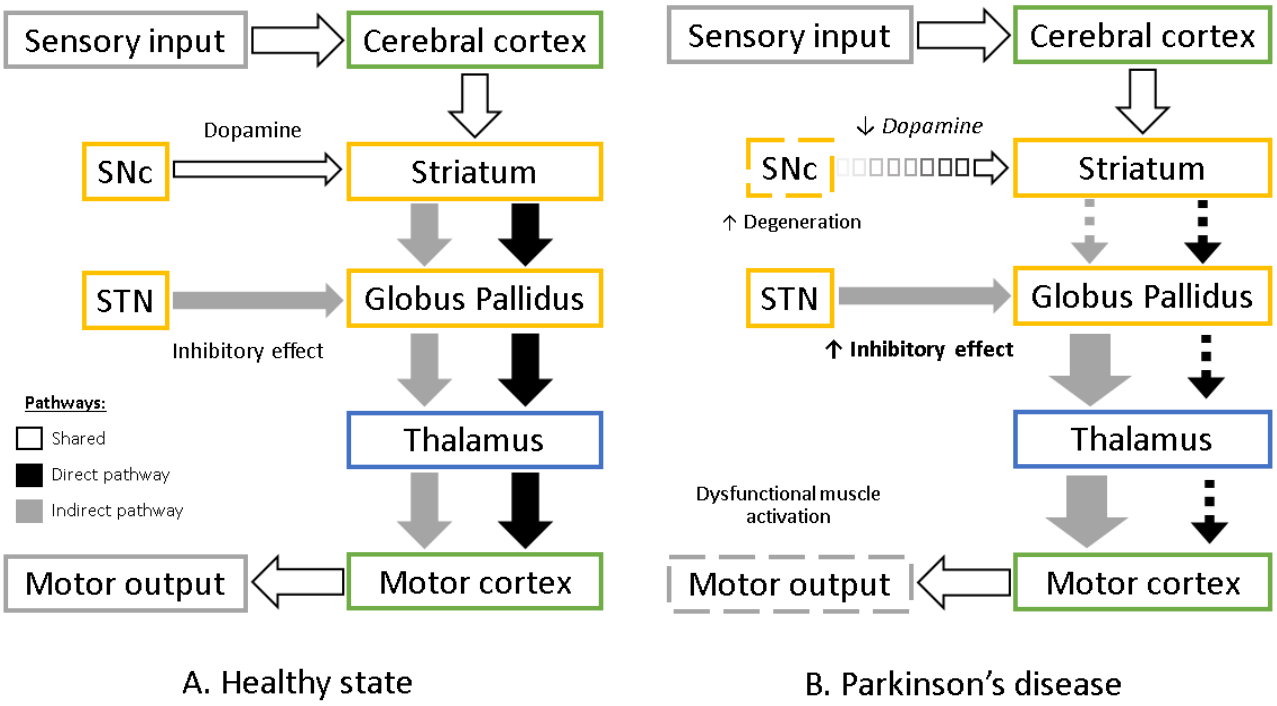


Figure 2.2: *Motor loop of the basal ganglia of individuals in a healthy state compared to individuals with Parkinson's disease.*

A. Sensory input activates the cerebral cortex, which sends a signal to the striatum. Dopamine is released from the SNc to the striatum and two pathways are activated via different dopamine receptors: 1) direct pathway from striatum send signal to globus pallidus which excites the thalamus, resulting in an excitatory signal to the motor cortex; and 2) indirect pathway from the striatum sends a signal to the globus pallidus, which then receives signals with inhibitory effects from the STN. This results in the thalamus being inhibited, and the signal to the motor cortex is also an inhibitory one. **B.** In PD, the SNc become degenerated and dopamine cannot effectively activate the two pathways; activation of the direct pathway become very reduced whereas the indirect pathway stimulates the STN more resulting in more inhibitory signals sent to the motor cortex via the thalamus. Grey boxes: input and output of motor programme; Green boxes: cortex; Yellow boxes: part of basal ganglia; Blue box: Thalamus. **SNc**: substania nigra pars compacta; **STN**: subthalamic nucleus

(Source: Personal collection of EM Atterbury©; adapted from Mtui, 2015)

Other pathophysiology and theories around PD have also been reported such as non-dopaminergic pathways, alpha-synuclein, Lewy bodies and physiological stress. Non-dopaminergic pathways involving other neurotransmitters, like epinephrine, norepinephrine and serotonin, have been found to be dysfunctional in PD and have been linked to symptoms such as depression, autonomic dysfunction, sleeping difficulties and sensory impairments [116,117]. Alpha-synuclein has been of special interest in research. Alpha-synuclein is a protein throughout the whole body, but predominantly found in the brain and is thought to aid in communication between synaptic and presynaptic terminals and play a role in the release of dopamine [118]. When a mutation of this protein occurs, it forms pathological clusters known as Lewy bodies. Lewy bodies have been strongly correlated to many neurodegeneration

diseases such as PD, dementia with Lewy bodies, and multiple systems atrophy [119]; the exact mechanism is not yet understood. A study by Braak (2006) [120] found that the neuropathology of PD changes as the disease progresses. They hypothesised that the disease initially affects the olfactory structures and other structures located in the brainstem, then progresses to affect the substantia nigra in the basal ganglia, and in the final stages it affects parts of the cortex [120–122]. Braak's (2006) hypothesis states that sporadic PD is caused by a pathogen that enters the body via the nasal cavity, and subsequently is swallowed and reaches the gut, initiating in the nose and the digestive tract. A staging system describing the spread of Lewy pathology from the peripheral to the central nervous system was also postulated by the same research group [121]. Lewy bodies become widely distributed throughout the whole body [104,119], including in the brain, spinal cord and visceral autonomic nervous system, and this widespread distribution can offer some explanation for the variety of motor and non-motor symptoms of PD, and the neurophysiological differences in disease stages [121].

Chronic physiological and psychological stress has a cascading effect in the body and may become detrimental when not controlled or managed. Part of this cascading effect involves increased secretion of nerve growth factor which has been linked to programmed neuron cell death (apoptosis) [123]. Furthermore, an increased nerve growth factor results in more sympathetic neurite growth which results in increased secretion of norepinephrine [124]. In animal studies, they have found that rats exposed to chronic stress have a decrease in dopamine neurons in the SNc and VTA [96,125]. In addition, an increased activation of the midbrain microglia during and after chronic stress results in the degeneration of dopamine neurons. Another possible reason is that chronic stress and trauma result in a heightened and exaggerated response of the hypothalamus-pituitary-adrenal (HPA) axis [51,126]. Hannibal (2014) [51] states that this leads to altered immune response and brain function, which also activates the midbrain microglia adding to dopamine cell death. Perhaps exposure to chronic stress (exacerbated by environmental factors) might trigger genes to mutate or become dysfunctional resulting in neurodegeneration [47,48,98], which leads to a wide variety of motor and non-motor symptoms.

2.1.4 SYMPTOMS

Since a variety of brain structures and function are affected by PD, it is easy to see why PD individuals have a wide variety of symptoms. Parkinson's disease is primarily diagnosed based on the manifestations of motor symptoms [2]. Non-motor symptoms manifest before motor symptoms; in recent studies they have found that individuals could start presenting with non-motor symptoms up to 20 years before being diagnosed [43,108].

Parkinson's disease is typically treated with pharmacological interventions. The main aim for the drug therapies is to minimize symptoms by trying to correct or prevent neurochemical imbalances. This can be done by supplying Levodopa which can be metabolized in the brain to produce and increase the dopamine available to the basal ganglia [127]. However, medications often do not address all the motor and non-motor symptoms. Moreover, drug therapies are a double-edged sword as stated and explained in a study by Curtze and colleagues (2015) [127]. Most PD medications have side effects, both central and peripheral, such as gastrointestinal distress, confusion and insomnia, to name a few [59]. For some IwPD they do not have distinct ON or OFF periods (periods when medications are effects and periods when medication have worn off), while many others experience quite severe symptoms during OFF periods. Long-term use of medication and disease progression can result in reduced responsiveness to medication

[127], and furthermore, can even cause movements disorders, such as dyskinesia, or dystonia as well as fluctuations of motor disability [2,59]. Levodopa medication use also does not address the other pathways involved in PD. Therefore, treatment and management of all PD symptoms are notoriously complex and difficult. Non-pharmacological treatments, like exercise, have shown to be beneficial (to be discussed in section 2). The section to follow, we'll investigate the motor and non-motor symptoms most applicable to IwPD and relevant to this study.

2.1.4.1 **Motor symptoms**

The four cardinal symptoms of PD are tremor, rigidity, bradykinesia and postural instability, which often results in gait disturbances. The first three cardinal symptoms can be somewhat controlled by medications, whereas postural instability often does not respond to medication or may even worsen with medication use [59,127]. Postural instability plays a critical role in balance and furthermore in mobility. Thus, postural instability and resulting gait disturbances directly affect IwPD independence and QoL [128]. Additional gait disturbances such as freezing of gait (FoG) further contributes to the decline in independence, and some researchers ever argue that FoG can be viewed as a separate symptom [17]. Table 2.1 summarises the most important motor symptoms [2,13,17,18,54,110,129–134]. Postural instability, and how it relates to balance and gait, is discussed below as it has special interest for this study.

Table 2:1: *Summary of Parkinson's disease motor symptoms*

Symptom	Definition & description
Tremor at rest	- Unintentional, oscillating rhythmical muscle movement involving one or more parts of the body, often unilaterally. - Often resolves with action or during sleep - Primarily distal, involving hands ("pill-rolling"); may also occur in feet, legs, lips, jaw, chin or tongue. - *Reported prevalence:* 60 - 90% - *Possible pathophysiology*: Degeneration of dopaminergic neurons of midbrain neurons

Bradykinesia	- General slowness & decreased amplitude of movements
	- Insufficient force production during the initiation of movement results in underestimating targets or under-scaling the muscle force needed to perform an action
	- Clinical manifestations are diverse & complex; can include difficulties with:
	  ○ **Gait**: shuffling, festination & reduced arm swing
	  ○ **Speech:** monotonic & soft dysarthria
	  ○ **Spontaneous movements:** gesturing, loss of facial expression (hypomimia), dysphagia (difficulty swallowing) & sialorrhoea (excessive production of saliva)
	- *Reported prevalence*: 80% to 90%
	- *Possible pathophysiology*: Disruption in normal motor cortex activity mediated by reduced dopaminergic function in basal ganglia

Rigidity	- Increased resistance in the muscles, proximally at neck, shoulder & hips, & distally at wrist & ankles - Present throughout the passive range of movement of a limb (flexion, extension or rotation about a joint) - Often accompanied by the ''cogwheel'' phenomenon & pain - *Reported prevalence*: 80% to 90% - *Possible pathophysiology*: Altered connectivity in widely distributed networks between cortical & subcortical - **Postural abnormalities** are common in IwPD & relate to rigidity: o Most prevalent postural abnormality is the "Stooped" posture, characterized by narrow stance with rounding of shoulders, flexed neck and truck, with increased flexion in hips, knees and elbows, reflecting an increased flexor tone o Other abnormalities or deformities might occur, including antecollis/dropped head (extreme neck flexion), camptocormia (forward trunk flexion), Pisa syndrome/scoliosis (lateral trunk flexion or rotation), striatal hands & striatal toes o Postural abnormalities might be an attempt to maintain balance, since posture & balance are closely linked o *Reported prevalence*: ~ 33%; often underreported & misdiagnosed o *Possible pathophysiology*: Complex combination of on-going Parkinsonian symptoms (rigidity & slowness), dystonia, musculoskeletal changes, loss of postural reflexes & influence of dopaminergic medications
Postural Instability	- Inability to keep oneself upright resulting in decreased postural control & a tendency to fall. - Predisposes IwPD to falls & injuries, & the resultant loss of mobility becomes an important factor QoL - Postural instability, or balance impairment, is not frequent in early stages of PD (first 5 years). - *Reported prevalence*: 50% within 5 years of diagnosis - *Possible pathophysiology*: Loss of postural reflexes attributed to dysfunctional visual, vestibular, & proprioceptive systems, incorrect neuromuscular response, & increased background muscle tone
Freezing of Gait	- Transient & sudden halt in walking ability described as the sensation of your feet being 'glued to the floor' - Five subtypes of freezing: start hesitation, turn hesitation, hesitation in tight quarters, destination hesitation & open space hesitation. - Risk factors for the development of freezing include the presence of rigidity, bradykinesia, postural instability & longer disease duration; more frequently in men than in women - *Reported prevalence*: 47 – 60% - *Possible pathophysiology*: Clinical expression of a dysfunction of the cortico-subcortical interplay & deficits in motor planning

QoL: Quality of life; IwPD: Individuals with Parkinson's disease; PD: Parkinson's disease

2.1.4.1.1 Postural instability

Postural instability in PD is of special interest because it often does not respond well to medication, but has a big impact on independence, activities of daily living (ADL) and QoL [13]. Postural instability and balance dysfunction in PD go hand-in-hand. Balance is defined as the ability to control your centre of mass (CoM) over your base of support (BoS). The ability to maintain balance and orientation is crucial to

mobility and independence [135]. Balance is therefore vital to ADL since you require balance to sit on a chair, when standing still, when walking and when performing dynamic activities.

Balance can be divided into static and dynamic balance. Static balance, or balance during quiet stance, is defined as the ability to maintain the position of the CoM in unsupported stance when the BoS does not change [136]. Dynamic balance is defined as the ability to exert on-going control of CoM when the BoS is changing [136], for example when walking, turning or performing postural transitions like standing up from a seated position. In order to perform any movement, the body must have postural control or stability – defined as a multisystem function that strives to aligns the body with respects to gravity, the support of the surface, and the visual environment and stabilizes the CoM of the body relative to its BoS during daily activities [132]. Postural instability occurs when an individual demonstrates an abnormal dynamic postural control [13].

There are several balance domains that can affect postural control. These domains include anticipatory postural adjustments, reactive postural responses, sensory orientation and stability in gait [135]. Anticipatory postural adjustments refer to the ability to shift the COM in anticipation of distinct voluntary movements, like stepping [136]. Reactive postural responses are defined as the ability to recover stability after an external perturbation by bringing the CoM within the BoS, through corrective movement strategy [136]. Sensory orientation is the integration of sensory information from proprioceptive, vestibular, and visual systems [13] to aid postural orientation and balance maintenance [135]. Stability in gait consider both the relative position and the velocity of the body's CoM over its BoS during straight line walking, avoiding obstacles, standing up from a chair and turning [132].

Increased postural instability, associated with poor balance and gait disturbance, is considered the most incapacitating sign and symptom as it can directly threaten independent-living. Due to impaired proprioception, PD individuals might experience an altered sense of verticality, meaning they have an inaccurate representation of gravitational alignment [132]. This affects the position of their CoM over their BoS, making them more vulnerable to falls. In fact, stage III on the H&Y severity rating scale, as mentioned before is delineated by postural instability, and is considered a critical stage for prognostic importance in that it may influence clinician-based interventions [128]. Postural instability, and the associated impairment in balance, have been linked to increased risk of falls and identified as one of the most debilitating symptoms of PD [137,138] which gradually increases with PD progression [139]. Recurrent falls are also common in people with PD [138]. This is further increased by the characteristic "stooped" posture observed, decreased joint range of motion, narrow foot stance and axial rigidity [139]. Schoneburg and colleagues (2014) [132] eloquently explain why walking is a challenge to balance, and how this leads to festination in PD. They state that during walking the person's CoM constantly shifts forward outside the anterior limits of stability and from side to side to take the weight of alternating legs. To counteract these shifts the person needs axial control of their lateral and forward stability as well as appropriate foot placement. In other words, the person places their foot in front of their CoM to prevent themselves from falling forward. However, if the first step is too small, which often occurs in PD, the individuals will have to take a subsequent step to try to regain balance, resulting is festinating gait [132].

Several other factors also influence the occurrence of postural instability in IwPD. These include other parkinsonian symptoms, orthostatic hypotension, medication state, age-related sensory changes and emotional state [13]. Perception has also been found to play a role in postural control, provide a clear

link between the mind and the body. For example, fear of falling, confidence about balance capabilities, confidence in ability to cope with a situation or anxiety have shown to have an influence on balance performance [62,63,115,140–142]. The fear of falling and a decrease in balance confidence can further impair balance control in IwPD [138,143,144]. Balance confidence, of all individuals, are affected by the extent to which individuals can return their CoM over their BoS when leaning toward their limits of stability [132]. With PD individuals these perceived limits of stability decrease, especially in the forward direction, and the speed of movements within these limits are reduced, possibly due to fear of falling [145]. This fear of falling is a natural protective mechanism and increases caution during the performance in all other ADL and hazardous activity. However, it can be maladaptive and subsequently compels individuals to restrict their mobility, independence and social participation, leading to further deconditioning, functional decline, and poorer QoL [84,146]. Increase in anxiety has been shown to affect balance control of IwPD [62,63] and thus a vicious cycle exists between postural instability, fear of falling with decreased balance confidence and associated anxiety. It stands to argue that to treat this postural instability it will be of value to focus on balance and thus increase IwPD confidence in their abilities, however, perhaps improving anxiety might break the cycle of fear of falling and reduced mobility. Perhaps an intervention that can address both balance deficits and anxiety would be ideal to improve postural instability.

2.1.4.2 **Non-motor symptoms**

Non-motor symptoms (NMS) are a major part of PD and have only recently received much attention as a potential bio-marker for early PD diagnosis as well as for the impact it has on the QoL of IwPD [108]. James Parkinson himself did not consider PD to be a motor disorder alone and in 1817, he referred to sleep disturbances, gastrointestinal dysfunction, bladder dysfunction, and even fatigue (extreme exhaustion) in his ‘Essay on the Shaking Palsy’ [42]. It is now widely accepted that PD is characterized not only by its motor aspects, but also by numerous NMS that encompass neuropsychiatric changes, sensory abnormalities, autonomic dysfunction, and fatigue/sleep disturbances, [147].

Non-motor symptoms often remain undiagnosed as IwPD do not know these symptoms form part of their condition, or they might be too embarrassed to share some details with their primary caregiver. The variety of and variation in NMS make them difficult to diagnose and treat. Some NMS respond to dopaminergic and non-dopaminergic medications, while others do not and as with most pharmacological interventions, medications often have quite noticeable side-effects [148]. Non-motor symptoms occur across all stages of PD and do increase with decrease progression, and some symptoms like REM behaviour disorder (RBD) and olfactory deficit precede the onset of motor symptoms by a number of years [108]. Research studies have found time and again than NMS impact QoL to a much greater extent than motor symptoms [149,150]. Recently new NMS questionnaire and scale have been developed and validated to help IwPD communicate their NMS better whilst also enhancing the possible treatment from health-care providers [151]. A summary of NMS experienced by IwPD are presented in Table 2.2 [2,12,58,108,113,116,131,147,151–156].

Table 2:2: *Summary of Non-motor Parkinson's symptoms*

Symptom	Definition & description
Neuropsychiatric behavioural changes	
Anxiety	- Umbrella term used to describe feelings of nervousness, fear, apprehension, & worrying - PD anxiety most often takes the form of generalized anxiety disorder, panic disorder, or social phobias - Commonly but not always accompanied by depressive moods in PD - Observed more in women, patients with disease onset at a young age & patients with advanced disease - May be prodromal symptoms; occur before diagnosis - *Reported prevalence*: 25 – 60% - *Possible pathophysiology*: Increases with motor fluctuation (associated with low dopamine levels)
Depressive moods	- Feelings of prolonged sadness and/or a loss of interest in activities once enjoyed; feeling "blue" - Clinical depression is serious medical illness with feelings of severe despondency & dejection - PD-related depression may occur at any time & is generally milder; i.e. depressive moods - Complex phenomenon may be a consequence of PD pathology, a reaction to the PD−associated disability, a separate phenomenon, or a combination of all three - Antidepressant medications can be effective in treating parkinsonian depressive moods however some do not respond well to the medication - Correlated with disease duration, severity & fluctuations - May be an early prodromal sign of PD - *Reported prevalence*: 35 – 58% - *Possible pathophysiology*: Related to reduced dopamine transporter availability in the striatum & limbic brain regions and changes in noradrenergic & serotonergic systems - **Apathy** often occurs with depressive moods. (Approximately 54%) o The indifference felt with apathy can affect QoL of IwPD & caregivers
Cognitive decline	- Defined as a slight but noticeable and measurable decline in cognitive abilities, including memory and thinking skills - Risk of dementia is increased ~6 fold in IwPD - Current treatment of cognitive impairment in PD is suboptimal. - *Reported prevalence*: 25 - 80% show cognitive decline - *Possible pathophysiology*: Plaques of Lewy bodies slow down synaptic communication
Abnormalities of sensation	
Olfactory deficits	- Decreased sense of smell (hyposmia) or loss of sense of smell (anosmia) - Usually occurs bilaterally & may predate the diagnosis of PD by several years - Olfactory deficits do not improve with dopaminergic medications - *Reported prevalence*: > 90 % - *Possible pathophysiology*: May be linked to cholinergic denervation or changes in central olfactory processing in midbrain

Visual disturbances	- Visual disturbances are often overlooked in PD - May include: decreased blinking, dry eyes syndrome, blurred vision, apraxia of eyelid opening, reduced visual acuity, decreased contrast sensitivity, impaired colour discrimination, convergence insufficiency, double vision (diplopia) - Incidence of visual hallucinations & diplopia increases with disease progression - Dopaminergic therapies do not improve visual disturbances & might even worsen some symptoms like hallucination - *Reported prevalence*: 22 – 78% - *Possible pathophysiology*: Thinning of the retinal nerve fibre layer & the inner retinal fovea are characteristic of PD, even when vision is normal. Hallucinations have been linked to Lewy bodies in occipital lobe & in retinal neurons
Pain & Somatosensory disturbances	- Pain in PD remain underreported & difficult to treat as pain can be due to various neural pathways & causes - Classifications for pain in PD: musculoskeletal pain (stiffness, dystonia-related & muscle cramps), radicular or neuropathic pain, central parkinsonian pain, Off-state fluctuation-related pain, nocturnal orofacial pain (temporomandibular joint disorders tightness), & peripheral pain (including burning sensations or akathisia discomfort for example restless legs syndrome) - Dopaminergic medication can raise pain thresholds, however is often not effective - *Reported prevalence*: 30–85% - *Possible pathophysiology*: Both dopaminergic & non- dopaminergic pain pathways are involved. Dysfunctional basal ganglia integrate sensory information & changes pain thresholds of IwPD
Autonomic dysfunction	
Gastrointestinal dysfunction	- Dysfunction occurs along the entire length of the gastrointestinal tract in PD - Gastrointestinal dysfunction in PD may include gastroparesis, small intestinal bacterial overgrowth, & constipation - Gastroparesis symptoms include early satiety, reduced appetite, bloating, abdominal distension, nausea, vomiting, & progressive weight loss. - Impaired gastric emptying may impair effective levodopa absorption, which occurs in small intestines - Might occur before diagnosis: Changes in vagus nerve (important for autonomic bowel control) occur early in PD development - *Possible pathophysiology*: Multiple systems involved → enteric nervous system & multiple neurotransmitters (acetylcholine, dopamine, serotonin, & noradrenaline) control bowel. Linked to increase Lewy bodies, alpha-synuclein aggregation in intestines
Cardiovascular features	- This dysfunction includes hypotension (orthostatic, nocturia & labile), higher resting rate, increase heart rate variability, & labile hypertension. - Orthostatic (postural) hypotension is the most widely recognized aspect of cardiovascular dysfunction in PD. - Symptoms might include light-headedness, blurred vision, foggy thinking or pain in lower back upon - OFF periods or motor fluctuation affect cardiovascular response standing, “coat hanger” headache, or just lethargy. - *Reported prevalence*: 60 - 80% - *Possible pathophysiology*: Dysfunction of sympathetic & parasympathetic autonomic fibres that control heart rate & contractility

Urinary dysfunction	- Urinary dysfunction in PD includes nocturia, & increased frequency & urgency of urination - Detrusor (muscle that controls bladder function) might be over- or underactive - Although urinary symptoms become more frequent in later PD stages, urinary dysfunction may develop early in the course of PD - Medications are available to treat overactive bladders. However, treatment of underactive bladder is limited - *Reported prevalence*: 25 - 50% - *Possible pathophysiology*: Urination regulation is facilitated by the hypothalamus, cerebellum, frontal cortex, & basal. Bladder dysfunction is related to loss of the inhibitory role of the basal ganglia.
Sexual dysfunction	- Sexual dysfunction is very common in both men & women with PD, but studies addressing this aspect are sparse. - Men typically experience erectile dysfunction, difficulty reaching orgasm, or premature ejaculation - Women often experience low sexual desire, difficulty with arousal, & difficulty with orgasm. - *Possible pathophysiology*: Testosterone deficiency has been identified in some men with PD experiencing sexual dysfunction.
Thermo-regulation	- Episodic drenching sweats occur with many IwPD - May be influenced by motor fluctuations, but sweating episodes can appear independent of motor status - Episodes can be embarrassing & inconvenient; significantly impact QoL - Little is known of the prevalence, mechanism or effective treatment of drenching sweats in PD
Fatigue & Sleep Disturbances	
Fatigue	- Defined as the feeling of tiredness or exhaustion, sometimes to the extent of not being able to do daily tasks - Very disabling symptoms of PD with the great impact on QoL - Little is known of the prevalence, mechanism or effective treatment of fatigue in PD

Sleep disorders	- Disturbances in sleep & wakefulness affect most IwPD
	- Prevalence increases with the duration of disease
	- Sleep disorders include daytime “sleep attacks”, insomnia, sleep fragmentation & frequent prolonged awakening, REM sleep behaviour disorder, periodic limb movements, & restless leg syndrome
	- *Reported prevalence*: 90%
	- *Possible pathophysiology*: Exacerbated by OFF periods, impaired “turnability” due to night-time rigidity & bradykinesia, dyskinesia and/or dystonia related to drug action, nightmares, hallucinations & nocturia
	- **REM sleep behaviour disorders (RBD)** is particularly of interest. 25-50% of IwPD have RBD
	  o Characterized by continued ability to move during REM sleep
	  o RBD may be present years before diagnoses

QoL: Quality of life; IwPD: Individuals with Parkinson’s disease; PD: Parkinson’s disease; REM: Rapid eye movement; RBD: REM-sleep behaviour disorder

2.2 EXERCISE THERAPIES AS TREATMENT

Exercise is a planned, structured physical activity which aims to improve one or more aspects of physical fitness and overall health [157]. The belief that exercise could be considered medicine, or part of medicine, is not new. This strong emphasis on health, rather than disease, dates to prominent ancient physicians such as Hippocrates [158]. Physical movement has always been a vital part of maintaining good health, and with the modern, more sedentary lifestyle exercise have been promoted. Exercise has been widely researched as a potential long-term, inexpensive way to modify physiological aspects of health to promote longevity. Further investigation also shows the positive effects exercise has on psychology, QoL, and possible beneficial effect on the brain [157,159]. This is a crucial part for the elderly who are at a higher risk of developing a disease and losing independence [160], and even more so for individuals with a neurodegenerative disease such as PD. In this section an overview for exercise modalities for PD will be covered, followed by Complementary and Alternative Medicine (CAM) therapies for PD and lastly, specific therapies utilizing vibrations and tremors will be reviewed.

2.2.1 OVERVIEW

Physical activity levels decline with advancing age and these reductions contribute to functional decline [161]. It has been shown that people with PD are more inactive than their healthy peers [162]. For IwPD, exercise could have potential neuroprotective mechanisms [85], in that regular exercise could stimulate brain function and also extend the period before medication starts to have a negative influence on motor tasks [163,164]. In PD, it has been found that exercise stimulates dopamine synthesis in remaining dopaminergic cells and thus reducing motor and non-motor symptoms by prolonging the progression of the disease [85]. Evidence suggests that exercise might promote brain repair and neuroplasticity in people with PD [165]. This reorganization can lead to behavioural recovery, affecting movement as well. Previous research indicates that functional improvements from exercise interventions stem from the activation of the motor cortex that overrides atypical basal ganglia function demonstrated in PD [101]. Thus, exercise in general can facilitate neuronal transmission and motor coordination that are essential for improved balance and overall function [164], and improvement in non-motor symptoms can greatly contribute to improved QoL [166] .

Various exercise modalities have been researched and many offer benefits towards motor and/or non-motor symptoms; although they are often short-lived [167]. Traditional exercise interventions focus on aerobic, strength or balance training, and are effective at improving physical functioning and health-related QoL, leg strength, balance, and gait [164,167,168]. Some of the popular exercise interventions include cycling, boxing, resistance training, aqua aerobics, treadmill gait training, cognitive movement strategies, sensory attention focused exercise and Lee Silverman Voice Therapy [169–172].

Complementary and alternative medicine (CAM) therapies have also gained popularity as they often offer improvements in motor and non-motor symptoms, and they are interesting and enjoyable (two aspects of great importance for neuroplasticity [165]). In the general public, CAM therapies are often used to improve stress management, promote relaxation and well-being, and even resolve psychological issues that modern-day pharmacology or mainstream psychology fail to improve. Given the impact of chronic stress and trauma could have on IwPD, alternative therapies might be a possible solution.

2.2.2 COMPLIMENTARY & ALTERNATIVE MEDICINE THERAPIES

Complementary and alternative medicine (CAM) is a broad term that describes a multitude of unrelated treatments and practices but is globally connected with a holistic approach to health and wellness. It can also be defined [173] as a

> *broad domain of healing resources that encompasses all health systems, modalities, and practices and their accompanying theories and beliefs, other than those intrinsic to the politically dominant health system of a particular society or culture in a given historical period*. (Institute of Medicine statement; 2005).

These CAM therapies can be classified into five categories (Table 2.3), however, many therapies can be classified into more than one category, for example, yoga and reflexology.

Table 2.3: *Classification of CAM therapies*

Category	Definition	Therapies
Mind-Body Medicine	Variety of techniques to enhance the mind's capacity to affect bodily function and symptoms; focussed on mindfulness	Tai Chi, biofeedback, hypnosis, meditation, play therapy, relaxation techniques, aromatherapy, dance therapy, drama therapy, music/sound therapy, sensory therapies, yoga
Natural Product Based Therapies	Uses substances found in nature to promote health	Diet therapies, hydrotherapy, chelation therapy, Dietary supplements, oxygen or ozone therapy, Plant extracts.
Manipulative and Body-Based Practices	Based on manipulation and/or movement of parts of the body	Alexander technique, chiropractic manipulation, Craniosacral massage, Feldenkrais method, massage, reflexology
Energy Medicine	Uses and/or manipulate electromagnetic fields that surround and penetrate the human body	Acupuncture therapy, acupressure, Qigong, distant healing, Reiki, Therapeutic touch, Ultrasound therapy, magnetic therapy.
Whole Medical Systems	Complete systems of theories and beliefs, and practice outside the conventional allopathic model.	Ayurveda medicine, Traditional Chinese, medicine. Homoeopathy, Naturopathy, Japanese traditional medicine

Not all possible therapies listed

Often individuals who do not find relief from the conventional mainstream allopathic model of medicine, turn to CAM therapies to help them resolve or manage their symptoms. The same is true for IwPD; it is estimated that about 40 – 76% of IwPD make use of some form of CAM [174,175]. Various CAM therapies for PD have been researched including yoga, Tai Chi, Qigong, various dance therapies, music therapy, drum circles, expressive writing, active theatre therapy, mindfulness therapy, acupuncture, massage, reflexology, Alexander technique, Feldenkrais method, stochastic resonance therapy, progressive relaxation, and whole-body vibration therapy [174,176]. These CAM therapies have shown to be beneficial for improving QoL, depressive moods, sleep and cognitions of IwPD. Specifically, we see that acupuncture and Tai Chi may help depressive moods, QoL and sleep, while dance and yoga have some evidence in improving cognition, apathy, and fatigue [174]. In a review by Kwok (2016) [176] they found that mind-body exercise therapies (specially looking at yoga, Tai Chi and dance therapies) demonstrated beneficial effects on motor symptoms, postural instability, and functional mobility among individuals with mild to moderate PD. Kwok and colleagues (2017) [177] further went on to propose an investigation of the effects of yoga versus stretching versus resistance training on IwPD in a randomized control study. They hypothesize that yoga might help IwPD through utilizing the theory of self-transcendence; by exploring their boundaries, redefining their experience of illness and self-transcending to attain a sense of wellbeing despite their vulnerable PD trajectory [177]. Evidence suggests that CAM therapies promoting relaxation can improve motor and non-motor PD symptoms. Mind-body therapies might be particularly well suited to address both motor and non-motor symptoms of IwPD, since there is sufficient evidence about how the mind and body affect and interact with each other as an expression of holistic health [176]. For this study therapies that involve therapeutic tremors or whole body vibrations are of special interest; and the background of such therapies this will be discussed and elaborated on in the following subsections.

2.2.3 THERAPEUTIC TREMOR AND VIBRATIONAL THERAPIES

One simply needs to look at the English language to realize that tremors are part of the human condition, with common phrases such as "shaking in my boots", "shook with anger", "my whole body was shaking with laughter". Furthermore, the notion that tremors (or vibrations) can be therapeutic is not new; with “shake it off” often referring to rid or free oneself from something that one finds aggravating, upsetting, or annoying. Therapeutic effects of vibrations might date back as far as 1892 [69]. Often vibrational therapies are induced by a therapist possibly through a machine while self-initiated tremors might be induced in the body through selective exercises, breathing techniques or possibly even sound. There are various theories behind why vibration and tremors might be beneficial for the human body including the biomechanical and sensorimotor stimulation [71,74], and allowing the body to reorganise itself through neural noise [74] and lastly that it may be the body’s innate mechanism to a stress response [8,66,178]. Firstly, vibration and tremor therapies that have been used with PD will be discussed, followed by tremor therapies that have not been researched but might have a promising effect on PD, which is the premise of this study.

2.2.3.1 **Therapeutic tremor and vibrational therapies for PD**

It seems counterintuitive to use vibrational or tremor therapy for individuals who already experience a tremor, however, the two types of tremors (i.e. PD tremors and therapeutic tremors) might originate from different parts of the brain. Two therapies have been used with PD include whole-body vibration (WBV) therapy (or stochastic resonance therapy) and Alexander technique.

Whole body vibration is a therapy were individuals stand, sit or lie down on a vibrating machine [71]. Charcot (1892) identified the beneficial effects of an external vibrational-type stimulus when he noticed in 1892 that IwPD were displaying fewer symptoms when they were travelling on a train [69]. Research results of WBV are varied as studies use different frequencies, intensities and amplitudes, and have found that some individuals respond, while others do not [72,179]. Some researchers applied set intensities for the intervention while other use random WBV, also term stochastic resonance [179]. Overall, studies on PD demonstrated mixed results in favour of WBV for improving postural instability, balance or mobility [71,72,179]. Most studies seem to suggest a favourable benefit following WBV for mobility and balance, but not when compared to other active intervention or placebo groups. The underlying mechanisms of why WBV might be beneficial remain elusive but suggest that neuromuscular activation and metabolic mechanisms play a significant role in promoting proprioception and stretch reflex sensitivity in weight-bearing joints and muscles [71,179].

Alexander technique is an educational therapeutic process that was created to retrain habitual patterns of movement and posture [180]. The founder Frederick Matthias Alexander believed that poor posture and movement habits damage spatial self-awareness as well as health, and that movement and mental efficiency could support overall physical well-being [181]. This therapy starts with a hands-on component with a therapist and later becomes an instructional therapy; lessons are individual private sessions. Although Alexander Technique does not aim to induce a tremor, many practitioners and clients have anecdotally reported a tremoring sensation, especially when lying in an "active rest" or semi-supine positions. This position is used often, and the subsequent tremoring sensation is encouraged. The Alexander Technique is widely used to reduce or prevent chronic back pain and other problems such as poor muscular respiratory function, both of which frequently occur in Parkinson's disease [181]. The mindful movement approaches used in Alexander Technique have shown to be beneficial for IwPD by improving balance and mobility PD by acutely facilitating increased upright postural alignment while decreasing rigidity [180], improving self-reported disease severity and depression ($p < 0.05$) [181].

2.2.3.2 **Therapeutic tremor therapies**

Tremoring is not new to humans; we typically shake after we have been in an accident, when we are nervous or angry. These tremors are often foregone by a stressful stimulus whether it is physical, psychological, emotional or mental, and is thought to be a self-induced natural mechanism to calm the body. Tremors of shaking to calm an individual or to promote feeling better are inherently part of humans – mothers instinctually rock their babies to smooth them, whole body laughter or crying is coupled with shaking resulting in an improvement in mental and physical state. Some individuals even experience tremoring during or after orgasms. However, humans suppress the tremoring after stressful events as we have been socially conditioned that it is a sign of weakness. This tremor was named by Robert Scaer (2001) [7] as a neurogenic tremor, and he stated that the dysregulation of the autonomic nervous system (ANS) homeostasis due to trauma causes dysregulated autonomic oscillations. He observed that animals in the wild will tremor spontaneously once they are out of harm's way [7], and theorized that this tremoring mechanism is genetically encoded in all animals. Thus the tremors are neurological and genetic; therefore the term of neurogenic tremors is appropriate. It has been theorized that these chaotic dynamic mechanisms in the body might have some physiological benefits.

In recent years therapies have developed around this tremoring mechanism which is thought to be a way for the body to re-organize itself and promote healing [74] as well as an innate part of the body's

response to stress or trauma [8,65]; these tremors will be more thoroughly explained in section 2.3. The three therapies are currently known to induce this tremoring mechanism that has not yet been researched in PD, namely Somatic Experiencing (SE), Neurophysics therapy (NPT), and Trauma and Tension Releasing Exercises (TRE). All three of these therapies have been used in practice for more than 15 years each and have all reported promising results in performance, pain, stress, sleep, depression, anxiety and QoL in a variety of populations including social workers, university students, trainees of the therapies, spastic paraplegics, muscle dystrophy and individuals with restless legs syndrome and PTSD [4,6,22,75,76,182–184]. Often these tremors are called by different names, but for the purpose of this study, any natural chaotic tremoring induced through therapy modalities will be referred to as therapeutic neurogenic tremors (TNT). The first two therapies will be briefly discussed below and TRE (the intervention used for this study) and theoretical basis for TNT will be elaborated on in section 2.3.

Somatic Experiencing (SE) method is a mind-body CAM therapy aimed at healing from trauma and other stress disorders through focusing on the individual's perceived body sensations (or somatic experiences); usually in one-on-one sessions with the individual lying down [8]. It was developed by Peter Levine over 45 years ago, using his insights from his multidisciplinary studies of stress physiology, psychology, ethology, biology, neuroscience, indigenous healing practices, and medical biophysics [8,22]. Conventional therapies to treat trauma or stress often involve mainstream cognitive psychology (such as talk therapy) or pharmacological medications, both of which are a top-down approach to dealing with PTSD and other stress-related disorders. Somatic experiencing method uses bottom-up processing by directing the individual's attention to internal physical (somatic) sensations, through interoception (including breathing, heart rate, gastric discomfort, etc.), proprioception and kinesthesis (including musculoskeletal discomfort, pain, muscle tightness, etc.) or many other sensations [22,185]. Post-traumatic stress symptoms are considered an expression of stress activation and an incomplete defensive reaction to a traumatic event; and these sensations are the carriers of a traumatic memory [9,183]. According to researchers this gentle approach to charged traumatic memories through body sensations helps to avoid re-traumatization through direct and intense evocation of traumatic memories and aids the recovery of the individual by generating new associations with specific somatic experiences [22]. Part of this internal awareness of interoception, proprioception, and kinesthesis, spontaneous body movements are encouraged, and an individual will often experience TNT. Levine (2010) [185]reports that he has observed through his years of clinical experience that individuals might tremor in body parts that have sustained injuries or were utilized during a traumatic event. In a randomized control study by Brom (2017) [183] they found that SE was an effective therapy for reducing depressing and traumatic-stress symptoms in individuals diagnosed with PTSD.

Neurophysics therapy (NPT) was developed by Ken Ware, who has been using the therapy for more than 25 years [74]. This therapy operates on a completely different approach than SE (or TRE), but also utilizes TNT to achieve clinically significant and relevant improvements in individuals. Ross and Ware (2013) [74] does not describe the tremor as part of the stress response but rather explains it as the body's natural self-healing and re-organizational processes, additionally explained most clearly by the dynamic systems theory and chaos theory [74]. Through these theories, they explained how the body incorporates knowledge of our surroundings, the task at hand and personal constraints to communicate and achieve more effective movement strategies. Neurophysics therapy is performed on gym equipment with limited degrees of freedom (like a leg press, lateral pulldown, chest press or seated leg curl) with minimal resistance at ultra-slow speeds (2.5cm per second), with the correct posture while maintaining a relaxed

state of mind [74]. According to Ross and Ware (2013), the slow speed allows the nervous systems to detect and adjust any imbalances which result in chaotic non-linear random rhythmic movements (i.e. TNT). If the client experiences slight dynamical movement in limbs or torso at a point during the structured exercise, the client has to hold that position to permit the dynamic response to surface and evolve [74]. “Such mild indicators are the system's first hint that a person is beginning to remove physical-emotional restraints and unbridle their system.” [74]. Anecdotal evidence claims that NPT has helped individuals with various disease ranging from arthritis, migraines, strokes, drug addition, scoliosis, fibromyalgia and even PD [74] however, research is limited. In a few recent case report studies, benefits have been reported on increased brainwave coherency [76], improved heart rate variability [184], and increased synchronization and coupling strength of muscles [184].

The third therapy mentioned previously is TRE, short for Trauma and Tension Releasing Exercises. This therapy evokes TNT through simple exercises and is of special interest for this research study. This therapy will be elaborated on in the next section, and described in detail as well as the theories behind it, how it compared to other mind-body therapies and the current available research.

2.3 THERAPEUTIC NEUROGENIC TREMORS

The therapeutic value of neurogenic tremors is an emerging concept, in its research infancy, with very few research conducted internationally or in South Africa. This self-induced TNT are claimed to be an innate survival mechanism [178], possibly enabling the body and nervous system to re-organize itself into more coherent states [184]. Trauma and Tension Releasing Exercises (TRE) is one of these therapies mentioned previously with great potential to possibly aid not only IwPD but all individuals. Interestingly even though the research into TNT are relatively new to the modern day way of life, this "healing shiver" have been part of various cultures as a healing ritual all over the world for years [67,68]. The most prominent culture who uses tremoring and shaking is the indigenous Khoi San “Bushmen” of the Kalahari located between South Africa and Namibia who have weekly dancing rituals which brings about spontaneous vibrations throughout the whole body and emotional releases, resulting in healing of the mind, body and spirit [68]. During these trance-like dancing rituals, healers may shudder and shake chaotically while laughter and tears never far away and help tribe members in need of healing tremor as well [67]. This practice resembles TRE where the individual’s whole body can tremor during a session and depending on the specific situation emotional responses can often occur [186]. Researchers in stress and trauma and its role in neurogenic tremors note that these tremors are spontaneous and theorized to be part of the recovery process after a stressful event; thereby returning the body to full functional mobility [8,65].

In this section, TNT will be discussed in detail, especially how it is utilized in TRE. Stress and trauma will be elaborated on and how it impacts the body; the mechanism and theories behind TNT as well as how it links to a normal stress response in the body. A typical TRE session will be described and a comparison will be made with other mind-body therapies. Lastly, all current research and the theory behind TRE will be discussed.

2.3.1 BACKGROUND ON TENSION AND TRAUMA RELEASING EXERCISES

Tension and Trauma Releasing Exercises was created by Dr David Berceli more than 15 years ago. At the time he developed TRE he was providing humanitarian aid in war-torn areas of the Middle East and Africa, and was a former monk, qualified social worker, psychologist and massage therapist [182]. He spent years observing how people react to big life events, causing trauma and how they behave and react to additional or subsequent stressors. These years gave him insights into how the human organism restructured itself to survive trauma, and noticed patterns in the body’s reaction, regardless of age, sex, culture, class, language or religion. Specifically, he noticed how people always curled their bodies inward, into a fetal position, when bombs exploded, and with his knowledge of the body concluded that the flexor muscles of the body react instinctively when threats are detected. Additionally, he started to notice that children would shake or tremor and began to associate this with a possible natural phenomenon of the body to discharge tension of an event. More importantly, he noted that the adults did not shake, and when he enquired about this they responded that they would but they did not want the children to know they were scared [65,66]. Berceli returned to the USA curious about what he had observed and began to research this tremoring mechanism.

Numerous animal studies have reported on physiological tremors after life-threatening events, but not much in humans. Studies on wild animals show that when animals survive a frightening experience, either by fighting, fleeing or freezing, they calm their nervous systems by shaking [7]. This is

noticed more prominently with animals experiencing a freezing or immobility response. Spontaneous recovery of the freeze response in animals, described as “repetitive, almost seizure-like motor activity” [185], have been linked to increased resilience, while not allowing spontaneous recovery have been linked to early death [7,32,187]. Van der Kolk (1991) [32] drew similarities between how animals respond to highly stressful situations and how humans respond; noting that no animal in the wild suffers from PSTD after a traumatic event. Interestingly it has also been observed that animals in captivity (e.g. circus animals, zoos or even domestic pets) do not display this response as strongly as their wild counterparts. This being said they do not have active predators, so this response is not activated as often; however, researchers have also noted that "caged" animals often have impaired health and shorter lifespan [7,8].

Levine (1997) [8] further postulated that the lack of recovery from the freeze response in humans results in storage of the “fight or flight” energy and leads to hyperarousal of the nervous system. Dissipating the retained energy build-up will aid the body to fully recover from the event and normalize into homeostasis [7,8,32]. Levine further speculated that PTSD might be a result of an incomplete freeze response in the body, and this theory is further independently supported by Van der Kolk (1991) who also noted that PTSD individuals’’ behaviours often reflect the traumatic event, as if they want to re-enact it, possibly as a way to subconsciously allow the body to complete the freeze response [32]. Levine developed Somatic Experiencing (a therapy discussed in the previous section) to treat traumatized clients, and initially he did not understand why his clients would tremble during the session but did note that they felt remarkably better afterwards [8,185]. Around the same time, Scaer [188] was conducting research on whiplash and came to the interesting conclusion that whiplash syndrome was due to a conditioned behavioural response to the trauma of the accident, and might be more due to the memory than a physical injury seeing as derby drivers never got whiplash. Van der Kolk (1995) describes memory as a somatic experience and thus states that any distress, whether psychological, social, or physical, has a profound impact of the body [32]. This supports the notion that chronic stress or trauma can be held in the body (not just the mind) when it is not fully discharged. Scaer (2001) further defined these neurogenic tremors as a primordial somatic experience originating in the natural processes of the brain’s procedural memory system when exposed to a situation of stress [7,8,189]. They are a natural part of the genetic composition of the human organism. This genetically based discharge of the human organism has a physiological rather than a psychological origin. Neurogenic tremors are hypothesised to be an innate adaptive mechanism by which the human organism can restore homeostasis [66]. Berceli (2007) [66] suggests that neurogenic tremors can also be activated therapeutically to discharge an incomplete stress response.

Armed with this knowledge, Berceli started to look into ways to induce this tremoring mechanism. He developed TRE over a few years and the end results is a very simple exercise routine designed to stretch and fatigue specific muscles in the legs and hips resulting in a spontaneous tremor. He suspected that the psoas muscle might be the prime muscle responsible for the flexor position, and thus aimed to find ways to encourage the psoas muscle to release; thereby aiding the body to release chronically held muscle tension [65,66]. Invoking these TNT worked for individuals who had acute stress or trauma as well as individuals who had chronic stress or experience trauma many years ago.

Since then Berceli has used this therapy to treat a variety of clients and TRE is taught globally, with South Africa having quite a large number of TRE practitioners compared to other larger countries. Today

it is used as a self-help tool or can be facilitated by a practitioner, either individually or in groups, and once learned it requires no special equipment or travel to a facility [190]. Berceli has worked with the USA military as well as several areas that have experienced natural disasters; there are several videos online reporting on this (https://traumaprevention.com/video-testmonials/). In some of the research on TRE they use the term "self-induced therapeutic tremor" since neurogenic tremors might sometimes be used to describe other types of tremors; however for this study, the term therapeutic neurogenic tremors will be used. Later in this chapter, a typical TRE session will be described as well as other factors to keep in mind when participating in the therapy, however, it is first important to understand the concept of stress.

2.3.2 MECHANISM OF STRESS

Stress has become a worldwide challenge resulting in more individuals being diagnosed with anxiety, depression, attention deficiency, bi-polar and other mood-related disorders. According to the World Health Organisation [33], a quarter to a third of the European population suffers from some form of mental health disorder. In addition, stress might accelerate or contribute to the increase in diseases such as diabetes, strokes, obesity, and high blood pressure [34,35]. Stress has even been postulated to affect neurological disorders such as Alzheimer's, dementia and PD; especially adding to the prevalence of depression [40,49,96] and mobility-related concerns [191]. In this section, the mechanism of stress and the physiological impact will be briefly discussed.

2.3.2.1 **Stress vs. Trauma**

The word ‘stress’ simply refers to force or influence being exerted on an object, including everything from physics, to language, to the body and nervous system. Therefore, stress can be seen as a stimulus to a system or can be seen as the arousal level of our nervous system. In other words, we actually need stress to function optimally; i.e. there is good and bad stress. Stress and performance have a bell-curve type of relationship to one another (Figure 2.3); too little and we lack motivation and energy to perform, too much and our system become overloaded and performance declines. Therefore stress can be defined as *“a state of psychological and physiological imbalance resulting from the disparity between situational demand and the individual's ability and motivation to meet those needs.”* [31]

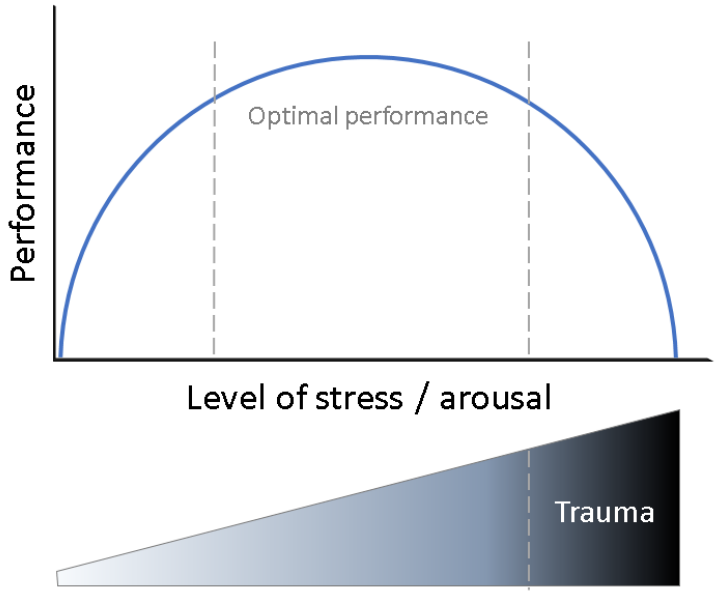


Figure 2.3: *Stress-performance curve and Stress continuum*

(Source: Personal collection of EM Atterbury ©)

Good stress is called eustress and acts as a motivator for peak performance in situations where there is an opportunity to gain something. Distress is the termed used for bad stress, although in modern living stress and distress are used interchangeably. Distress can occur when a person faces social, physical, organizational and emotional problems. Both are essential in life, as eustress is responsible for achieving your highest potential whereas distress, on the other hand, is very unpleasant, but according to Van der Kolk (2001) [9], it is a time where we as humans make social connections, deepen our appreciation for life and each other and form lifelong friendships. To live a balanced life, we aim for optimal performance and therefore it is important to know what the effects of stress are and how to manage it.

Stress exists along a continuum (Figure 2.3) of events that may be experienced as mild to the more severe and extremely traumatic, as well as being brief or continuous. Stress has a big impact on the body and results in neurological signals to be fired and chemicals to be released throughout the body. Stress can therefore also be described as a physiological change in the body chemicals [31]; whereas anxiety is the psychological sensation or association with the change in chemicals [11]. Anxiety is considered a normal response to stress, with some individuals being more sensitive to it; however, prolonged exposure to individually perceived stress may lead to adverse consequences, including the development of general anxiety [53]. Wiegner (2015) found that individuals with higher perceived stress also had a higher prevalence towards anxiety and/or depression [53]. In several studies they have found the symptoms of perceived stress, anxiety, depression and somatization (the expression of psychosomatic symptoms such as physical bodily discomfort or pain caused by disturbed psychology) to overlap [24,37,155,192,193]. Therefore it stands to reason that a measurement of two or more of these symptoms would give a valid score for the level of stress an individual is experiencing in their body.

Trauma is part of the stress continuum and can be seen as an acute bout of very high intensity stress or it can be accumulative [22,65]. In this regard stress on a person's psyche can be compared to how bone reacts to stress: repetitive stress on bone can strengthen it (Wolff's law), stress applied in an abnormal direction during overuse activities results in stress fractures, or a massive amount of stress can be applied during a single event (e.g. accident or fall) resulting in a bone fracture. Trauma is often thought of as a life-threatening physical event, such as natural disasters or acts of crime (very common in South Africa). However, with growing research into trauma a new definition of trauma has emerged: "A shocking or stressful experience that occurs in a state of helplessness" [32]. Therefore, trauma can occur in various situations. Different types of trauma have also been identified [66], namely "hard" trauma (tsunami, high jacking, sexual abuse, motor vehicle accident, contact sport, operations) and "soft" trauma (emotional abuse, loss of a loved one, bullying, job loss, break-ins, divorce, witnessing violence, diagnosis of incurable diseases). It is clear to see that helplessness, or the absence of control, defines a traumatic experience. It is important to note that trauma is a highly individualized experience and is associated with an individual's nervous system, genetics, psyche and life experiences, and not with the event [22]; since two individuals can experience the same extreme event but not both be traumatized, or traumatized to the same extent.

2.3.2.2 **Stress in the body**

The body is evolutionarily designed to adapt and survive when reacting to a stimulus of perceived danger, and it uses a multitude of bodily systems to stay alive. These systems include the central and peripheral nervous system, endocrine, immune and musculoskeletal systems [7]. The stress-related physiological response is activated and sustained by the ANS and sets off a cascade of emotional, cognitive and behavioural responses, which offsets homeostasis [7] to achieve its goal at hand, and once the perceived danger has passed the body usually restores homeostatic balance. However, sometimes this natural response is disrupted (possibly due to sustained perceived danger due to insufficient recovery) which results in an aggravated stress response when a new perceived danger is encountered. Below the stress response will be explained to illustrate how symptoms of stress manifest across the entire mind-body continuum and are underpinned by neurobiological processes that mostly remain outside of conscious awareness [182].

The brain processes hundreds of thousands of sensory signals within a second and has to sort through the signals that might be a threat to the organism. The amygdala, situated in the midbrain and part of the basal ganglia (Figure 2.1), operates as the early-warning-system or watchdog of the brain, receiving information from the environment and all the senses via the sensory cortex [194]. This process occurs within milliseconds outside of conscious thinking, and have been termed neuroception by Porges (1995) [194]. This might sometimes be referred to as the "sixth sense" as it so accurately alerts the body to danger or safety/pleasure before the conscious brain can explain why, including micro-expressions, tone of voice, pheromones and possibly even the frequencies of electromagnetic field emitted by the body [195,196]. When danger is perceived, the "watchdog" alerts the hypothalamus and the sympathetic nervous system, activating what is commonly known as the "fight or flight" response. This response range from slight to intense regardless of if the nature of the threat (physical or psychological). The body does not know the difference and therefore reacts the same. Multiple systems are activated or inhibited by this response; the effects on the ANS, brain, Hypothalamus-pituitary-adrenal (HPA) axis and psoas muscles will be briefly discussed below. Furthermore common symptoms that occur due to acute or chronic

activation of the stress response as well as showing the overlap of these symptoms with PD symptoms. Lastly the effects of stress (and subsequent anxiety) on postural control will be highlighted.

2.3.2.2.1 Autonomic nervous system

The whole nervous system is a complex network throughout the body and can be divided into different branches (Figure 2.4). The ANS primarily controls the stress response, and therefore the two branches of the ANS are of special interest, namely the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS). Usually, these two systems work in a reciprocal manner and fluctuate slightly throughout the day to maintain homeostasis [7]. When danger is perceived, big or small, the body will do whatever it takes to stay alive by triggering the SNS to prepare the body for action, which involves activating the cardiovascular system, skeletal muscles and the release of necessary hormones to provide energy while simultaneously inhibiting bodily functions not necessary for immediate survival, like digestion, reproduction, immune and secretory systems [22].

Therefore the signs of acute stress are increased heart rate and breathing, pupil dilation and perspiration and symptoms of stress are hypertension, decreased salivation, indigestion, constipation, increased blood glucose and cortisol [197]. These symptoms are commonly associated with anxiety and perceived stress as well. Chronic stress, and therefore chronic dysregulation of homeostasis, have been linked to heart disease, gastrointestinal disease, diabetes, adrenal fatigue, increase inflammation and reproductive problems [7,9,185,197] as these systems in the body are either chronically overactive or inhibited. Important to note that IwPD suffer from autonomic dysregulation [198], which includes cardiovascular problems, gastrointestinal complaints, urinary and sexual dysfunction, and autonomic dysregulation is associated with fatigue in IwPD and other conditions [198].

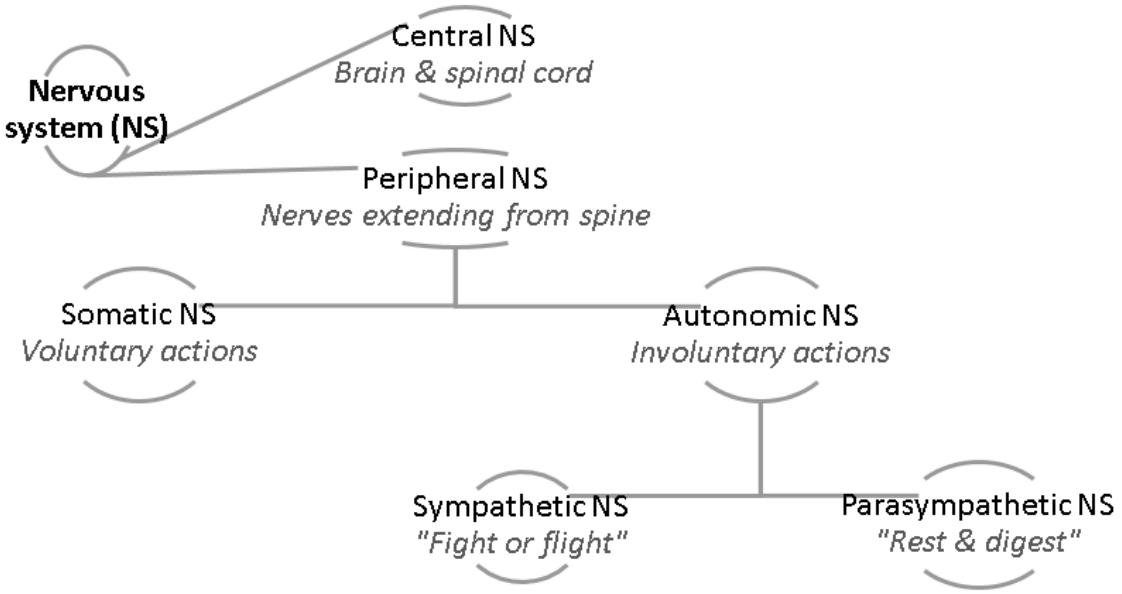


Figure 2.4: *Branches of the nervous system*

(Source: Personal collection of EM Atterbury©)

2.3.2.2.2 Brain

During a stress response, the brain function changes. Liston (2009) [199] found that prefrontal processing and attentional control decreases with stress, and postulates that chronic stress might even lead to executive dysfunction. In the 1950s Dr MacLean put forth a theory that the human brain evolved to consist of three distinct brains [200]; the reptilian brain, the mammalian or mid-brain, and the neocortex or primate brain. The reptilian brain is simply concerned with staying alive, thus responsible for basal physiological functions such as heart rate, breathing, temperature control and digestions while also being able to detect danger; think of how lizards live. The mammalian brain or mid-brain is connected with the limbic system and is concerned about emotions, nurturing of young, social engagement; think about how rats nurse and engage with rat pups. And lastly the neocortex or primate brain is concerned with all aspects of consciousness like higher thinking, learning and understanding; behaviours observed in primates but humans have the largest neocortex which is represented in our philosophy, moral reasoning, religion, belief systems, spirituality, imagination, problem-solving, innovation, language capacity, creativity and rational thinking. MacLean's triune brain concept has been challenged and critiqued (even by himself) as researchers understood more about the brain [98,200,201] however, his concept has intrigued researchers as a theory and has helped to explain certain behaviours [98,197,200]. Interestingly this triune brain concept is very comparable to Maslow's hierarchy of needs. When applying this theory to the stress response; it can be suggested that during a stress response the neocortex becomes inhibited, while the reptilian and mammalian brains are stimulated; also known as a state of hyperarousal [195]. This occurs as the body is just concerned with survival or survival of offspring, and not concerned with what is the most logical or politically-correct way to solve the problem at hand. This supports Liston's findings and can explain why stressed individuals are accident prone, more forgetful and less likely to make smart rational decisions. Interestingly the two "brains" activated during a stressful event, possibly resulting in trauma, are non-verbal and more visceral, somatic and emotional. This might give insight into why conventional "talk therapy" with psychologists do not offer much relief from symptoms associated with PTSD.

Stress signs and symptoms that are related to brain changes include decrease in executive functioning which can include difficulty concentrating and making decisions, racing thoughts, forgetfulness, and confusion [199]. Chronic stress can lead to permanent damage or changes in the brain, making it more susceptible to disease and illness [202]. Mild cognitive impairment has been linked to chronic stress, and this is also a symptoms that is often seen in IwPD [7,54,125,203,204]. Also of interest to note is that the interaction and relationship between cognition and motor performance is a well establish phenomenon [205], perhaps exhibited by IwPD more clearly as their brain chemistry is more sensitive to changes [61].

2.3.2.2.3 Hypothalamic-pituitary-adrenal axis

A multitude of hormonal changes occur during a stress response to prepare the body for action. Hyperarousal has been associated with changes in the levels of cortisol, glucocorticoids, catecholamines (norepinephrine and epinephrine), growth hormone, thyroid hormone, vasopressin, insulin, and prolactin [206]. The hypothalamic-pituitary-adrenal (HPA) axis is of particular interest because the end-result

production of cortisol has been termed the stress hormone [34]. This axis is responsible for the neuroendocrine adaptation component of the stress response and is an eloquent and dynamic intertwining of the central nervous system (hypothalamus and pituitary gland) and the endocrine system (adrenal glands). After perceiving danger via the amygdala, the hypothalamus secretes corticotropin-releasing factor which binds to a receptor in the pituitary gland, thereby activating it to secrete adrenocorticotropic hormone which binds to receptors on the adrenal cortex and stimulates adrenal release of cortisol [105]. This response to a stressor can continue for several hours, however, at a certain blood cortisol concentration sufficient protecting is apparently achieved, and then the cortisol has a negative feedback to the hypothalamus and the pituitary gland to return the system to homeostasis [105,178]. Cortisol is responsible for harnessing all systems to resist, tolerate and manage stress in the short-term by activating the energy stores throughout the body and suppressing systems not vital to survival, but Scaer (2005) points out that this comes at the cost of homeostasis. In chronic stress, the HPA axis is repeatedly stimulated and the axis becomes desensitised to the negative feedback loop [7,197]. The problem rests with the inability of an individual to switch off the HPA axis. The HPA axis remains switched on, keeping the body in a chronic state of preparedness for any potential future danger, resulting in dysregulated physical, mental and emotional states [34,51].

High cortisol levels also suppress the immune system, rendering the stressed individual susceptible to infection and physical illness, while the increased arousal and the disruption of normal hormone balance affects mental and emotional functioning [34]. The body remains in a state of physiological hyperarousal causing perceived stress and resultant anxiety to be exacerbated. Furthermore dysfunction of the HPA axis increases inflammation and pain in the body, and have been linked to an increase in depressive moods [51]. Individuals with PD experience unexplained pain and have a high prevalence for depressive moods, which might indicate a HPA axis that has become over-activated and thus desensitised, and perhaps IwPD could benefit from addressing this overactive HPA axis through effective relaxation methods [3].

2.3.2.2.4 Psoas muscles

Muscle tension increases with a stress response and Berceli (2007)[66] argues that the psoas muscles are the primary muscles to be activated when danger is perceived. The two psoas muscles (one attaching on either side of the lumbar spine) link the ribcage and trunk with the legs, passes through the pelvis, over the hip joint, and attach on the inner side of each femur [207]. This core muscle is responsible for posture, directly affects range of motion, movement and rotation of the pelvis and legs, as well as the ability to breathe as its tendons are contented to the diaphragm [207]. It is richly supplied by nerve fibres of the somatic and autonomic nervous systems, and thus responds to and is affected by both visceral (organ) and skeletal systems [208]. The psoas muscles are activated during the stress response and play a role in one's ability to cope with and adapt to stress. Scaer (2005)[178] concurs that the healthy functioning of the psoas muscle is tantamount to overall health and vitality of an individual. By its unifying function, it is implicated in the fight, flight, or freeze response. In the face of danger all internal systems (skeletal and visceral) work in unison to prepare for action. The role of the psoas is to enable locomotion (flight), offensive manoeuvres (fight) or defensive postures (freeze) by bringing the extremities together, into the foetal position, to protect all vulnerable parts (genitals, vital organs, head, eyes, ears, nose, and mouth)

(Koch 2005). This contraction is referred to as 'flexor withdrawal'. Koch (2005) further explains that under optimum functioning conditions, once the stress response concludes, the body should be able to restore homeostasis and return to a state of relaxation, with all muscles lengthening and relaxing. However, Levine (1997) [8] highlights that this is often not the case, due to a maladaptive conditioning of the stress response, either due to repeated firing with little opportunity for recovery and/or an inability to complete the process. Thus, a conditioned response is set in motion that maintains the body in a state of tension, which accumulates over time.

Chronic tension patterns are held within the body which has a cascading effect on health and wellbeing [66]. Muscles in constant hyper-activated tension not only result in physical discomfort or pain but also decrease physical functioning by increasing energy expenditure and movement limitations. Shortened psoas muscles result in exaggerated lordosis and have been linked to lower back pain [209] and sleeping difficulties [210] as well as chronic muscle tension [8,66,178,207]. Interestingly, research has found that specific muscles in the lower back (namely quadratus lumborum and psoas major) in IwPD are hypertrophic and therapies aimed at releasing muscle tension might be of benefit to investigate [211].

The symptoms of stress, chronic stress and trauma affects the whole body. As illustrated by Scaer (2014) [189] physiological or somatic symptoms include, for example, muscle tension, increased heart rate, shallow breathing, disturbed sleep patterns, and fatigue of adrenal glands and the pancreas. Emotional symptoms are expressed as anxiety, fear, dread, irritability or depression [34,197]. Cognitive symptoms include hypervigilance, problems with learning and memory, unrealistic worries, or a fear of loss of control, and finally, behavioural symptoms include escape, avoidance, aggression or freezing [8,206]. It is an interesting observation to note that several of the general stress symptoms overlap with PD symptoms [40,51–54] , as can be seen in Table 2.4.

Table 2.4: *Similarities between Parkinson's disease and general stress symptoms*

	Parkinson's disease	General stress symptoms
Motor	• Resting tremor • Bradykinesia • Rigidity • Postural instability	• Tremors, trembling of lips, hands • Stuttering or stammering; rapid or mumbled speech, dry mouth • Frequent headaches, back pain, muscle spasms & pain
Non-motor	• Neuropsychiatric behavioural changes → *Anxiety, depressive moods, apathy & cognitive impairments* • Abnormalities of sensation → *Olfactory & visual disturbances, & unexplained pain)* • Autonomic dysregulation → *Gastrointestinal, urinary & sexual dysfunction, cardiovascular features, thermoregulation)* • Fatigue & sleep disturbances	• Excess anxiety, worry, nervousness, depression, social withdrawal and isolation • Difficulty concentrating and making decisions, racing thoughts, forgetfulness, confusion • Light headedness, dizziness, palpitations, rapid pulse, sweating, heartburn, nausea, constipation, frequent urination, diminished sexual desire or performance • Constant tiredness, weakness, fatigue, insomnia, nightmares, disturbing dreams

Previously in this chapter, the effects of perception, such as fear of falling or anxiety, on postural control and balance performance was highlhlighted. In table 2.5, the main effects of stress and the resultant effect on postural control in highlighted.

Table 2.5: *Link between stress and postural control*

Effects of stress	Resultant effect of postural control
Increase in anxiety (perception/ association of stress)	Effects postural control in PD [62] Evokes balance deficits [63]
Decrease in executive functioning [199]	Decreases postural control [205] Decreases effect of Levadopa [61]
Greater cortisol and norepinephrine secretion [124,212]	Increases perception of pain, alters brain function and adds to dopamine cell death [34,51]
Greater demand on neurotransmitters, such as dopamine [55,123]	Increase apoptosis leads to less dopamine secreted → reduction in automated movements [63,123,125]

Interestingly, in a study by Keller (2012) [213], they found that an individual's perception of stress on the body (thus perceiving stress to be bad for your health) has a significant impact on how the body reacts to it and this negative perception might be linked to premature death [213]. One researcher uses the example of being in love, which elicits a stress response based on emotional vulnerability, but the individual's perception or association with this physiological stress is positive and therefore is not detrimental to health [213].

2.3.2.3 **Stress response and therapeutic neurogenic tremors**

With the body primed for action, and depending on the level of danger, there are several options to choose from- flight, fight or freeze. The first option is flight, to avoid the danger; the second option is fight, if flight is not possible and there is a chance of escaping the danger or the need to protect offspring [7]. The third option is freeze, if the danger is inescapable and too life-threatening to fight [214,215]. Humans can exhibit the freeze response by physically becoming immobile [215,216] or by dissociating [7,217]. Scaer (2001) defines dissociation as a clinical psychiatric condition associated with the fragmentation and splitting of the mind, and perception of the self and the body [7]. Clinical manifestations include altered perceptions and behaviour, numbing and avoidance. This frozen state can be seen as a pronounced instinctual extreme co-activation of the PNS, marked by bradykinesia, decreased heart rate and breathing and a release of opioids (theorized to make possible imminent death less painful) [7,22,32]. All three reactions are hypothesized to be mediated by the vagal nerve [194]. Porges (1995) [194] puts forth the polyvagal theory stating that the vagal nerve has three distinct functions: 1) to stimulate the SNS for fight or flight; 2) to stimulate instinctual extreme co-activation of the PNS via the unmyelinated dorsal vagal nerve; and lastly 3) to stimulate the PNS via the myelinated ventral vagal nerve promoting social engagement, groundedness, open-mindedness and curiosity (all the positive aspects of the human condition).

The body's aim is to be in the ventral vagal activation as much as possible, and it is theorized that neurogenic tremors are the natural genetically encoded off-switch or completion of the stress response to return to the ventral vagal state [7]. This spontaneous recovery after hyperarousal is less when the organism (human or animal) can respond by fleeing or fighting, which are not helpless states [8], whereas as the freeze response (associated with trauma and feelings of helplessness) elicits a bigger and more urgent recovery [9]. There are several theories about what triggers the body to start the tremoring process, and they are discussed below, with special focus on the Dynamic Systems Theory (DST) as it pertains to this study.

The first theory or concept to highlight is neuroception which describes how neural circuits distinguish whether situations or people are safe, dangerous, or life-threatening [194]and links to the polyvagal theory with the three outcomes mediated by the vagal nerve (Figure 2.5). The neurogenic tremors will only occur when the neural system, through neuroception, can detect it if the environment is "safe enough" and therefore deactivates the hyper-aroused nervous system. It does not have to be 100% safe as observed in animals who might tremor after the immediate threat has disappeared but before they are completely isolated [188]. It has been theorized that the neurogenic tremor has to give

an animal a physiological benefit to improve survival if it is often prioritized before moving to a “safer” area.

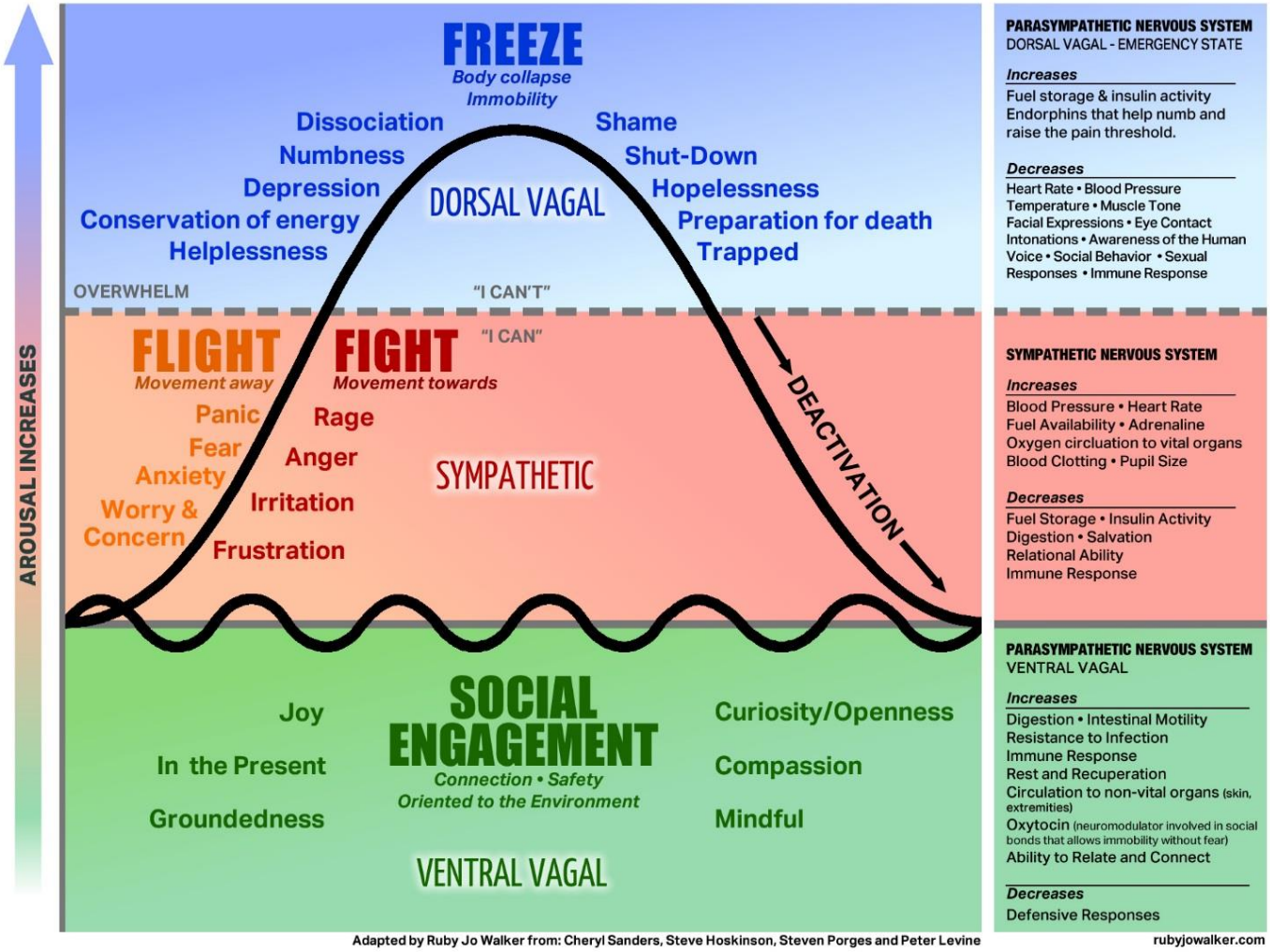


Figure 2.5: *Poly-vagal theory’s stress response (Porges 1995)*

(Source: Reused with permission from Ruby Jo Walker, 2017 rubyjowalker.com)

The neurogenic tremors might also be beneficial to the body by providing the system with mechanical somatosensory stimulation, not only re-tuning the nervous system but also releasing the psoas muscle in the process. It has been postulated that the psoas muscle has a feedback loop to the brain; thus when danger is perceived the brain activates the psoas muscles, but the tightness or tension in the psoas muscle can also send signals to the brain about safety [66,207]. If the muscle is tightened, it reinforces the signal that danger is still present; whereas if the psoas muscle is relaxed it can send a signal to the brain that all is well; the environment is safe enough. This signal possibly aids the HPA-axis to switch off [212]. Berceli noticed this and therefore thought that by inducing the tremoring mechanism it can possibly operate as a mechanical off switch to a hyper-aroused and stress system.

2.3.2.3.1 Dynamic Systems Theory

The novelty of a new therapy always makes it difficult to understand and explain the changes that the new therapy causes; however, with a well-reasoned theory explanation can be extrapolated. For this reason, the Dynamic Systems Theory (DST) have been selected as the most suited theory for this research to explain TNT.

The DST states that human movement is propagated through the self-organization of ever-changing complex interactions amongst different systems in the body, environment/context and task; and is formulated to achieve a movement or behavioural solution [16]. Based on environmental, biomechanical, and morphological/task constraints, any biological system will self-organize to find the most stable solution. These stable solutions are often referred to as attractor states [218]. Behaviourally, an attractor state refers to a preferred state which serves the body in the best way (i.e. increase postural control on an uneven surface, or walk slowly). Describing the attractors of chaotic dynamical systems is often is the focus of the theory of chaos [219]. Increased variability to the system, through addition or subtraction of constraints, will eventually drive the system to react non-linearly and find new attractor states. This is a nonlinear system because the input does not lead to a linear predictable change in output, thus small changes could have a big impact and vice versa [218,219].

The clinical value of understanding DST is important as it provides a way to explain certain non-linear results often observed in a clinical or practical setting [218]. Clinical therapies or certain healing modalities might cause certain constraints to exchange, for example, body constraints around muscle strength, fitness, balance or even psychological aspects such as perceptions, assumptions, anxiety or fears (figure 2.6). A change in any of these aspects might result in changes to the behavioural output observed [16,218,220], often in a non-linear fashion. The body is designed to make sense of chaos and to adjust to ever-changing environments, and is thus poised at the edge of chaos - not too chaotic and therefore incoherent, and not too ordered, and thus unchanging – and in modern day life we are too busy to allow the body to adapt, resulting in disease [39,202,219]. Stress can further impact on any of the three domains – i.e. the task changes, the environment becomes unpredictable or individual perception is altered. The result effect of stress entering into the dynamic system is an increase in individual constraints, such as physiological, neurological, anatomical or psychological changes as described previously in the section. The increase in individual constraints will result in a change in the selective movement solution, and the most fundamental human movement springs form postural control [16,220]. Thus it can be postulated that an increase in stress or inability to manage stress will result in an increase in individual constraints which will impact on postural control. Individuals with PD might start off with more individual constraints, thus even slight additions of stress could impact their functional movement solution to a greater extent.

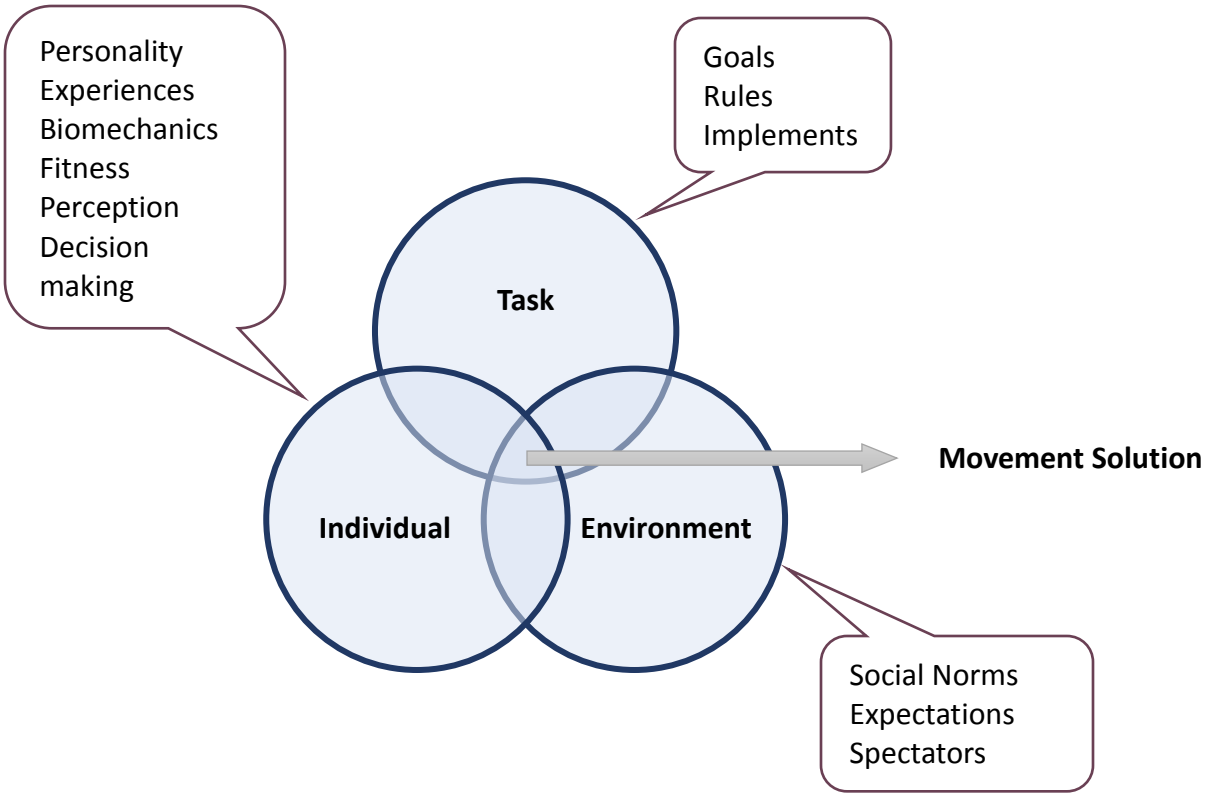


Figure 2.6: *Dynamic Systems Theory*

(Personal collection of EM Atterbury ©)

Perhaps therapies such as TRE that utilizes TNT are an exciting new way to stimulate the body to change existing attractor states, constraints and help the body self-organize into more effective behavioural or movement patterns. During a typical TRE session, great care is taken to minimize the impact of task and environmental constraints (as will be discussed in the following section) by keeping the exercises as simple as possible and curating a "safe-enough" environment. Through minimizing the impact of the constraints from these two domain, the body (or individual constraints) can spontaneously re-organize itself to find the most stable form. It is theorized that these neurogenic tremors is the physical expression of this self-organization plus the physical movements aid in achieving better results through adaptation [74]. Ross and Ware (2013) [74] used DST as well as chaos theory to explain the tremoring phenomenon as it relates to their therapy utilizing TNT, called Neurophysics therapy (NPT), as previously explained in section 2 of this chapter. Ross and Ware (2013) explained this tremoring mechanism as the body's way of re-organizing itself and promoting self-healing. This chaotic dynamic non-linear movements might be elicited by the nervous system during the end-phase of the freeze response when bradykinesia is prominent, and perhaps through the presence of the very-slow movements, heart-rate and breathing the nervous system can detect any additional abnormalities in the organism often overlooked during sympathetic responses [22,74]. Therefore the tremoring actually allows the body to re-adjust, learn and grow from the stressful experience. This is supported by research studies showing the benefits of stress [125,213,221].

2.3.3 TYPICAL TRE SESSION

Trauma and Tension Releasing Exercises are a series of simple exercises that stretch and fatigue specific muscle patterns throughout the body evoking neurogenic tremors in a controlled and sustained manner [66]. These exercises were designed to evoke neurogenic tremors as a way of releasing deep chronic tension patterns held in the body. Trauma and tension releasing exercise can be performed alone as a self-help tool or can be facilitated by a practitioner in a one-on-one basis or groups. Group sessions often bring about greater changes as individuals experience greater enjoyment and perhaps feel safer when sessions are facilitated by a practitioner. A typical session entails the exercise routine, followed by tremoring and concluded with an integration period. Facilitated sessions are top-and-tailed by a check-in and check-out period, which will be explained. Lastly a comparison will be made between TRE and other mind-body therapies.

The exercises used in the sessions do not involve the traditional aerobic components of endurance, intensity or resistance, but is made up of simple stretching and fatiguing exercises of the muscles in the legs and pelvic area (Addendum E – note that exercises have been adapted to accommodate all levels of PD; the last level of the exercises are the original TRE exercises prescribed). Exercises are done on or next to an exercise mat; and are performed at a very low intensity and without any pain. There are very little progression in the exercise routine and individuals are encouraged to perform at the level they feel comfortable for the session. The more individuals become accustom to the exercises the less effort should be used to achieve the same result. The exercises do not require a high physical and/or cognitive functioning or load, and are therefore very applicable to a variety of populations.

The exercise routine starts with a brief breathing exercise to just bringing awareness to heart rate and breathing tempo, followed by ankle stretches and calve raises to fatigue the gastrocnemius and soleus. This exercise is done slow and controlled, and is stopped when the individuals experience the muscle fatigue to be at about 7/10 on a visual analogue fatigue scale. The fourth exercise is a stretch of the posterior line of the leg, focussing on the hamstring group mainly, followed by a stretch on the adductors, hamstrings and back. The sixth exercise is designed to stretch the hip flexors, possibly the psoas as well, and including a gentle spine twist. The next exercise individuals have to perform a wall sit for at least three minutes. This can be quite a fatiguing exercise but individuals are instructed to only work on the level they feel comfortable and if they feel that the exercise becomes too fatiguing they should bring their buttock and lower back higher on the wall. The reason behind these exercises is to fatigue all the muscles in the upper thigh (mainly the quadriceps), including the fast-twitch and slow-twitch fibres of the muscles. Depending on the individual's fitness level they can modulate the level and the length of the exercise. This fatiguing results in a slight tremor, which for novices might be due to physiological exhaustion of the muscles but it allows the individuals to get a feel for the sensation of tremors. Individuals are also encouraged to "let it happen", thus overcoming the social reflex for suppressing tremors. After the wall-sit exercise, individuals can step away from the wall and hang forward from their hips; providing some relief for the fatigued muscles and stretching the hamstrings and spine. The last exercise is performed on the floor and is aimed at fatiguing the muscles in the lower back and hip region. In these positions neurogenic tremors often occur already in the form of bouncing, legs butterflying or swaying

from side to side. After this, individuals are instructed to lie comfortably with their legs in a diamond shape and by closing their legs very slowly tremors occur somewhere in the range of movement (Figure 2.7).

Figure 2.7*: Position in which tremoring mechanism is evoked after the exercises*

(Personal collection of EM Atterbury ©)

Tremors may differ between individuals in a group, between different sessions of one individual and even during a session. Tremors range from being non-visible and feeling like electricity running through a body part, to very small intense movements or large fluttering movements. With TRE the tremors usually start in the legs or lower body, and the more the individual performs the therapy the more the tremor moves to the pelvis, abdominal, chest, fingers, shoulder, head and even jaw. Sometimes tremors occur as muscle contractions of stretches and can be localised or move wave-like throughout the body. The frequency, intensity and amplitude of tremors are extremely individualized. Questions about whether the tremor is purely just due to fatigue can be answered by phenomenon experienced like the tremoring of body parts not exercised, some individuals can initiate the tremor without any exercises, and the tremor continues even when participants are cognitively distracted showing it is not a conscious movement. The tremors can be controlled and stopped by extending the legs (this acts like an “off switch”) and can easily be restarted. Participants are encouraged to stop the tremors as much as they feel necessary, perhaps when they experience any physical or emotional discomfort or overwhelment; this is referred to as self-regulation. After the desired period of tremoring is over (usually between 10 – 20 minutes), individuals are asked to stop the tremors using the self-regulation "off switch" and are then encouraged to lie in a comfortable position for a few minutes. This is called the integration period and it gives the individuals and their body time to integrate the new state they might find themselves in.

The environment the therapy takes place in is important. Ideally, it should be a place where there are minimal distractions since the main aim of TRE is to induce the body to relax. Unknown or sudden

sounds, smells or movements might trigger a stress response and will not help individuals become calm. Therefore, their body will not allow the tremor to happen, as it is in essence a vulnerable act and thus great care must be taken to create a “safe enough” environment. Practitioners of TRE undergo an 8-month training process to obtain a level 2 certification (level 1 certifies practitioners to work with individuals, level 2 certifies practitioners to work with groups, and level 3 certifies the practitioner to train of new practitioners) with the main objective to achieve a very calm and grounded state. This calm nervous system of the practitioner provides an anchor for the stressed and erratic nervous system of the client and thereby helping the client achieve a calmer state. This concept is supported by Porges' polyvagal theory and neuroception, through which our nervous systems pick up on perceived danger. Sessions in a group, facilitated by TRE practitioners, are often a very powerful experience for individuals who seek out help with their trauma or related problems. However, some clients prefer one-on-one session and other might prefer performing the session alone at home, which TRE is perfectly suited to as well.

Before and after the exercises and TNT, check-in and check-out sessions are done; whether in a group, one-on-one with a therapist, or done alone. Check-ins facilitate the practitioner to check in with each group member about any discomforts or express any concerns. It also serves as an opportunity for group members to check in with their own body and notice their physical, emotional and mental state. Check-outs are necessary as the practitioners need to establish the current state of the individual since some might experience some dissociation during the session and practitioners then need to help the individuals become more grounded. It also offers the chance to talk about how the individuals feel after the session and what they experienced during the session, for example, "I tremored in my arms for the first time" or expressing emotions or sensations they experienced. Trauma and Tension Releasing Exercises do not require the person to talk about any traumatic experiences, but often after a session an individual is in such a calm state that recalling an event does not lead to re-traumatization and actually helps the person come to terms with his/her experience. The increase in self-awareness and bodily-awareness is encouraged.

Currently, TRE is usually offered as private sessions or as group sessions that run for 6-week periods, as a minimal timeframe to see beneficial results. Often there is only one supervised session in a week with clients being encouraged to perform the exercises twice at home during the week. Supervised sessions are often coupled with some form of client education into how the body reacts to stress, the stress response, emotions such as empathy or shame, breathing techniques and other mindfulness topics. Individuals are encouraged to continue with their tremoring process after the 6-week period as it is believed that after approximately three months of tremoring regularly the body experiences permanent changes towards restoring homeostasis. In Table 2.6 a comparison is made between a typical group TRE session and other mind-body therapy session (such as Tai Chi, Yoga, Qi Gong and dance therapies) [174,176]. The table highlights the differences in time spent of various aspects in class, as well as how physical and cognitive load of the therapies might differ. In the following section, anecdotal evidence will be discussed and the current available research will be summarized.

Table 2.6: *Comparison between typical session for mind-body therapies and TRE*

Session aspects	Various Mind-body therapies	Trauma and Tension Releasing Exercises
Typical session layout	- Warm-up (10 minutes) - Exercises (40 minutes) - Cool-down (10 minutes)	- Check-in (5 – 10 minutes) - Exercises (20 minutes) - Tremor (10 – 20 minutes) - Integration (5 minutes) - Check-out (5 – 10 minutes)
Time spent on (can occur simultaneously):		
Physical activity	40 – 50 minutes	15 – 40 minutes
Relaxation	5 – 10 minutes	15 – 20 minutes
Social / group interaction	2 – 5 minutes	5 – 10 minutes
Personal expression	n/a	5 – 10 minutes
Self-reflection	2 – 5 minutes	5 – 10 minutes
Physical load	- Intensity ranges from low to moderate - Focus on specific muscles and movements throughout - Progressions are encouraged	- Exercises at low intensity - Use minimal effort to achieve specific exercise aim - Tremoring can range from low to moderate intensity
Cognitive load	- Most mind-body therapies have specific techniques, postures or sequences to remember & focus on	- Exercise routines stays the same - Tremoring requires no cognitive involvement

2.3.4 CURRENT RESEARCH ON TRE & ANECDOTAL EVIDENCE

Trauma and Tension Releasing Exercises have been used in practice for more than 10 years and have gained surprising popularity in South Africa. To gain a more clear understanding of TRE the anecdotal evidence and current research must be evaluated since research on TRE are very limited, and thus anecdotal evidence serves as a motivation for the use of the therapy.

Anecdotal evidence of the benefits of TRE is well reported on a multitude of TRE-related websites with video testimonials, case studies and blogs about experiences. Prominent benefits include increased relaxation and calmness, decrease in discomfort and pain, and changes in depression and anxiety levels. Table 2.7 displays a summary of benefits compiled by an advanced level 3 TRE practitioner in South Africa

on changes she has noticed by over her 8 years in practice and as TRE level 3 trainer as well as reports from countless other TRE practitioners.

Table 2.7: *Summary of anecdotal evidence from South African TRE practitioners*

After 6 tremors **(approx. 2 weeks)**	**After 12 tremors** **(approx. 4 weeks)**	**After 18 tremors** **(approx. 6 weeks)**	**After 36 tremors** **(approx. 3 months)**
✓ Calm ✓ Relaxation ✓ Improved sleep pattern ✓ Less anxiety	✓ Sustained calm & relaxation ✓ Deeper sleep ✓ Less anxiety and panic ✓ Hyper-vigilance & ADD/ADHD improve ✓ Back and neck pain dissipate ✓ Improvements of painful medical ✓ Conditions such as headaches, arthritic pains ✓ More centred & focused with improvement in cognitive functioning	✓ Feeling grounded & centred ✓ Relationships improve ✓ Connectedness with self and with others ✓ General health improvements ✓ Improvement in mental functioning noticeable ✓ Decreased depressive moods	✓ Sustainable & permanent groundedness with the capacity to stay centred amidst chaos ✓ Resilient & bouncing back rapidly after emotional triggers ✓ Relaxed & "*accepting what is*" approach to life comes naturally ✓ Significant changes in all relationships due to increased connectedness & increased tolerance ✓ Calm, focused concentration with good memory recall ✓ Children with bed-wetting, ADD, ADHD & poor school performance are reported to improve ✓ Health changes in all areas are significant. Improvements noted in diabetes, blood pressure, epilepsy, & asthma ✓ Increased creativity ✓ People report feeling able to enjoy life again

ADD: Attention deficiency disorder, ADHD: Attention deficiency hyperactivity disorder

The current available research on TRE is inadequate, with small sample sizes, no controls groups and limited quantitative data. There are several articles found online about conference proceedings, proposal and reviews regarding TRE; not all published but available on TRE websites. For the purpose of this study, only experimental studies will be elaborated on, of which there are only six to date, as well as several theses and dissertations, of which only six can be found online, will be briefly summarized. The five experimental studies are by Berceli (2014) [4], Herold and Nibel (2016) [78], Johnson (2017a&b) [5,77], do Amoral (2018) [79] and Harrison (2018) [6]. There are several academic scriptures (thesis and dissertation) on TRE on a variety of population and the most relevant ones will be highlighted. Interestingly almost half of the articles mentioned above are based on research conducted in South Africa. The studies are summarized and discussed below.

2.3.4.1 **Experimental research studies**

In a 2014 study, Berceli and colleagues [4] conducted a single-armed, non-controlled pilot study to investigate the effect of a 10-week TRE intervention on self-reported health-related QoL on non-

professional caregivers. The study was conducted with the staff members working at an SOS Children's Village (a government-supported orphanage in South Africa) in 2012. The 21 staff members who elected to participate in the study consisted of one professional psychologist, 17 "house mothers" and three support staff (46.6 ±9.63 years old; 91% women). Participants completed the Health, Wellness, and QoL Questionnaire (measuring physical health, mental and emotional health, stress evaluation, life enjoyment, and overall QoL) before and after the intervention. The intervention included educational talks on anatomy, psychology and physiology and practical TRE sessions which took place once a week for 10 weeks. The participants received a total of 20 hours of educational talks and 30 hours of experimental supervised practice. Participants were required to perform 2-3 TRE sessions independently at home each week. Researchers elected to use an alpha value of 0.10 due to the small sample size. Results show that the intervention had a very good adherence rate (91.3%) and participants reported statistically significant improvements in "life enjoyment" ($p < 0.05$), and overall impression of improvements in all five domains of QoL ($p < 0.05$). According to the researchers, participants experienced more life satisfaction with more frequent positive emotions and greater confidence in their ability to handle stress. The study concluded that a 10-week TRE intervention is highly feasible among non-professional caregivers and can be a potential therapeutic method for improving QoL for a population with high levels of caregiver-fatigue and burnout. This study did not have a control group and it is therefore difficult to extrapolate the effect that attention and potential educational effect in the subject area could have had on participants.

A study conducted in Ukraine by Herold and Nibel (2016) [78] shares their preliminary results of several small sample studies during TRE training. The main aim was to see if TRE can reduce the symptoms of stress-induced illnesses and other health complaints of TRE trainees, consisting of psychotherapist and related academic fields. In total 71 participants (72% women, average age of 42.5 ± 4.3 years) completed the study between March – August 2016. Groups consisted of 12 – 30 participants and were trained by an experienced psychotherapist and certified level 3 TRE trainer. The article does not state how many sessions participants attended, however, training per level usually takes four months with at least twice a week sessions, however, only a quarter of the sessions are with the supervision of the trainer. Data was collected via a questionnaire asking participants to quantify and comment on several areas, including job satisfaction, strain and stress reaction, health complaints, over-all pain and treatments for health conditions; the questionnaire used was developed by the German labour agency. No inferential statistics were reported in this article, however, observing the means values health complaints decreased after training and treatments for medical complaints decreased by 50% after TRE training. These results suggest that TRE might be a promising healing technique to help professional psychotherapists, who experience a high amount of secondary traumatization. This study also did not have a control group and results should be interpreted with caution.

In 2017, Johnson and Naido published two articles [5,77] from Johnson's 2013 dissertation investigating the impact of stress and burnout interventions on educators in high-risk secondary schools in South Africa. The two articles will be summarized together as they pertain to the same research study; with a focussed look at TRE as an intervention. The study focused on the impact of meaningful interventions to help reduce high levels of perceived stress and burnout of high-risk secondary schools teachers working in the Cape Flats, South Africa. The Cape Flats is an overpopulated urban area outside Cape Town with extreme levels of poverty, unemployment, crime, violence, drug abuse, and gang activity. The children and teachers alike are affected by this surroundings through chronic stress, trauma and eventually burnout. In total 63 teachers (age range 40 – 50 years; means 46 years) from four secondary

schools participated in this pre-post pilot study which took place over a 10 week period. Participants were cluster randomized into three intervention groups, namely TRE group (n = 17), transpersonal psychology (n = 16), transactional analysis (n = 10), and a control group n = 20). Both sexes were equally represented. Outcome measures included questionnaires on perceived stress and burnout on personal, work, and learner levels for quantitative data and were completed before and after the interventions. For qualitative data focus groups were held after the intervention. Intervention sessions took place once a week for 90 minutes over a 10 week period, totalling 15 contact hours. The TRE intervention yielded a statistically significant reduction in perceived stress ($p < 0.001$) and burnout relating to learners ($p < 0.02$), comparable to changes observed in the transactional analysis intervention. Qualitative analysis of TRE revealed that participants felt more calm and relaxed after the intervention with increased body-awareness and self-understanding. The participants viewed the intervention as a self-help tool with physical and emotional impacts to improve self-control and increase coping strategies. More centeredness and groundedness were reported by teachers who undertook the TRE intervention. According to the researchers, these results suggest that TRE enabled teachers to cope better with perceived stress in a relatively relative short period.

An observational study conducted in Brazil [79] investigated innovative solutions for mental health promotion of adolescents and their family members in Primary Care. Two groups were observed over a period of 11 years; the first group was focused on parents and caregivers aiming to help them with the education of their children and give them support to deal with the specific challenges of adolescence; with 888 parents and caregivers participating in 47 parents support groups. The other group, focused on youngsters as well as caregivers, participated in a TRE intervention; 1263 individuals participated in 121 regular TRE groups. Group meetings were held weekly, and adolescence and parents were asked to share their experiences. The main results observed during the 11-year period of the parent support groups were the improvement of family relationships, the reduction and prevention of domestic violence, the prevention of teenage involvement in risk situations and an improvement in QoL as a whole. Participants in the TRE group reported improvements in anxiety, stress, depression, panic syndrome insomnia, muscular pains, fibromyalgia, and PTSD symptoms, resulting in a reported better QoL for the adolescents, their families and the community. This shows that the application of TRE might be a viable effective low-cost option for working with large groups and effecting changes in behaviours and symptoms. The data of this study is not well documented, and no standardized tests were used, and thus results rely solely on participants testimonies.

A new study published in 2018 by Harris and colleagues [6] investigated the effects of TRE on restless legs syndrome (RLS) severity, which is a sensorimotor disorder that can negatively impact on sleep and quality of life. The researchers state that the potential merit of TRE for RLS was formulated by the unsubstantiated and speculative hypothesis that RLS may be the result of chronic stress. This randomized controlled trial set out to compare TRE intervention to a discussion control group and included 18 participants who were randomly allocated (stratified by age and RLS severity) to one of the groups. The study was conducted over six weeks with once a week sessions of approximately 60 min with a certified TRE practitioner or expert facilitator for the control group. Participants in the TRE group were encouraged to perform the exercises at home when they felt they needed it while the control group held discussions around the syndrome, the problems they encounter and how they dealt with the symptoms. Outcomes measures were recorded prior to each week's session and included the International Restless Legs Syndrome Rating Scale scores, visual analogue scale on global syndrome severity and stress ratings,

Pittsburgh insomnia rating scale and Major Depression Inventory scores. Nine participants (56.2 ± 9.1 years, 11% man) completed the TRE intervention and showed clinically meaningful improvements in symptoms severity scores as well as improvements in depression and sleep quality, although these results were not statistically significant ($p > 0.05$). The control group ($n = 9$, 60.4 ± 12.5; 67% men) showed similar improvements and thus research theorized the effect of the small group setting and attention might have played a beneficial role in the control group as well. The researchers state that this is an important preliminary study and future research into this subject field should aim for larger samples size, double-blinding of experimental design and stratifying for sex as well during randomization.

2.3.4.2 **Theses and dissertations**

There were five academic scriptures found, three of which are from South African Universities. Only one master thesis [182] and one dissertation [66] are summarized below due to one thesis not being in English [222] and the other two for the following reasons: The main findings in the dissertation by Johnson (2013) have already been elaborated on previously with regards to two published articles [5,77]; and in the dissertation by Blom (2015) [186] TRE is promoted as a possible intervention to effect change in the South African business sectors but the dissertation does not entail any experimental work regarding TRE.

Berceli's dissertation (2007) [66] evaluated the effects of TRE on stress and anxiety and heart rate variability. College students between the ages of 22 – 35 years ($n = 61$) participated in this study. They were divided into a TRE group ($n = 28$) and a control group ($n = 33$); where the controls performed exactly the same exercises as the TRE group but without allowing the tremor to happen. Outcome measures were State-Trait Anxiety Inventory, Activation-Deactivation Adjective Check List (AD-ACL) results and heart rate variability (HRV). Six sessions were performed in both groups over a two-week period. Results indicated a significant reduction ($p < 0.05$) in anxiety-present and an increase in anxiety-absent in both the subscale and total scores. The AD-ACL scores did not reveal any significant changes in the individual categories or subscales, and HRV showed an increase in Parasympathetic Nervous System (PNS) activity but it was not statistically significant ($p > 0.05$). Berceli (2007) concluded that additional research is needed as it is difficult to draw a strong conclusion from the study, but the results of TRE as a therapeutic modality is promising. Furthermore, he highlighted that the control group might have experienced the tremors to a lesser degree, and therefore did not serve as the best comparison group for anxiety and HRV measure.

A Master thesis by McCann (2011) [182] evaluated the effects of a TRE training programme on QoL. Research was conducted on 50 participants (21 – 70 years, 16% men) who attended a four-day Introductory Level 1 TRE Training Course presented by Berceli in April 2010. Participants completed three QoL self-report measures (36-Items Short-Form Health Survey, and the Psychological General Well-Being Index and State-Trait Anxiety Inventory) before and after the four-day training course (including approximately 7 TRE sessions). The main findings showed that the training course resulted in significant improvements in the QoL variables of anxiety ($p = 0.000012$) and general well-being ($p = 0.000014$). No significant differences were established for the variables of state anxiety, physical functioning or mental functioning ($p > 0.05$). While the results are to be interpreted with caution, due to the nature of the study design, there are some evidence to support the ability of TRE and neurogenic tremors to reduce stress and anxiety and improve QoL in a short and intensive training period. However, the researcher states that it remains for future research to delineate the neurological mechanism and the potential therapeutic benefits of neurogenic tremors.

CHAPETR 3 – PROBLEM STATEMENT

3.1 STUDY PURPOSE

Stress has become a worldwide problem resulting in more diagnosis made for mood-related disorders, such as anxiety and depression, with the presence of physical somatic symptoms as well [37]. The symptoms of stress, perceived stress, anxiety, depression and somatisation often overlap and are frequent comorbidities of one another [36,193,223]. Additional evidence for the link between how psychology and the physical body affect each other is seen by the association found between higher anxiety, perceived stress or fear of falling and decreases in postural control [114,140,224]. Stress has even been postulated to influence neurological disorders such as Alzheimer's disease, dementia and Parkinson's disease (PD) especially in areas related to depressive moods [49] and mobility-related concerns [191]. Stress has been shown to reduce mobility in Parkinsonian rats [45,225], and it is believed by Smith and colleagues (2008) that this pathway exists in human as well. In recent studies, the link between anxiety and postural instability have been highlighted in individuals with Parkinson's disease (IwPD), however, further research is needed to strengthen the relationship [62,63].

It is necessary to find methods to relieve stress-based symptoms, especially in a population such as PD, who are influenced by daily stressors [3,60] and chronic stress [3,40]. Perhaps through alleviating the impact of stress on IwPD it will subsequently result in improvements in PD symptoms considering how many of the symptoms overlap [2,51–54]. Therefore finding alternative solutions to provide relief from motor and non-motor symptoms of IwPD are vital. Given the fact that stress can worsen PD motor and non-motor symptoms in the short and long-term [48,60,226], it is of value to investigate stress-relief therapies. Taken together with the knowledge of how stress and trauma affect the body in multiple ways; relaxation exercises with therapeutic neurogenic tremors might hold the key to discharged chronic tension in the body, and improve the quality of life (QoL) of IwPD.

Individuals with PD suffer from a wide range of motor and non-motor symptoms which affects their independence and QoL. As explained in the previous chapter, the main motor symptoms include rigidity, slowness of movement, postural instability, gait dysfunctions, and tremors. Non-motor symptoms include depressive moods, sleep disorders, apathy, cognitive decline, autonomic dysfunction, pain and fatigue [55]. Individuals with PD might be more vulnerable to stress symptoms as stress places greater demand on the neurotransmitters, endocrinology and skeletal muscles. It furthermore inhibits systems IwPD already struggle with, such as sleep cycles, digestion, reproduction, mental health and immune system [55]. According to Hemmerle et al. (2012) [49], IwPD might be at risk of experiencing more chronic stress due to the disease itself and/or might not be able to cope with stress effectively. For instance, QoL is influenced by many different factors including personal (age, co-morbidities, disease duration and severity) and environmental aspects (social support), which contribute to daily stress. Furthermore, the decline in QoL and independence, due to limited functional mobility, is a major problem for IwPD. The frequency and severity of non-motor symptoms have also been associated with higher levels of perceived stress and decrease in QoL [226,227]. Increased perceived stress and anxiety and future loss of independence due to poor mobility may lead to a greater stress-based physiological effect, which in turn amplifies stress response and increases postural instability. It is a vicious cycle that not only impact IwPD but also burdens their caregivers and the healthcare system.

Trauma and Tension Releasing Exercises (TRE) were designed to evoke neurogenic tremors; believed to be an innate genetically-encoded mechanism in all animals as part of the stress response. Chronic stress and anxiety can cause havoc in the body on a physiological and psychological level, resulting in chronic muscles tension patterns held in the body and a multitude of psychological and physical symptoms due to dysfunction of the nervous and endocrine system[21,32,212]. A therapy like TRE might be able to help IwPD manage stress symptoms better and improve their QoL via a reduction in non-motor symptoms, such as anxiety, depression, pain, autonomic dysfunction, etc., as well as possibly improving postural instability. It is theorised that TRE might promote muscle relaxation, especially the psoas major muscles, however, it is not in the scope of the current study to investigate this possible link. Taken together, the use of TRE as a treatment for IwPD to reduce their perceived stress and thereby improving their motor and non-motor symptoms is a worthwhile endeavour.

Very few studies have investigated TRE, and none to date have explored its effect on Parkinsonian symptoms. There are currently six experimental studies on the effects of TRE [4–6,77–79]. These studies were performed on a large variety of populations either suffering from stress-related problems and health complaints, including non-professional caregivers of orphans, teachers at high-risk secondary schools, psychotherapist, adolescents with mental health concerns and their parents, lastly individuals suffering from restless legs syndrome. The currently available research on TRE is inadequate, with small sample sizes, no controls groups and limited quantitative data. However, the studies show promising results for TRE towards improvements in enjoyment of life, QoL, teachers' burnout, and quality of sleep. Moreover, decreases in health complaints, perceived stress, anxiety, depression, and pain was noted by the researchers after a TRE intervention. Anecdotal evidence suggests that therapies using therapeutic neurogenic tremors (TNT) such as TRE could possibly address motor and non-motor symptoms by allowing the body to self-heal and re-organise itself [74]. The TNT may help to restore homeostasis in the body [7], through somatosensory stimulation of the body, releasing chronic muscle tension as well as reducing perceived stress and anxiety.

In South Africa, TRE might be of particular benefit as South Africans have increased daily stress due to crime, income inequality, mental health disorders, risk factors, corruption and low life expectancy [228]. In addition, South Africans have additional barriers to seeking the necessary health care as transportation, cost, personal preference can limit participation. Therefore, TRE might be a successful therapy to implement as it can easily be practised in a group or as a self-help tool at home.

Therefore, this exploratory study set out to investigate the effect of self-induced therapeutic neurogenic tremors (TNT) via TRE on selective motor and non-motor symptoms of IwPD. This study aims to investigate global aspects of the possible benefits of relaxation-based exercises with TNT on IwPD, since PD symptoms, stress-related symptoms and the effects of relaxation are highly heterogeneous and non-linear. It is postulated that exercise with neurogenic tremors will be effective in bringing about significant beneficial changes to selective motor and non-motor symptoms. This improvement may result in less postural instability, improved gait, a decrease in non-motor complaints such as anxiety, depression or autonomic dysregulation which will ultimately lead to enhancing QoL. This is the first study to explore the effects of TNT with exercise on IwPD and the first study to investigate the effects of TNT on motor symptoms.

3.2 RESEARCH QUESTION

This exploratory experimental study design endeavours to answer the following research questions:

3.2.1 PRIMARY RESEARCH QUESTION

Does a nine-week relaxation-based exercise intervention with TNT (Trauma and Tension Releasing Exercises (TRE)) influence selective motor and non-motor symptoms to a greater extent compared to the same intervention without TNT (Exercise and Relaxation (EAR)) or no exercise intervention in individuals with Parkinson's disease?

In other words, the study specifically set out to investigate if a nine-week relaxation-based exercise intervention with TNT influence could:

- reduce general anxiety and improve postural instability to a greater extent compared to the same intervention without TNT or no exercise intervention in individuals with Parkinson's disease?
- influence functional mobility and subsequently reduce gait disturbances to a greater extent compared to the same intervention without TNT or no exercise intervention in individuals with Parkinson's disease?
- influence non-motor and stress-related symptoms reduce to a greater extent compared to the same intervention without TNT or no exercise intervention in individuals with Parkinson's disease?

3.2.2 SECONDARY RESEARCH QUESTION

Additionally, what changes, related to these selective motor and non-motor symptoms, are retained or lost three-weeks after the two interventions are completed?

3.2.3 HYPOTHESIS STATEMENT

It is hypothesised that if IwPD do exercises with TNT over nine weeks, then selective motor (specifically postural instability and gait disturbances) and non-motor (specifically depressive moods and autonomic dysregulation) symptoms will improve due to a reduction in general anxiety and somatisation, as a measure of perceived stress.

Therefore, the null hypothesis, for the preceding research hypothesis, is that there will be no difference in mean motor and non-motor symptoms between the groups who did the relaxation-based exercises with or without therapeutic neurogenic tremors, as well as the no exercise condition. Thus H_0: $\mu_1 = \mu_2 = \mu_3$

The alternative hypothesis states that the mean motor and non-motor symptoms are not all equal between those participants who did the relaxation-based exercises with or without therapeutic neurogenic tremors, as well as the no exercise condition. Thus H_1: The means are not all equal.

3.3 AIMS AND OBJECTIVES

This exploratory study aims to measure the global changes in selective PD motor and non-motor symptoms due to TNT. This study aims to investigate the non-linear effects of relaxation-based exercises with and without TNT on IwPD. This preliminary study aims to add to the knowledge base for more comprehensive PD rehabilitation programmes.

3.3.1 PRIMARY AIM(S)

A. To investigate the effects of exercise with and without TNT on selective motor symptoms of IwPD, especially postural instability and gait disturbances, compared to no exercise.
B. To investigate the effect of exercise with and without TNT on non-motor symptoms of IwPD, specifically including depressive moods, autonomic dysregulation, anxiety and somatisation compared to no exercise.

3.3.2 SECONDARY AIMS

C. To investigate the effect of exercise with and without TNT on disease severity of IwPD, compared to no exercise.
D. To investigate the effect of exercise with and without TNT on self-perceived balance confidence and QoL of IwPD, compared to no exercise.
E. To investigate the retention effect of exercise with and without TNT three weeks after a nine-week intervention compared to no exercise.

3.3.3 OBJECTIVES

The following objectives were used to assess the above-mentioned aims.

3.3.3.1 Primary objectives

To measure and compare the effects of relaxation-based exercises with or without TNT interventions, and a no exercise group, before, during and after a nine-week intervention period as well as after a three-week retention period, on:

- Objective 1: Postural instability, including balance domains of anticipatory control, reactive balance, sensory integration and stability of gait
- Objective 2: Gait disturbances through evaluating gait performance and quality of gait through parameters such as stride length, time in double support, arm swing, trunk rotation, gait asymmetries and coordination
- Objective 3: Non-motor symptoms severity and frequency
- Objective 4: Selective non-motor symptoms which relate the research hypothesis, including depressive moods, anxiety and somatisation

3.3.3.2 Secondary objectives

To measure and compare the effects of relaxation-based exercises with or without TNT interventions, and a no exercise group, before, during and after a nine-week intervention period as well as after a three-week retention period, on:

- Objective 5: Parkinson's disease severity and symptoms, including motor and non-motor experiences of ADL and motor examination
- Objective 6: Self-perceived balance confidence
- Objective 7: Quality of life of IwPD

To collect descriptive characteristics prior to the start of the study for:

- Objective 8: Age, height, years since diagnosis, subtype classification, medication, and global cognition

And to monitor:

- Objective 9: Intrinsic motivation and perceived value of intervention after the nine-week period only
- Objective 10: Intensity of sessions throughout the intervention period
- Objective 11: Parkinson's-related medication use throughout the intervention period

3.4 VARIABLES

3.4.1 DEPENDENT VARIABLES

This exploratory study do not have a singular primary outcome due to the heterogeneity of PD symptoms and the individualized effects of stress and/or relaxation, and thus the study set out to investigate global scores, and specific symptoms where possible, to establish a general idea of the effectiveness of this novel intervention. Singular primary outcomes have several limitations and drawbacks [229] and in an exploratory study it is acceptable to have several primary outcomes, however this limits the conclusions that can be drawn from the results [230]. Keeping this in mind, exploratory studies are necessary to open the doorway to future research and help them focus their attention and aid with hypothesis generation [230]. Human beings are non-linear complex systems and therefore investigating the effects of a novel intervention would require a wide net to explore the effects. This approach increases the likely would of type 1 errors and make results difficult to interpret and generalized to a population [229]. However it is the opinion of the researcher that this approach is essential for this exploratory study.

The dependent variables included the primary outcome variables such as postural instability and gait, non-motor symptoms frequency and severity (specifically stress-related symptoms such as autonomic dysregulation, depressive moods, anxiety and somatisation), as well as the secondary outcome variables like disease severity, balance confidence, QoL and intrinsic motivation.

3.4.2 INDEPENDENT VARIABLES

The independent variables were the nine-week exercise interventions with TNT (TRE) and without TNT (EAR) intervention.

3.4.3 CATEGORICAL VARIABLES

Categorical variables are the participants' age, sex, disease duration, disease severity, as well as freezers and non-freezers (i.e. IwPD who experience freezing of gait and IwPD who do not).

3.4.4 CONFOUNDING VARIABLES

Medication, sex, motor subtype, the presence of freezing of gait and cognition was identified as possible confounding variables. Medication use was assessed as a confounding variable, especially since individuals might change medications during the research process and therefore the effect of medication changes of variables was accounted and controlled for.

3.4.5 ASSUMPTIONS

Certain assumptions regarding the research participants were made at the start of the study. It was assumed that participants would complete the forms honestly and answer specific questions as completely as possible. It was assumed the participants would execute each test to the best of their ability. It was assumed that participants would attend at least two of the three sessions per week and adhere to a minimum of 70% attendance rate. Moreover, it was assumed that participants were willing and motivated to part take in the intervention. In addition, it was assumed that participants would be forthcoming about any problems they experience, and honestly inform the researchers about any changes in medication at each testing session. Lastly, certain assumptions were made concerning the study itself. It was assumed all IwPD have some problems with mobility to a certain extent and that they have a high level of stress [191].

3.4.6 DELIMITATIONS

Certain delimitations were set at the beginning of the study to help control external factors. The study was delimited to diagnosed men and women with PD aged between 40 to 85 years old, from H&Y stage I to IV and who reside within a 70km radius of Stellenbosch in the Western Cape. Participants had to be able to execute dynamic balance activities (i.e. walking 10m and sit–to–stand) without support other than customary walking aids, to be able to complete the testing. Practitioners were instructed to follow strict guidelines to keep the exercise sessions comparable. All tests were done while the participants were on medication and tests took place at the same time of day to accommodate for fluctuations due to medication.

CHAPTER 4 – METHODOLOGY

4.1 STUDY DESIGN

This exploratory experimental study followed a double-blinded randomised time-series design. Multiple measurements from time-series studies are essential to observe changes over time and understand the nonlinear dynamics of human behaviour [219,231]. Participants were randomly allocated to one of three groups following baseline pre-tests: i) Group 1 performing Trauma and Tension Releasing Exercises (TRE) (i.e. exercises with therapeutic neurogenic tremors (TNT)) ii) Group 2 performing an Exercise and Relaxation (EAR) intervention (i.e. exercises without TNT) and iii) Group 3 (CON) is a non-exercising waitlist control group (Figure 4.1). Waitlist control refers to a control group which receive the intervention as a waiting period; where they serve as the control for the study and afterwards receive the intervention. This is an established method for including a control group in intervention studies on individuals with Parkinson's disease (IwPD) [167,232].

The intervention followed a tapered supervision design and took place over nine weeks and participants were tested every three weeks (i.e. baseline, 3, 6 and 9 weeks). A retention test was conducted three weeks after the intervention; thus, participants were tested up to five times throughout the study at set intervals. A retention period is a good method to see if changes are maintain after the secession of an intervention programme. Furthermore researchers suggest that the passage of time is essential to infer learning [233] and therefore retention tests are used to establish long-lasting changes or acquisition of motor skill execution [234]. For the current study, a retention phase have been shown to be useful for research on IwPD [235] and the Dynamic Systems Theory [236], which are two pertinent aspects of the current study.

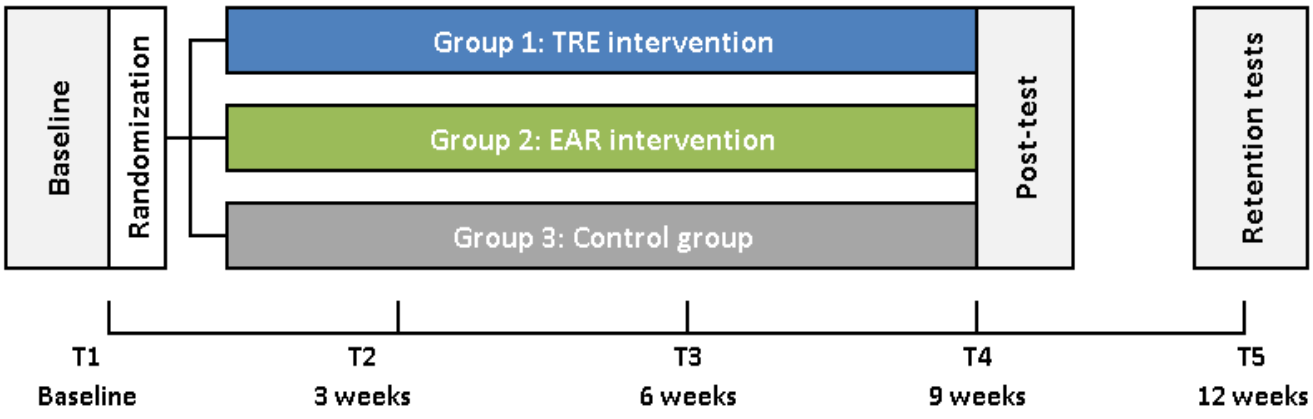


Figure 4.1: Illustration of the study design over 12 weeks

TRE: Trauma and Tension Releasing Exercises; EAR: Exercise and Relaxation
(Source: Personal collection of EM Atterbury ©)

4.2 PARTICIPANTS

4.2.1 SAMPLING METHODS

Due to the nature of the intervention, the study population consisted of a convenience sample of idiopathic individuals with PD using the suburbs that showed the largest likelihood for maximal participant inclusion and attendance. Sampling areas used had the similar socioeconomic status [237].

4.2.2 RECRUITMENT

All participation in this research study was voluntary; and possible interested individuals were contacted via the following three platforms: a) an existing database from the Movement laboratory at Stellenbosch University of IwPD who have previously taken part in research studies and/or have expressed interest in future research; b) the principle investigator presented talks at various support groups in the Cape Metropolitan area to invite IwPD; and c) e-flyers (Addendum M) were shared online and via email to old-age homes, healthcare practitioners and other possibly interested parties. The study was conducted in the Western Cape Province of South Africa. Participants were recruited in a 70km radius from Stellenbosch; predominantly focusing on the Cape Metropolitan's northern and southern suburbs, as well as Cape Winelands, Helderberg, Cape Peninsula and Atlantic Seaboard.

4.2.3 INCLUSION AND EXCLUSION CRITERIA

Volunteers who expressed interest in the study were telephonically contacted for the initial screening. Prior to any data collection, informed consent was verbally explained to volunteers and their questions were answered. Only after initial screening and written consent were obtained were the individuals included in the study. Participants were included based on the criteria in Table 4.1.

Table 4.1: *Inclusion and Exclusion criteria*

Inclusion criteria
• Men and women aged 40-85 years with idiopathic PD • Able to execute dynamic balance activities (e.g. ambulate > 10m, perform sit-to-stand) • Approval to exercise & diagnosis confirmed by primary physician • Stably medicated: same medication for past 4 weeks prior to first testing
Exclusion criteria
• Participants $\geq$ Type IV PD on H&Y Scale • Other neurological conditions (e.g. neuropathy assoicated with Diabetes, stroke) • Visual problems that can not be corrected & vestibular problems • Surgery or injuries in previous 3 months • Major adverse effects due to medication • Severe cognitive impairment (MoCA score < 17) • < 70% attendance of intervention sessions at the end of the 9-week intervention

PD, Parkinson's disease; H&Y, Hoehn and Yahr; MoCA, Montreal Cognitive Assessment

4.2.4 SAMPLE SIZE

Prior to the research, the Centre for Statistical Consultation (Stellenbosch University, South Africa) was consulted. Since this was the first study on the effects of exercises with TNT on selective symptoms of IwPD, a priori power analysis was not possible due to the novelty of this study. Previous studies on TRE are difficult to use for an estimation of sample size as they do not include clinical populations, and consisted of younger participants than the current study. The most comparable study [6] included 18 adults with restless legs syndrome (58.3 ± 10.1 years) divided evenly into an experimental (TRE) group and control group. The researchers found statistically significant results with their sample size, and suggested that their study had adequate power. For the current study, the principal investigator was advised to recruit as many participants as possible to increase the power of the results from this exploratory study. The use of multiple time points add additional statistical power [238]. The principal investigator aimed to recruit and include as many as possible participants, but logistical aspects (such as the availability and distribution of willing TRE practitioners to facilitate the interventions) restricted the execution of a study with a large sample size. However, a post-hoc power analysis on G*Power software (Version 3.1.9.2) [239] for multivariate analysis of variance (ANOVA) demonstrated adequate statistical power (0.97) for the non-motor symptoms (NMS) related to perceived stress [226] as well as for the collective spatial-temporal parameters of gait disturbances (i.e. arm swing, trunk rotation, phase coordination index, stride velocity, stride length, and gait asymmetries) typically associated with IwPD (0.93). The Partial Eta-squared, of the interaction (GROUPxTIME) effect, and alpha value of 0.05 was used.

4.2.5 RANDOMISATION AND BLINDING

After baseline testing (discussed later under procedures), participants were randomly allocated in a 1:1 ratio into one of three groups based on age and sex by an independent controller, not involved in testing or the intervention. This study was double-blinded as an independent investigator conducted the tests and was not involved in the intervention and the group allocation was also concealed during testing sessions. Participants were not informed of the true nature of the study; and they did not know which therapy was being used, only that it was a relaxation therapy. They were also not in contact with participants of other allocated groups. The control group was told that due to limited hall space they could not participate in the first round of the interventions, however after a period of observation they will be offered the opportunity to participate in the better of the two interventions.

4.2.6 PLACE OF STUDY

Volunteers were concentrated in three major suburbs in the Cape Metropolitan area, specifically in the Southern Suburbs of Cape Town (including Simon's Town, Fish Hoek and Muizenberg); Northern Suburbs (Bellville, Durbanville, Brackenfell) and the Cape Winelands region (incorporating Strand and Somerset West). Due to logistical reasons only these three suburbs were included in the study; more specifically the intervention took place in Fish Hoek, Strand and Durbanville. These areas were also locations where TRE practitioners, assisting in the study, resided or were able to travel to within their schedules. Moreover, these three areas were of the same socio-economical class [237]. Within each area, participants were

randomly allocated to the three groups. The entire data collection and intervention period intervention ran from July to December 2017.

At least two suitable halls were identified in each town where testing and interventions could take place; including church halls, scout halls, and exercise studios. Halls used for testing sessions had at least 8m of hard surfaces for straight line walking with good lighting. Halls used for interventions also had approximately $3m^2$ surface area per person with adequate privacy and safety.

4.3 ETHICAL CONSIDERATIONS

Ethical approval (HS S16/10/232) was granted by the Health Research Ethics Council of Stellenbosch University, South Africa (Addendum B). All tests were conducted with professionalism and in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. All possible risks were explained to participants and non-consequential withdrawal from the research study was emphasized. The primary investigator made use of a research team including an independent investigator (qualified clinical exercise therapist or Biokineticist); an independent controller (qualified clinical exercise therapist), and ten certified TRE practitioners (including the principal investigator who is also a qualified clinical exercise therapist).

4.4 PROCEDURES

4.4.1 SCREENING

Volunteers' eligibility was evaluated with a basic information and screening form (Addendum N), which were completed electronically, manually or telephonically. Major aspects of the form included age, perceived functional ability, health questions (comorbidities and recent injuries) and availability. In South Africa individuals with chronic diseases, like PD, need to see their neurologist or primary physician for on-going management every six months. Participants were asked to confirm with the primary physician if they are cleared for exercise prior to participation. After the initial screening form was completed and the individuals met the requirements, participants were visited at their homes to conduct a final screening. During this visit, the written informed consent form (Addendum D) was explained and signed, followed by tests to access global cognitive status with the Montreal Cognitive Assessment (MoCA) and establish motor functionality, such as at least ambulate for 10m or perform a sit-to-stand. Only once participants met the requirements of the inclusion and exclusion criteria (Table 4.1) were they included in the study.

4.4.2 TESTING SESSIONS

Participants were assessed at baseline (T1), twice during the 9-week intervention (T2 & T3), post-intervention (T4) as well as three weeks post-intervention (T5) (Figure 4.1). All five testing sessions were performed in the same hall for each of the three locations, by the same independent assessor. Testing procedures for each session followed the same protocol, lasting approximately 30 – 40 minutes. The baseline testing lasted approximately 50 – 60 minutes and included additional questionnaires for baseline characteristic purposes.

4.4.2.1 Testing protocol

Participants were tested on medication, approximately at the same time of day as their baseline testing to control for their medication state or possible symptom fluctuations; the time since their last medication was also recorded. Upon arrival, participants were asked if they had any changes in activity status, over and above the intervention, or in medication, and their levodopa equivalence daily dosage (LEDD) was recorded at each testing session. Levodopa equivalent daily dose scores were calculated using a website programmed (https://www.parkinsonsmeasurement.org) according to established methods [240,241]. Participants were tested by an independent investigator who is a clinical exercise therapist (biokineticist) and researcher trained to use the assessment modalities. This investigator was not involved in the interventions and was blinded to group allocations. Caregivers were allowed to be present during testing sessions.

Assessments started with questions and a seated motor examination, which then progressed to standing balance assessments and walking tests (Figure 4.2). All tests were conducted barefoot. After the testing protocol was completed, participants were given questionnaires to complete privately at the testing location or at home, and the questionnaires had to be returned to the research team within 72 hours. Tests were conducted in the following order: Part III of Movement Disorder Society's – Unified Parkinson's Disease Rating Scale (MDS-UPDRS), Mini Balance Evaluation Systems Test (BESTest) and 2-Minute Walk (2MW). Questionnaires included non-motor and motor experiences of ADL measured with Part Ib and II of MDS-UPDRS, while the severity and frequency of non-motor symptoms (NMS) were assessed with Non-motor Symptoms Questionnaire (NMSQuest) and Non-motor Symptoms Scale (NMSS), as well as depressive moods with the 9-item Patient Health Questionnaire (PHQ-9). Self-perceived balance confidence was assessed with Activity-specific Balance Confidence (ABC) scale and Quality of Life (QoL) with the 8-item Parkinson's disease Questionnaire (PDQ-8).

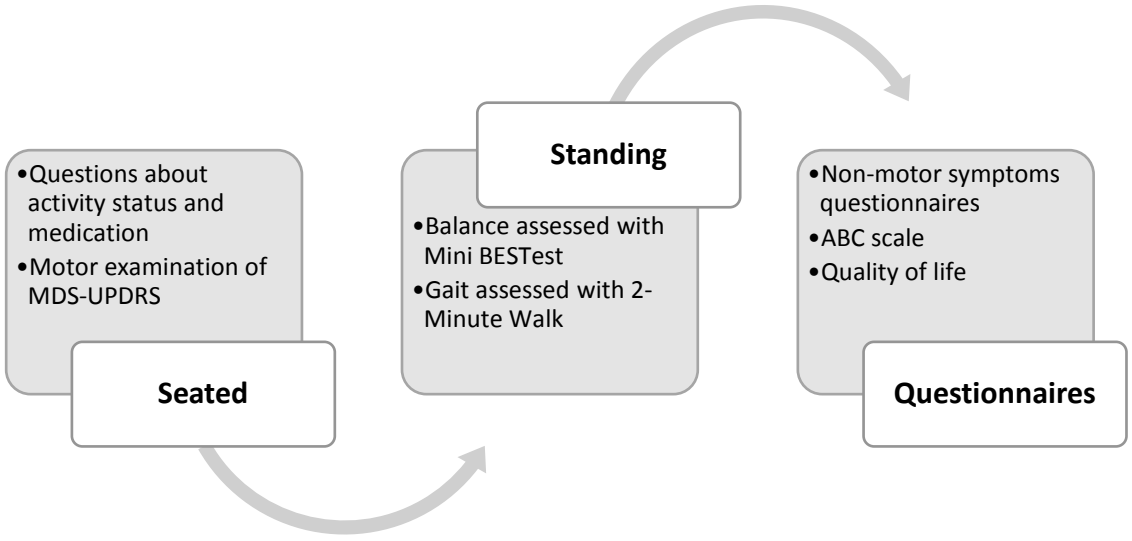


Figure 4.2: *Testing protocol progression*

MDS-UPDRS: Movement Disorder Society's – Unified Parkinson's disease Rating scale; BESTest: Balance Evaluation Systems Test; ABC: Activity-specific Balance confidence scale

The TRE and ER groups were asked to complete additional questionnaires during the interventions. After each session during the intervention, participants were asked to give their rate of perceived exertion (RPE) score (explained in section 4.5.1.5). After the last session of the intervention, participants were asked to complete an Intrinsic Motivation Inventory (IMI).

4.4.2.2 Baseline testing

During baseline testing, participants' height was measured and Part Ia and IV of the MDS-UPDRS were completed by the principal investigator (not the independent investigator) with the participant, with or without their caregiver present. Information and/or questions concerning the interventions were shared and answered by the principal investigator to ensure the independent investigator remained blinded.

4.5 INTERVENTIONS

Two of the three groups took part in active interventions for nine weeks while the third was a non-exercising wait-list control group. As explained previously, Group 1 performed TRE which entails exercise with TNT; Group 2 followed an Exercise and Relaxation (EAR) intervention, which was the same as the TRE intervention, in terms of the environment and exercise routine performed, but without TNT. Both interventions ran for nine weeks with three sessions a week of approximately 50 - 60 minutes. All three groups were asked to complete sleep diaries daily and to report any changes in medication or physical activity. In Table 4.2 the structure of the exercise sessions and the intervention environment are described which provides a summary of the differences and similarities between the two interventions.

Table 4.2: *Summary of differences and similarities in TRE and EAR interventions*

Intervention type	TRE (Trauma & Tension Releasing Exercises)	EAR (Exercise and Relaxation)
Check-in	YES (3 - 5 minutes on talk topics)	YES (3 - 5 minutes on talk topics)
Exercise routine	6 simple and safe exercises (15 – 30 min) Performed on exercise mat with chair	6 simple and safe exercises (15 - 30 min) Performed on exercise mat with chair
Neurogenic tremors	YES (for maximum of 10 minutes)	NO
Relaxation period	YES (3 – 5 minutes)	YES (for maximum of 10 minutes)
Check-out	YES, share current state and RPE of session	YES, share current state and RPE of session
Setting	Small group (3 - 6 per group) Local exercise hall & home	Small group (3 - 6 per group) Local exercise hall & home

Frequency	3 x week (50 – 60 min) for 9 weeks 27 sessions in total	3 x week (50 – 60 min) for 9 weeks 27 sessions in total
Supervision	Certified TRE practitioner Tapered design of 17 supervised sessions	Certified TRE practitioner Tapered design of 17 supervised sessions

RPE, Rate of perceived exertion

4.5.1 SESSION STRUCTURE

Trauma and Tension Releasing Exercises are a series of simple exercises designed to fatigue and stretch certain muscles to help evoke a neurogenic tremor [65]. Session structure included check-in, exercises, relaxation period and check-out. Participants' caregivers could participate in the intervention as well.

4.5.1.1 Check-in

'Check-in's' took place at the beginning of each session. It was a way for participants to introduce themselves and become familiar with the group and the practitioners. It also helped participants feel at ease and promoted coherence which helps with relaxation. As the intervention progressed participants were asked to briefly state if they have noticed any changes in their behaviour or body, mostly as a way for the TRE practitioners to become aware of anyone who might struggle with the exercises during the session. After the short response from everyone in the room, the practitioners were instructed to share a brief 3 - 5 minute topic with the group (more on this in section 4.5.2.2). The aim of including the topics was to educate and explain how to recognize stress, how it affects the body and why stress management is important. During other exercise inventions, the therapist would often explain why certain exercises are being used of how the body reacts and for the purpose of this research study, it was more suited to do it prior to the exercises.

4.5.1.2 Exercises

The exercises used for the intervention are very simple and easy to perform. The primary investigator also modified the original TRE exercises to further simplify the movements and make it very accessible for IwPD to perform. Almost every exercise had two to three levels of difficulty, with the last level being the original TRE exercise (Addendum E). The aim of the exercises was to achieve the stretch or the fatiguing point for each individual and therefore participants were strongly encouraged to do the exercise at the level they felt comfortable with for each session. The exercise routine was performed at a low intensity and participants were instructed to adjust the movement or position when they experienced any pain. Additionally, participants were also asked not to push past a 7/10 of a rate of perceived exertion (RPE) scale when performing fatiguing exercises. Exercises were performed on a 3mm thick exercise mat alongside a chair for balance and safety. Since the aim of the whole intervention was to induce relaxation in the body, too high intensity of pain or fatigue or the feeling of being unsteady or unsafe during the exercises would have been counterproductive.

The exercise routine with modifications can be viewed in Addendum E; however please note that that this is shortened version. All sessions started with a breathing exercise to reduced heart rate variability (Shankar 2012) and thereby aid in calming their nervous systems for the session. Participants were also asked to perform a standing body scan and become aware of any discomfort they might feel in their body. Stretches included the ankles, hamstrings, adductors and hip flexors. Fatiguing exercises focussed on the calves, quadriceps and gluteus muscles. Exercises often progressed from double leg to single leg; from using the chair to without the chair, or from limited range of motion (RoM) to full as possible RoM. The majority of exercises were performed standing, with the second last exercise performed at the wall and the last exercise was performed on the ground. These last two exercises were fatiguing exercises (including a wall-sit and modified pelvic bridge) performed for at least two minutes to ensure that fast-twitch and slow-twitch muscle fibres were fatigued. These exercises are often accompanied by a slight tremor, which initially might be a simple physiological muscle fatigue tremor. However, it is used as a tool for participants to notice how a tremor might feel. The sensation or experience of these tremors during the exercises was encouraged in both the TRE and EAR groups to keep the exercise routine the same for both groups. Participants were shown how to go down to the floor in a safe and systematic way, as well how to get up from the floor as well. Some participants opted to not go down to the floor, so the last part of the exercise routine was performed on a chair.

4.5.1.3 Therapeutic neurogenic tremors (TNT)

Once the exercises were completed and participants were lying on their exercise mat, the tremor mechanism was activated for the TRE group. This activation occurred through very slow movements of the legs to a certain point where each participant felt their tremors initiating. As the intervention progressed, TRE participants were able to find their initiation point easier. The TRE group only tremored for a maximum of 10 minutes per session. Participants were taught to self-regulate, i.e. stop the tremors whenever they felt the need to do so, by straightening their legs and locking their knees. After the 10-minute tremor period, the TRE group were asked to stop their tremors through the self-regulation movement.

The EAR group performed the same exercises but was instructed to “self-regulate”, i.e. straighten their legs and lock their knees, immediately after they performed the last exercise thus they did not initiate the tremoring mechanism at the end of the exercise routine.

4.5.1.4 Relaxation period

The EAR group started with the relaxation period directly after the exercises for a maximum of 10 minutes, whereas the TRE group had a shorter relaxation period (3 - 5 minutes) after their tremors. The relaxation period is the same as the integration period described in the literature review. Participants were instructed to lie in a comfortable position of their choice; on their back, side, stomach, etc. They were allowed to bring a pillow or blanket to increase their comfort. While lying down, they were encouraged to perform a body scan once again throughout their whole body. Additionally, they were also reminded to keep their attention to their breathing or body sensations and not their thoughts. The practitioners did not guide participants through any form of progressive relaxation techniques or methods; they merely gave reminders such as “be aware of your breathing” or “adjust your body to feel as comfortable and

relaxed as possible". After the relaxation period was over, participants were instructed to roll to their side and push themselves in a seated position. Participants could choose if they wanted to remain seated on the floor or arise to sit on a chair for the check-out.

4.5.1.5 Check-out

The aim of the 'check-out' for the purpose of this research was firstly to hear verbal confirmation that each participant was fully awake after the session. Participants were asked to briefly state how they felt after the session (i.e. share their current state), and if they experienced anything during the session, such as the tremor occurring in a different body part or a new sensation throughout the body. Therapists were instructed not to inquire further about any participants' personal psychology or emotional state than what they shared voluntarily, which is customary for usual practice of TRE sessions, in an attempt to control the environment and experience of each group. Participants were asked to provide their rate of perceived exertion (RPE). The RPE is a visual analogue scale (Addendum L) from 0 – 10 indicating how much exertion was used during the session including shortness of breath, muscle fatigue and overall body exertion (not just the exertion of singular exercises). A score of 0 indicates no exertion or effort and 10 indicates maximal exertion of effort. The RPE scale is used as a method to determine the intensity participants experienced during a session. The aim was to keep the exercise intensity below 5 out of 10 on the RPE scale [242].

4.5.2 INTERVENTION ENVIRONMENT

The environment in which the intervention took place was very important and therefore great care was taken when the surroundings were curated; predominantly the focus was on the TRE practitioners who led the sessions. Both exercise interventions were supervised TRE practitioners in a small group setting of 3 – 6 individuals per group. A relaxing environment was strongly encouraged since a "not-safe" environment can stimulate a stress response from the sympathetic nervous system [195]. Porges (2007) emphasizes the effect the environment could have on an individual's nervous system. A small group setting has also been found to be very beneficial to enhance enjoyment, QoL and motivation of IwPD, thereby ensuring the best possible environment for the intervention [243,244].

4.5.2.1 TRE practitioners

Certified level 2 TRE practitioners were recruited to help with the intervention. A total of nine practitioners (excluding the principal investigator) located within the three main locations of the study volunteered their time and effort. Practitioners were randomly assigned to the TRE or EAR groups. The primary investigator wanted to use TRE practitioners for both groups as they are trained to facilitate sessions through modulating their own internal state of wellbeing or "groundedness", which is the quality of maintaining emotional equilibrium and calm demeanour. Therefore, the assumption was that the quality of the environment created by the practitioners was the same for both groups. The holistic approach to the body, movements and the tremors were of greater importance than the precise execution of exercises, as would have been provided by a clinical exercise therapist. Where it was possible, groups were facilitated by two practitioners, especially during the first two weeks.

4.5.2.2 Intervention manual

The TRE practitioners attended an introductory talk by the primary investigator to explain the research plan and inform them about the practical aspects of working with IwPD. Prior to the start of the intervention, practitioners met with the primary investigator to discuss details about the intervention and all exercise modifications were shown and explained. A manual with all the necessary information regarding the sessions were handed to each practitioner. The manual contained emergency contacts, attendance sheets, RPE sheets, session notes, pre-existing conditions of participants in their group, topics to be covered during check-ins, exercise descriptions and a short fact sheet (Addendum C) about practical considerations for working with IwPD.

Practitioners were given 17 topics to be covered during the 17 supervised sessions. A script of each topic was included in the manual. Practitioners did not have to communicate the script exactly but were asked not to elaborate or give more information about the topics. Topics included were not new to TRE practitioners; and included a definition of stress and trauma, how the body reacts to stress, sleep, mindfulness, resilience, self-regulation, breathing, and boundaries (Addendum O).

4.5.2.3 Supervision and attendance

Trauma and Tension Releasing Exercises were designed to be a self-help tool that can easily be done in groups, one-on-one with a practitioner, or at home after several sessions with a TRE practitioner. Individuals often claim that facilitated sessions with a practitioner felt more beneficial. For this research study, the intervention followed a tapered supervision plan to ascertain if home-based exercises would be sustainable for IwPD. The added additional benefit of the graded supervision plan is that participants were not dependent on the practitioner to facilitate sessions or guide them through the exercises. Thus, the research intervention could also be used as a self-help tool after the study, which is ethically considered to be a better approach to intervention studies. The first two weeks were fully supervised with three sessions per week. The following four weeks participants only had two of the three sessions with the practitioners, and participants were asked to complete one session at home per week; exercise mats were provided to participants if they required it. The last three weeks individuals only attended one supervised class and had to perform two sessions at home. In total, the intervention consisted of 17 supervised sessions and 10 home sessions.

Participants had to report successful completion of home sessions during their following supervised session and were strongly encouraged to maintain the 3-times a week frequency throughout the 9-week intervention. A minimum attendance of 70% was required for participants to be included in the analysis of the results. Thus, individuals had to perform a minimum of 19 of the 27 sessions to reach the mandatory attendance. Therefore, the intervention consisted of 17 supervised sessions and a minimum of three sessions and a maximum of 10 sessions at home.

4.6 TESTS AND ASSESSMENTS

Primary and secondary outcome measure are described below. Participants' descriptive and demographic measurements were recorded with the personal information forms that participants completed during

screening. These outcome variables included age, sex, age of onset, disease duration, most affected side and mediation. The height of participants was measured using the Frankfort plane method and a steel anthropometer (Siber-Hegner GPM, Switzerland) at baseline testing.

4.6.1 PRIMARY OUTCOME VARIABLES

4.6.1.1 Postural instability and gait disturbances

Postural instability and balance were assessed by using the Mini Balance Evaluations Systems Test (Mini BESTest), and gait disturbances were assessed by the instrumented 2-Minute Walk (2MW) with the APDM Mobility Lab™ system (APDM, Inc., Portland, USA).

The Balance Evaluation Systems Test (BESTest) was developed in 2009 by Horak and colleagues as a clinical assessment tool [245]. It aims to identify and evaluate the six different balance domains (previously discussed) however this very comprehensive test procedure took more than 30 minutes to complete which made it a time-consuming evaluation with too much information for research purposes. Thus, the Mini BESTest was developed by Franchignoni in 2010 as a shortened version of the original test, and aimed to focus on the assessments of the balance domains thought to underlie postural instability [143,245]. The Mini BESTest (Addendum F) is a 14-item evaluation that can be administered in 10 to 15 minutes, and addresses 4 of the 6 constructs included in the BESTest: anticipatory control, reactive postural control, sensory orientation, and dynamic gait [143]. The Mini BESTest exhibits excellent reliability and validity across stages of PD, can discriminate between fallers and non-fallers, and is responsive to change with rehabilitation interventions [246]. The activities in the four domains are simple tasks, many of whom are valid tests on their own, for example, the timed-up-and-go (TUG) task. Some activities tested the right and left side and participants were offered more than one trial to complete the task, however, the worse side between left and right was used to calculate total scores. The TUG was one of the tasks in the fourth domain (stability in gait) and participants were instructed to stand up from a chair, walk 3m, turn, and walk back and sit down again at their comfortable walking pace [247]. Participants were given a test trial followed by two recorded trials. A higher Mini BESTest score indicates better balance performance.

Gait disturbances are common in IwPD and can be very limiting to ADL and QoL [20]. The 2MWT is a valid and reliable test to not only establish functional capacity (measured as gait speed or distance covered) but also assess any gait disturbances in PD[248,249]. For objective measurement, the Instrumented 2MW or iWalk (from the Mobility Lab™ system) used six tri-axial accelerometers with a gyroscope (placed on the lower back, chest, wrists and ankles) to automatically processes input signals and provide data on gait and transitional movements [250]. The performance measures collected from the 2MW were distance, used as a descriptive variable for functional capacity, and gait speed. The data collected to quantify gait parameters were selected for their association with balance and PD-specific gait disturbances [20,131,132,137,161,250,251]. These parameters included stride length (SL), SL asymmetry, time in double support (DS), trunk rotation, coefficient of variance (CoV) of trunk rotation, range of motion (RoM) of arm swing, arm swing asymmetry and phase coordination index (PCI) [247,252]. These parameters were further used to express improvements in a few of the gait quality criteria, put forth by

Vienne and colleagues (2017) [253]. The criteria (and corresponding gait parameters) investigated include sturdiness (SL, trunk rotation and arm swing RoM), steadiness (trunk rotation CoV), symmetry (asymmetry of SL, and arm swing RoM), and synchronization (time in DS and PCI). Stride length parameters were normalized to each participant's height as men usually have a longer SL than women [254]. Consequently, these values are expressed as a percentage of stature rather than in meters. Participants were instructed to walk at their comfortable pace for two minutes between two-line markers place 7 – 8 meters apart. Two trials were performed, and the total distance covered in each trial were recorded. For the variables pertaining to gait performance, such as gait speed, only the best of the trials were used whereas variables looking at quality of gait used the average of validated trials.

4.6.1.2 Non-motor symptoms

Two questionnaires were used to assess the severity and frequency of NMS. A study by Chaudhuri and Martinez-martin (2008) stated that it is best to use both questionnaires [150] as Non-motor Symptoms Questionnaire (NMSQuest) accurately detects the non-motor symptoms, and Non-motor Symptoms Scale (NMSS) gives information about the frequency and severity of NMS in IwPD. Both questionnaires are self-administered pen and paper questionnaires and were given to participants to complete with or without their caregiver at every testing session (T1 – T5).

The Non-motor Symptoms Questionnaires (NMSQuest) was developed by Chaudhuri and colleagues (2006) and their studies showed that NMSQuest (Addendum H) is a feasible, valid, and accepted tool to detect the presence of NMS [150,255,256]. The NMSQuest is comprised of 30 items and is a screening tool designed to draw attention to the presence of non-motor symptoms and initiate further investigation [255]. Questions asked to require a simple "yes/no" response and on average take 5 – 7 minutes to complete [255]. This questionnaire covers 10 domains, namely 1) Gastrointestinal tract (8 items); 2) Urinary tract (2 items); 3) Sexual function (2 items); 4) Cardiovascular (2 items); 5) Apathy, attention and memory (3 items); 6) Hallucinations and delusions (2 items); 7) Depression, anxiety and anhedonia (2 items); 8) Sleep and fatigue (5 items); 9) Pain (unrelated to other causes) (1 item); and 10) Miscellaneous (e.g. diplopia, weight loss) (3 items). There was a significant association of total score in individuals with PD and their H&Y stage ($r = 0.31$; $p = 0.0006$) [255]. A similar result was found in a study by Bostantjopoulou (2013) were IwPD's NMSQuest total scores differed significantly in the disease stages ($p = 0.001$) and due to disease duration ($r = 0.282$; $p=0.000$) [257]. The parameters of the questionnaire indicate a low ceiling (0.8%) and floor (2.4%) effect [255].

The Non-motor Symptoms Scale (NMSS) is also a 30-item scale for the assessment of non-motor symptoms in PD developed by Chaudhuri and colleagues in 2007 to assess the severity and frequency of non-motor symptoms. The NMSS (Addendum I) contains nine domains: cardiovascular, sleep/fatigue, mood/cognition, perceptual problems, attention/memory, gastrointestinal, urinary, sexual function, and miscellany [150]. Each item evaluates frequency and severity separately, and score per each item or "symptom burden" is calculated by the multiplication of frequency and severity score. Scores range from 0 (not present) to 12 (maximum frequency and severity) by multiplication of both, and domains sub-scores are the sum of the items in a domain. The scale was validated [150] and has internal consistency (mean Cronbach's $\alpha = 0.61$) and satisfactory test-retest reproducibility (ICC > 0.80). The scale showed modest

association with indicators of motor symptom severity and disease progression but a high correlation with other measures of non-motor symptoms such as the NMSQuest and health-related QoL measure (PDQ-8) (both, r = 0.70) [150]. The scale showed an overall low floor and ceiling effect for the total NMSS score were 0.42% [150].

Researchers have also demonstrated that several severity and frequency items of the NMSS are associated with perceived stress and QoL [226,227]. The domains associated with perceived stress were mood/cognition severity and frequency scores, as well as frequency scores of attention/memory and urinary domains [226], while QoL was associated with the above-mention domains as well as perceptual problems/hallucinations [227]. Based on these associations with the NMSS scores, additional analysis were performed to give insight regarding participants' level of perceived stress. In conclusion, the NMSQuest and the NMSS are a valid screening tools and a holistic measures, respectively, to detect any non-motor symptoms as well as to assess the symptoms and to plan effective treatment [258].

4.6.1.3 Depressive moods, anxiety and somatization

The Patient Health Questionnaire (PHQ) was developed in 1999 as a shortened and self-reported questionnaire based on the "Primary Care Evaluation of Mental Disorders" physician report to detect depressive, anxiety, somatoform, alcoholism and eating disorders [259]. Although the PHQ was originally developed to detect five disorders, the depression, anxiety, and somatoform modules have turned out to be the most popular [260]. The co-occurrence of somatic, anxiety and depressive symptoms (the SADS triad) is exceptionally common [193,261,262]. This is the rationale behind the PHQ-SADS screener [261] (Addendum K). Each PHQ module can be used alone, together with other modules, or as part of the full PHQ and the modules have been shown to be accurate in detecting and monitoring symptoms [260]. The three questionnaires used are the PHQ-9 to screen for depressive moods, generalized anxiety disorder (GAD)-7 to screen for anxiety and PHQ-15 to screen for somatic (psychosomatic symptoms relating to the body) symptoms. The benefit of using the PHQ-SADS screener is that all three questionnaires use the same cut-off scores, namely scores of 5, 10, 15, and 20 represent cut-off scores for mild, moderate, moderately severe and severe depressive moods/anxiety or somatization, respectively[260]. No ceiling effects have been found with the PHQ-SADS. All three questionnaires are self-administered pen and paper questionnaires.

Depressive moods can be screened for with the 9 questions asking the individual to rate the frequency of specific occurrences or moods in the past two weeks.The points for questions rage from 0 (not at all) to 3 (nearly every day). The questionnaire is quick and easily administered, and can be completed under 5 minutes. Although a score of 10 is generally accepted as the cut-off to identify major depressive moods, with PD scores of 0 – 4 denotes minimal depression and scores of 5 – 9 indicates moderate depression; and thus a score of 9 offers optimal sensitivity and specificity for screening for major depressive moods in the PD population [263]. The PHQ-9 has excellent test-retest reliability (ICC = 0.91). The GAD-7 is a 7-question screening tool to assess the frequency of anxiety symptoms over a 2-week period. Though originally developed as a screening and severity measure for generalized anxiety disorder, the GAD-7 also proved to have good sensitivity and specificity as a screener for three other common anxiety disorders – panic disorder, social anxiety disorder, and post-traumatic stress disorder

[264]. Question scores range from 0 (not at all) to 3 (nearly every day), in which scores > 5 indicate mild anxiety, > 10 indicate moderate anxiety, and > 15 indicate severe anxiety. A cut-off score of 10 has 89% sensitivity and 82% specificity for identifying GAD in a primary care setting [264]. Finally, the PHQ-15 is used to assess somatic symptom severity and the potential presence of somatization and somatoform disorders [265]. The PHQ-15 is calculated by assigning scores of 0 (not at all), 1 (bothered a little), and 2 (bothered a lot) to 13 somatic symptoms of the PHQ and also 2 items from the depression module. The score ranges from 0 to 30, and the reliability and validity of the PHQ-15 are high in clinical care settings [29,265].

4.6.2 SECONDARY OUTCOME VARIABLES

4.6.2.1 Disease severity

The Unified Parkinson's Disease Rating Scale (UPDRS) was originally developed in the 1980s and was revised in 2008 by the Movement Disorder Society (MDS). The new MDS-UPDRS is more comprehensive and inclusive of non-motor symptoms and is currently the most valid and widely used scale to measure disease severity in PD [266]. The validity of the MDS-UPDRS for rating PD is supported by the combined clinometric results of the study by Goetz (2008). The MDS-UPDRS consist of the following four parts: Part I (13 items on non-motor experiences of daily living), Part II (13 items on motor experiences of daily living), Part III (18 items on motor examination) and Part IV (6 items on motor complications) (available online at https://www.movementdisorders.org/MDS/Education/Rating-Scales.htm). Part I has two components: a) behaviours evaluated by the investigator with all relevant information from participants and caregivers, and b) was completed by the participant with or without the help of their caregiver, but independently of the investigator. Part II was also a self-administered questionnaire like Part Ib; these sections could have been reviewed by the investigator to ensure extensiveness and clarity [266]. Part III was a motor examination of the participant completed by the investigator. Motor examination assessed the amount of rigidity, bradykinesia, resting tremor and other motor manifestations of PD. Some of the tests included finger taps, rigidity of limbs, arising from a chair, and observations of posture and gait, to name a few. Part IV integrated patient-derived information and was completed with the investigator's clinical observations. A higher total score indicates greater disease severity; and higher scores in the separate parts indicate greater difficulty with experiences of non-motor and motor symptoms during ADL (Part I and II), a greater presence of motor symptoms (Part III) and more motor complications (Part IV), respectively. Part Ib, II and III were measured repeatedly throughout the research period (T1 – T5); whereas part Ia and IV were only measured at baseline.

The scores obtained from part II and III of the MDS-UDRS were further used to calculate participants' sub-type scores and classify them as an individual who experiences freezing of gait (FoG); i.e. freezers vs. non-freezers. These subtypes included postural instability and gait disturbance (PIGD), tremor-dominant (TD) or akinetic-rigid (AR). These sub-type scores were calculated using established methods [25,267]. Freezers were identified by using the answers from part II (self-reported) and part III (clinically observed) pertaining to FoG. Previous researchers have found this method to be effective [268,269].

4.6.2.2 Global cognition

The Montreal Cognitive Assessment (MoCA) assesses global cognition [270] with a simple pen-and-paper test (Addendum G) and is considered to be a more sensitive screening instrument to detect cognitive dysfunction than the "Mini Mental State Examination" [271]. The MoCA was completed with participants before baseline testing as a screening tool. Cognitive dysfunction can present with impaired working memory, executive function, visuospatial function, attention, as well as decrease in dual-tasking abilities [272], and the MoCA assesses all these domains. The MoCA can effectively identify cognitive changes in PD and is able to successfully differentiate both dementia and mild cognitive impairment (MCI) in PD [273]. The MoCA is a 30 point test conducted on a single page. A result ≥ 26 is considered a typical global cognitive ability [270]. Individuals with PD who score above 17 are considered not to have severe cognitive impairment [271]. There are a variety of MoCA test pages to control for the learning effects with repeated testing of participants; as well as multiple versions in different languages, of most important is English and Afrikaans for this study. The MoCA has a high test-retest reliability (r = 0.92) and good internal consistency (Cronbach α = 0.83 on standardized items) [270,271].

4.6.2.3 Self-perceived balance confidence

Self-perceived balance confidence was measured with the Activity-specific Balance Confidence (ABC) questionnaire; which is particularly relevant in IwPD who have an increased fear of falling due to low balance confidence. It is valuable for detecting an individual's balance confidence in performing a variety of functional daily activities in individuals with balance disorders. The 16-item questionnaire (Addendum A) is quick and easy to administered, asking the individuals to indicate how confident they feel with an activity (e.g. going up or down stairs, climbing into or out of a car) using a scale from 0% (no confidence) to 100% (complete confidence) (Adkin et al. 2003). The ABC Scale has excellent internal consistency (Cronbach's alpha = 0.96) when used on IwPD (Lohnes & Earhart, 2010) 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. Participants were asked to complete the ABC scale at all testing sessions (T1 – T5), with or without their caregiver present.

4.6.2.4 Quality of Life

The Parkinson's Disease Questionaire-8 is derived from the Parkinson Disease Questionaire-39, which measures functioning and well-being in those with PD [274]. The main aim is to measure QoL of IwPD. The 39-item questionnaire tested 8 domains and the short form, PDQ-8, is comprised of one question of each domain that correlated the strongest to the total score of the domain (Addendum J). These domains include mobility, activities of daily living, emotional well-being, stigma, social support, cognition, communication, and bodily discomfort. Each question is scored from 0-4 points and the total scores are summed, from which a percentage is calculated. The questionnaire is self-administered and can be completed in 5-12min [274,275]. The test has excellent test-retest validity (ICC = 0.72) [146] and inter-rater reliability (ICC = 1.00) [274]. This questionnaire has an adequate correlation with higher Hoehn and Yahr stages (r = 0.53), and adequate to excellent correlations with UPDRS sub-scores (r = 0.47 to 0.60)

[274]. No studies have found floor or ceiling effects in this questionnaire [274,275]. Participants were asked to complete the PDQ-8 at every test session after they have completed all other questionnaires.

4.6.2.5 Intrinsic Motivation Inventory

The intrinsic motivation inventory (IMI) is a questionnaire used to measure motivation and perceptions following a specific task [276]. Motivation is of particular interest in IwPD since dopamine is the governing neurotransmitter of the reward-seeking system in the brain. Intrinsic motivation is also a good estimate of the value individuals perceive from an intervention. The IMI includes five subscales to tests the degree of motivation of a participant; subscales include interest/enjoyment, perceived competence, effort/Importance, pressure/tension and value/usefulness [277]. The IMI questionnaires were completed on the last day of the intervention during the check-out.

4.7 STATISTICAL ANALYSIS

Statistical analyses were performed with STATISTICA® 13.2 (Dell Corp, Round Rock, TX, USA) and Microsoft® Excel 2010 (Microsoft Corp, Redmond, WA, USA).

To determine if the continuous data followed a normal distribution the Shapiro-Wilk test was used. Outcome variables with possible outliers were winsorized by 10% to minimize the effect of outliers [278]. Discrete variables were compared by Chi-square test. Baseline characteristics were compared using one-way analysis of variance (ANOVA). All measures were normally distributed. Descriptive variables are reported as mean ($\acute{x}$) and standard deviation (±SD) with the range, unless otherwise specified. The tabulated continuous variables are reported as mean ($\acute{x}$) and standard deviation (±SD) with the 95% confidence intervals (CI). The graphs are presented as the mean with standard error of measurement (SEM).

For comparisons of measurements done over time, mixed model repeated measures ANOVA's were conducted with GROUP, TIME and TIME* GROUP (interaction) as fixed effects. The intention-to-treat principles were followed, allowing calculations to be done when there are missing data, therefore preserving the sample size and while maintaining sufficient power for statistical tests (Chakraborty 2009). For the Post-hoc comparison, the Fisher's Least Significant Difference (LSD) analysis was performed to evaluate the effect between the three groups (i.e. TRE, EAR and CON) and within the five time points (i.e. T1 - T5). Data were analysed separately over the intervention period (T1 to T4) and for the retention phase (T4 - T5). In addition, measures were assessed for possible covariates (i.e. Levodopa Equivalent Daily Dose (LEDD), sex, freezing status and PD subtype), however none of these possible covariates differed between the groups at baseline. Only LEDD covariate was included in an analysis of covariance (ANCOVA), to control for and investigate if any changes in medications could have affected the data. The alpha level was set to ≤ 0.05. Statistics are reported with one decimal or significant decibels, were additional precision is needed, and p-values are displayed with at least two decimals.

Effect sizes (ES) were calculated to give insight into the magnitude of statistical differences [279]and their practical significance[280] within groups. Hedges' g ES size was used as it is more sensitive for smaller samples sizes by using a sample size weighted pooled SD [281]. Effect sizes are reported with statistically significant p-values; unless otherwise specified. Additional statistical analysis was performed

on ES to calculate the 95% confidence intervals (CI) indicate practical significance [280]. However some variables' practical significance were interpreted in context with the use of established minimal clinical important differences (MCID), where MCID were available and applicable to the relevant population [279,281].

CHAPTER 5 – RESULTS

This chapter reviews the results of the study, starting with descriptive characteristics of the participants followed by primary outcome variables, including motor and non-motor symptom measures. The secondary outcome measures (balance confidence, QoL, intrinsic motivation) are presented and the chapter concludes with a summary of the main findings. Variables are firstly described over the intervention period (T1 – T4), where T1 represents baseline data, T2 and T3 represent mid-way testing sessions at three and six weeks into the interventions, and T4 represent post intervention data at nine weeks. Secondly, the results for the three week retention period (T4 – T5) follows after each variable.

5.1 PARTICIPANTS

In total, a hundred and forty-six individuals with Parkinson's disease (IwPD) were contacted via the existing database and responses to advertisements. Seventy-three individuals expressed interest to participate in the study. However, only 45 individuals completed the screening forms and three of those individuals were excluded as they did not meet the inclusion and exclusion criteria. Forty-two individuals were included in the study and randomized into one of the three groups (Figure 5.1). Baseline descriptive characteristics are summarized in Table 5.1. Groups did not differ significantly for any baseline descriptive variables ($p > 0.05$).

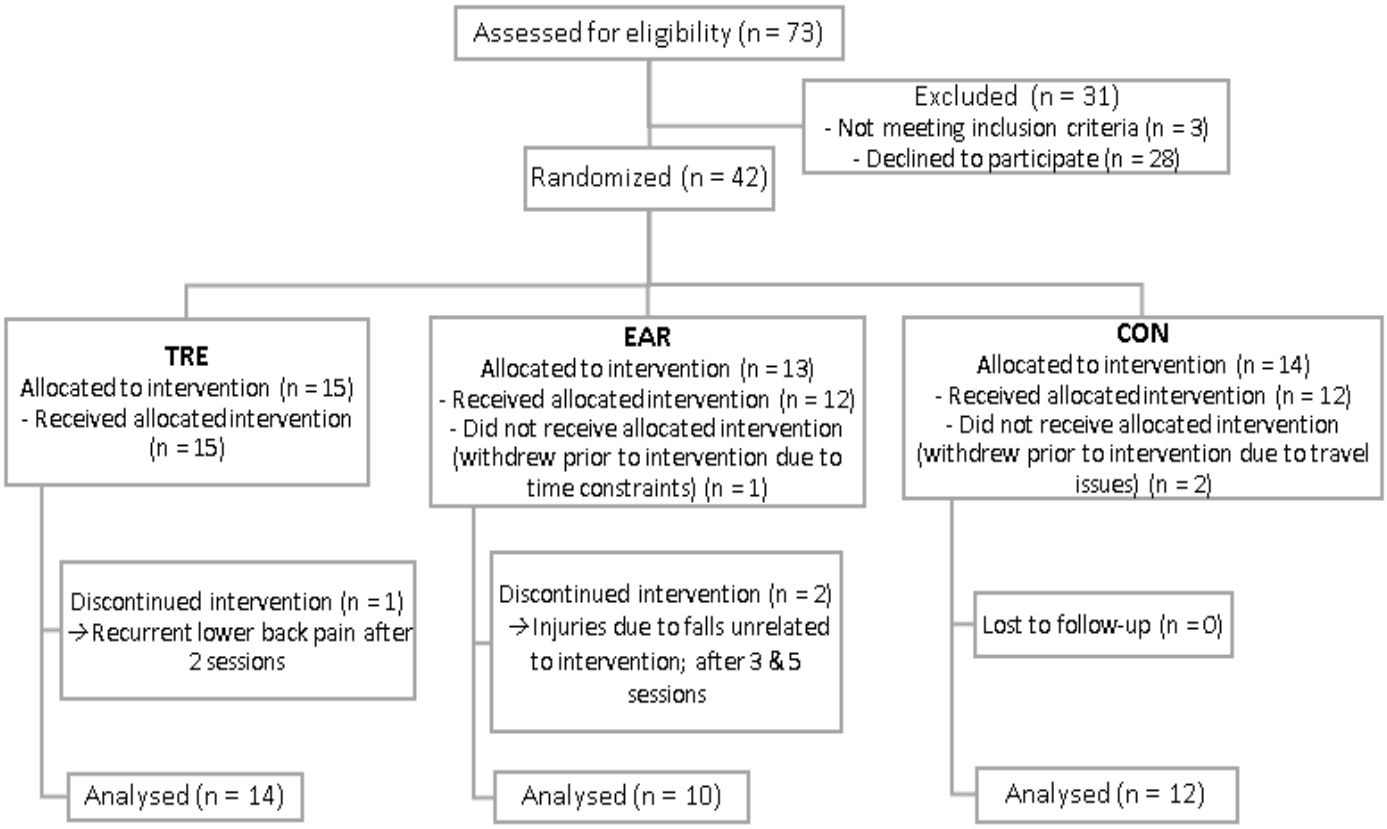


Figure 5.1: *Flow-diagram of participant inclusion and analysis*

Table 5.1: *Baseline demographic and clinical characteristics of participants; reported as $\bar{x}$ ± SD (range), unless otherwise specified*

Variable	TRE (n = 14)	EAR (n = 10)	CON (n = 12)	p-Value
Sex (% men)	64%	70%	75%	0.90
Age (years)	72.7 ± 7.5 (58 - 84)	70.3 ± 5.7 (61 - 76)	69.6 ± 8.3 (55 - 84)	0.58
H&Y Stage (%)				
I	29%	30%	42%	0.11
II	57%	50%	17%	
III	14%	10%	41%	
Disease severity				
MDS-UPDRS total (A.U.)	57.1 ± 21.7 (18 - 90)	60.9 ± 28.4 (26 - 106)	57.1 ± 22.4 (26 - 88)	0.4
MDS-UPDRS I (A.U.)	12.1 ± 6.0 (3 - 23)	12.6 ± 7.1 (4 - 29)	11.5 ± 6.1 (2 - 20)	0.98
MDS-UPDRS IV (A.U.)	1.5 ± 2.7 (0 - 9)	3.3 ± 3.5 (0 - 10)	2.8 ± 4.1 (0 - 12)	0.37
Years with PD (years)	5.1 ± 3.5 (0 - 12)	7.0 ± 5.9 (2 - 21)	5.8 ± 5.6 (1 - 17)	0.47
LEDD	500.0 ± 236.2 (0 - 800)	619.0 ± 404.1 (0 - 1400)	624.6 ± 302.9 (200 - 1250)	0.11
Side most affected (%)				
Right	43%	40%	42%	
Left	14%	40%	17%	
Both	43%	20%	41%	
Subtype scores (A.U.)				
TD	4.2 ± 5.0 (0 - 15)	5.7 ± 4.8 (0 - 15)	4.8 ± 5.6 (0 - 14)	0.79
PIGD	4.9 ± 2.7 (1 - 10)	5.4 ± 4.4 (1 - 14)	7.2 ± 3.8 (1 - 14)	0.26
AR	17.4 ± 7.5 (6 - 29)	17.9 ± 12.3 (1 - 41)	17.3 ± 8.9 (4 - 35)	0.99
Freezers (%)	29	50	58	0.81
Global cognition (A.U.)	24.9 ± 3.3 (18 - 29)	23.7 ± 2.8 (20 - 28)	24.8 ± 3.0 (18 - 29)	0.74
Functional capacity (m)	99.5 ± 26.3 (40.6 - 131.8)	86.8 ± 17.9 (61.0 - 108.8)	89.0 ± 30.0 (40.0 - 129.8)	0.43

TRE: Trauma and Tension Releasing Exercises group; CON: Control group; EAR: Exercise and Relaxation group; H&Y: Hoehn and Yahr; MDS-UPDRS: Movement disorder society - unified Parkinson's disease rating scale; A.U.: Arbitrary units; PD: Parkinson's disease; LEDD: Levodopa Equivalency Daily Dosage; TD: Tremor Dominant; PIGD: Postural Instability and Gait Disturbances; AR: Akinetic Rigidity

5.2 PRIMARY OUTCOME MEASURES

Results will be reported in the following order: baseline to post-intervention (T1-T4); retention (T4-T5). Tables show mean, standard deviations (SD) and 95% confidence intervals (CI), unless otherwise indicated. The relevant p-values are given in text, and differences are reported with the Hedges' g effect size (ES) along with the 95% CI of ES.

5.2.1 MOTOR SYMPTOMS

5.2.1.1 **Postural instability** – Mini BESTest

i) Intervention (T1-T4):

No treatment effect (GROUP x TIME) was found for the Mini BESTest total score or any of its domains nor were any influenced by the LEDD covariate ($p > 0.05$). A TIME effect was observed for domain 2 (Reactive balance) ($p = 0.04$). Table 5.2 summarizes the results of the Mini BESTest. No group differences were observed at baseline; however, at T4 the TRE group differed from CON group in their Mini BESTest domain 1 (Anticipatory control) score ($p = 0.047$), and at T2 the EAR and CON groups tended to differ in domain 3 (Sensory integration) ($p = 0.052$). No significant changes were observed in the total score of the Mini BESTest, except in the TRE group where T3 differed from T1 by 5,7% ($p = 0.04$, ES = 0.37^{S}, CI of ES: -0.8 – 1.5). The scores of the Mini BESTest domain 2 for the TRE group showed a 23.6% decrease from T1 – T2 ($p = 0.004$, ES = 0.59^{M}, CI of ES: -0.1 – 1.2) and a 12.7% decrease from T1 – T3 ($p = 0.046$; ES = 0.36^{S}, CI of ES: -0.1 – 0.9). Domain 2 for the EAR group showed a 16.2% decrease from T1 - T2 ($p = 0.04$, ES: 0.31^{S}, CI of ES: -0.5 – 1.1), and from T1 - T3 ($p = 0.04$, ES: 0.32^{S}, CI of ES: -0.4 – 1.1), as well as from T1 - T4 ($p = 0.04$, ES: 0.32^{S}, CI of ES: -0.4 – 1.1). Domain 3 showed that T2 scores were lower than baseline scores for TRE and EAR groups by 7.4% (ES = 0.69^{M}, CI of ES: 0.5 – 0.9) and 9.1% (ES = 0.39^{S}, CI of ES: -0.1 – 0.9), respectively ($p < 0.05$), however, the EAR group showed an increase from T2 – T3 by 14% ($p = 0.01$, ES = 0.61^{M}, CI of ES: -1.1 - -0.1). In domain 4 (Dynamic Balance) only the EAR group showed changes over time, with 15.8% increase at T3 from baseline ($p = 0.04$, ES = 0.51^{M}, CI of ES: -1.3 – 0.2) and 22.8% increase from T1 – T4 ($p = 0.02$; ES = 0.64^{M}, CI of ES: -15 – 0.2). As a whole, no meaningful changes towards improved postural instability occurred over time, between or within groups; although some fluctuations in performance are present especially for the TRE group.

ii) Retention (T4 - T5):

A treatment effect (GROUP x TIME) was found for Mini BESTest domain 1 ($p = 0.04$) in the retention phase, but not for the total score or the other domains ($p > 0.05$). The LEDD covariate did not influence any of the Mini BESTest scores in the retention phase ($p > 0.05$). A TIME effect was observed for the total score ($p = 0.01$) and domain 2 ($p = 0.04$) and domain 3 ($p = 0.04$). Increases from T4 to T5 were seen for the TRE group's Mini BESTest total scores ($p = 0.02$, ES = 0.48^{M}, CI of ES: -1.7 – 0.7); CON domain 1 ($p = 0.02$, ES = 0.65^{M}, CI of ES: -1.2 - -0.2), and EAR group's domain 3 ($p = 0.04$, ES = 0.57^{M}, CI of ES: -1.0 - -0.1). The CON group also showed a non-significant tendency to increase their total score at T5 ($p = 0.059$, ES = 0.42^{M}, CI of ES: -2.1 – 1.3). Table 5.2 summarizes the results of the Mini BESTest retention results.

Table 5.2: *Balance performance before, during and after interventions and at retention; reported as $\bar{x}$ ± SD (95% CI)*

Variable	Group	T1	T2	T3	T4	T5
Mini BESTest Total	TRE	21.5 ± 3.0 (19.0 – 24.0)	20.3 ± 3.4 (17.9 - 23.0)	20.3 ± 3.3 *S (17.8 - 22.8)	21.1 ± 3.0 (18.3 - 23.4)	22.5 ± 2.6 #M (19.7 – 26.0)
	EAR	18.3 ± 4.9 (15.4 - 21.2)	17.9 ± 4.9 (15.0 - 20.9)	18.9 ± 4.8 (16.0 - 21.9)	18.5 ± 7.5 (15.6 - 21.4)	19.6 ± 6.9 (15.7 - 22.4)
	CON	18.7 ± 4.8 (16.0 - 21.4)	16.6 ± 5.3 (15.5 - 21.0)	19.6 ± 5.6 (16.6 - 22.1)	19.5 ± 3.5 (15.8 - 21.2)	21.1 ± 3.8 (17.9 - 24.4)
Mini BESTest Domain 1 *Anticipatory control*	TRE	4.4 ± 0.9 (3.7 - 5.2)	4.3 ± 0.7 (3.6 - 5.2)	4.4 ± 0.8 (3.6 - 5.1)	4.6 ± 0.8 ac (4.0 - 5.5)	4.7 ± 0.7 (3.8 - 5.5)
	EAR	3.4 ± 2.2 (2.5 - 4.3)	3.9 ± 1.7 (3.0 - 4.8)	3.5 ± 1.7 (2.6 - 4.4)	4.2 ± 1.5 (3.0 - 4.8)	3.8 ± 1.8 (2.7 - 4.5)
	CON	3.7 ± 1.6 (2.9 - 4.5)	3.0 ± 1.4 (2.5 - 4.2)	3.9 ± 1.5 (3.0 - 4.7)	3.8 ± 1.1 (2.8 - 4.4)	4.6 ± 1.1 #M (3.8 - 5.5)
Mini BESTest Domain 2 *Reactive balance*	TRE	3.9 ± 1.4 (3.1 - 4.8)	3 ± 1.7 #M (2.2 – 4.0)	3.4 ± 1.3 *S (2.6 - 4.3)	3.7 ± 1.5 (2.8 - 4.5)	4.0 ± 1.3 (3.2 - 5.1)
	EAR	3.7 ± 1.6 (2.7 - 4.7)	3.1 ± 2 #S (2.1 - 4.1)	3.1 ± 1.9 *S (2.1 - 4.1)	3.1 ± 1.9 *S (2.1 - 4.1)	3.9 ± 1.9 (2.8 - 4.9)
	CON	3.0 ± 1.2 (2.1 - 3.9)	2.7 ± 1.1 (2.2 – 4.0)	3.0 ± 1.9 (2.1 – 4.0)	3.3 ± 1.1 (2.1 - 3.9)	3.9 ± 1.1 (2.7 - 4.9)
Mini BESTest Domain 3 *Sensory integration*	TRE	6.0 ± 0.0 (5.6 - 6.4)	5.6 ± 0.9 #M (5.0 – 6.0)	5.7 ± 0.8 (5.3 - 6.2)	6.0 ± 0.0 (5.5 - 6.4)	6.0 ± 0.0 (5.6 - 6.4)
	EAR	5.5 ± 0.8 (5.0 - 6.0)	5 ± 1.5 #S (4.5 - 5.5)	5.7 ± 0.5 #M (5.2 - 6.2)	5.3 ± 1.3 (4.8 - 5.8)	5.9 ± 0.4 #M (5.5 - 6.3)
	CON	5.8 ± 0.9 (5.3 - 6.2)	5.7 ± 0.7 bc (5.2 - 6.2)	5.7 ± 1.0 (5.2 - 6.2)	6.0 ± 0.0 (5.3 - 6.3)	6.0 ± 0.0 (5.6 - 6.4)
Mini BESTest Domain 4 *Dynamic Balance*	TRE	7.1 ± 1.5 (6.1 - 8.2)	7.4 ± 2.1 (6.3 - 8.6)	6.8 ± 2.5 (5.7 - 7.9)	7.4 ± 1.5 (6.1 - 8.3)	7.8 ± 1.4 (6.7 - 9.2)
	EAR	5.7 ± 1.7 (4.4 – 7.0)	6.6 ± 1.9 (5.2 - 7.8)	6.6 ± 1.6 *M (5.3 - 7.9)	7 ± 2.2 *M (5.5 - 8.0)	7.0 ± 2.4 (5.3 - 8.1)
	CON	6.3 ± 2.3 (5.1 - 7.4)	5.9 ± 1.8 (5.2 - 7.6)	7.0 ± 1.9 (5.5 - 7.9)	6.5 ± 2.0 (5.1 - 7.4)	6.7 ± 2.1 (5.4 - 8.1)

SD: Standard deviation; CI: Confidence Intervals; BESTest – Balance Evaluation Systems Test
[a]TRE: Trauma and Tension Releasing Exercises; [b]EAR: Exercise and Relaxation; [c]CON: Control
Between-group differences indicated by ab, ac or bc.
** Significant within-group differences from T1, p < 0.05*
 # Significant within-group changes from previous time point, p < 0.05
Hedges' g effect size: S – Small, M – Medium, L – Large

5.2.1.2 **Gait Disturbance** – Instrumented 2-Minute walk

i) Intervention (T1-T4):

No treatment effect (GROUP x TIME) was found for the gait parameters (p > 0.05); LEDD showed no influence on gait parameters (p > 0.05). A TIME effect was observed for gait speed (p = 0.01). Results for gait parameters are shown in Table 5.3. No baseline differences were observed; except between TRE and

CON for the variability (CoV) of trunk rotation range of motion (RoM) ($p = 0.04$). Group differences were observed only in stride length asymmetry at T2 between TRE and EAR ($p = 0.02$) and CON ($p = 0.01$).

For gait speed, the EAR group significantly improved from T1 to T3 by 0.07 m/s ($p = 0.01$, ES = 0.39^{S}, CI of ES: -0.7 - -0.5) and from T2 to T3 ($p = 0.01$, ES = 0.32^{S}, CI of ES: -0.6 - -0.4), while the CON group significantly decreased their gait speed ($p = 0.02$, ES = 0.13^{N}, CI of ES: -0.1 – 0.1) from T3 – T4. Interesting to note, the TRE group improved their overall (T1 – T4) gait speed by 0.07 m/s (ES = 0.33^{S}, CI of ES: -0.4 - -0.2) while the EAR had a 0.05 m/s (ES = 0.16^{S}, CI of ES: -0.2 - -0.1) overall improvement from T1 – T4 albeit not statistically significant ($p > 0.05$). The TRE group had significant changes in their stride length (SL) with a decrease of 4.9% at T2 followed by an increase in stride length at T3 by 4.7% ($p < 0.05$, with non-significant small ES). The SL asymmetry of the TRE group experienced an increase from T1 to T2 by 124% (ES = 0.52^{M}, CI of ES: -3.0 – 2.0) followed by a decrease of 56.4% (ES = 0.52M, CI of ES: -2.1 – 3.2) from T2 to T3 ($p < 0.01$). There were no significant changes in the EAR or CON groups in SL or the respective asymmetry parameter ($p > 0.05$). No differences were found for time spent in double support for all three groups ($p > 0.05$). No statistically significant changes were observed for trunk rotation, except for the EAR group who increased their trunk rotation by 14.4% from T1 to T4 ($p = 0.02$, ES = 0.19^{S}, CI of ES: -2.1 – 1.7). The CoV of trunk rotation showed statistically significant decreases ($p < 0.05$) for the TRE group only, with a decrease of 11.65% (ES = 0.32^{S}, CI of ES: 0.26 – 0.34) from T1 to T2 and an overall (T1 – T4) decrease of 8.23% (ES = 0.27^{S}, CI of ES: 0.2 – 0.3). Arm swing RoM increased by 40.4% from T1 to T2 for TRE group ($p = 0.02$, ES = 0.49^{M}, CI of ES: -6.6 – 5.7) followed by a decrease of 25.1% from T2 to T3 ($p = 0.04$, ES = 0.41^{M}, CI of ES: -6.2 – 7.0). Both EAR and CON group showed no significant changes in arm swing RoM ($p = 0.05$). Only the TRE group had less arm swing asymmetry at T4 albeit not significant ($p = 0.21$, ES = 0.48^{M}, CI of ES: -5.7 – 6.6) while the EAR group had a large increase in arm swing asymmetry of 30.12% and 31.7%, from T1 to T4 ($p = 0.02$, ES = 0.64^{M}, CI of ES: -8.5 – 7.2) and from T3 to T4 ($p = 0.017$, ES = 0.60^{M}, CI of ES: -9.4 – 8.2), respectively. Phase coordination index (PCI) showed only the TRE group significantly decreased their score from T3 to T4 by 21% ($p = 0.04$, ES = 0.55^{M}, CI of ES: -0.6 – 1.7) with a tendency to decrease from T1 – T4 ($p = 0.06$, ES = 0.46M, CI of ES: -0.7 – 1.6), while both EAR and CON groups had higher scores at the end of the intervention time, although increases were non-significant ($p > 0.05$, with non-significant small ES).

ii) Retention (T4 - T5):

No treatment effect (GROUP x TIME) was found for the gait parameters of the retention phase, except for arm swing asymmetry ($p = 0.01$); and LEDD covariate showed to have no influence on retention gait parameters ($p > 0.05$). A TIME effect was observed for stride length ($p = 0.01$). Only two variables showed significant changes at T5 (Table 5.3). Stride length of the CON group decreased ($p = 0.01$, ES = 0.05^{N}, CI of ES: -5.8 – 5.9) and arm swing asymmetry of the EAR group significantly decreased ($p = 0.003$, ES = 0.8^{L}, CI of ES: -7.9 – 9.5). Trunk rotation CoV showed a non-significant tendency to differ at T5 for EAR group ($p = 0.06$; ES = 0.60M, CI of ES: -0.4 - -0.3).

Table 5.3: *Gait parameters measured during 2-Minute Walk before, during and after the interventions and at retention; reported as $\bar{x}$ ± SD (95% CI)*

	Variable	Group	T1	T2	T3	T4	T5
Gait performance	2-Minute Walk Gait speed (m/s)	TRE	0.84 ± 0.23 (0.72 – 0.96)	0.86 ± 0.16 (0.68 - 0.92)	0.85 ± 0.24 (0.73 – 0.96)	0.91 ± 0.17 (0.71 – 0.95)	0.90 ± 0.19 (0.77 - 1.06)
		EAR	0.74 ± 0.15 (0.60 - 0.88)	0.75 ± 0.17 (0.61 - 0.89)	0.81 ± 0.18 #S *S (0.67 – 0.95)	0.77 ± 0.20 (0.63 - 0.91)	0.80 ± 0.24 (0.64 - 0.94)
		CON	0.76 ± 0.26 (0.63 - 0.88)	0.71 ± 0.23 (0.64 - 0.90)	0.79 ± 0.22 (0.66 - 0.92)	0.75 ± 0.26 #N (0.60 - 0.86)	0.71 ± 0.29 (0.65 - 0.94)
	Gait Quality						
Sturdiness	Stride length (%stature)	TRE	69.3 ± 10.3 (63.0 - 75.5)	65.9 ± 19.6 #S (56.0 - 69.8)	69 ± 11.1 #S (62.7 - 75.4)	71.4 ± 8.9 (62.7 – 76.0)	72.4 ± 8.2 (66.0 - 79.8)
		EAR	66.0 ± 11.1 (58.6 - 73.4)	68.1 ± 9.8 (58.8 - 73.9)	66.2 ± 11.4 (58.8 - 73.6)	65.8 ± 11.7 (58.4 - 73.2)	67.7 ± 10.3 (58.7 - 73.2)
		CON	65.0 ± 11.1 (58.2 - 71.7)	63.9 ± 11.1 (59.1 - 73.6)	67.7 ± 8.6 (60.7 - 74.8)	64.4 ± 13 (57.0 - 70.7)	63.7 ± 12.1 #N (60.2 - 74.1)
	Trunk rotation RoM (degrees)	TRE	4.9 ± 1.7 (59.1 - 73.4)	4.9 ± 1.5 (51.9 - 67.4)	4.9 ± 1.8 (59.5 – 74.0)	4.4 ± 1.3 (59.4 - 74.4)	4.6 ± 1.5 (2.6 - 6.7)
		EAR	5.9 ± 4.2 (53.2 - 70.1)	6.5 ± 4.3 (54.1 - 71.2)	6.2 ± 4.4 (54.8 - 71.7)	6.7 ± 4.4 *S (53.6 - 70.5)	7.0 ± 5.8 (4.4 - 8.8)
		CON	5.6 ± 2.2 (54.8 - 70.2)	5.8 ± 2.2 (56.7 - 73.0)	5.7 ± 2.8 (57.9 – 74.0)	6.3 ± 4.1 (54.0 - 69.6)	5.4 ± 2.7 (2.9 - 7.4)
	Arm swing RoM (degrees)	TRE	18.5 ± 10.0 (12.8 - 24.2)	25.9 ± 20.8 #M (19.6 - 33.4)	19.4 ± 11.1 #M (13.6 - 25.3)	17.3 ± 7.1 (10.8 - 23.6)	20.2 ± 11.6 (13.8 - 27.2)
		EAR	18.6 ± 11.4 (11.9 - 25.4)	21 ± 8.7 (13.6 - 27.5)	21.7 ± 10.8 (14.9 - 28.4)	22.9 ± 9.3 (16.2 - 29.7)	24.3 ± 14.2 (16.3 - 30.9)
		CON	20.3 ± 9.6 (14.1 - 26.4)	18.7 ± 6.6 (11.5 - 25.5)	23.7 ± 11 (17.5 – 31.0)	21.9 ± 10.7 (15.2 - 27.9)	21.1 ± 7.1 (17.2 - 32.3)
Symmetry	Stride length Asymmetry (%)	TRE	2.6 ± 0.9 (1.2 - 4.1)	5.9 ± 10.1 #M (4.0 - 7.9)	2.6 ± 0.7 #M (1.1 - 4.1)	2.5 ± 0.8 (0.8 - 4.3)	2.4 ± 0.9 (1.5 - 3.2)
		EAR	2.8 ± 1.6 (1.0 - 4.5)	2.7 ± 1.4 ab (0.9 - 4.6)	2.9 ± 1.7 (1.2 - 4.7)	3.0 ± 1.8 (1.3 - 4.8)	3.3 ± 2 (2.3 - 4.1)
		CON	2.8 ± 0.9 (1.2 - 4.4)	2.5 ± 0.8 ac (0.6 - 4.4)	2.3 ± 1.0 (0.5 - 4.2)	3.0 ± 1.7 (0.9 - 4.4)	3.0 ± 1.1 (2.0 - 3.9)

	Arm swing RoM Asymmetry (%)	TRE	50.9 ± 14.1 (41.9 - 59.9)	51.9 ± 17.9 (40.0 - 61.7)	49.2 ± 18.3 (40.1 - 58.7)	43.2 ± 17.1 (34.6 - 54.8)	46.4 ± 17.4 (36.6 - 61.1)
		EAR	39.9 ± 16.3 (29.2 - 50.6)	42.9 ± 11.7 (33.5 - 55.6)	39.4 ± 20.5 (28.7 - 50.1)	51.9 ± 19.4 #^{M} *^{M} (41.2 - 62.6)	36.2 ± 17.9 #^{L} (22.9 - 49.4)
		CON	41.2 ± 15.7 (31.5 - 51)	39.8 ± 18.8 (31.1 - 53.3)	43.7 ± 14.2 (31.8 - 53.1)	47.7 ± 20.4 (37.8 - 57.9)	46.4 ± 22.2 (31.9 - 58.6)
Steadiness	Trunk rotation RoM CoV (degrees)	TRE	0.24 ± 0.08 ^{ac} (0.20 - 0.28)	0.21 ± 0.09 #^{S} (0.16 - 0.25)	0.22 ± 0.07 (0.18 - 0.26)	0.22 ± 0.05 *^{S} (0.17 - 0.25)	0.21 ± 0.07 (0.16 - 0.26)
		EAR	0.19 ± 0.06 (0.15 - 0.24)	0.19 ± 0.06 (0.14 - 0.23)	0.18 ± 0.06 (0.14 - 0.23)	0.17 ± 0.04 (0.13 - 0.22)	0.20 ± 0.06 (0.15 - 0.25)
		CON	0.18 ± 0.06 (0.14 - 0.22)	0.18 ± 0.08 (0.15 - 0.24)	0.21 ± 0.08 (0.16 - 0.24)	0.20 ± 0.11 (0.16 - 0.24)	0.20 ± 0.06 (0.16 - 0.26)
Synchronisation	Time in Double support (%)	TRE	24.1 ± 5.3 (21.1 - 27.1)	21.2 ± 4.7 (19.6 - 26.1)	24 ± 5.6 (21.1 - 27.2)	22.4 ± 5.2 (20.7 – 27.0)	23.6 ± 4.2 (19.2 - 26.9)
		EAR	24.9 ± 6 (21.3 - 28.4)	26.9 ± 6.5 (22.5 - 29.7)	25.7 ± 6.3 (22.1 - 29.2)	25.6 ± 6.6 (22.0 - 29.1)	27.7 ± 7.6 (23.1 - 31.3)
		CON	24.8 ± 4.9 (21.5 - 28.0)	24.8 ± 6.7 (20.5 - 27.3)	24.2 ± 4.4 (20.3 - 27.0)	24.6 ± 5.9 (21.5 - 28.1)	26.8 ± 6.3 (20.7 - 28.8)
	Phase coordination index (%)	TRE	7.5 ± 2.9 (5.8 - 9.2)	8 ± 4.9 (6.1 - 9.9)	7.8 ± 2.8 (5.9 - 9.4)	6.1 ± 2.9 #^{M} (4.3 – 8.0)	6.6 ± 2.4 (4.5 - 8.4)
		EAR	6.5 ± 2.8 (4.5 - 8.5)	6 ± 2.9 (4.3 - 8.3)	7.4 ± 5.3 (4.8 - 8.8)	7.6 ± 4.7 (5.4 - 9.4)	6.9 ± 2.3 (5.3 - 9.5)
		CON	7.4 ± 2.9 (5.6 - 9.2)	7.7 ± 3.3 (5.4 - 9.4)	6.5 ± 2.7 (5.1 – 9.0)	9.1 ± 6.8 (5.8 - 9.6)	6.9 ± 2.0 (5.11 - 9.5)

SD: Standard deviation; CI: Confidence Intervals; RoM: Range of Motion; CoV: Coefficient of variance

[a]TRE: Trauma and Tension Releasing Exercises; [b]EAR: Exercise and Relaxation; [c]CON: Control;

Between-group differences indicated by ab, ac or bc.

** Significant within-group differences from T1, p < 0.05;*

 # Significant within-group changes from previous time point, p < 0.05

Hedges' g effect size: N – Negligible, S – Small, M – Medium, L – Large

5.2.2 NON-MOTOR SYMPTOMS

5.2.2.1 **Non-motor symptom frequency and severity** – NMSQuest & NMSS

i) Intervention (T1 – T4):

No treatment effect (GROUP x TIME) was found for Non-motor symptoms Questionnaire (NMSQuest) or Non-motor symptoms scale (NMSS) ($p > 0.05$); the NMSQuest did show a GROUP effect ($p = 0.01$) while only domain 1 (Cardiovascular) of the NMSS was influenced by LEDD as covariate ($p = 0.01$). Table 5.4 summarizes the central tendencies of the NMSQuest and NMSS and furthermore highlights the differences from T1 to T4. Baseline differences were observed at domain 3 (Mood/Cognition) and 5 (Attention/Memory) with the TRE and CON differing at both ($p < 0.05$). Differences between TRE and CON groups were found at T2, T3 and T4 of the NMSQuest ($p < 0.03$).

Post hoc analysis showed no significant changes within groups for NMSQuest, NMSS total, domain 2 (Sleep/Fatigue), 5 (Attention/Memory), and 7 (Urinary) ($p > 0.05$). Within-group changes were seen for CON group in domain 1 (Cardiovascular) from T1 - T3 ($p = 0.01$, ES = 0.42^{M}, CI of ES: -0.9 – 1.4). In domain 3, a non-significant tendency to decrease from T1 to T4 was observed for the TRE group ($p = 0.06$, ES = 0.37^{S}, CI of ES: -5.6 – 6.3) while the TRE group also showed a tendency in domain 4 (Perceptual problems/Hallucinations) to increase from T1 to T4 ($p = 0.07$, ES = 0.74^{M}, CI of ES: -1.2 - -0.4). In domain 6 (Gastrointestinal), the TRE group decreased significantly from T1 to T4 ($p = 0.048$, ES = 0.57^{M}, CI of ES: -1.6 – 1.7), the EAR group decreased by 12.5%, from T2 to T3 ($p = 0.050$, ES = 0.66^{M}, CI of ES: -1.5 – 1.7), while the CON group showed a tendency to decrease by 28.0% from T1 to T2 ($p = 0.06$, ES = 46^{M}, CI of ES: -2.5 – 3.0). Domain 8 (Sexual dysfunction) showed tendencies to decrease from T1 to T4 for EAR ($p = 0.089$, ES = 0.63^{M}, CI of ES: -2.0 – 2.8) and CON ($p = 0.06$, ES = 0.79^{L}, CI of ES: -1.7 – 3.0). The CON group showed a tendency to decrease their score in domain 9 (Miscellaneous) from T1 to T4 ($p = 0.06$, ES = 0.35^{S}, CI of ES: -4.1 – 4.3).

Additional analysis of the NMS subscales associated with perceived stress [226] revealed no interaction effect for any of the variables ($p > 0.05$) and only a TIME effect for the severity scores of the mood/cognition domain ($p = 0.02$) and frequency scores for Nocturia (in urinary domain) ($p = 0.05$). Post-hoc analysis indicated statistically significant improvement in mood severity for both TRE ($p = 0.01$, ES = 0.49^{M}, CI of ES: 1.6 – 2.4) and EAR ($p = 0.03$, ES = 0.73^{M}, CI of ES: 1.9 – 3.0) over T1 to T3. While frequency scores for anxiety, depression, flat moods & lacking pleasure (Mood domain) only showed an improvement in TRE group's T1 – T3 ($p = 0.02$, ES = 0.60^{M}, CI of ES: 2.0 – 2.5). Similar frequency scores for difficulty concentrating (domain 5 – attention/memory) only improved for the TRE group over T1 to T3 ($p = 0.04$, ES = 0.53^{M}, CI of ES: 2.2 – 2.4). For forgetting task frequency the TRE group improved over all from T1 to T4 ($p = 0.049$, ES = 0.49^{M}, CI of ES: 2.1 – 2.3). Finally, the Nocturia frequency only indicated a non-significant tendency to improve in the TRE group over the intervention ($p = 0.06$, ES = 0.34^{S}, CI of ES: 1.7 – 2.0). No other statistical or practical significant differences where observed in the other two group.

ii) Retention (T4 - T5):

No treatment effect (GROUP x TIME) was found for NMSQuest or NMSS ($p > 0.05$) of the retention phase, except for NMSQuest ($p = 0.04$). Tendencies was observed for treatment effect for domain 4 of NMSS ($p = 0.05$), TIME effect for domain 7 ($p = 0.07$) and GROUP effect for domain 9 ($p = 0.06$). The LEDD covariate showed to have no influence on retention for NMSQuest or NMSS ($p > 0.05$). Only NMSQuest of the TRE group showed to be significantly lower at T5 ($p = 0.04$, ES = 0.56^{M}, CI of ES: -1.7 – 1.9). No other variables had statistically significant changes at T5 (Table 5.4).

Additional analysis of the NMS subscales that are associated with perceived stress [226] showed no main effects over the retention phase. Post-hoc analysis revealed large practical significant differences from T4 – T5 for the TRE group's frequency score for concentration ($p = 0.07$, ES = 0.86^{L}, CI of ES: 2.7 – 3.0). No other statistical or practical significant differences where observed in the other two group.

Table 5.4: *Non-motor symptoms questionnaire and scale before during and after the interventions and at retention; reported as $\bar{x} \pm SD$*

Variable	Group	T1	T2	T3	T4	T5	% Change T1 - T4	T1 - T4 p-value & ES
NMSQuest	TRE	10.0 ± 4.5	9.7 ± 4.4	8.2 ± 3.8	8.1 ± 4.1	7.8 ± 3.8 #M	-1.9 (-19.1%)	0.87 N
	EAR	9.7 ± 4.3	9.5 ± 4.5	7.7 ± 5.3	7.7 ± 6.0	7.3 ± 4.2	-2.0 (-21.0%)	0.60 S
	CON	8.0 ± 4.1	8.2 ± 4.2 ac	8.2 ± 4.2 ac	8.3 ± 5.3 ac	7.0 ± 4.1	0.3 (3.8%)	0.12 M
NMSS total	TRE	47.6 ± 37.6	42.3 ± 29.8	31.8 ± 21.7	34.3 ± 26.4	32.8 ± 36.1	-13.3 (-27.9%)	0.27 S
	EAR	47.5 ± 46.1	32.3 ± 39.4	25.1 ± 42.9	25.0 ± 32.4	17.4 ± 23.4	-22.5 (-47.4%)	0.41 S
	CON	44.3 ± 30.2	28.9 ± 19.8	36.6 ± 30	35 ± 25.3	29.2 ± 26.6	-9.3 (-20.9%)	0.25 M
NMSS D1 *Cardiovascular*	TRE	2.2 ± 2.5	1.3 ± 1.2	1.6 ± 2.4	2.0 ± 4.0	1.1 ± 2.6	-0.2 (-9.7%)	0.36 M
	EAR	0.8 ± 1.2	0.9 ± 1.4	0.8 ± 2.0	1.0 ± 1.4	0.4 ± 0.8	0.2 (25.0%)	0.69 N
	CON	2.7 ± 2.9	1.8 ± 2.9	1.9 ± 2.1 *M	2.1 ± 2.3	2.4 ± 3.6	-0.6 (-20.8%)	0.31 S
NMSS D2 *Sleep/Fatigue*	TRE	9.3 ± 8.1	7.2 ± 5.8	6.8 ± 5.1	5.5 ± 5.4	7.4 ± 8.1	-3.8 (-40.9%)	0.11 M
	EAR	13.0 ± 10.1	9.3 ± 9.4	6.0 ± 8.6	6.0 ± 8.4	6.0 ± 6.6	-7.0 (-53.9%)	0.57 S
	CON	7.2 ± 7.3	5.1 ± 5.6	7.3 ± 7.3	7.3 ± 5.6	7.2 ± 7.3	0.8 (2.3%)	0.44 S
NMSS D3 *Mood/Cognition*	TRE	11.9 ± 16.8 ac	8.7 ± 14.9	5.7 ± 8.6	6.4 ± 11.3	10.4 ± 15	-5.5 (-46.4%)	0.06 S
	EAR	9.0 ± 11.0	5.7 ± 10.2	5.3 ± 12.9	3.6 ± 6.8	1.6 ± 2.3	-5.4 (-59.7%)	0.57 S
	CON	5.5 ± 7.6	1.8 ± 2.3	4.8 ± 8.4	3.7 ± 4	2.8 ± 3.4	-1.8 (-33.3%)	0.97 N
NMSS D4 *Perceptual problems/ Hallucinations*	TRE	0.1 ± 0.5	0.3 ± 1.0	0.5 ± 1.1	1.0 ± 1.6	0.1 ± 0.4	0.9 (600.0%)	0.07 M
	EAR	2.4 ± 4.2	0.5 ± 0.9	0.1 ± 0.4	0.7 ± 1.3	0.3 ± 0.8	-1.73 (-70.8%)	0.16 S
	CON	0.1 ± 0.3	0.0 ± 0.0	0.1 ± 0.3	0.6 ± 1.3	0.0 ± 0.0	0.5 (566.7%)	0.32 N

NMSS D5 *Attention/Memory*	TRE	7.7 ± 9.9 [ac]	7.3 ± 6.8	4.5 ± 4.4	5.7 ± 6.4	3.5 ± 5.0	-2.0 (-26.1%)	0.10 [S]
	EAR	6.7 ± 10.4	5.5 ± 10	6 ± 11.1	5.1 ± 8.7	2.7 ± 3.9	-1.5 (-22.9%)	0.73 [N]
	CON	4.8 ± 5.5	3.5 ± 4.3	3.1 ± 3.5	4.0 ± 6.1	2.4 ± 2.2	-0.8 (-15.8%)	0.97 [N]
NMSS D6 *Gastrointestinal*	TRE	3.3 ± 4.0	3.4 ± 3.9	2.3 ± 2.9	3.1 ± 4.0	3.6 ± 4.6	-0.2 (-5.7%)	0.048*[M]
	EAR	7.0 ± 8.3	3.0 ± 2.4	2.6 ± 4.0 #[M]	3.0 ± 2.7	1.1 ± 1.5	-4 .0 (-57.1%)	0.45 [S]
	CON	5.3 ± 7.8	3.8 ± 5.3	5.1 ± 7.9	4.3 ± 6.0	4.2 ± 7.4	-0.9 (-17.5%)	0.26 [S]
NMSS D7 *Urinary*	TRE	7.1 ± 6.5	7.8 ± 4.8	5.7 ± 4.7	4.8 ± 4.5	6.0 ± 6.2	-2.3 (-32.2%)	0.69 [N]
	EAR	9.6 ± 8.2	10.0 ± 9.9	7.3 ± 7.7	5.7 ± 7.2	5.8 ± 8.7	-3.8 (-40.2%)	0.78 [N]
	CON	8.3 ± 9.0	6.0 ± 7.4	7.5 ± 8.8	6.0 ± 8.3	8.4 ± 9.4	-2.3 (-27.3%)	0.45 [N]
NMSS D8 *Sexual dysfunction*	TRE	2.6 ± 4.7	2.3 ± 4.2	2.2 ± 3.7	2.8 ± 5.7	1.5 ± 2.1	0.16 (6.2%)	0.90 [N]
	EAR	2.9 ± 6.3	2.0 ± 3.5	0.7 ± 1.3	0.9 ± 1.6	0.3 ± 0.8	-2.0 (-70.2%)	0.09 [M]
	CON	4.6 ± 6.7	2.4 ± 6.0	5.9 ± 8.5	1.3 ± 1.4	0.3 ± 0.6	-3.4 (-73.0%)	0.06 [L]
NMSS D9 *Miscellaneous*	TRE	5.0 ± 6.3	4.2 ± 5.1	3.1 ± 3.3	3.0 ± 3.9	1.8 ± 2.5	-23.0 (-40.0%)	0.91 [N]
	EAR	2.4 ± 3.0	2.1 ± 2.0	1.7 ± 2.2	1.3 ± 2.8	1.3 ± 3.0	-1.2 (-48.9%)	0.49 [M]
	CON	6.9 ± 12.0	6.1 ± 7.7	4.0 ± 7.2	5.9 ± 5.4	1.6 ± 2.1	-1.0 (-14.8%)	0.06 [S]

SD: Standard deviation; CI: Confidence Intervals; ES: Effect size; NMSQuest: Non-motor symptoms Questionnaire; NMSS: Non-motor Symptoms Scale; D: Domain.
[a]TRE: Trauma and Tension Releasing Exercises [b]EAR: Exercise and Relaxation; [c]CON: Control
Between-group differences indicated by ab, ac or bc.
** Significant within-group differences from T1, $p < 0.05$*
 # Significant within-group changes from previous time point, $p < 0.05$
Hedges' g effect size: S – Small, M – Medium, L – Large

5.2.2.2 **Other NMS measures** – MDS-UPDRS Ib & PHQ-SADS

i) Intervention (T1 – T4):

No treatment effect (GROUP x TIME) was found for Patient Health Questionnaire – Somatization Anxiety Depression Symptoms (PHQ-SADS), which includes the PHQ-9 for depressive moods, 7-item General Anxiety disorder (GAD-7) and PHQ-15 for somatization ($p > 0.05$). Only PHQ-15 was influenced by the LEDD covariate ($p = 0.01$). There were no between-group differences observed at any of the time points (Table 5.5). Scores of the PHQ-9 for the TRE group decreased from T1 with 30.5% to T2 ($p = 0.02$, ES = 0.37^{S}, CI of ES:-1.9 – 2.6), with 30.1% to T3 ($p = 0.04$, ES = 0.36^{S}, CI of ES: -1.7 – 2.4), and 29.6% to T4 ($p = 0.02$, ES = 0.38^{S}, CI of ES: -1.6- 2.4). The GAD-7 scores showed no significant changes over time except between T1 and T3 for the EAR group, where scores decreased by 51.1% ($p = 0.04$, ES = 0.75^{M}, CI of ES: -0.7 – 2.2). Interesting to note, the TRE group decreased their score by 29.6% from T1 – T4 and the EAR had an overall improvement of 31.1% from T1 – T4, albeit not significant ($p > 0.05$). Within-group changes were observed for PHQ-15 from T1 - T4 for TRE ($p = 0.02$, ES = 0.60^{M}, CI of ES: -1.5 – 1.7) and from T1 to T2 for EAR group ($p = 0.02$, ES = 0.58^{M}, CI of ES: -2.3 – 2.4).

Table 5.5: *Depressive moods, anxiety and somatization before, during and after interventions and at retention; reported a $\bar{x} \pm SD$ (95% CI)*

Variable	Group	T1	T2	T3	T4	T5
Patient Health Questionniare-9 *Depressive moods*	TRE	6.7 ± 5.7 (4.1 - 9.3)	4.7 ± 4.9 #^{S} (1.4 - 7.1)	4.7 ± 5.2 *^{S} (2.1 - 7.4)	4.7 ± 4.1 *^{S} (1.6 - 7.1)	4.6 ± 6.1 (0.9 - 7.0)
	EAR	4.5 ± 6.4 (1.4 - 7.6)	4.7 ± 6.2 (1.6 - 7.8)	4.2 ± 7.6 (0.9 - 7.2)	3.1 ± 5.7 (-0.1 - 6.3)	3.3 ± 6.2 (-0.4 - 6.4)
	CON	3.8 ± 4.0 (1.0 - 6.7)	3.6 ± 2.5 (0.8 - 6.7)	3.3 ± 2.8 (-0.1 - 5.9)	4.4 ± 3.0 (1.4 - 7.4)	4.0 ± 3.2 (0.5 - 7.4)
General Anxiety Disorder -7 *General anxiety*	TRE	4.0 ± 6.2 (1.6 - 6.4)	4.8 ± 6.8 (2.4 - 7.8)	3.8 ± 5.2 (1.2 - 6.1)	2.8 ± 3.7 (0.3 - 5.4)	3.3 ± 3.4 (-0.4 - 4.8)
	EAR	5.0 ± 3.8 (2.2 - 7.8)	4.6 ± 3.5 (1.8 - 7.4)	2.4 ± 2.5 *^{M} (-0.5 - 5.3)	3.4 ± 3.7 (0.3 - 6.1)	3.0 ± 3.3 (0.1 - 5.7)
	CON	2.1 ± 3.3 (0.0 - 5.3)	3.6 ± 3.3 (0.5 - 6.1)	3.4 ± 4.1 (0.0 - 5.6)	3.0 ± 4.8 (0.2 - 5.6)	2.6 ± 4.7 (-0.01 - 5.6)
Patient Health Questionnaire-15 *Somatization*	TRE	6.1 ± 4.3 (6.6 - 11.2)	5.4 ± 3.7 (4.8 - 10.1)	5.8 ± 3.4 (5.1 - 9.9)	5.6 ± 3.7 *^{M} (3.4 - 8.6)	4.5 ± 5.1 (3.8 - 11.2)
	EAR	8.1 ± 5.5 (1.4 - 6.8)	7.9 ± 5.3 #^{M} (4.4 - 9.9)	7.7 ± 6.7 (3.3 - 8.7)	6.0 ± 5.1 (3.7 - 9.1)	5.9 ± 6.1 (1.7 - 9.5)
	CON	5.9 ± 3.4 (3.7 - 8.8)	7.0 ± 3.8 (3.4 - 8.9)	7.4 ± 4.6 (2.3 - 7.7)	7.3 ± 5.3 (2.1 - 7.4)	5.6 ± 3.6 (1.5 – 7.9)

SD: Standard deviation; CI: Confidence Intervals. [a]TRE: Trauma and Tension Releasing Exercises; [b]EAR: Exercise and Relaxation; [c]CON: Control. Between-group differences indicated by ab, ac or bc.
** Significant within-group differences from T1, $p < 0.05$;*
 # Significant within-group changes from previous time point, $p < 0.05$;
Hedge's G effect size: S – Small, M – Medium, L – Large

i) Retention (T4 - T5):

No treatment effect (GROUP x TIME) for the retention phase was found for PHQ-9, GAD-7 or PHQ-15 ($p > 0.05$); nor were any of these variables influenced by LEDD as a covariate ($p = 0.05$). Seen in Table 5.5, post hoc tests revealed that changes occurred at T5 ($p > 0.05$).

5.3 SECONDARY OUTCOME MEASURES

5.3.1 DISEASE SEVERITY – MDS-UPDRS Ib, II AND III

i) Intervention (T1-T4):

No interaction effect (GROUP x TIME) was found for Movement Disorders Society – Unified Parkinson's disease rating scale (MDS-UPDRS) Ib, II or III, or Postural Instability and Gait Disturbances (PIGD) subscore ($p > 0.05$). The covariate of Levodopa Equivalency Daily Dosage (LEDD) significantly influenced MDS-UPDRS II ($p = 0.01$) and PIGD ($p = 0.02$). A TIME effect was observed for MDS-UPDRS II ($p = 0.01$). Post-hoc analysis revealed there were no group differences at baseline of the variables displayed in Table 5.6. Between-group differences were observed at T3 between Trauma and Tension Releasing Exercises (TRE) and Control group (CON) ($p = 0.048$). No within-group differences are observed for MDS-UPDRS Ib ($p > 0.05$). Decreases in MDS-UPDRS II scores by 17.9% ($p = 0.01$, ES = 0.51^{M}, CI of ES: -1.4 – 2.6) and 11.2% ($p = 0.02$, ES = 0.29^{S}, CI of ES: -1.7 – 2.8) were seen for the TRE group between T1 to T3 and T4, respectively, as well as for the CON group from T1 to T4 by 23.7% ($p = 0.01$, ES = 0.51^{M}, -2.8 – 3.6). The TRE group showed a decrease of 28.9% in PIGD scores from T1 to T4 ($p = 0.046$, ES =0.6^{M}, CI of ES: -0.3 – 1.5).

ii) Retention (T4 - T5):

No treatment effect (GROUP x TIME) in the retention phase (T4 - T5) was found for MDS-UPDRS Ib, II, III, or PIGD subscore ($p > 0.05$). The covariate of LEDD significantly influenced MDS-UPDRS II ($p = 0.001$) and PIGD ($p = 0.01$). A TIME effect was observed for PIGD ($p = 0.01$). No statistically significant changes with groups were observed at T5 for MDS-UPDRS II or III (Table 5.6). Decreases were seen at T5 of PIGD scores for Exercise and Relaxation group (EAR) (16.7%, ES = 0.25^{S}, CI of ES: -1.5 – 1.9) and CON (23.9%, ES = 0.33^{S}, CI of ES: -1.3 – 2.0) ($p < 0.05$). The TRE group reduced their PIGD score by 21.8% albeit not significant ($p = 0.16$, ES = 0.56^{M}, CI of ES: -0.01 – 1.2).

Table 5.6: *Disease severity measured by MDS-UPDRS Ib, II and III before, during and after intervention and at retention; reported as $\bar{x}$ ± SD (95% CI)*

Variable	Group	T1	T2	T3	T4	T5
MDS - UPDRS Ib *Non-motor experiences of ADL*	TRE	7.6 ± 3.8 (5.2 - 10.1)	8.2 ± 4.2 (5.3 - 10.6)	7.9 ± 3.4 (5.7 - 10.6)	7.6 ± 4 (5.0 - 10.1)	6.5 ± 4.1 (4.7 - 10.0)
	EAR	8 ± 5.5 (5.1 - 10.9)	8.2 ± 5.7 (5.3 - 11.1)	7.7 ± 5.4 (4.4 - 10.3)	7.4 ± 5.1 (4.3 - 10.3)	6.3 ± 3.9 (3.5 - 9.8)
	CON	8.3 ± 3.7 (5.6 - 10.9)	9.9 ± 5.7 (6.7 - 12.3)	9 ± 6.5 (5.80 - 11.3)	7.2 ± 4.1 (4.1 - 9.5)	6.4 ± 4.1 (4.3 - 10.1)
MDS - UPDRS II *Motor experiences of ADL*	TRE	15.9 ± 6.2 (12.5 - 19.7)	14.3 ± 6.5 (10.2 - 17.8)	12.7 ± 3.9 *^{M} (9.4 - 16.6)	12.7 ± 4.5 *^{S} (9.7 - 17.0)	12.4 ± 7.2 (11 - 19)
	EAR	16.7 ± 9.1 (10.7 - 19.0)	16 ± 8.9 (10.5 - 18.9)	15.8 ± 9.3 (9.8 - 18.3)	15.1 ± 9.1 (9.2 - 17.9)	13.1 ± 7.3 (5.4 - 14.8)
	CON	15.4 ± 8.0 (12.7 - 20.4)	17 ± 7.0 (11.3 - 19.3)	13.1 ± 8.2 (10.3 - 18.3)	12.4 ± 7.3 *^{M} (9.3 - 17.1)	12.6 ± 9.0 (8.9 - 18.0)
MDS - UPDRS III *Motor examination*	TRE	27.5 ± 11.8 (19.5 - 33.7)	30.1 ± 11.3 (21.3 - 36.3)	27.2 ± 10.7 (19. 7 - 33.9)	29.6 ± 10.1 (19.3 – 34.0)	28.9 ± 9.1 (20.4 - 39.0)
	EAR	28.3 ± 16.6 (21.2 - 38.0)	28.5 ± 14.7 (23.1 - 39.9)	29.8 ± 15.9 (22.9 - 39.7)	30.2 ± 16.1 (22.1 - 38.9)	29.9 ± 16.8 (24.8 - 44.7)
	CON	27.3 ± 12.9 (21.1 - 36.5)	30.9 ± 13.1 (20.4 - 36.3)	28.2 ± 12.7 (21.0 - 36.9)	28.2 ± 15.6 (19.1 - 34.6)	25.3 ± 10.9 (20.0 - 39.7)

PIGD score *Postural instability & gait disturbances*	TRE	4.9 ± 2.7 (3.5 - 6.9)	4.1 ± 2.2 (2.6 - 6.3)	4.1 ± 1.8 [ac] (2.5 – 6.0)	3.5 ± 1.4 *[M] (2.1 - 5.7)	2.7 ± 1.3 (1.5 - 4.9)
	EAR	5.4 ± 4.4 (3.2 - 7.3)	5.5 ± 4.9 (3.4 - 7.4)	5.8 ± 4 (3.7 - 7.7)	5.4 ± 3.7 (3.2 - 7.2)	4.5 ± 3.6 #[S] (2.1 - 5.6)
	CON	7.2 ± 3.8 (5.2 - 8.9)	7.3 ± 3.5 (4.1 - 8)	6.9 ± 5 (4.9 - 8.8)	5.8 ± 3.4 (4.13 - 7.9)	4.4 ± 3.9 #[S] (2.71 - 6.2)

SD: Standard deviation; CI: Confidence Intervals; MDS – UPDRS: Movement Disorder Society – Unified Parkinson's disease rating scale; ADL –Activities of daily living; PIGD: Postural Instability and Gait Disturbances.
[a]TRE: Trauma and Tension Releasing Exercises; [b]EAR: Exercise and Relaxation; [c]CON: Control;
Between-group differences indicated by ab, ac or bc.
** Significant within-group differences from T1, p < 0.05*
 # Significant within-group changes from previous time point, p < 0.05
Hedges' g effect size: S – Small, M – Medium, L – Large

5.3.2 BALANCE CONFIDENCE – ABC SCALE

i) Intervention (T1 – T4):

No treatment effect (GROUP x TIME) was observed for Activity-specific balance confidence (ABC) scale scores over the intervention nor were scores influenced by LEDD ($p > 0.05$). As depicted in Figure 5.2, no between-group differences were shown for all groups between T1 and T4. No changes were observed for ABC scores over the intervention period ($p > 0.05$), where the EAR group improved their overall T1-T4 ABC score by 4.6%, and the TRE group increased their score by more than 8% from T1 – T4.

ii) Retention (T4 - T5):

No treatment effect (GROUP x TIME) was found for ABC scale retention scores, nor were scores influenced by LEDD ($p > 0.05$). However, a non-significant GROUP effect tendency was found ($p = 0.08$). The TRE and CON groups differed at T5 ($p = 0.02$), but no other statistically significant differences were observed ($p > 0.05$). A steady increase of the TRE ABC scores (Figure 5.2) was observed, with a 9.4% increase between T4 – T5 ($p > 0.05$).

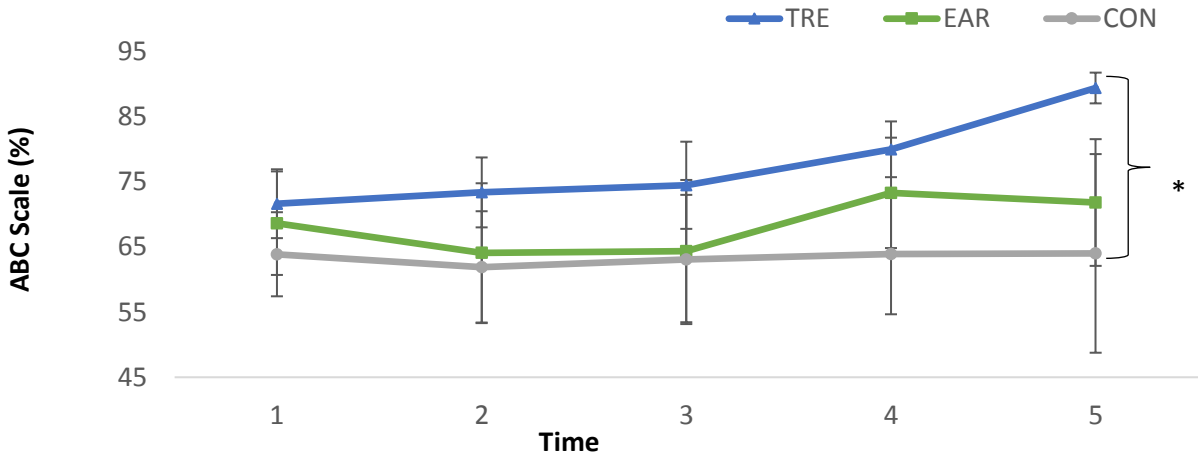


Figure 5.2: *Changes of balance confidence before, during and after the intervention and at retention ($\bar{x}$ ± SEM); *p < 0.05*

ABC: Activity-specific balance confidence scale; SEM: Standard error of measurement; TRE: Trauma and Tension Releasing Exercises; EAR: Exercise and relaxation; CON: Control

5.3.3 QUALITY OF LIFE – PDQ-8

i) Intervention (T1 – T4):

A treatment effect (GROUP x TIME) was observed for the Parkinson's disease questionnaire (PDQ-8) over the intervention ($p = 0.01$). Scores were not influenced by LEDD ($p > 0.05$). As depicted in Figure 5.3, no between-group differences were shown for all groups between T1 and T4. Over the intervention period, statistically significant changes were observed for TRE group from T2 – T3 ($p = 0.045$, ES = 0.59^{M}, CI of ES: -1.2 – 2.4), where the EAR group showed significant changes from T1 - T2 ($p = 0.04$, 0.30^{S}, CI of ES:-2.4 – 3.0) and T3 – T4 ($p = 0.01$, 0.40^{M}, CI of ES: -2.6 – 3.4). An overall (T1-T4) PHQ-8 score of the EAR group showed a decrease of 37.5% ($p = 0.002$, ES = 0.45^{M}, CI of ES: -2.3 – 3.12) while a non-significant decrease was observed for the TRE group (22.1%, $p = 0.07$, ES = 0.35^{S}, CI of ES: -1.3 – 2.0).

ii) Retention (T4 - T5):

No treatment effect (GROUP x TIME) was observed for the retention scores of PDQ-8 nor were scores influenced by LEDD ($p > 0.05$). As shown in Figure 5.3, no statistically significant differences were observed for the retention phase ($p > 0.05$).

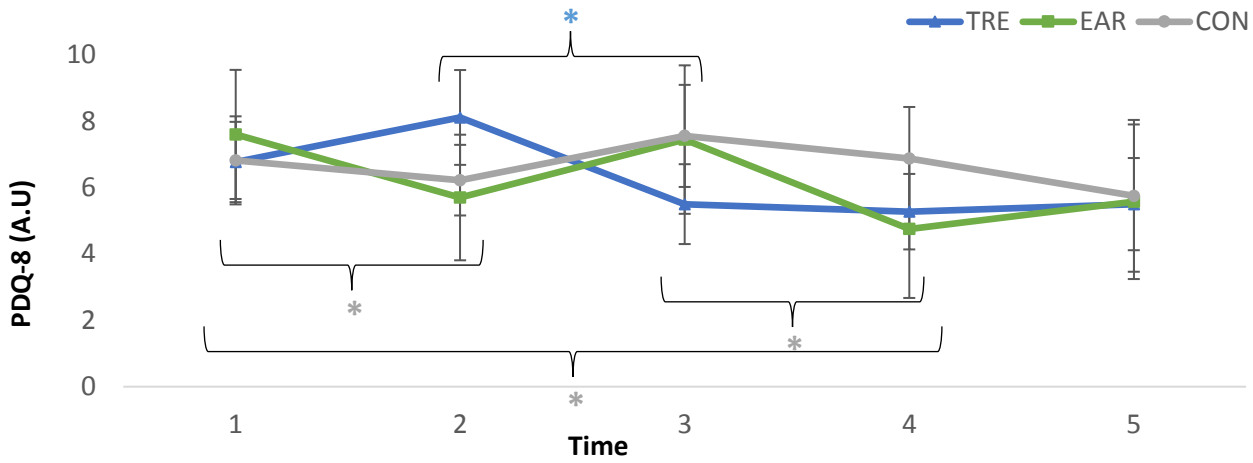


Figure 5.3: *Changes of PDQ-8 before, during and after the interventions and at retention ($\bar{x} \pm SEM$); *p < 0.05*

PDQ-8: Parkinson's disease questionnaire; SEM: Standard error of measurement; TRE: Trauma and Tension Releasing Exercises; EAR: Exercise and relaxation; CON: Control

5.3.4 MOTIVATION AND INTENSITY – IMI & RPE

Intrinsic motivation inventory (IMI) was measured after the 9-week intervention (Figure 5.4), which assessed five domains. No statistical differences were found between TRE and EAR in any of the domains ($p > 0.05$).

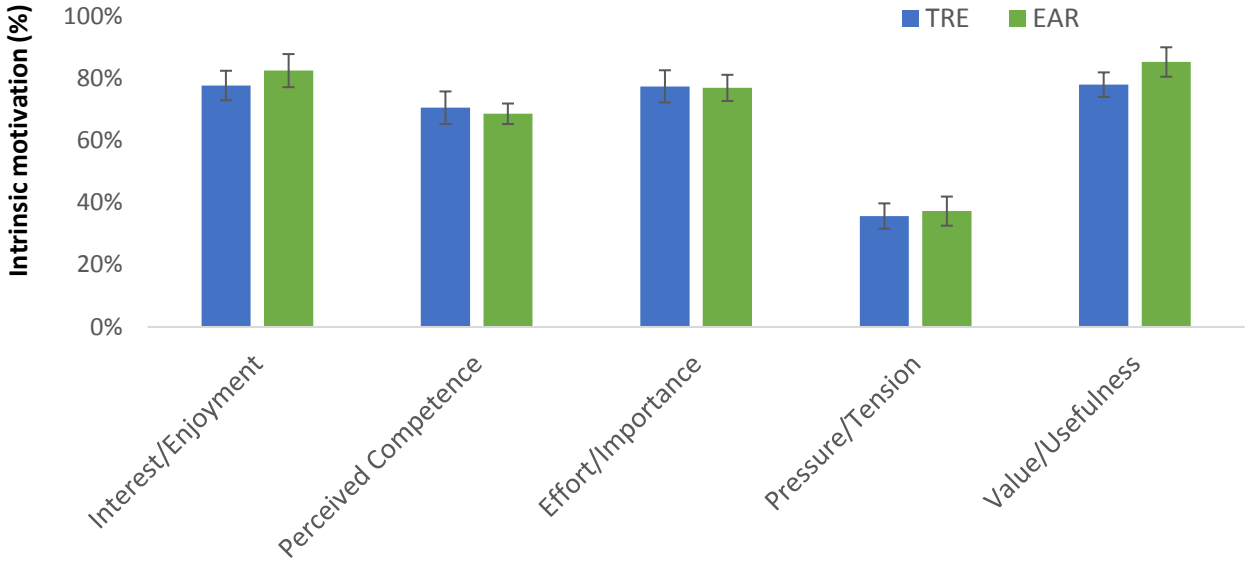


Figure 5.4: *Five domains of intrinsic motivation measured after interventions ($\bar{x}$ ± SEM)*

SEM: Standard error of measurement; TRE: Trauma and Tension Releasing Exercises; EAR: Exercise and relaxation

The intensity of the exercise interventions was recorded throughout the 9 weeks (Figure 5.5). The overall average Rate of perceived exertion (RPE) of both groups were 2.6 ± 1.0 for TRE group and 3.1 ± 0.6 for EAR group ($p > 0.05$).

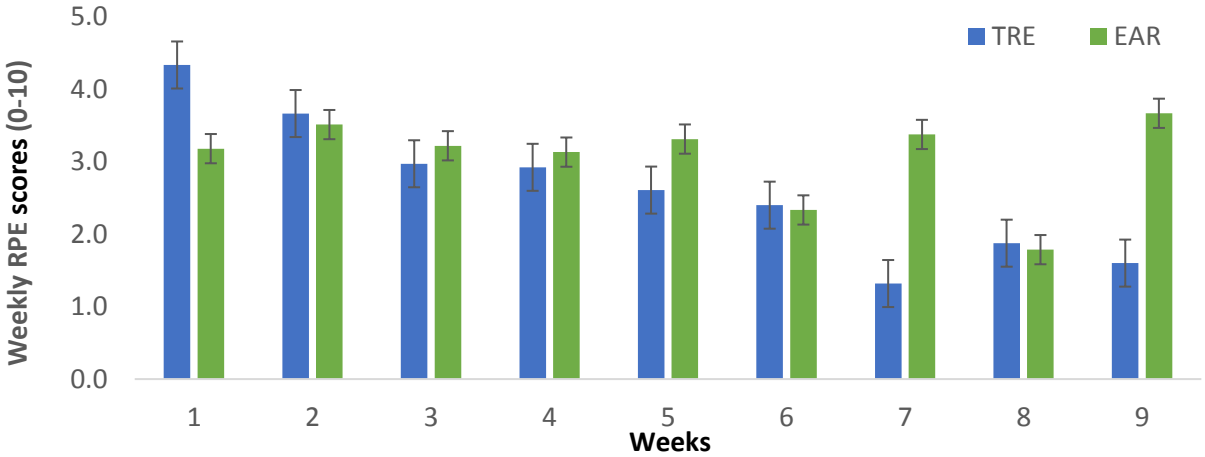


Figure 5.5: *Weekly RPE scores over the 9-week interventions ($\bar{x}$ ± SEM)*

SEM: Standard error of measurement; TRE: Trauma and Tension Releasing Exercises; EAR: Exercise and relaxation; CON: Control; RPE: Rate of perceived exertion

5.4 SUMMARY OF RESULTS

The main effects (GROUP*TIME GROUP, or TIME) and LEDD covariate of the intervention and retention periods are summarized in Table 5.7. A summary of the results is displayed in Table 5.8 per group over time. The table indicates increases and decreases of scores, as well as whether the change indicates an improvement or decline in performance.

Table 5.7: *Summary of significant main effects and covariate over intervention and retention periods*

Variables	Intervention	Retention
MDS - UPDRS II	LEDD: 0.01; TIME: 0.01	LEDD: 0.001
PIGD score	LEDD: 0.02	TIME: 0.001
Mini BESTest total		TIME: 0.01
Mini BESTest Domain 1		GROUP*TIME: 0.04
Mini BESTest Domain 2	TIME: 0.04	TIME: 0.04
Mini BESTest Domain 3		GROUP: 0.04
2MW gait speed	TIME: 0.01	
Stride length		TIME: 0.01
Arm swing RoM Asym		GROUP*TIME: 0.01
NMSQuest	GROUP: 0.01	GROUP*TIME: 0.04
NMSS Domain 1	LEDD: 0.01	
PHQ-15	LEDD: 0.01	
PDQ-8	GROUP*TIME: 0.01	

MDS-UPDRS: Movement Disorder Society – Unified Parkinson's disease rating scale; LEDD: Levodopa Equivalency Daily Dosage; BESTest: Balance Evaluation Systems Test; 2MW: 2-Minute walk; RoM: Range of motion, Asym: Asymmetry; NMSQuest: Non-motor symptoms questionnaire; NMSS: Non-motor symptoms scale; PHQ: Patient health questionnaire; PDQ: Parkinson's disease questionnaire; PIGD: Postural instability and gait disturbance.

Table 5.8: *Summary of statistically significant changes over time for all outcome variables (p < 0.05)*

Group	Outcome variables	T2 (3 weeks)	T3 (6 weeks)	T4 (9 weeks)	T5 (3 weeks retention)
TRE	Disease severity		*MDS-UPDRS II ↓ √	*MDS-UPDRS II ↓ √ * PIGD ↓ √	
	Postural instability	# Mini BESTest D2 ↓ X # Mini BESTest D3 ↓ X^{PS}	*Mini BESTest total ↓ X *Mini BESTest D2 ↓ X		#Mini BESTest total ↑ √
	Gait disturbances	# Stride length ↓ X	# Stride length ↑ √	* Trunk rotation CoV ↓ √^{PS}	
		# Stride length asym ↑ X	# Stride length asym ↓ √	# PCI ↓ √	
		# Stride velocity ↓X	# Stride velocity ↑ √		
		# Trunk rotation CoV ↓ √^{PS} # Arm swing RoM ↑ √	# Arm swing RoM ↓ X		
	Non-motor	# PHQ-9 ↓ √	# PHQ-9 ↓ √	*NMSS D6 ↓ √	# NMSQuest ↓ √
				* PHQ-9 ↓ √ * PHQ-15 ↓ √	
	Quality of life		# PDQ-8 ↓ √		
EAR	Disease severity				# PIGD ↓ √
	Postural instability	# Mini BESTest D2 ↓ X	* Mini BESTest D2 ↓ X	* Mini BESTest D2 ↓ X	# Mini BESTest D3 ↑ √^{PS}
		# Mini BESTest D3 ↓ X	# Mini BESTest D3 ↑ √^{PS} * Mini BESTest D4 ↑ √	# Mini BESTest D4 ↑ √	
	Gait disturbances		*# Gait speed ↑ √^{PS}	* Trunk rotation RoM ↑ √ *# Arm swing asym ↑ X	# Arm swing asym ↓ √
	Non-motor	# PHQ-15 ↓ √	# NMSS D6 ↓ √ * GAD-7 ↓ √		
	Quality of life	# PDQ-8 ↓ √	# PDQ-8 ↓ √	* PDQ-8 ↓ √	
CON	Disease severity			* MDS-UPDRS II ↓ √	# PIGD ↓ √
	Postural instability				# Mini BESTest D1 ↑ √^{PS}
	Gait disturbances			# Gait speed ↓ X	# Stride length ↓ X
	Non-motor		* NMSS D1 ↓ √		

TRE: Trauma and Tension Releasing Exercises; EAR: Exercise and Relaxation; CON: Control; BESTest: Balance Evaluation Systems Test; Asym: Asymmetry; CoV: coefficient of variance; RoM: Range of motion, PHQ: Patient health questionnaire; PDQ: Parkinson's disease questionnaire; MDS-UPDRS: Movement Disorder Society – Unified Parkinson's disease rating scale; NMSQuest: Non-motor symptoms questionnaire; NMSS: Non-motor symptoms scale; PIGD: Postural instability and gait disturbance; PCI: Phase coordination index; GAD: General anxiety disorder; D: domain

** Significant within-group differences from T1, p < 0.05; # Significant within-group changes from previous time point, p < 0.05*

↑ / ↓ Increase or decrease in score; √ / X Improvement or decline in performance; ^{PS}Practical significant effect size

CHAPTER 6 – DISCUSSION

In this chapter, the main findings are discussed as a support for or against the study hypothesis. The outcome measures are deliberated in the same order as the results of the previous chapter. Additionally, the retention period is discussed separately, as well as specific aspects of the intervention. Followed by the limitations whilst also highlighting the recommendations and considerations for future research. Lastly, the hypothesis statement is discussed in the conclusion which brings the chapter to a close.

This study set out to investigate the effects of relaxation-based exercises with therapeutic neurogenic tremors (TNT) on selective motor and non-motor symptoms of individuals with Parkinson's disease (IwPD). The main findings of this study indicate that relaxation-based exercises with TNT (Trauma and Tension Releasing exercise (TRE)) might cause beneficial changes in gait steadiness and synchronization, non-motor symptoms such as depressive moods and somatisation as well as motor experiences of activities of daily living (ADL), specifically postural instability and gait disturbances (PIGD). However the results are not clear on whether TRE is better that EAR since no significant between-group changes were found. Improvements were seen in both the EAR and TRE groups for gastrointestinal complaints and quality of life (QoL), as well as both groups showed a deterioration in reactive balance performance. Furthermore, the Relaxation and Exercise (EAR) group showed improvements in sturdiness and stability of gait, and anxiety; with significant fluctuations (referring to the changes from one time point to another) in sensory integration. The control group (CON) had deterioration in gait speed and cardiovascular-related non-motor symptoms, but improved in motor experiences of ADL. Based on the main statistical significant findings, both the TRE and the EAR interventions show to be beneficial towards motor and non-motor symptoms to some degree. More insights are derived when the results are discussed in a practical context.

6.1 PARTICIPANTS

Participants in the three groups did not differ in terms of descriptive characteristics. However there are several factors that were interesting to observe, for example, the EAR group had a larger range of disease duration which is reflected in the large range of MDS-UPDRS total score. As Parkinson's disease (PD) is a progressive disorder, the longer the disease duration the greater the impact on motor function, QoL and ADL [282]. Another aspect to note is the distribution of H&Y stages in the groups, with TRE and EAR groups being similar with a higher prevalence of H&Y stage II individuals, while the CON group had higher distribution in H&Y stages I and III. This distribution is also represented in the higher PIGD score in Table 5.6 for the CON group; as postural instability increases with disease progression marked with a higher H&Y stage [2,13]. Interestingly the TRE group had a relatively low PIGD score and few participants with freezing of gait (FoG), thus changes in those variables are of value since their improvements were possibly due to the intervention, and not subject to the "regression to the mean" phenomenon [283]. Sex and FoG were not tested as covariates for this current study since they did not differ at baseline, and therefore it was assumed that these variables would not influence the results of the current study.

6.2 PRIMARY OUTCOME MEASURES

6.2.1 MOTOR SYMPTOMS

6.2.1.1 **Postural instability**

The interventions did not have a clinically significant effect on the overall balance performance of the groups since a change of more than 4-5 points on the mini BESTest is considered the minimal detectable change [245,284]. Research has indicated that a score lower than 21 could differentiate between IwPD with and without postural instability [285], and the current study's results support this notion since the group that had the lowest PIGD score also had the highest mini BESTest score (i.e. TRE group).

Within the separate domains and across time points there are several fluctuations in scores which make interpretations difficult. Therefore the statistical significant changes with practical significance, based on the effect sizes, are mainly discussed. Worse performance in sensory integration (domain 3) was noted for the TRE group three weeks into the intervention. Although this decrease in sensory integration has practical significance, when observing this score across the intervention it can be noted that the TRE group achieved their baseline score again after 9 weeks. A similar pattern is observed for TRE reactive balance scores, however, the results do not indicate any practical significance. For the EAR group a significant improvement is noted from T2 to T3, however, this improvement is preceded by a non-significant decrease in performance between T1 to T2. Furthermore, the EAR group showed worse reactive balance performance, but better dynamic gait performance after 9 weeks; albeit not have practical significance.

Fluctuations and changes in balance most likely did not result in clinically significant deteriorations or improvements in performance. However, these fluctuations in performance allude to the possibility that these interventions might have caused attractor states to shift [74]. Ross and Ware (2013) used the dynamic systems theory to explain the phenomenon of TNT, where they theorize the tremor is an innate way for the body to reorganize itself through seemingly chaotic movements to shift attractor states of movement. Thus detriments or even improvements in balance performance might be due to changing attractor states which results in fluctuations in outcome measures. Harbourne and Stergiou (2009) [219] argue that fluctuations are a normal healthy part of a complex dynamic system, and that attractor states might take some time to settle into a new state or revert back to the old one once the stimulus to the organism changes. Furthermore the human organism is a complex non-linear system and changes that occur should not be viewed in isolation but as part of the whole. Part of the unpredictability of a non-linear system is determining where and to what extent changes might occur. Thus it could be that both the TRE and EAR interventions caused dynamic states to fluctuate, either through the addition of TNT and/or possibly through minimizing the individual constraints (such as perceived stress, mood, flexibility, etc.) placed on the participants motor behaviour. In other complementary and alternative medicine (CAM) therapies often used on IwPD, such as yoga, Thai Chi, mindfulness-training, researchers have found these therapies to reduce stress and improve mood [286], which could possibly influence balance performance and postural instability [63].

However, another possible reason could explain the fluctuations marked in both interventions groups. The EAR group might have experienced the TNT to a lesser degree as it could be that the EAR intervention was not completely devoid of any possible TNT [66,190]. Two researchers and founders of different exercise therapies utilizing TNT, namely David Berceli (TRE) and Ken Ware (Neurophysics Therapy), both suggested that the tremoring mechanism affects individuals at different times and in different ways. Some individuals might experience very slight tremors, not noticeable from the

outside, and even though participants are instructed to stop any tremoring, it might be too slight for novices to recognise it [66]. For the purpose of this research, the exercises played an important role to ensure participants physically performed the same tasks to ascertain the effect on the TNT above the relaxation-based exercises. As this was the first study investigating the effect of TRE of motor aspects such as balance and gait, it was important to ensure the experimental (TRE) and sham (EAR) groups followed the same exercise protocol. Thus the EAR group might have experienced the tremor even without their awareness of it while participating in the sham intervention. These factors make it difficult to draw plausible conclusions with a high degree of certainty and findings, significant and/or practical, should be interpreted with caution.

6.2.1.2 **Gait Disturbance**

The findings demonstrate the fluctuation of gait disturbances experienced by IwPD (seen in the CON group's non-significant changes). The only baseline differences between groups were observed for the variation (CoV) in trunk rotation with the TRE group presenting with a higher trunk rotation CoV than the CON group. This is an interesting observation since the control has more freezers, and thus more gait variability would be expected [287], and the opposite is observed. Information regarding gait performance and quality were measured. Gait performance was measured with gait speed, which is a clinically important factor as it plays a role in independent living [20]. The EAR group demonstrated a statistically significant improvement in gait speed of 0.07 m/s after 6 weeks of the intervention and maintained their faster speed to the end of the intervention. This improvement had a small effect and did not show any practical significance, however, research suggests that improvements in gait speed between 0.05 - 0.13m/s is a small clinically significant difference for IwPD [288]. Interestingly the TRE group also showed an increase in gait speed of 0.07 m/s at the end of the intervention, and although this change is not statistically significant it did show a small practical and clinical significance.

Quality of gait can be considered of almost greater important than performance as it gives an indication of safe and effective ambulation and is an indication of better motor control [20,101,253]. For the TRE group several gait parameters underwent changes, however, some of these changes can be explained by an anomaly in the data (i.e. stride length and asymmetries) while changes in trunk rotation CoV and phase coordination index (PCI) are possible due to the intervention. In the formerly mentioned variables, a pronounced spike occurred from T1 to T2 and back to T3 for stride length (SL) and its asymmetry as well as arm swing range of motion (RoM). Upon additional investigation into individual participant data, it revealed that this spike occurrence did not occur in all participants, and this anomaly can be explained by one participant's data that impacted the group average significantly. Even though the data was trimmed through winsorization to minimize the effect of any possible outliers [278], the spike is still prominent in the mean values of the variables. It could be possible that the particular participant was influenced by the TRE intervention, or the participant did not test well on that specific day. Part of the research process is that we make the assumption that participants will try their best during test sessions, however, this is sometimes not the case. However, a benefit of the current study's design is the multiple testing times which allows us to track changes over time and conclude that this anomaly in data only occurred once in one participant and it did not have a long-term effect.

A significant reduction in trunk rotation CoV after the intervention was observed for the TRE group with a small practical significance. This indicates that the TRE group walked with less variation in trunk rotations [247,253]. This finding is supported with the lower score in the phase coordination index (PCI) observed at T3-T4 and the tendency towards a lower score at T1-T4, both with a moderate effect size. A lower PCI indicates better coordination between the body segments involved in

ambulation [18], which is a valuable finding since IwPD notorious have impaired coordination and synchronization compared to healthy controls [289], furthermore impaired coordination is associated with risk of falling in the elderly [290]. Researchers have found that IwPD have more in-phase coordination when walking [223,291], which means their upper and lower body move with one another rather than opposite one another as is seen in normal opposite-arm-and-leg walking. This in-phase coordination contributes to increased trunk immobility and reduced arm swing [130,289]. Another interesting gait parameter that could have been influenced by the TRE intervention is arm swing asymmetry, noted with a lower score after the intervention with moderate effect size, albeit not statistically significant. Asymmetrical arm swing and reduced trunk rotation are some of the earliest signs of gait dysfunction in untreated PD [132,292] and might influence each other resulting in greater coordination problem for IwPD [289]. Furthermore improved inter-limb coordination might explain the clinical improvement in gait speed observed for the TRE group [293]. Therefore it can be stated that after the nine-week intervention the TRE group walked faster with more coordination due to improvements in gait steadiness, synchronization and symmetry [253].

For the EAR group, more trunk rotation was seen after the intervention, although it was not practically significant, however, it could possibly have helped with the improvement in gait speed [293]. Interestingly a significant increase of arm swing asymmetry was observed in the EAR group at T4. Perhaps the exercises helped to increase trunk rotation and as result, more movements in the trunk resulted in more movement in arm swing [132,289], which can be seen be the insignificant but consistent increases in arm swing RoM over the intervention. Although based on the data, it can be concluded that only one arm's swing was increased thus adding to the significant arm swing disparity seen in the asymmetry scores. Therefore it can be stated that after the nine-week intervention the EAR group walked faster with greater trunk rotation coupled with great arm swing asymmetry, indicating improvements in sturdiness and detriments in symmetry.

Taken together, these results from the gait parameters give interesting insights into the interventions. Both groups improved in gait speed which might indicate a practical impact of relaxation-based exercises. It cannot be stated with scientific certainty that the TRE group had better gait after the nine weeks, however the results show that the TNT might have had a more beneficial effect that the relaxation intervention without the additional self-initiated tremors. The TRE group showed greater practical and clinically significant improvements in gait performance and quality (noted by the decrease in the variability of trunk rotation). It can be speculate that these improvements might have been due to the TNT that are theorized to release the tight psoas muscles, associated with chronic stress and trauma [8,65,207], and have been identified as a problematic muscle in IwPD [211]. Perhaps the addition of deliberate TNT, compared to unintentional TNT possibly experienced by the EAR group, helped the body to utilize these mobility gains in a productive way, through self-organization and the Dynamic Systems Theory [74], into functional improvements in synchronization.

6.2.2 NON-MOTOR SYMPTOMS

6.2.2.1 **Non-motor symptom frequency and severity**

Between-group differences were observed at baseline with the TRE group having a higher score than the CON group for mood/cognition (domain 3) and attention/memory (domain 5) in the Non-motor symptom scale (NMSS). These higher scores might be explained with the TRE group's non-significant higher depressive moods and anxiety scores as measured by the PHQ-9 and GAD-7 respectively. Depression and anxiety have been linked to cognition [155,294], however, the TRE and CON groups showed no significant differences in baseline score of global cognition, which measures attention and

memory. It could be that the Montreal Cognitive Assessment is a more objective measurement of global cognition while the NMSS is a subjective scale about how IwPD perceive their attention and memory to be; which could have led to the contradicting findings. The amount of non-motor symptoms (NMS) identified by the NMS questionnaire (NMSQuest) decreased by an average of 2 points (or symptoms) after the intervention for the TRE and EAR groups, but not for the CON group. The frequency and severity of global NMS scores decreased from T1 to T4 by 13.27 points for the TRE group and 22.5 points for the EAR group, which according to Martinez-Martin (2009)[256], signifies a MCID of 13.91 points. No noteworthy statistical of practical changes occurred in the domains of cardiovascular and attention/memory. Several changes with practical significance were noted in the sleep/fatigue, mood/cognition, perceptual problems/hallucinations, gastrointestinal, urinary, sexual dysfunction and miscellaneous domains.

The sleep/fatigue domain of the EAR group improved above the MCID of 4.31 points [256] while the TRE group almost showed a MCID at T4 with a decrease of 3.81 points. For mood/cognition both the TRE and EAR group achieved a MCID from T1-T4 with decreases in scores of more than 4.28 points [256], however, only the TRE group showed a statistical tendency to improve. The TRE group showed a tendency to experience more perceptual problems/hallucinations as measured by domain 4 with a moderate practical significance although this increased score did not qualify as a MCID. Gastrointestinal complaints decreased for both groups after the intervention, with the TRE group showing a statistically significant lower score while the EAR group achieved a clinically significant difference (Martinez-martin 2009). Additionally, the EAR group's urinary symptoms showed a MCID from T1-T4, while the CON group showed an MCID improvement in sexual dysfunction domain scores with a tendency to decrease (Martinez-martin 2009). Lastly, miscellaneous aspects were measured in domain 9, such as unexplained pain or weight loss, and the CON group showed a strong tendency towards improvements, however without any clinical of practical significance.

Investigating the changes in each group as well as changes that overlap might give insight into what effects the interventions could have had. The relaxation-based exercises, regardless of TNT, seems to have a beneficial effect on global NMS severity and frequency since both the TRE and EAR groups lowered their total NMSS scores. The domains that seem to be influenced in both these groups are mood/cognition and gastrointestinal complaints (which falls under autonomic dysregulation symptoms of IwPD), indicating that relaxation-based exercises might improve these symptoms. Improvements could possibly be due to the intervention causing deep relaxation and thus helping a hyper-aroused nervous system calm down [66]. It is difficult to say if the improvements are solely due to the relaxation-based exercises, or if the EAR group also experienced TNT to a lesser extent, as mentioned previously. However, regardless of the cause of the reduction in severity and frequency of these two domains, their impact of the QoL of IwPD should not be overlooked. Additional analysis on the NMS relating to perceived stress [226], indicate that the TRE was more effective in minimizing the frequency and severity of mood with a moderate practical significance, as well as improve the scores for concentration, forgetfulness and nocturia with practical significance. The EAR group only improved their severity mood score. These results attest to the beneficial effect relaxation-based exercises have on the severity of mood as it relates to perceived stress, and furthermore, it shows that exercise with TNT could have a beneficial effect of the frequency of symptoms that relates to perceived stress.

Over and above the improvements in mood/cognition and gastrointestinal complaints, the TRE group showed a tendency towards worse perceptual problems/hallucinations, and this might be explained by therapy possibly bringing forth certain emotional or psychological states, and since TRE practitioners were asked not to dwell on this it might have limited participants to make sense of their internal state, which is usually assisted with during normal TRE sessions without the limitations of the

research. In the EAR group, improvements were observed in the domains for sleep/fatigues, and urinary. These improvements could suggest that the relaxation-based exercises might have increased awareness of participants' physical state and sensations more so than the exercises with TNT. Interestingly improvements in the CON group were also observed in sexual dysfunction and miscellaneous aspects such as unexplained fatigue, sweating and changes in weight and smell. These changes are non-significant but might allude to the placebo effect of being observed and learning effect of being asked the same questions, perhaps making them more aware of certain physical complaints [283]. Important to note that the placebo effect has been shown to be quite powerful in IwPD [295] and that the expectation that drives placebo effect is influenced by trust [112] which might be increased during the repeated measures of the current study.

6.2.2.2 **Other NMS measures**

The other NMS measures (such as depressive moods, anxiety and somatic symptoms) were included to investigate specific NMS in isolation, specifically depressive moods, and to gain further insight into perceived stress experienced. It is important to measure anxiety, somatic symptoms, and depressive moods together as researchers have found their comorbidity to be 50% in individuals in primary care [261] and the symptoms very importantly overlap with perceived stress symptoms [36,37,155,193]. This triad of symptoms or the individual subscales have been found to be a valid measure of perceived stress and posttraumatic stress disorder [29,75,260,265,296]. In this current study, the CON group had no meaningful changes in the depressive moods, general anxiety and somatisation. In both the TRE and EAR groups a gradual decline in symptoms of depressive moods, general anxiety and somatisation were observed, with the TRE group showing a statistically significant decline from T1 to T4 for depressive moods and somatisation. The EAR group had a significant decline in general anxiety from T1 to T3, and showed a tendency towards lower scores for somatisation with moderate practical effect.

When the ≥ 9 cut-off score is applied to participants' depressive mood baseline scores, it shows that 19.4% of participants had moderate levels of depressive moods. Researchers have found that IwPD generally experience a milder form of depression; i.e. depressive moods [113,116], thus if the ≥ 5 cut-off score is applied it reveals that 38.9% of participants had mild depression at baseline which is similar to the expected prevalence between 35 – 58% [2,156]. In a 2018 article by Herman and colleagues, they state that depressive moods might be a predictor for future prevalence of FoG [297], thus finding methods to decrease depressive moods become of greater value since FOG is a substantial contributor to the decline in QoL and independence of IwPD. Participants' general anxiety baseline scores show that 16.7% of participants could be classified with generalized anxiety disorder (GAD) which is similar to the 14% prevalence found by Spitzer and colleagues (2006) [298]. The GAD-7 is useful as a rapid screening and monitoring tool for GAD (possibly also panic disorder, social phobia and post-traumatic stress disorder), but not to clinically assess and diagnosed a full spectrum of anxiety disorders [299]. Researchers have found that individuals with higher anxiety had more postural difficulties [62,63,191], which supports the study's findings where the TRE group had the lowest anxiety score as well as the lower PIGD score. Somatisation classification according to the mild and moderate cut-off scores reveal that 44.5% of participants had mild somatic symptoms and 22.2% had moderate somatic symptoms, which is similar to studies reporting that often more than 50% of IwPD present with somatic symptoms [300]. Somatisation is a controversial issue in PD, mainly due to a neglect in the clinical relevance of a psychological factor of a disease [301]. Despite this, in a recent systematic review in somatisation in PD, they found a prevalence of somatisation up to 67% of IwPD [300,302]. Despite this high prevalence and impact on QoL, it is currently not recognized as a clinical symptom [300]. Carrozzino and colleagues (2017) urge that the old idea of somatisation as a pseudo-

clinical condition only mimicking real symptoms of a medical disease be revised. A multifactorial definition of somatisation was provided in the 1980's by Lipowski who identified this clinical aspect as "*a specific individual tendency to experience and communicate somatic symptoms in response to psychological distress and to seek medical help for it*" [28]. In this regard, it is clinically valid assuming somatisation in PD as a true somatic symptom arising from a multifactorial causation consisting of several medical and psychological factors. Somatisation detection and monitoring are of clinical importance, and thus a treatment for somatic symptoms should also be a high priority using an integrative and holistic approach to PD symptoms.

Upon further investigation of baseline depressive moods, anxiety, and somatic symptoms by applying the standard cut-off scores (as explained in Chapter 4) to mean values, the TRE group can be described as presenting with mild depressive moods and somatic symptoms, the EAR group presenting with mild anxiety and somatic symptoms, and lastly the CON group can also be classified with mild somatic symptoms. After the intervention, only somatisation was still considered as mild in all three groups with the TRE and EAR groups showing a decrease in scores and the control group showing an increase. Exercises with or without TNT seems to be able to lower depressive moods, anxiety and somatic symptoms with the TRE invention (exercises with TNT) showing a possible greater advantage over the nine-week intervention. However further research is needed to confirm these effects with more statistically conclusive evidence.

Overall both interventions played a role in reducing the depressive moods, general anxiety and somatic symptoms of the participants compared to the CON group. Following this, it can be suggested that relaxation-based exercises, regardless of the TNT, are useful tools to reduce perceived stress symptoms and thereby helping IwPD to decrease their moderate or mild symptoms of anxiety, somatisation and depressive moods. Unfortunately, these findings do not provide a definitive answer towards the benefit of TNT over relaxation-based exercises.

6.3 SECONDARY OUTCOME MEASURES

6.3.1 DISEASE SEVERITY

Non-motor experiences of ADL did not show any changes over the intervention period. Part 1(a + b) of the MDS-UPDRS have shown a good correlation to NMS in previous studies [303,304], however the results from the current study does not support this since a clinically significant decrease was observed in NMS frequency and severity but not in MDS-UPDRS Ib (which is a larger portion of part I than section a) for any of the groups. Perhaps the intervention was too short or sample size too small to have enough power to result in changes in the non-motor experiences of ADL.

No changes were observed in motor proficiency scores related to disease severity over time, however, improvements in motor experiences of daily living were found for TRE group from baseline to T3 (6 weeks) and to T4 (9 weeks), and for the CON group from T1-T4. These improvements in this participant-completed questionnaire are important to note as they decrease by more than 3.05 points, which constitutes a minimal clinically important difference (MCID) [305], which has practical significance for the groups. It means that the participants from the TRE and CON group experienced more ease when performing their ADL. Furthermore, these improvements could have contributed to the improved PIGD sub-score seen at T1-T4 for the TRE group, since the subtype score was calculated by using two items from part II and three items from part III of the MDS-UPDRS [25]. The improvement in their motor experiences of daily living is an unexpected finding, however, it might give some insight into the effect the research process itself had on participants.

Reasons for CON group to seemingly improve inexplicably might be attributed to perceptual factors such as reactivity of measurement [306] and the Hawthorne effect [283]. Becker (2003) explains that testing can act as an intervention itself, and this coupled with participants possibly adjusting their behaviour, or questionnaire answers, because they were being observed over multiple testing times might result in improved scores. Furthermore, questions asked in MDS-UPDRS II could have made participants more aware of their motor difficulties with ADL, and thus their behaviour in reality could have changed [283]. This improvement of the CON group makes it difficult to verify whether the TRE intervention caused the improvements seen in the TRE group. However, if perceptual factors such as Hawthorne effect and reactivity to measurement affected all groups, then the EAR group should have shown improvements as well. Furthermore, the TRE group was the only group to significantly improve their PIGD subscores, which is supported by their improvements in gait, thus we suggest that the TRE intervention had an additional influence on the participants, over and above perceptual factors such as Hawthorne effect and reactivity of measurement.

6.3.2 BALANCE CONFIDENCE

Poor balance confidence has been correlated to poor balance performance and IwPD who score less than 69% might be more at risk to fall or suffer a recurrent fall [138]. The normative score for IwPD is 73.6% [138], which places all three groups below the norm with the EAR and CON groups at additional risk of falling. After the interventions, the EAR group improved their average ABC score to be on par with the population average, while the TRE group increase their score to be well above the population average, possibly reducing their risk of falling [144] although the 8% improvement does not qualify as a of 11% [307]. Granting no statistical or practical significant changes occurred over time; the slight improvements in the TRE group might support the previously mentioned Dynamic Systems Theory of the intervention causing attractor states to shift. Thus although poorer balance performance was measured between time points with the Mini BESTest, the performance did not influence their perceived balance confidence. Additionally, the improvements in gait parameters and PIGD subscores could have influenced their balance confidence.

6.3.3 QUALITY OF LIFE

Quality of life is an important measure when evaluating treatments for IwPD since the large amount of motor and non-motor symptoms present might fluctuate but the perception and life enjoyment the IwPD experiences is extremely relevant [274]. Worse QoL scores have been associated with higher levels of perceived stress along with frequency and severity of NMS [227], thus a treatment that can reduce stress can therefore improve QoL. In this current study, lower QoL scores were seen for the TRE and EAR group after the intervention, which indicates an improvement in QoL of 22.1% and 37.5% respectively. The EAR group had a significant change over time, while the TRE group showed a non-significant tendency towards change, although both do not have practical significance. Quality of life scores as determined by PDQ-8 have a very good correlation with ADL measured by the MDS-UPDRS ($r = 0.60$) [274], and this current study support this relationship with decreases seen in part II of MDS-UPDRS, although only the TRE group had a significant change in the motor experience of ADL. These changes in QoL did not meet the MCID for the PDQ-8 [308], nevertheless, the changes over time still hold value as a comment on the effect of the interventions. Relaxation-based exercises, regardless of the TNT, seem to cause a change in the perceived QoL of IwPD. Previous research on TRE has also shown improvements in QoL [5,6,65], as well as previous research on other body-based or mind-body CAM therapies, such as yoga and Thai Chi [168,174]. In a 2011 study by Bucks and colleagues, they showed that coping strategies relating to daily stressors were correlated with health-related QoL, and

emphasized that stress management and coping mechanism are important for IwPD, and mindfulness-based intervention might be of great value [309].

6.3.4 RETENTION

A retention period is a good method to see if changes are maintained after the secession of an intervention programme. Furthermore, the passage of time is essential to infer if learning has occurred or if motor performances changed [233]. Keeping the Dynamic Systems Theory in mind, retention, interventions might cause attractor states to settle once the stimulus to the system changes or is removed, and therefore changes that occurs during retention period are of value to discuss. For the most part, the variables stayed the same with a few significant changes for each group, mostly indicating improvements. Looking at the data overall it seems to show that the majority of the TRE group's variables showed improved scores at T5 compared to baseline. A similar pattern is observed for the EAR group however with a few detriments in gait variables; whereas the CON group is almost evenly divided between improved and worse scores at T5 compared to T1. For the TRE group, significant improvements in overall balance (Mini BESTest total score) and amount of NMS are observed; both with moderate effect size although not practically significant. A practical significant improvement was observed for the frequency score of concentration for the TRE group over retention. For the EAR group, significant improvements are observed for sensory integration with moderate practical significance, with statistically significant changes observed in PIGD sub-scores, and arm swing asymmetry. Unexpectedly the CON group showed a significantly better score for anticipatory control with a moderate practical significance.

These improvements after the intervention offer possibly additional support for the Dynamic Systems Theory. For example, after the intervention the TRE group had worse scores for overall balance and perceptual problems/hallucinations, and after a retention period both those scores improved to be not just above score at nine weeks, but better than the scores obtained during baseline. This could mean that the intervention causes the body to self-organize, as hypothesized by Ross and Ware (2013), as a way for the body to detect and correct problems in the system, i.e. the body, brain, nervous system, etc. The intervention might cause certain constraints on the body to be less, either through increasing the individual's abilities or perceptions, removing obstacles or limitations from the environment, or by becoming more familiar with the task at hand. Through self-organization, and the decrease of constraints, the body can more easily shift to another attractor state possible better suited. This shifting might cause performance measures to fluctuate, which is often observed in a non-linear system. However perhaps with the implementation of a retention period, it allows the body to settle into a new attractor state, resulting in improved performance. An interesting observation is made with regards to balance confidence, which increased with every testing session for the TRE group. The final balance confidence score is 17.7% higher than T1, which is above the estimated MCID of 11.12% [307]. Perhaps a retention period is needed for new attractor states to settle. This theory should be view with caution, as further research in this field is needed with regards to the mechanistic properties on TNT.

6.3.5 ADDITIONAL INTERVENTION-SPECIFIC ASPECTS

6.3.5.1 **Motivation and Perceived Intensity**

Intrinsic motivation is the result of internal factors and can influence how participants are impacted by the interventions [276]. Intrinsic motivation drives individuals to participate in activities for the enjoyment, interest or satisfaction derived from of it, rather than due to external awards [276], which is especially important in IwPD since apathy and loss of motivation are common [310]. Although the

positive effect of the group environment is a particularly important benefit in PD populations, it might also be viewed as a limitation of the study. For instance, if one intervention/group environment made participants experience too much pressure or tension or they did not find it enjoyable or saw the value of the intervention; their variables might differ considerably from the comparison group. However, luckily in this current study, participants in both intervention groups had very comparable intrinsic motivation scores with a high rating for interest/enjoyment, effort/importance and value/usefulness and low scores for pressure/tension.

The rate of perceived exertion collected after each session allowed the researcher to track the intensity of the interventions. Both exercise interventions were performed at an RPE of 5 or lower. Thus the exercises were performed at a light intensity [242]. It is interesting to note that the TRE group's RPE rating decrease over the weeks, whereas the EAR group's intensity remained approximately the same. The decrease RPE scores could be interpreted as the TRE intervention resulting in more relaxation throughout the whole body and therefore participants rated their RPE's lower as the weeks progressed.

6.3.5.2 **Supervision**

The current study shows supervised sessions had greater results (refer back to the summary table of results, Table 5.8), as more changes occurred at three weeks and six weeks, than at nine weeks. Although some positive changes were still noted even with minimal supervision. Furthermore, a minimum of eight supervised sessions (or 3 weeks) are necessary to cause changes in depressive moods, somatisation and possibly steadiness of gait; although in some cases temporary deteriorations in performance might be observed. The sessions were very well attended with 86% and 88% attendance rates achieved for the TRE and EAR groups. Only about 48% of participants in both intervention groups completed all the home sessions and stated that they did not achieve the same level of relaxation when exercise routine was performed at home.

6.4 LIMITATIONS & RECOMMENDATIONS FOR FUTURE STUDIES

Limitations are an important part of research as it offers the opportunity to learn from your own mistakes. The limitations highlight the circumstances and conditions that could have influenced or limited the outcome of the study. Transparency in study limitations allows future research to improve upon ideas and theory, and therefore all limitations are broadly discussed. The current study is limited by the following factors:

- The TRE intervention as it was used in this study, might not have had all the benefits of the usual TRE therapy since the researcher tried to control for interpersonal aspects. By limiting the psychological and emotional guidance often received during TRE sessions participants in the TRE group did not experience the full therapy of TRE in an attempt to curate comparable environments between groups. The normal full therapy of TRE was designed to use the physical exercises to induce the TNT which in turn helps the individual reduce hyper-arousal of the nervous system [66], and additionally share any physical, psychological and emotional problems that they become aware of during the session with the TRE practitioner or group members. Individuals who seek out help for dealing with trauma and stress-related problems have found great benefits not only from the physical tremoring but through sharing memories, sensations or experiences [5,182]. With this research, individuals were randomly assigned to intervention groups with only the necessary information, to minimize their expectation of possible results, which possibly restricted their motivation about the intervention according to the self-determination theory [311]. In an attempt

to control for any psychological or emotional experiences, practitioners were restricted for asking questions to prompt additional self-awareness of participants' internal state. Since the researcher was interested in the effect of exercises with TNT on PD symptoms, the psychosocial or psychosomatic aspects of the therapy itself were neglected in an attempt to only investigate the TNT. Furthermore, this approach was chosen so the study follows a randomized controlled trial, which is currently the golden standard for research. However, this controlled approached has been a critique recently since the holistic effect of interventions are often limited by creating a controlled setting for a carefully included/excluded population rather than observing the effectiveness in a practical setting [231,312]. Medical claims from IwPD for treatments bares values and future studies should consider benchmarking controlled trials [312] to establish effectiveness. Benchmarking controlled trials is a method of controlled observation; thereby allowing treatments and interventions to proceed as practitioners usually would without the strict guidelines of researchers. The additional benefits of such an approach are that participants can decide what type of intervention or treatment they want, and taking self-determination theory into consideration this is a valuable point. Self-determination theory (SDT) is an empirically based theory of human motivation, development, and wellness [313]. Researchers state that individuals who have autonomous motivation, through making their own choice, have better predictions for performance and well-being outcomes [313]. Bloem and colleagues (2018) [231] state that there is merit in performing "real world" analyses using medical claims data, and this also mitigates the issue with the perceptual factors involved in research such as the Hawthorne effect.

- Additionally, the "sham" EAR group performing only the exercise without the TNT might not have been the most appropriate intervention to choose since the EAR group could have unintentionally experienced TNT without their or the researchers/practitioners knowing. Again in an attempt to control the environment and information that participants received, the TRE practitioners leading the EAR groups were asked not to mention anything concerning such tremors as to not stimulate additional curiosity. In his dissertation, Berceli (2007) [66] noted the same limitation, however since balance and mobility were tested for the current study, the principal investigator wanted to ensure that both groups perform the same exercises as the same intensity. Future research on TRE might do well by using a different comparison intervention or by modifying the intervention to ensure TNT are not experienced.

- The exercises part of TRE used in this study are very simple and easy to do, and often become part of the "ritual" or process leading up to the experience of the tremor, and often the accompanied relieve from emotional or psychological burdens. With the limits placed of the emotional and psychological aspects, plus the fact that participants did not seek out this therapy, the exercises experienced might have been too mundane and simple for some of the younger and more agile participants. Although the exercises can be used as a form of movement meditation, and future research should consider explaining the exercises in that way.

- Although the non-exercising waitlist CON group provides valuable information regarding normal PD symptoms and fluctuations; they could not fully account for non-intervention-related benefits. Future studies can include an attention-matched control group, to account for the efforts of small group gatherings and interaction. A small group setting has been shown to be very beneficial for

a neurological disorder such as PD as compared to individuals who attend one-on-one sessions or do sessions at home [243,244].

- This study had a tapered design for supervision since home sessions are currently part of the recommendation for TRE. However, sessions performed at home are often not performed with the same conscious intention than supervised sessions. Therefore session at home might not be the best recommendation for TRE as a therapy or for IwPD. The tapered designed also makes it difficult to extrapolate which changes are due to the possible influence of supervision or would have happened in the absence of supervision. Future studies should consider rather having different groups with different levels of supervision to ascertain the influence session facilitated by a certified practitioner might have.

- A bigger sample size would have allowed the researcher to investigate how different subtypes within IwPD might have responded to the therapy. The researcher aimed to include more participants however the amount and distributions of willing TRE practitioners made it difficult to include more than the three areas chosen. A greater sample sized would have made it possible to subdivide participants into freezer/non-freezers or into their various motor subtypes (PIGD, Tremor dominant, etc.), or occurring to their sex to make it possible to observe how the different group might have responded to the therapy. For this reason, future studies on IwPD or TNT should aim to include a larger sample size to determine what the best treatment options are for men/women, freezer/non-freezers, or different subtypes. Although the post hoc power analysis showed the power to be adequate, there has been some debate regarding the usefulness of such post-hoc analyses [314,315]. Regardless, research into therapies utilization TNT should aim to include a large sample size and use standardized testing, so that future studies can use their data to predict the optimal sample size. Consequently, a small sample size makes it difficult to extrapolate the findings to the larger PD population.

- Future research can be improved by using more sensitive questionnaires for specific symptoms. The anxiety questionnaires used in the current study was not designed to measure or differentiate between state or trait anxiety, nor different types of anxiety. A questionnaire could also be included to determine different non-motor subtypes of anxiety and depressive moods present in IwPD. Questionnaires or scales to measure perceived stress, sleep quality, fatigues or specific autonomic dysregulation can add value to future research on TNT, TRE or the effect of exercise on the NMS of IwPD.

- Future studies into TRE or other body-based stress relieve therapies would benefit from using objective measures of stress, such as heart rate variability or saliva markers for inflammation. Researcher of the current study could not include these measure due to financial limitation. Unfortunately, it was not one of the aims of this study to include objective measures of stress to support findings from this study, and it was outside of the scope of this study to establish causal relationships or mechanistic links. Future studies investigating the physiological effect of TRE should include such measures.

- Only spatiotemporal measures were used in the current study to evaluate gait, however, using kinematic analysis of gait in combination with spatiotemporal measures would have allowed the

researcher to describe characteristics of gait more accurately [131]. This was not possible in the current study due to equipment limitations. Furthermore, only straight line walking variables were used for this research, future studies are recommended to include turning and transitional variables as they might give more insight into functional mobility.

- A mixed-method approach would be highly recommended for future studies on TRE and other similar therapies. A mixed-model approach would allow for qualitative and quantitative research and outcome measures, which might be more insightful with regards to participants shared experience and subjective benefits.

6.5 CONCLUSION

From researchers theorizing that chronic stress or trauma might trigger PD to the quite acute effect of perceived stress on IwPD motor and non-motor symptoms; the influence of stress of IwPD cannot be overlooked. However current treatment modalities do not seem to be addressing the problem by not promoting body-based stress relief therapies. Given the impact of chronic stress and trauma have on IwPD, alternative therapies should be investigated and promoted as possible treatment options.

The current exploratory study show promising preliminary results for the use of TNT with relaxation-based exercises. It was hypothesized that if IwPD do exercises with TNT over nine weeks then selective motor (specifically postural instability and gait disturbances) and non-motor (specifically depressive moods and autonomic dysregulation) symptoms will improve due to a reduction in general anxiety and somatisation, as a measure of perceived stress. The main findings of this study indicate that relaxation-based exercises are beneficial, regardless of the addition of TNT, for non-motor symptoms, such as gastrointestinal complaints, the severity of mood, anxiety, and QoL; supporting the notion that relaxation therapies are valuable to include in treatments for PD. Furthermore, relaxation-based exercises with TNT might cause beneficial changes in motor experiences of ADL, PIGD subscore, gait speed and steadiness, as well as depressive moods, somatisation, and frequency of perceived stress-related symptoms. The EAR group showed improvements in sturdiness and speed of gait, and anxiety. These findings partially support the hypothesis, as improvements are seen in selective motor and non-motor symptoms. No between-group differences were observed and therefore conclusions cannot be made regarding which intervention was better with a high degree of statistical and scientific certainty. Although significant changes occurred over time within the groups, the results that have a clinical and practical bearing are of greater interest. Thus Table 6.1 displays a summary of only the results that are practically and statistically significant or that show an improvement equivalent to the MCID of that specific variable.

Table 6.1: *Summary of practically and clinically significant results*

	Tension & Trauma Releasing exercises (TRE)	Exercise & relaxation (EAR)	Control
Motor	↑ Gait steadiness [T1-T2 & T4] (Prac. Sig.)		
	↑ Gait speed[T1-T4] (MCID)[NS]	↑ Gait speed [T1-T3] (Prac. Sig.)	
Non-motor	↓ Global NMS[T1-T4] (MCID)[NS]	↓ Global NMS[T1-T4] (MCID)[NS]	
	↓Mood/cognition[T1-T4] (MCID)[NS]	↓Mood/cognition[T1-T4] (MCID)[NS]	
		↓Sleep/fatigue, gastrointestinal, & Urinary[T1-T4] (MCID)[NS]	↓Sexual dysfunction [T1-T4] (MCID)[NS]
	↓ Severity & frequency of stress-related NMS (mood, concentration, forgetfulness & nocturia)[T1-T4] (Prac. Sig.)		
Secondary	↑ Motor ADL[T1-T3 & T4] (MCID)		↑ Motor ADL[T1-T4] (MCID)
	↑ Balance confidence[T1-T5] (MCID)[NS]		

MCID – Minimal Clinical Important difference; Prac. Sig. – Practical significance; NS – Not statistically significant

However, the questions of whether the TRE intervention offers more benefits than the EAR intervention remain inconclusive, although results look promising towards improvements in perceived stress-related non-motor symptoms. Thus it can be stated that relaxation-based exercises, regardless of TNT, are beneficial towards PD symptoms compared to a non-exercising CON group, but we cannot state with relative scientific certainty that the addition of TNT results in greater improvements. The overlap of results are displayed in Figure 6.1 to indicate the congruent and divergent results from a relaxation-based exercise intervention between the TRE and EAR groups. This figure shows that the TRE group possibly experienced more benefits, however, further research is needed to confirm these results. The motor and non-motor benefits from the simply relaxation-based exercise intervention seems promising, and future rehabilitation programmes should aim to place a greater emphasis on relaxation or stress management for IwPD.

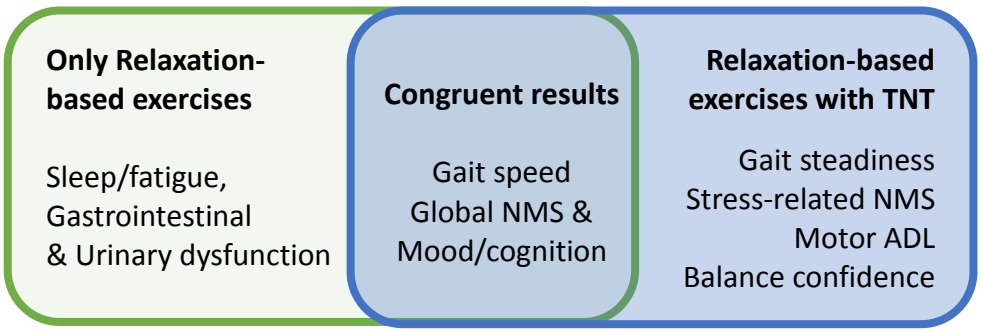


Figure 6.1: *Summary of congruent and divergent result of relaxation-based exercise intervention with and without TNT*

TNT: Therapeutic Neurogenic tremors; NMS: Non-motor symptoms; ADL: Activities of Daily Living

For the purpose of this research, the exercises and a calming environment played important roles in controlling for variance in both interventions and thus the exact same exercise protocol was followed. Thus the TRE group was possibly hampered from experiencing the full effect of the therapy while the EAR group might have experienced the tremor even without their awareness of it while participating in the sham intervention. These factors make it difficult to draw plausible conclusions with a high degree of certainty and findings, significant and/or practical, should be interpreted with caution. However, the preliminary results from this exploratory study look promising for TRE and other relaxation-based exercises as a possible treatment modality for the selective symptoms of IwPD.

This is the first study to explore the effects of relaxation-based exercises with TNT on IwPD; it is also the first study to investigate the possible motor improvements that might be obtained through this therapy. Further research is warranted to establish the possible benefits to be gained from of using TNT on IwPD or in other populations vulnerable to stress. More research is needed to establish the physiological effects of TNT and their influence on psychological and somatic symptoms to gain a better understanding of the mechanism. A benchmark controlled trial could be of more value than a randomized control trial, in light of how self-determined motivation could influence outcomes. Lastly, future research studies on TNT need to include multiple testing sessions and a retention period to get a clear understanding of how the therapy influences acutely and in the long term.

The use and benefits of therapeutic tremors are worth investigating and exploring since it holds the promise that the utilization of such tremors in treatment address the biopsychosocial model of illness. Wade and Halligan (2017) state that the biopsychosocial model of illness have to be implemented in treatment regimes in light of more evidence supporting this model as a basis for pathologies [316], and the use of this approach could improve clinical outcomes [317]. Therapeutic tremors could address the biological as well as psychological aspects of stress, which is linked to the development of several diseases, and through the effective mind-body management of stress, individuals will be better equipped to handle social environments. Researchers recommend this biopsychosocial model for the management for PD as well [318,319] and state that this multi-disciplinary approach could be highly effective and beneficial for IwPD.

In conclusion, supervised relaxation-based exercises in a group might be a valuable form of exercise therapy for IwPD. Individuals participating in relaxation-based exercise utilizing TNT could see improvement in non-motor symptoms that relate to stress. If TNT are a method to relieve body-based stress and aid the body to self-organize, and possibly self-heal, the use of TNT should be strongly encouraged and promoted in South Arica. Given the fact how stress and resulting mood disorders can influence somatic symptoms and postural instability, promoting therapies that aid in stress management should be emphasized, not only for IwPD to minimize symptoms and promote QoL, but to the general public as well.

REFERENCES

[1] Postuma RB, Berg D, Adler CH, Bloem BR, Chan P, Deuschl G, et al. The new definition and diagnostic criteria of Parkinson's disease. Lancet Neurol 2016;15:546–8. doi:10.1016/S1474-4422(16)00116-2.

[2] Jankovic J. Parkinson's disease: Clinical features and diagnosis. J Neurol Neurosurg Psychiatry 2008;79:368–76. doi:10.1136/jnnp.2007.131045.

[3] Austin KW, Ameringer SW, Cloud LJ. An Integrated Review of Psychological Stress in Parkinson's Disease: Biological Mechanisms and Symptom and Health Outcomes. Parkinsons Dis 2016;2016. doi:10.1155/2016/9869712.

[4] Berceli D, Salmon M, Bonifas R, Ndefo N. Effects of Self-induced Unclassified Therapeutic Tremors on Quality of Life among Non-professional Caregivers: A Pilot Study. Glob Adv Heal Med 2014;3:45–8. doi:10.7453/gahmj.2014.032.

[5] Johnson S. A Body-Based Group Intervention for Teacher Stress and Burnout in High-Risk Schools. Acta Psychopathol 2017;03:1–4. doi:10.4172/2469-6676.100151.

[6] Harrison EG, Keating JL, Morgan P. Novel Exercises for Restless Legs Syndrome: A Randomized, Controlled Trial. J Am Board Fam Med 2018;31:783–94. doi:10.3122/jabfm.2018.05.180065.

[7] Scaer RC. The neurophysiology of dissociation and chronic disease. Appl Psychophysiol Biofeedback 2001;26:73–91. doi:10.1023/A:1009571806136.

[8] Levine P. Walking the Tiger: Healing trauma: The innate capacity to transform overwhelming experiences. vol. 17. North Atlantic Books; 1997.

[9] Van Der Kolk BA, Roth S, Pelcovitz D, Sunday S, Spinazzola J. Disorders of extreme stress: The empirical foundation of a complex adaptation to trauma. J Trauma Stress 2005;18:389–99. doi:10.1002/jts.20047.

[10] Harrison MB, Wylie SA, Frysinger RC, Patrie JT, Huss DS, Currie LJ, et al. UPDRS activity of daily living score as a marker of Parkinson's disease progression. Mov Disord 2009;24:224–30. doi:10.1002/mds.22335.

[11] Zautra AJ, Affleck GG, Tennen H, Reich JW, Davis MC. Dynamic approaches to emotions and stress in everyday life: Bolger and Zuckerman reloaded with positive as well as negative affects. J Pers 2005;73:1511–38. doi:10.1111/j.0022-3506.2005.00357.x.

[12] Siddiqui MF, Rast S, Lynn MJ, Auchus AP, Pfeiffer RF. Autonomic dysfunction in Parkinson's disease: A comprehensive symptom survey. Park Relat Disord 2002;8:277–84. doi:10.1016/S1353-8020(01)00052-9.

[13] Rinalduzzi S, Trompetto C, Marinelli L, Alibardi A, Missori P, Fattapposta F, et al. Balance dysfunction in Parkinson's disease. Biomed Res Int 2015;2015:434683. doi:10.1155/2015/434683.

[14] Kemper KJ, Shannon S. Complementary and Alternative Medicine Therapies to Promote Healthy Moods. Pediatr Clin North Am 2007;54:901–26. doi:10.1016/j.pcl.2007.09.002.

[15] Williams JR, Hirsch ES, Anderson K, Bush AL, Goldstein SR, Grill S, et al. A comparison of nine scales to detect depression in Parkinson disease: Which scale to use? Neurology 2012;78:998–1006. doi:10.1212/WNL.0b013e31824d587f.

[16] Shumway-Cook A, Woollacott MH. Motor Control: Translationg Research Into Clinical Practice. 4th ed. Wolters Kluwer, Lippinicot Williams & Wilkins; 2011.

[17] Rahman, S., H.J. Griffin NPQ. The factors that induce or overcome freezing of gait in Parkinson's disease. Behav Neurol 2008;19:127–36.

[18] Plotnik M, Giladi N, Hausdorff JM. Bilateral coordination of gait and Parkinson's disease: The effects of

dual tasking. J Neurol Neurosurg Psychiatry 2009;80:347–50. doi:10.1136/jnnp.2008.157362.

[19] Bryant MS, Rintala DH, Hou JG, Collins RL, Protas EJ. Gait variability in Parkinson's disease: Levodopa and walking direction. Acta Neurol Scand 2016;134:83–6. doi:10.1111/ane.12505.

[20] Boucą-Machado R, Maetzler W, Ferreira JJ. What is functional mobility applied to Parkinson's disease? J Parkinsons Dis 2018;8:121–30. doi:10.3233/JPD-171233.

[21] Kudielka BM, Schommer NC, Hellhammer DH, Kirschbaum C. Acute HPA axis responses, heart rate, and mood changes to psychosocial stress (TSST) in humans at different times of day. Psychoneuroendocrinology 2004;29:983–92. doi:10.1016/j.psyneuen.2003.08.009.

[22] Payne P, Levine PA, Crane-Godreau MA. Somatic experiencing: Using interoception and proprioception as core elements of trauma therapy. Front Psychol 2015;6:1–18. doi:10.3389/fpsyg.2015.00093.

[23] Mestre TA, Beaulieu-Boire I, Aquino CC, Phiellipp N, Poon YY, Lui JP, et al. What is a clinically important change in the Unified Dyskinesia Rating Scale in Parkinson's disease? Parkinsonism Relat Disord 2015;21:1349–54. doi:10.1016/j.parkreldis.2015.09.044.

[24] Cohen S, Kamarck T, Mermelstein R, Health J, Behavior S, Dec N. A Global Measure of Perceived Stress A Global Measure of Perceived Stress 2008;24:385–96. doi:http://dx.doi.org/.

[25] Stebbins GT, Goetz CG, Burn DJ, Jankovic J, Khoo TK, Tilley BC. How to identify tremor dominant and postural instability/gait difficulty groups with the movement disorder society unified Parkinson's disease rating scale: Comparison with the unified Parkinson's disease rating scale. Mov Disord 2013;28:668–70. doi:10.1002/mds.25383.

[26] Chaudhuri KR, Sauerbier A, Rojo JM, Sethi K, Schapira AHV, Brown RG, et al. The burden of non-motor symptoms in Parkinson's disease using a self-completed non-motor questionnaire: A simple grading system. Park Relat Disord 2015;21:287–91. doi:10.1016/j.parkreldis.2014.12.031.

[27] Morris ME, Huxham F, McGinley J, Dodd K, Iansek R. The biomechanics and motor control of gait in Parkinson disease. Clin Biomech 2001;16:459–70. doi:10.1016/S0268-0033(01)00035-3.

[28] Lipowski ZJ. Physical illness and psychopathology. Int J Psychiatry Med 1974;5:483–97. doi:10.2190/7279-X24X-FPV9-E8WV.

[29] Han C, Pae C-U, Patkar AA, Masand PS, Woong Kim K, Joe S-H, et al. Psychometric Properties of the Patient Health Questionnaire–15 (PHQ–15) for Measuring the Somatic Symptoms of Psychiatric Outpatients. Psychosomatics 2009;50:580–5. doi:10.1016/S0033-3182(09)70859-X.

[30] Bloem BR, Hausdorff JM, Visser JE, Giladi N. Falls and freezing of Gait in Parkinson's disease: A review of two interconnected, episodic phenomena. Mov Disord 2004;19:871–84. doi:10.1002/mds.20115.

[31] Hobfoll SE. Conservation of resources - A new way at conceptualizing stress. Am Psychol 1989;44:513–24.

[32] van Der Kolk BA, Saporta J. The biological response to psychic trauma: Mechanisms and treatment of intrusion and numbing. Anxiety Res 1991;4:199–212. doi:10.1080/08917779108248774.

[33] WHO Europe. Fact sheet - Mental Health. RC63 Fact Sheet Ment Heal Geneva, World Heal Organ 2013:1–3.

[34] Gaffey AE, Bergeman CS, Clark LA, Wirth MM. Aging and the HPA axis: Stress and resilience in older adults. Neurosci Biobehav Rev 2016;68:928–45. doi:10.1016/j.neubiorev.2016.05.036.

[35] Piazza JR, Charles ST, Sliwinski MJ, Mogle J, Almeida DM. Affective reactivity to daily stressors and long-term risk of reporting a chronic physical health condition. Ann Behav Med 2013;45:110–20. doi:10.1007/s12160-012-9423-0.

[36] Haftgoli N, Favrat B, Verdon F, Vaucher P, Bischoff T, Burnand B, et al. Patients presenting with somatic complaints in general practice: Depression, anxiety and somatoform disorders are frequent and associated with psychosocial stressors. BMC Fam Pract 2010;11. doi:10.1186/1471-2296-11-67.

[37] Bener A, Al-Kazaz M, Ftouni D, Al-Harthy M, Dafeeah EE. Diagnostic overlap of depressive, anxiety, stress and somatoform disorders in primary care. Asia-Pacific Psychiatry 2013;5:29–38. doi:10.1111/j.1758-5872.2012.00215.x.

[38] Polusny MA, Ries BJ, Schultz JR, Calhoun P, Clemensen L, Johnsen IR. PTSD Symptom Clusters Associated With Physical Health and Health Care Utilization in Rural Primary Care Patients Exposed to Natural Disaster. J Trauma Stress 2008;21:75–82. doi:10.1002/jts.

[39] Song H, Fang F, Tomasson G, Arnberg FK, Mataix-Cols D, De La Cruz LF, et al. Association of stress-related disorders with subsequent autoimmune disease. JAMA - J Am Med Assoc 2018;319:2388–400. doi:10.1001/jama.2018.7028.

[40] Goldstein DS, Kopin IJ. Linking Stress, Catecholamine Autotoxicity, and Allostatic Load with Neurodegenerative Diseases: A Focused Review in Memory of Richard Kvetnansky. Cell Mol Neurobiol 2018;38:13–24. doi:10.1007/s10571-017-0497-x.

[41] Sulzer D, Surmeier DJ. Neuronal vulnerability, pathogenesis, and Parkinson's disease. Mov Disord 2013;28:41–50. doi:10.1002/mds.25095.

[42] Alves G, Forsaa EB, Pedersen KF, Dreetz Gjerstad M, Larsen JP. Epidemiology of Parkinson's disease. J Neurol 2008;255:18–32. doi:10.1007/s00415-008-5004-3.

[43] Kalia L V., Lang AE. Parkinson's disease. Lancet 2015;386:896–912. doi:10.1016/S0140-6736(14)61393-3.

[44] Ascherio A, Schwarzschild MA. The epidemiology of Parkinson's disease: risk factors and prevention. Lancet Neurol 2016;15:1257–72. doi:10.1016/S1474-4422(16)30230-7.

[45] Sugama S, Conti B, Kakinuma Y. Effect of Chronic Stress in the Onset of Parkinson's Disease: Possible Role of Microglial Cells in Neuroinflammation. J Neurol Disord 2015;s2:6895. doi:10.4172/2329-6895.S2-001.

[46] Chan YLE, Bai YM, Hsu JW, Huang KL, Su TP, Li CT, et al. Post-traumatic Stress Disorder and Risk of Parkinson Disease: A Nationwide Longitudinal Study. Am J Geriatr Psychiatry 2017;25:917–23. doi:10.1016/j.jagp.2017.03.012.

[47] Smith AD, Castro SL, Zigmond MJ. Stress-induced Parkinson's disease: A working hypothesis. Physiol Behav 2002;77:527–31. doi:10.1016/S0031-9384(02)00939-3.

[48] Djamshidian A, Lees AJ. Can stress trigger Parkinson ' s disease ? Mov Disord 2014;85:879–82. doi:10.1136/jnnp-2013-305911.

[49] Hemmerle AM, Herman JP, Seroogy KB. Stress, depression and Parkinson's disease. Exp Neurol 2012;233:79–86. doi:10.1016/j.expneurol.2011.09.035.

[50] Dallé E, Mabandla M V. Early Life Stress, Depression and Parkinson's Disease: A New Approach. Mol Brain 2018;11:1–13. doi:10.1186/s13041-018-0356-9.

[51] Hannibal KE, Bishop MD. Chronic Stress, Cortisol Dysfunction, and Pain: A Psychoneuroendocrine Rationale for Stress Management in Pain Rehabilitation. Phys Ther 2014;94:1816–25. doi:10.2522/ptj.20130597.

[52] Goldstein DS, Kopin IJ. Evolution of concepts of stress. Stress 2007;10:109–20. doi:10.1080/10253890701288935.

[53] Wiegner L, Hange D, Björkelund C, Ahlborg G. Prevalence of perceived stress and associations to symptoms of exhaustion, depression and anxiety in a working age population seeking primary care - An observational study. BMC Fam Pract 2015;16:1–8. doi:10.1186/s12875-015-0252-7.

[54] DeMaagd G, Philip A. Parkinson's Disease and Its Management: Part 1: Disease Entity, Risk Factors, Pathophysiology, Clinical Presentation, and Diagnosis. P T 2015;40:504–32. doi:10.1016/j.expneurol.2017.10.002.

[55] Sauerbier A, Jenner P, Todorova A, Chaudhuri KR. Non motor subtypes and Parkinson's disease. Park Relat Disord 2016;22:S41–6. doi:10.1016/j.parkreldis.2015.09.027.

[56] Zhang T-M, Yu S-Y, Guo P, Du Y, Hu Y, Piao Y-S, et al. Nonmotor symptoms in patients with Parkinson disease: A cross-sectional observational study. Medicine (Baltimore) 2016;95:e5400. doi:10.1097/MD.0000000000005400.

[57] Dibilio V, Nicoletti A, Mostile G, Toscano S, Luca A, Raciti L, et al. Dopaminergic and non-dopaminergic gait components assessed by instrumented timed up and go test in Parkinson's disease. J Neural Transm 2017;124:1539–46. doi:10.1007/s00702-017-1794-8.

[58] Chaudhuri KR, Schapira AH. Non-motor symptoms of Parkinson's disease: dopaminergic pathophysiology and treatment. Lancet Neurol 2009;8:464–74. doi:10.1016/S1474-4422(09)70068-7.

[59] Ng B, Varoquaux G, Poline JB, Thirion B, Greicius MD, Poston KL. Distinct alterations in Parkinson's medication-state and disease-state connectivity. NeuroImage Clin 2017;16:575–85. doi:10.1016/j.nicl.2017.09.004.

[60] Lee HJ, Lee WW, Kim SK, Park H, Jeon HS, Kim HB, et al. Tremor frequency characteristics in Parkinson's disease under resting-state and stress-state conditions. J Neurol Sci 2016;362:272–7. doi:10.1016/j.jns.2016.01.058.

[61] Zach H, Dirkx MF, Pasman JW, Bloem BR, Helmich RC. Cognitive Stress Reduces the Effect of Levodopa on Parkinson's Resting Tremor. CNS Neurosci Ther 2017;23:209–15. doi:10.1111/cns.12670.

[62] Jazaeri SZ, Azad A, Mehdizadeh H, Habibi SA, Najafabadi MM, Saberi ZS, et al. The effects of anxiety and external attentional focus on postural control in patients with Parkinson's disease 2018:1–13. doi:10.1371/journal.pone.0192168.

[63] Ehgoetz Martens KA, Lefaivre SC, Beck EN, Chow R, Pieruccini-Faria F, Ellard CG, et al. Anxiety provokes balance deficits that are selectively dopa-responsive in Parkinson's disease. Neuroscience 2017;340:436–44. doi:10.1016/j.neuroscience.2016.11.011.

[64] Kwakkel G, de Goede CJT, van Wegen EEH. Impact of physical therapy for Parkinson's disease: a critical review of the literature. Parkinsonism Relat Disord 2007;13 Suppl 3:S478–87. doi:10.1016/S1353-8020(08)70053-1.

[65] Berceli D, Napoli M. A Proposal for a Mindfulness-Based Trauma Prevention Program for Social Work Professionals. Complement Health Pract Rev 2006;11:153–65. doi:10.1177/1533210106297989.

[66] Berceli D. Evaluating the effects of stress reduction exercises 2007:1–141.

[67] Schweitzer E. Trembling With Joy: Anthropology, Trembling Practices Worldwide. Shake It Off Nat Reduce Stress Anxiety, AndTension with TRE 2015:15–24.

[68] Keeney H, Keeney B, Boo K. The "trance dance" of the Ju/'hoan Bushmen (San) of Southern Africa: implications for hypnotic means of healing. Int J Heal Promot Educ 2016;54:137–44. doi:10.1080/14635240.2016.1142063.

[69] Charcot JM. Vibratory therapeutics.—The application of rapid and continuous vibrations to the treatment of certain diseases of the nervous system. J Nerv Ment Dis 1892;17:880–6. doi:10.1097/00005053-189212000-00002.

[70] Orr R. The effect of whole body vibration exposure on balance and functional mobility in older adults: A systematic review and meta-analysis. Maturitas 2015;80:342–58. doi:10.1016/j.maturitas.2014.12.020.

[71] Sharififar S, Coronado RA, Romero S, Azari H, Thigpen M. The effects of whole body vibration on mobility and balance in Parkinson disease: A systematic review. Iran J Med Sci 2014;39:318–26.

[72] Turbanski S, Haas CT, Schmidtbleicher D, Friedrich A, Duisberg P. Effects of random whole-body vibration on postural control in Parkinson's disease. Res Sport Med 2005;13:243–56. doi:10.1080/15438620500222588.

[73] Harris MA, Marion SA, Spinelli JJ, Tsui JKC, Teschke K. Occupational Exposure to Whole-Body Vibration and Parkinson's Disease: Results from a Population-based Case-Control Study. Am J Epidemiol 2012;176:299–307. doi:10.1093/aje/kws017.

[74] Ross SN, Ware K. Hypothesizing the body's genius to trigger and self-organize its healing: 25 years using a standardized neurophysics therapy. Front Physiol 2013;4 NOV:1–18. doi:10.3389/fphys.2013.00334.

[75] Winblad NE, Changaris M, Stein PK. Effect of Somatic Experiencing resiliency-based trauma treatment training on quality of life and psychological health as potential markers of resilience in treating professionals. Front Neurosci 2018;12:1–10. doi:10.3389/fnins.2018.00070.

[76] Ware K, Conte E, Marvulli R, Ianieri G, Megna M, Pierangeli E, et al. Case Report: Generalized Mutual Information (GMI) Analysis of Sensory Motor Rhythm in a Subject Affected by Facioscapulohumeral Muscular Dystrophy after Ken Ware Treatment. World J Neurosci 2015:67–81. doi:10.4236/wjns.2015.52018.

[77] Johnson S, Naidoo A. Can evolutionary insights into the brain's response to threat suggest different group interventions for perceived stress and burnout of teachers in high-risk schools? South African J Psychol 2017;47:401–15. doi:10.1177/0081246316675588.

[78] Herold A, Nibel H. Preliminary results of several small sample studies in the Ukraine, during TRE trainings on different levels. Psychol Couns Psychother 2016;2:29–38.

[79] Amaral MA do, Andrade EAR, Angnes GM, Sardeiro ER, Carvalho LBS, Fonseca VMAC, et al. Innovative Solutions for the Promotion of Adolescent Mental Health in Primary Care. Off J Nucl Adolesc Heal Stud 2018;15.

[80] Fahn S. Description of Parkinson's Disease as a Clinical Syndrome. Ann New York Acad Sci 2003;991:1–14.

[81] Lees AJ, Hardy J, Revesz T. Parkinson's disease. Lancet 2009;373:2055–66. doi:10.1016/S0140-6736(09)60492-X.

[82] Van Der Merwe C, Haylett W, Harvey J, Lombard D, Bardien S, Carr J. Factors influencing the development of early- or late-onset Parkinson ' s disease in a cohort of South African patients. South African Med J 2012;102:848–54. doi:10.7196/SAMJ.5879.

[83] Abbruzzese G, Marchese R, Avanzino L, Pelosin E. Rehabilitation for Parkinson's disease: Current outlook and future challenges. Park Relat Disord 2016;22:S60–4. doi:10.1016/j.parkreldis.2015.09.005.

[84] Mazilu S, Calatroni A, Gazit E, Mirelman A, Hausdorff JM, Tr G. Prediction of Freezing of Gait in Parkinson ' s From Physiological Wearables : An Exploratory Study. IEEE J Biomed Heal Inf 2015;19:1843–54. doi:10.1109/JBHI.2015.2465134.

[85] Monteiro-Junior RS, Cevada T, Oliveira BRR, Lattari E, Portugal EMM, Carvalho A, et al. We need to move more: Neurobiological hypotheses of physical exercise as a treatment for Parkinson's disease. Med Hypotheses 2015;85:537–41. doi:10.1016/j.mehy.2015.07.011.

[86] Liu CC, Li CY, Lee PC, Sun Y. Variations in incidence and prevalence of Parkinson's disease in Taiwan: A population-based nationwide study. Parkinsons Dis 2016;2016. doi:10.1155/2016/8756359.

[87] Wirdefeldt K, Adami H-O, Cole P, Trichopoulos D, Mandel J. Epidemiology and etiology of Parkinson's disease: a review of the evidence. Eur J Epidemiol 2011;26:1–58. doi:10.1007/s10654-011-9581-6.

[88] Kieburtz K, Wunderle KB. Parkinson's disease: Evidence for environmental risk factors. Mov Disord 2013;28:8–13. doi:10.1002/mds.25150.

[89] Cilia R, Akpalu A, Sarfo FS, Cham M, Amboni M, Cereda E, et al. The modern pre-levodopa era of Parkinson's disease: insights into motor complications from sub-Saharan Africa. Brain 2014;137:2731–42. doi:10.1093/brain/awu195.

[90] Dorsey E, Constantinescu R, Thompson J, Biglan K, Holloway R, Kieburtz K. Projected number of people

with Parkinson disease in the most poplous nations, 2005 through 2030. Neurology 2007;68:384–6. doi:10.1212/01.wnl.0000271777.50910.73.

[91] Berg D, Postuma RB, Bloem B, Chan P, Dubois B, Gasser T, et al. Time to redefine PD? Introductory statement of the MDS Task Force on the definition of Parkinson's disease. Mov Disord 2014;29:454–62. doi:10.1002/mds.25844.

[92] Blanckenberg J, Bardien S, Glanzmann B, Okubadejo NU, Carr JA. The prevalence and genetics of Parkinson's disease in sub-Saharan Africans. J Neurol Sci 2013;335:22–5. doi:10.1016/j.jns.2013.09.010.

[93] Okubadejo NU, Bower JH, Rocca WA, Maraganore DM. Parkinson's disease in Africa: A systematic review of epidemiologic and genetic studies. Mov Disord 2006;21:2150–6. doi:10.1002/mds.21153.

[94] Velkoff VA, Kowal PR. Population aging in Sub-Saharan Africa: demographic dimensions 2006. Curr Popul Reports, P95/07-1 Popul 2007:38.

[95] Haylett WL, Keyser RJ, du Plessis MC, van der Merwe C, Blanckenberg J, Lombard D, et al. Mutations in the parkin gene are a minor cause of Parkinson's disease in the South African population. Park Relat Disord 2012;18:89–92. doi:10.1016/j.parkreldis.2011.09.022.

[96] Sugama S, Sekiyama K, Kodama T, Takamatsu Y, Takenouchi T, Hashimoto M, et al. Chronic restraint stress triggers dopaminergic and noradrenergic neurodegeneration: Possible role of chronic stress in the onset of Parkinson's disease. Brain Behav Immun 2016;51:39–46. doi:10.1016/j.bbi.2015.08.015.

[97] Sulzer D, Surmeier DJ. Neuronal vulnerability, pathogenesis, and Parkinson's disease. Mov Disord 2013;28:41–50. doi:10.1002/mds.25095.

[98] Diederich NJ, Parent A. Parkinson's disease: Acquired frailty of archaic neural networks? J Neurol Sci 2012;314:143–51. doi:10.1016/j.jns.2011.10.003.

[99] Rabkin JG, Struening EL. Life Events, Stress, and Illness. Scien 1975;194:1013–20.

[100] Sulzer D, Alcalay RN, Garretti F, Cote L, Kanter E, Agin-Liebes J, et al. T cells from patients with Parkinson's disease recognize α-synuclein peptides. Nature 2017;546:656–61. doi:10.1038/nature22815.

[101] Takakusaki K, Saitoh K, Harada H, Kashiwayanagi M. Role of basal ganglia-brainstem pathways in the control of motor behaviors. Neurosci Res 2004;50:137–51. doi:10.1016/j.neures.2004.06.015.

[102] Groenewegen HJ. The basal ganglia and motor control. Neural Plast 2003;10:107–20. doi:10.1155/NP.2003.107 [doi].

[103] Lanciego JL, Luquin N, Obeso JA. Functional neuroanatomy of the basal ganglia. Cold Spring Harb Perspect Med 2012;2:1–20. doi:10.1101/cshperspect.a009621.

[104] Dickson DW. Neuropathology of Parkinson disease. Park Relat Disord 2018;46:S30–3. doi:10.1016/j.parkreldis.2017.07.033.

[105] Mtui E, Gruener G, Dockery P. Fitzgerald's clinical neuroanatomy and neuroscience. Seventh ed. Philadelphia: Elsevier; 2016.

[106] Hegarty S V., Sullivan AM, O'Keeffe GW. Midbrain dopaminergic neurons: A review of the molecular circuitry that regulates their development. Dev Biol 2013;379:123–38. doi:10.1016/j.ydbio.2013.04.014.

[107] Mejias-Aponte CA, Drouin C, Aston-Jones G. Adrenergic and Noradrenergic Innervation of the Midbrain Ventral Tegmental Area and Retrorubral Field: Prominent Inputs from Medullary Homeostatic Centers. J Neurosci 2009;29:3613–26. doi:10.1523/JNEUROSCI.4632-08.2009.

[108] Gaenslen A, Wurster I, Brockmann K, Huber H, Godau J, Faust B, et al. Prodromal features for Parkinson's disease - baseline data from the TREND study. Eur J Neurol 2014;21:766–72. doi:10.1111/ene.12382.

[109] Keeler JF, Pretsell DO, Robbins TW. Functional implications of dopamine D1 vs. D2 receptors: A "prepare and select" model of the striatal direct vs. indirect pathways. Neuroscience 2014;282:156–75. doi:10.1016/j.neuroscience.2014.07.021.

[110] Berardelli a, Rothwell JC, Thompson PD, Hallett M. Pathophysiology of bradykinesia in Parkinson's disease. Brain 2001;124:2131–46. doi:10.1093/brain/124.11.2131.

[111] Nieuwboer A, Kwakkel G, Rochester L, Jones D, van Wegen E, Willems AM, et al. Cueing training in the home improves gait-related mobility in Parkinson's disease: the RESCUE trial. J Neurol Neurosurg Psychiatry 2007;78:134–40. doi:10.1136/jnnp.200X.097923.

[112] de la Fuente-Fernández R. The placebo-reward hypothesis: dopamine and the placebo effect. Park Relat Disord 2009;15:72–4. doi:10.1016/S1353-8020(09)70785-0.

[113] Schapira AHV, Chaudhuri KR, Jenner P. Non-motor features of Parkinson disease. Nat Rev Neurosci 2017;18:435–50. doi:10.1038/nrn.2017.62.

[114] Balaban CD, Thayer JF. Neurological bases for balance-anxiety links. J Anxiety Disord 2001;15:53–79.

[115] Staab JP, Balaban CD, Furman JM. Threat Assessment and Locomotion : Clinical Applications of an Integrated Model of Anxiety and Postural Control. Semin Neurol 2013;33. doi:10.1055/s-0033-1356462.

[116] Remy P, Doder M, Lees A, Turjanski N, Brooks D. Depression in Parkinson's disease: Loss of dopamine and noradrenaline innervation in the limbic system. Brain 2005;128:1314–22. doi:10.1093/brain/awh445.

[117] Bonnet A. Involvement of Non-Dopaminergic Pathways in Parkinson's Disease Pathophysiology and Therapeutic Implications 2000;13:351–64.

[118] Swart C, Haylett W, Kinnear C, Johnson G, Bardien S, Loos B. Neurodegenerative disorders: Dysregulation of a carefully maintained balance? Exp Gerontol 2014;58:279–91. doi:10.1016/j.exger.2014.09.003.

[119] Baba M, Nakajo S, Tu PH, Tomita T, Nakaya K, Lee VM, et al. Aggregation of alpha-synuclein in Lewy bodies of sporadic Parkinson's disease and dementia with Lewy bodies. Am J Pathol 1998;152:879–84. doi:10.1086/281267.

[120] Braak H, Müller CM, Rüb U, Ackermann H, Bratzke H, de Vos RAI, et al. Pathology associated with sporadic Parkinson's disease --- where does it end? In: Riederer P, Reichmann H, Youdim MBH, Gerlach M, editors. Park. Dis. Relat. Disord., Vienna: Springer Vienna; 2006, p. 89–97.

[121] Braak H, Del Tredici K. Invited Article: Nervous system pathology in sporadic Parkinson disease. Neurology 2008;70:1916–25. doi:10.1212/01.wnl.0000312279.49272.9f.

[122] Braak H, Del Tredici K. Neuropathological Staging of Brain Pathology in Sporadic Parkinson's disease: Separating the Wheat from the Chaff. J Parkinsons Dis 2017;7:S73–87. doi:10.3233/JPD-179001.

[123] Bachis A, Cruz MI, Nosheny RL, Mocchetti I. Chronic unpredictable stress promotes neuronal apoptosis in the cerebral cortex. Neurosci Lett 2008;442:104–8. doi:10.1016/j.neulet.2008.06.081.

[124] Morilak DA, Barrera G, Echevarria DJ, Garcia AS, Hernandez A, Ma S, et al. Role of brain norepinephrine in the behavioral response to stress. Prog Neuro-Psychopharmacology Biol Psychiatry 2005;29:1214–24. doi:10.1016/j.pnpbp.2005.08.007.

[125] Dhabhar FS, Malarkey WB, Neri E, McEwen BS. Stress-induced redistribution of immune cells-From barracks to boulevards to battlefields: A tale of three hormones - Curt Richter Award Winner. Psychoneuroendocrinology 2012;37:1345–68. doi:10.1016/j.psyneuen.2012.05.008.

[126] Smith SM, Vale WW. The role of the hypothalamic-pituitary-adrenal axis in neuroendocrine responses to stress. Dialogues Clin Neurosci 2006;8:383–95. doi:10.1038/nrendo.2011.222.

[127] Curtze C, Nutt JG, Carlson-Kuhta P, Mancini M, Horak FB. Levodopa Is a Double-Edged Sword for

Balance and Gait in People With Parkinson's Disease. Mov Disord 2015;30:1361–70. doi:10.1002/mds.26269.

[128] Goetz CG, Poewe W, Rascol O, Sampaio C, Stebbins GT, Counsell C, et al. Movement Disorder Society Task Force report on the Hoehn and Yahr staging scale: Status and recommendations. Mov Disord 2004;19:1020–8. doi:10.1002/mds.20213.

[129] Allen NE, Moloney N, Van Vliet V, Canning CG. The rationale for exercise in the management of pain in Parkinson's disease. J Parkinsons Dis 2015;5:229–39. doi:10.3233/JPD-140508.

[130] Wu T, Hallett M, Chan P. Motor automaticity in Parkinson's disease. Neurobiol Dis 2015;82:226–34. doi:10.1016/j.nbd.2015.06.014.

[131] Albani G, Cimolin V, Fasano A, Trotti C, Galli M, Mauro A. "Masters and servants" in parkinsonian gait: A three-dimensional analysis of biomechanical changes sensitive to disease progression. Funct Neurol 2014;29:99–105. doi:10.11138/FNeur/2014.29.2.099.

[132] Schoneburg B, Mancini M, Horak FB, Nutt J. Framework for Understanding Balance Dysfunction in Parkinson's Disease. Mov Disord 2014;28:1474–82. doi:10.1002/mds.25613.Framework.

[133] Doherty KM, van de Warrenburg BP, Peralta MC, Silveira-Moriyama L, Azulay JP, Gershanik OS, et al. Postural deformities in Parkinson's disease. Lancet Neurol 2011;10:538–49. doi:10.1016/S1474-4422(11)70067-9.

[134] Pandey S, Garg H. Postural & striatal deformities in Parkinson's disease: Are these rare? Indian J Med Res 2016;143:11–7. doi:10.4103/0971-5916.178577.

[135] Horak FB, Wrisley DM, Frank J. The Balance Evaluation Systems Test (BESTest) to Differentiate Balance Deficits. Phys Ther J 2015;89:484–98. doi:10.1111/j.1467-9639.1991.tb00167.x.

[136] Sibley KM, Beauchamp MK, Van Ooteghem K, Straus SE, Jaglal SB. Using the systems framework for postural control to analyze the components of balance evaluated in standardized balance measures: A scoping review. Arch Phys Med Rehabil 2015;96:122–132.e29. doi:10.1016/j.apmr.2014.06.021.

[137] Hubble RP, Naughton GA, Silburn PA, Cole MH. Wearable sensor use for assessing standing balance and walking stability in people with Parkinson's disease: A systematic review. PLoS One 2015;10:1–22. doi:10.1371/journal.pone.0123705.

[138] Mak MKY, Pang MYC. Balance confidence and functional mobility are independently associated with falls in people with Parkinson's disease. J Neurol 2009;256:742–9. doi:10.1007/s00415-009-5007-8.

[139] Conradsson D, Löfgren N, Ståhle A, Hagströmer M, Franzén E. A novel conceptual framework for balance training in Parkinson's disease-study protocol for a randomised controlled trial. BMC Neurol 2012;12. doi:10.1186/1471-2377-12-111.

[140] Carpenter MG, Adkin AL, Brawley LR, Frank JS. Postural, physiological and psychological reactions to challenging balance: Does age make a difference? Age Ageing 2006;35:298–303. doi:10.1093/ageing/afl002.

[141] Talkowski JB, Brach JS, Studenski S, Newman AB. Impact of health perception, balance perception, fall history, balance performance, and gait speed on walking activity in older adults. Phys Ther 2008;88:1474–81. doi:10.2522/ptj.20080036.

[142] Hadjistavropoulos HD, Amy J, Bourgault-fagnou MD. Core cognitions related to health anxiety in self-reported medical and non-medical samples. J Beh 2012;35:167–78. doi:10.1007/s10865-011-9339-3.

[143] Franchignoni F, Horak F, Godi M, Nardone A, Giordano A. Using psychometric techniques to improve the Balance Evaluation System's Test: the mini-BESTest. J Rehabil Med 2011;42:323–31. doi:10.2340/16501977-0537.Using.

[144] Huang TT, Wang WS. Comparison of three established measures of fear of falling in community-dwelling older adults: Psychometric testing. Int J Nurs Stud 2009;46:1313–9. doi:10.1016/j.ijnurstu.2009.03.010.

[145] Graham DF, Carty CP, Lloyd DG, Lichtwark GA, Barrett RS. Muscle contributions to recovery from forward loss of balance by stepping. J Biomech 2014;47:667–74. doi:10.1016/j.jbiomech.2013.11.047.

[146] Franchignoni F, Giordano A, Ferriero G. Rasch analysis of the short form 8-item Parkinson's Disease Questionnaire (PDQ-8). Qual Life Res 2008;17:541–8. doi:10.1007/s11136-008-9341-6.

[147] Pfeiffer RF. Non-motor symptoms in Parkinson's disease. Park Relat Disord 2016;22:S119–22. doi:10.1016/j.parkreldis.2015.09.004.

[148] Massano J, Bhatia KP. Clinical approach to Parkinson's disease: Features, diagnosis, and principles of management. Cold Spring Harb Perspect Med 2012;2:1–15. doi:10.1101/cshperspect.a008870.

[149] Martinez-Martin P, Chaudhuri KR, Rojo-Abuin JM, Rodriguez-Blazquez C, Alvarez-Sanchez M, Arakaki T, et al. Assessing the non-motor symptoms of Parkinson's disease: MDS-UPDRS and NMS Scale. Eur J Neurol 2015;22:37–43. doi:10.1111/ene.12165.

[150] Chaudhuri KR, Martinez-Martin P, Brown RG, Sethi K, Stocchi F, Odin P, et al. The metric properties of a novel non-motor symptoms scale for Parkinson's disease: Results from an international pilot study. Mov Disord 2007;22:1901–11. doi:10.1002/mds.21596.

[151] Chaudhuri KR, Odin P, Antonini A, Martinez-martin P. Parkinsonism and Related Disorders Parkinson ' s disease : The non-motor issues. Park Relat Disord 2011;17:717–23. doi:10.1016/j.parkreldis.2011.02.018.

[152] Broetz D, Eichner M, Gasser T, Weller M, Steinbach JP. Radicular and nonradicular back pain in Parkinson's disease: A controlled study. Mov Disord 2007;22:853–6. doi:10.1002/mds.21439.

[153] Nakamura T, Hirayama M, Hara T, Hama T, Watanabe H, Sobue G. Does cardiovascular autonomic dysfunction contribute to fatigue in Parkinson's disease? Mov Disord 2011;26:1869–74. doi:10.1002/mds.23744.

[154] Shiba M, Bower JH, Maraganore DM, McDonnell SK, Peterson BJ, Ahlskog JE, et al. Anxiety disorders and depressive disorders preceding Parkinson's disease: a case-control study. Mov Disord 2000;15:669–77. doi:10.1002/1531-8257(200007)15:4<669::AID-MDS1011>3.0.CO;2-5.

[155] Rutten S, Ghielen I, Vriend C, Hoogendoorn AW, Berendse HW, Leentjens AFG, et al. Anxiety in Parkinson's disease: Symptom dimensions and overlap with depression and autonomic failure. Park Relat Disord 2015;21:189–93. doi:10.1016/j.parkreldis.2014.11.019.

[156] Reijnders JSAM, Ehrt U, Weber WEJ, Aarsland D, Leentjens AFG. A systematic review of prevalence studies of depression in Parkinson's disease. Mov Disord 2008;23:183–9. doi:10.1002/mds.21803.

[157] Swisher AK. Yes, "Exercise is Medicine"....but It Is So Much More! Cardiopulm Phys Ther J 2010;21:4.

[158] Berryman JW. Exercise is Medicine: A Historical Perspective. Curr Sports Med Rep 2010;9:195–201. doi:10.1249/JSR.0b013e3181e7d86d.

[159] Russell E. Exercise is medicine. CMAJ 2013;185:4501. doi:10.1503/cmaj.109-4501.

[160] Schutzer KA, Graves BS. Barriers and motivations to exercise in older adults. Prev Med (Baltim) 2004;39:1056–61. doi:10.1016/j.ypmed.2004.04.003.

[161] Morris ME, Martin CL, Schenkman ML. Striding out with Parkinson disease: evidence-based physical therapy for gait disorders. Phys Ther 2010;90:280–8. doi:10.2522/ptj.20090091.

[162] Van Nimwegen M Van, Speelman AD, Hofman-Van Rossum EJM, Overeem S, Deeg DJH, Borm GF, et al. Physical inactivity in Parkinson's disease. J Neurol 2011;258:2214–21. doi:10.1007/s00415-011-6097-7.

[163] Luk KC, Lee VM, Petzinger GM, Fisher BE, Leeuwen J Van, Akopian G, et al. Enhancing Neuroplasticity in the Basal Ganglia: The Role of Exercise in Parkinson's Disease. Mov Disord 2014;25:1–9. doi:10.1002/mds.22782.Enhancing.

[164] Earhart GM, Duncan RP, Huang JL, Perlmutter JS, Pickett K a. Comparing interventions and exploring

neural mechanisms of exercise in Parkinson disease: a study protocol for a randomized controlled trial. BMC Neurol 2015;15:9. doi:10.1186/s12883-015-0261-0.

[165] Hirsch MA, Iyer SS, Sanjak M. Exercise-induced neuroplasticity in human Parkinson's disease: What is the evidence telling us? Park Relat Disord 2016;22:S78–81. doi:10.1016/j.parkreldis.2015.09.030.

[166] Šumec R, Filip P, Sheardová K, Bareš M. Psychological Benefits of Nonpharmacological Methods Aimed for Improving Balance in Parkinson's Disease: A Systematic Review. Behav Neurol 2015;2015. doi:10.1155/2015/620674.

[167] Goodwin VA, Richards SH, Taylor RS, Taylor AH, Campbell JL. The effectiveness of exercise interventions for people with Parkinson's disease: A systematic review and meta-analysis. Mov Disord 2008;23:631–40. doi:10.1002/mds.21922.

[168] Hackney ME, Earhart GM. Health-related quality of life and alternative forms of exercise in Parkinson disease. Park Relat Disord 2009;15:644–8. doi:10.1016/j.parkreldis.2009.03.003.

[169] Ebersbach G, Ebersbach A, Edler D, Kaufhold O, Kusch M, Kupsch A, et al. Comparing exercise in Parkinson's disease - The Berlin LSVT®BIG study. Mov Disord 2010;25:1902–8. doi:10.1002/mds.23212.

[170] Sage MD, Almeida QJ. Symptom and gait changes after sensory attention focused exercise vs aerobic training in Parkinson's disease. Mov Disord 2009;24:1132–8. doi:10.1002/mds.22469.

[171] Hirsch MA, Toole T, Maitland CG, Rider RA. The effects of balance training and high-intensity resistance training on persons with idiopathic Parkinson's disease. Arch Phys Med Rehabil 2003;84:1109–17. doi:10.1016/S0003-9993(03)00046-7.

[172] Dashtipour K, Johnson E, Hadi E, Whites E, Ghamsary M, Chen J, et al. Impact of exercise on the motor and non-motor symptoms of Parkinson disease. J Parkinsons Dis 2013;3:141. doi:http://dx.doi.org/10.1155/2015/586378.

[173] Wieland LS, Manheimer E, Berman BM. Development and classification of an operational definition of complementary and alternative medicine for the Cochrane collaboration. Altern Ther Health Med 2013;17:50–9. doi:10.1016/j.immuni.2010.12.017.Two-stage.

[174] Subramanian I. Complementary and Alternative Medicine and Exercise in Nonmotor Symptoms of Parkinson's Disease. Int Rev Neurobiol 2017;134:1163–88. doi:10.1016/bs.irn.2017.05.037.

[175] Scorza FA, Fiorini AC, Scorza CA, Finsterer J. Complementary Medicine in Parkinson Disease: Once Again, Surprisingly Effective. Arch Phys Med Rehabil 2018;99:1438–9. doi:10.1016/j.apmr.2018.01.033.

[176] Kwok JYY, Choi KC, Chan HYL. Effects of mind–body exercises on the physiological and psychosocial well-being of individuals with Parkinson's disease: A systematic review and meta-analysis. Complement Ther Med 2016;29:121–31. doi:10.1016/j.ctim.2016.09.016.

[177] Kwok JJYY, Kwan JCY, Auyeung M, Mok VCT, Chan HYL. The effects of yoga versus stretching and resistance training exercises on psychological distress for people with mild-to-moderate Parkinson's disease: Study prxotocol for a randomized controlled trial. Trials 2017;18:1–13. doi:10.1186/s13063-017-2223-x.

[178] Scaer RC. The Trauma Spectrum: Hidden wounds and human resiliency. New York, USA: W W Norton & Co; 2005.

[179] Kaut O, Brenig D, Marek M, Allert N, Wüllner U. Postural Stability in Parkinson ' s Disease Patients Is Improved after Stochastic Resonance Therapy. Park Dis 2016;2016. doi:10.1155/2016/7948721.

[180] Cohen RG, Gurfinkel VS, Kwak E, Warden AC, Horak FB. Lighten up: Specific postural instructions affect axial rigidity and step initiation in patients with Parkinson's disease. Neurorehabil Neural Repair 2015;29:878–88. doi:10.1177/1545968315570323.

[181] Stallibrass C, Sissons P, Chalmers C. Randomized controlled trial of the Alexander Technique for idiopathic Parkinson's disease. Clin Rehabil 2002;16:695–708. doi:10.1191/0269215502cr544oa.

[182] McCann T. An Evaluation of the Effects of a Training Programme in Trauma Release Exercise on Quality of Life. Master Diss Univ Cape T 2011;8.

[183] Brom D, Stokar Y, Lawi C, Nuriel-Porat V, Ziv Y, Lerner K, et al. Somatic Experiencing for Posttraumatic Stress Disorder: A Randomized Controlled Outcome Study. J Trauma Stress 2017;30:304–12. doi:10.1002/jts.22189.

[184] Conte E, Ware K, Marvulli R, Ianieri G, Megna M, Conte S, et al. Analysis of Brain-Neuromuscular Synchronization and Coupling Strength in Muscular Dystrophy after NPT Treatment. World J Neurosci 2015;5:302–21.

[185] Levine PA. In an Unspoken Voice: How the Body Releases Trauma and Restores Goodness. Berkeley: North Atlantic Books; 2010.

[186] Blom T. Fusing organisational change and leadership into a practical roadmap for South African organisations. 2015.

[187] Felitti VJ, Anda RF, Nordenberg D, Williamson DF, Spitz AM, Edwards V, et al. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: The adverse childhood experiences (ACE) study. Am J Prev Med 1998;14:245–58. doi:10.1016/S0749-3797(98)00017-8.

[188] Scaer RC. Observations on traumatic stress utilizing the model of the “Whiplash syndrome.” Int Soc Study Subtle Energies Energy Med 1997.

[189] Scaer R. The Body Bears the Burden. Third edit. New York, USA: 2014. doi:10.4324/9780203836361.

[190] Swann B. Trauma Releasing Exercises – A Potential Treatment for Co-Occurring Post-Traumatic Stress Disorder and Non-Specific Chronic Low-Back Pain: A Systematic Review. Saybrook University, 2016.

[191] Ghielen I, van den Heuvel O a, de Goede CJT, Houniet-de Gier M, Collette EH, Burgers-Bots I a L, et al. BEWARE: Body awareness training in the treatment of wearing-off related anxiety in patients with Parkinson’s disease: study protocol for a randomized controlled trial. Trials 2015;16:283. doi:10.1186/s13063-015-0804-0.

[192] Lu W, Bian Q, Wang W, Wu X, Wang Z, Zhao M. Chinese version of the Perceived Stress Scale- 10 : A psychometric study in Chinese university students 2017:1–8.

[193] Kohlmann S, Gierk B, Hilbert A, Brähler E, Löwe B. The overlap of somatic, anxious and depressive syndromes: A population-based analysis. J Psychosom Res 2016;90:51–6. doi:10.1016/j.jpsychores.2016.09.004.

[194] Porges SW. Orienting in a defensive world: Mammalian modifications of our evolutionary heritage - A Polyvagal theory. Psychophysiology 1995:301–18.

[195] Porges SW. The polyvagal perspective. Biol Psychol 2007;74:116–43. doi:10.1016/j.biopsycho.2006.06.009.

[196] Mccraty R, Atkinson M, Tomasino D, Tiller W a. The Electricity of Touch : Detection and measurement of cardiac energy exchange between people. Methods 1998:1–14.

[197] Ogden P, Pain C, Fisher J. A sensorimotor approach to the treatment of trauma and dissociation. PsychiatrClinNorth Am 2006;29:263–xii.

[198] Chou KL, Gilman S, Bohnen NI. Association between autonomic dysfunction and fatigue in Parkinson disease. J Neurol Sci 2017;377:190–2. doi:10.1016/j.jns.2017.04.023.

[199] Liston C, McEwen BS, Casey BJ. Psychosocial stress reversibly disrupts prefrontal processing and attentional control. Proc Natl Acad Sci 2009;106:912–7. doi:10.1073/pnas.0807041106.

[200] Porges SW. The Polyvagal Theory: Phylogenetic contributions to social behavior. Physiol Behav 2003;79:503–13. doi:10.1016/S0031-9384(03)00156-2.

[201] Porges SW. The polyvagal theory: New insights into adaptive reactions of the autonomic nervous system. Cleve Clin J Med 2009;76. doi:10.3949/ccjm.76.s2.17.

[202] De Kloet ER, Joëls M, Holsboer F. Stress and the brain: From adaptation to disease. Nat Rev Neurosci 2005;6:463–75. doi:10.1038/nrn1683.

[203] Mcewen BS. Stress Mediators 2009;583:174–85.

[204] Petzinger, G., Fisher, B., McEwen, S., Beeler, S., Walsh, J., Jakowec MENT. Cognitive Circuitry in Parkinson's Disease. Lancet Neurol 2013;12:716–26. doi:10.1016/S1474-4422(13)70123-6.Exercise-enhanced.

[205] Montero-Odasso M, Verghese J, Beauchet O, Hausdorff JM. Gait and cognition: A complementary approach to understanding brain function and the risk of falling. J Am Geriatr Soc 2012;60:2127–36. doi:10.1111/j.1532-5415.2012.04209.x.

[206] Ranabir S, Reetu K. Stress and hormones. Indian J Endocrinol Metab 2011;15:18. doi:10.4103/2230-8210.77573.

[207] Koch L (Core A. The Psoas Book. California: Guinea Pig Publications; 1997.

[208] Masaki M, Ikezoe T, Fukumoto Y, Minami S, Aoyama J, Ibuki S, et al. Association of walking speed with sagittal spinal alignment, muscle thickness, and echo intensity of lumbar back muscles in middle-aged and elderly women. Aging Clin Exp Res 2016;28:429–34. doi:10.1007/s40520-015-0442-0.

[209] Licciardone JC, Kearns CM, Crow WT. Changes in biomechanical dysfunction and low back pain reduction with osteopathic manual treatment: Results from the OSTEOPATHIC Trial. Man Ther 2014;19:324–30. doi:10.1016/j.math.2014.03.004.

[210] Iglesias-gonzález JJ, Rey U, Carlos J, De A. Musculoskeletal section. Pain Med 2013;14:1964–70.

[211] Kataoka H, Sawa N, Ueno S. Identification of a new target muscle for treatment in patients with Parkinson's disease who have lateral trunk flexion? J Neurol Sci 2015;358:435–9. doi:10.1016/j.jns.2015.09.014.

[212] Belda X, Fuentes S, Daviu N, Nadal R, Armario A. Stress-induced sensitization: The hypothalamic-pituitary-adrenal axis and beyond. Stress 2015;18:269–79. doi:10.3109/10253890.2015.1067678.

[213] Keller A, Litzelman K, Wisk LE, Maddox T, Cheng ER, Creswell PD, et al. Does the Perception that Stress Affects Health Matter? The Association with Health and Mortality. Heal Psychol 2013;31:677–84. doi:10.1037/a0026743.Does.

[214] Marx BP, Forsyth JP, Gallup GG, Fusé T, Lexington JM. Tonic immobility as an evolved predator defense: Implications for sexual assault survivors. Clin Psychol Sci Pract 2008;15:74–90. doi:10.1111/j.1468-2850.2008.00112.x.

[215] Volchan E, Souza GG, Franklin CM, Norte CE, Rocha-Rego V, Oliveira JM, et al. Is there tonic immobility in humans? Biological evidence from victims of traumatic stress. Biol Psychol 2011;88:13–9. doi:10.1016/j.biopsycho.2011.06.002.

[216] Sagliano L, Cappuccio A, Trojano L, Conson M. Approaching threats elicit a freeze-like response in humans. Neurosci Lett 2014;561:35–40. doi:10.1016/j.neulet.2013.12.038.

[217] Nijenhuis ERS, Vanderlinden J, Spinhoven P. Animal defensive reactions as a model for trauma-induced dissociative reactions. J Trauma Stress 1998;11:243–60. doi:10.1023/A:1024447003022.

[218] Cano-de-la-Cuerda R, Molero-Sánchez A, Carratalá-Tejada M, Alguacil-Diego IM, Molina-Rueda F, Miangolarra-Page JC, et al. Theories and control models and motor lear[1] Cano-de-la-Cuerda R, Molero-Sánchez A, Carratalá-Tejada M, Alguacil-Diego IM, Molina-Rueda F, Miangolarra-Page JC, et al. Theories and control models and motor learning: Clinical applications in neurorehabilit. Neurol (English Ed 2015;30:32–41. doi:10.1016/j.nrleng.2011.12.012.

[219] Harbourne R., Stergiou N. Movement variability and the use of nonlinear tools: principles to guide

physical therapist practice. Phys Ther 2009;89:267–82.

[220] Woollacott M, Shumway-Cook A. Attention and the control of posture and gait: A review of an emerging area of research. Gait Posture 2002;16:1–14. doi:10.1016/S0966-6362(01)00156-4.

[221] Kirby ED, Muroy SE, Sun WG, Covarrubias D, Leong MJ, Barchas LA, et al. Acute stress enhances adult rat hippocampal neurogenesis and activation of newborn neurons via secreted astrocytic FGF2. Elife 2013;2013:1–23. doi:10.7554/eLife.00362.

[222] de Macedo DS. Exercises to release stress and trauma (TRE): Application to situations of marital violence. 2013.

[223] Yang WC, Hsu WL, Wu RM, Lu TW, Lin KH. Motion analysis of axial rotation and gait stability during turning in people with Parkinson's disease. Gait Posture 2016;44:83–8. doi:10.1016/j.gaitpost.2015.10.023.

[224] Doumas M, Morsanyi K, Young WR. Cognitively and socially induced stress affects postural control. Exp Brain Res 2018;236:305–14. doi:10.1007/s00221-017-5128-8.

[225] Smith LK, Jadavji NM, Colwell KL, Katrina Perehudoff S, Metz GA. Stress accelerates neural degeneration and exaggerates motor symptoms in a rat model of Parkinson's disease. Eur J Neurosci 2008;27:2133–46. doi:10.1111/j.1460-9568.2008.06177.x.

[226] Cusso M, Sewram A, Pountney D, Donald K, Khoo TK. The association of perceived stress and the frequency and severity of non-motor symptoms in Parkinson's disease. Parkinsonism Relat Disord 2018;46:e12. doi:10.1016/j.parkreldis.2017.11.040.

[227] Cusso M, Sewram A, Pountney D, Donald K, Khoo TK. The association of stress with non-motor symptoms and quality of life in Parkinson's disease. J Neurol Sci 2017;381:188–373. doi:10.1016/j.parkreldis.2017.11.040.

[228] Herman AA, Stein DJ, Seedat S, Heeringa SG, Moomal H, Williams DR. The South African Stress and Health (SASH) study: 12-month and lifetime prevalence of common mental disorders. South African Med J 2009;99:339–44.

[229] De Los Reyes A, Kundey SMA, Wang M. The end of the primary outcome measure: A research agenda for constructing its replacement. Clin Psychol Rev 2011;31:829–38. doi:10.1016/j.cpr.2011.03.011.

[230] Wight D, Hallingberg B, Simpson SA, Craig P, Segrott J, Turley R, et al. Exploratory studies to decide whether and how to proceed with full-scale evaluations of public health interventions: a systematic review of guidance. Pilot Feasibility Stud 2018;4:1–12. doi:10.1186/s40814-018-0290-8.

[231] Bloem BR, Ypinga JHL, Willis A, Canning CG, Barker RA, Munneke M, et al. Using medical claims analyses to understand interventions for Parkinson patients. J Parkinsons Dis 2018;8:45–58. doi:10.3233/JPD-171277.

[232] Kluger BM, Rakowski D, Christian M, Cedar D, Wong B, Crawford J, et al. Randomized, Controlled Trial of Acupuncture for Fatigue in Parkinson's Disease. Mov Disord 2016;31:1027–32. doi:10.1002/mds.26597.

[233] Kantak SS, Winstein CJ. Learning-performance distinction and memory processes for motor skills: A focused review and perspective. Behav Brain Res 2012;228:219–31. doi:10.1016/j.bbr.2011.11.028.

[234] Shishov N, Melzer I, Bar-Haim S. Parameters and Measures in Assessment of Motor Learning in Neurorehabilitation; A Systematic Review of the Literature. Front Hum Neurosci 2017;11. doi:10.3389/fnhum.2017.00082.

[235] Kakar C, Zia N, Sehgal S, Khushwaha S. Effect of external and internal focus of attention on acquisition, retention, and transfer phase of motor learning in Parkinson's disease. Hong Kong Physiother J 2013;31:88–94. doi:10.1016/j.hkpj.2013.02.001.

[236] Cano-de-la-Cuerda R, Molero-Sánchez A, Carratalá-Tejada M, Alguacil-Diego IM, Molina-Rueda F, Miangolarra-Page JC, et al. Theories and control models and motor learning: Clinical applications in

neurorehabilitation. Neurol (English Ed 2015;30:32–41. doi:10.1016/j.nrleng.2011.12.012.

[237] City of Cape Town. Socio-economical profile of Western Cape. City Cape T 2017.

[238] Bretherton CS, Widmann M, Dymnikov VP, Wallace JM, Bladé I. The effective number of spatial degrees of freedom of a time-varying field. J Clim 1999;12:1990–2009. doi:10.1175/1520-0442(1999)012<1990:TENOSD>2.0.CO;2.

[239] Faul F, Erdfelder E, Buchner A, Lang A-G. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. Behav Res Methods 2009;41:1149–60. doi:10.3758/BRM.41.4.1149.

[240] Smith C. Levodopa Dpse Equivalency - A systematic review [presentation]. Present Birmingham Clin Trials Unit 2010.

[241] Tomlinson CL, Stowe R, Patel S, Rick C, Gray R, Clarke CE. Systematic review of levodopa dose equivalency reporting in Parkinson's disease. Mov Disord 2010;25:2649–53. doi:10.1002/mds.23429.

[242] Riebe D, Ehrman JK, Liguori G, Magal M. ACSM's guidelines for exercise testing and prescription. 2018.

[243] Atterbury EM, Welman KE. Balance training in individuals with Parkinson's disease: Therapist-supervised vs. home-based exercise programme. Gait Posture 2017;55:138–44. doi:10.1016/j.gaitpost.2017.04.006.

[244] King LA, Wilhelm J, Chen Y, Blehm R, Nutt J, Chen Z, et al. Effects of group, individual, and home exercise in persons with Parkinson disease: A randomized clinical trial. J Neurol Phys Ther 2015;39:204–12. doi:10.1097/NPT.0000000000000101.

[245] Leddy AL, Crowner BE, Earhart GM. Utility of the Mini-BESTest, BESTest, and BESTest sections for balance assessments in individuals with Parkinson disease. J Neurol Phys Ther 2011;35:90–7. doi:10.1097/NPT.0b013e31821a620c.

[246] Kegelmeyer D, Ellis T, Esposito A, Gallagher R, Harro CC, Hoder J, et al. Measurement Characteristics and Clinical Utility of the Mini BESTest in Individuals With Parkinson Disease. Arch Phys Med Rehabil 2015;96:1367–8. doi:10.1016/j.apmr.2015.02.021.

[247] Dewey DC, Miocinovic S, Bernstein I, Khemani P, Querry R, Chitnis S, et al. Automated gait and balance parameters diagnose and correlate with severity in Parkinson disease. J Neurol Sci 2014;345:131–8. doi:10.1016/j.jns.2014.07.026.

[248] Light KE, Behrman AL, Thigben M, Triggs WJ. The 2-minute walk test: a tool for evaluating endurance in clients with Parkinson's disease. Neurol Rep 1997;21:136–9.

[249] White DK, Wagenaar RC, Ellis TD, Tickle-Degnen L. Changes in Walking Activity and Endurance Following Rehabilitation for People With Parkinson Disease. Arch Phys Med Rehabil 2009;90:43–50. doi:10.1016/j.apmr.2008.06.034.

[250] Zampieri C, Salarian A, Carlson-Kuhta P, Aminian K, John G, Horak FB, et al. The instrumented timed up and go test: potential outcome measure for disease modifying therapies in Parkinson's disease. J Neurol Neurosurg Psychiatry 2010;81:171–6. doi:10.1136/jnnp.2009.173740.

[251] Stack E, Agarwal V, King R, Burnett M, Tahavori F, Janko B, et al. Identifying balance impairments in people with Parkinson's disease using video and wearable sensors. Gait Posture 2018;62:321–6. doi:10.1016/j.gaitpost.2018.03.047.

[252] Mancini M, Horak FB. Potential of APDM Mobility Lab for the monitoring of the progression of Parkinson's disease. Expert Rev Med Devices 2016;42:407–20. doi:10.1002/jmri.24785.Free-Breathing.

[253] Vienne A, Barrois RP, Buffat S, Ricard D, Vidal PP. Inertial sensors to assess gait quality in patients with neurological disorders: A systematic review of technical and analytical challenges. Front Psychol 2017;8:1–12. doi:10.3389/fpsyg.2017.00817.

[254] Hollman J, McDade E. Normative Spatiotemporal Gait Parameters in Older Adults. Gait Posture

2012;34:111–8. doi:10.1016/j.gaitpost.2011.03.024.Normative.

[255] Chaudhuri KR, Martinez-Martin P, Schapira AHV, Stocchi F, Sethi K, Odin P, et al. International multicenter pilot study of the first comprehensive self-completed nonmotor symptoms questionnaire for Parkinson's disease: The NMSQuest study. Mov Disord 2006;21:916–23. doi:10.1002/mds.20844.

[256] Martinez-Martin P, Rodriguez-Blazquez C, Abe K, Bhattacharyya KB, Bloem BR, Carod-Artal FJ, et al. International study on the psychometric attributes of the Non-Motor Symptoms Scale in Parkinson disease. Neurology 2009;73:1584–91. doi:10.1212/WNL.0b013e3181c0d416.

[257] Bostantjopoulou S, Katsarou Z, Karakasis C, Peitsidou E, Milioni D, Rossopoulos N. Evaluation of non-motor symptoms in Parkinson's Disease: An underestimated necessity. Hippokratia 2013;17:214–9.

[258] Chaudhuri KR, Martinez-martin P. Quantitation of non-motor symptoms in Parkinson's disease. Eur J Neurol 2008;15:2–8.

[259] Spitzer RL, Kroenke K, Williams JBW. Validation and utility of a self-report version of PRIME-MD: The PHQ Primary Care Study. J Am Med Assoc 1999;282:1737–44. doi:10.1001/jama.282.18.1737.

[260] Kroenke K, Spitzer RL, Williams JBW, Löwe B. The Patient Health Questionnaire Somatic, Anxiety, and Depressive Symptom Scales: A systematic review. Gen Hosp Psychiatry 2010;32:345–59. doi:10.1016/j.genhosppsych.2010.03.006.

[261] Löwe B, Spitzer RL, Williams JBW, Mussell M, Schellberg D, Kroenke K. Depression, anxiety and somatization in primary care: syndrome overlap and functional impairment. Gen Hosp Psychiatry 2008;30:191–9. doi:10.1016/j.genhosppsych.2008.01.001.

[262] Hanel G, Henningsen P, Herzog W, Sauer N, Schaefert R, Szecsenyi J, et al. Depression, anxiety, and somatoform disorders: Vague or distinct categories in primary care? Results from a large cross-sectional study. J Psychosom Res 2009;67:189–97. doi:10.1016/j.jpsychores.2009.04.013.

[263] Chagas MHN, Tumas V, Rodrigues GR, Machado-De-Sousa JP, Filho AS, Hallak JEC, et al. Validation and internal consistency of patient health questionnaire-9 for major depression in parkinson's disease. Age Ageing 2013;42:645–9. doi:10.1093/ageing/aft065.

[264] Achey RL, Yamamoto E, Sexton D, Hammer C, Lee BS, Butler RS, et al. Prediction of depression and anxiety via patient-assessed tremor severity, not physician-reported motor symptom severity, in patients with Parkinson's disease or essential tremor who have undergone deep brain stimulation. J Neurosurg 2018:1–10. doi:10.3171/2017.8.JNS1733.

[265] Kocalevent R, Hinz A, Brähler E. Standardization of a screening instrument (PHQ-15) for somatization syndromes in the general population. BMC Psychiatry 2013;13:11–3.

[266] Goetz CG, Tilley BC, Shaftman SR, Stebbins GT, Fahn S, Martinez-Martin P, et al. Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale presentation and clinimetric testing results. Mov Disord 2008;23:2129–70. doi:10.1002/mds.22340.

[267] Eggers C, Pedrosa DJ, Kahraman D, Maier F, Lewis CJ, Fink GR, et al. Parkinson Subtypes Progress Differently in Clinical Course and Imaging Pattern. PLoS One 2012;7. doi:10.1371/journal.pone.0046813.

[268] Josiah AF, Gruber-Baldini AL, Anderson KE, Fishman PS, Weiner WJ, Reich SG, et al. The effects of gait impairment with and without freezing of gait in Parkinson's disease. Park Relat Disord 2012;18:239–42. doi:10.1016/j.parkreldis.2011.10.008.

[269] Barthel C, Mallia E, Debû B, Bloem BR, Ferraye MU. The Practicalities of Assessing Freezing of Gait. J Parkinsons Dis 2016;6:667–74. doi:10.3233/JPD-160927.

[270] Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc 2005;53:695–9. doi:10.1111/j.1532-5415.2005.53221.x.

[271] Hoops S, Nazem S, Siderowf AD, Duda JE, Xie SX, Stern MB, et al. Validity of the MoCA and MMSE in

the detection of MCI and dementia in Parkinson disease. Neurology 2009;73:1738–45. doi:10.1212/WNL.0b013e3181c34b47.

[272] Schneider JS, Sendek S, Yang C. Relationship between motor symptoms, cognition, and demographic characteristics in treated mild/moderate Parkinson's disease. PLoS One 2015;10:1–11. doi:10.1371/journal.pone.0123231.

[273] Dalrymple-Alford JC, MacAskill MR, Nakas CT, Livingston L, Graham C, Crucian GP, et al. The MoCA: Well-suited screen for cognitive impairment in Parkinson disease. Neurology 2010;75:1717–25. doi:10.1212/WNL.0b013e3181fc29c9.

[274] Huang TT, Hsu HY, Wang BH, Chen KH. Quality of life in Parkinson's disease patients: validation of the Short-Form Eight-item Parkinson's Disease Questionnaire (PDQ-8) in Taiwan. Qual Life Res 2011;20:499–505. doi:10.1007/s11136-010-9777-3.

[275] Jenkinson C, Clarke C, Gray R, Hewitson P, Ives N, Morley D, et al. Comparing results from long and short form versions of the Parkinson's disease questionnaire in a longitudinal study. Park Relat Disord 2015;21:1312–6. doi:10.1016/j.parkreldis.2015.09.008.

[276] McAuley E, Duncan T, Tammen V V. Psychometric properties of the Intrinsic Motivation Inventory in a competitive sport setting: a confirmatory factor analysis. Res Q Exerc Sport 1989;60:48–58. doi:10.1080/02701367.1989.10607413.

[277] Brunet J, Gunnell KE, Gaudreau P, Sabiston CM. An integrative analytical framework for understanding the effects of autonomous and controlled motivation. Pers Individ Dif 2015;84:2–15. doi:10.1016/j.paid.2015.02.034.

[278] Keselman HJ, Algina J, Lix LM, Wilcox RR, Deering KN. A Generally Robust Approach for Testing Hypotheses and Setting Confidence Intervals for Effect Sizes. Psychol Methods 2008;13:110–29. doi:10.1037/1082-989X.13.2.110.

[279] Aarts S, Van Den Akker M, Winkens B. The importance of effect sizes. Eur J Gen Pract 2014;20:61–4. doi:10.3109/13814788.2013.818655.

[280] Lee DK. Alternatives to P value: Confidence interval and effect size. Korean J Anesthesiol 2016;69:555–62. doi:10.4097/kjae.2016.69.6.555.

[281] Durlak JA. How to select, calculate, and interperet effect sizes. J Pediatr Psychol 2009;34:917–28. doi:10.1093/jpepsy/jsp004.

[282] Maetzler W, Liepelt I, Berg D. Progression of Parkinson's disease in the clinical phase: potential markers. Lancet Neurol 2009;8:1158–71. doi:10.1016/S1474-4422(09)70291-1.

[283] McCambridge J, Witton J, Elbourne DR. Systematic review of the Hawthorne effect: New concepts are needed to study research participation effects. J Clin Epidemiol 2014;67:267–77. doi:10.1016/j.jclinepi.2013.08.015.

[284] Godi M, Franchignoni F, Caligari M, Giordano A, Turcato AM, Nardone A. Comparison of Reliability, Validity, and Responsiveness of the Mini- BESTest and Berg Balance Scale in Patients With Balance Disorders. Phys Ther J 2013;93.

[285] King LA, Priest KC, Salarian A, Pierce D, Horak FB. Comparing the Mini-BESTest with the Berg Balance Scale to evaluate balance disorders in Parkinson's disease. Parkinsons Dis 2012;2012. doi:10.1155/2012/375419.

[286] Ghaffari BD, Kluger B. Mechanisms for alternative treatments in Parkinson's disease: Acupuncture, tai chi, and other treatments. Curr Neurol Neurosci Rep 2014;14. doi:10.1007/s11910-014-0451-y.

[287] Weiss A, Herman T, Giladi N, Hausdorff JM. New evidence for gait abnormalities among Parkinson's disease patients who suffer from freezing of gait: insights using a body-fixed sensor worn for 3 days. J Neural Transm 2015;122:403–10. doi:10.1007/s00702-014-1279-y.

[288] Hass CJ, Bishop M, Moscovich M, Stegemöller EL, Skinner J, Malaty IA, et al. Defining the clinically

meaningful difference in gait speed in persons with Parkinson disease. J Neurol Phys Ther 2014;38:233–8. doi:10.1097/NPT.0000000000000055.

[289] Vaugoyeau M. Axial rotation in Parkinson's disease. J Neurol Neurosurg Psychiatry 2006;77:815–21. doi:10.1136/jnnp.2004.050666.

[290] James EG, Leveille SG, Hausdorff JM, Barton B, Cote S, Karabulut M, et al. Coordination Impairments Are Associated With Falling Among Older Adults. Exp Aging Res 2017;43:430–9. doi:10.1080/0361073X.2017.1369634.

[291] Van Emmerik REA, Wagenaar RC, Winogrodzka A, Wolters EC. Identification of axial rigidity during locomotion in parkinson disease. Arch Phys Med Rehabil 1999;80:186–91. doi:10.1016/S0003-9993(99)90119-3.

[292] Mirelman A, Bernad-Elazari H, Thaler A, Giladi-Yacobi E, Gurevich T, Gana-Weisz M, et al. Arm Swing as a Potential New Prodromal Marker of Parkinson's Disease. Mov Disord 2016;31:87–92. doi:10.1016/j.coviro.2015.09.001.Human.

[293] Lin C-C, Wagenaar RC. The impact of walking speed on interlimb coordination in individuals with Parkinson's disease. J Phys Ther Sci 2018;30:658–62. doi:10.1589/jpts.30.658.

[294] Dissanayaka NNNW, White E, O'Sullivan JD, Marsh R, Pachana NA, Byrne GJ. The clinical spectrum of anxiety in Parkinson's disease. Mov Disord 2014;29:967–75. doi:10.1002/mds.25937.

[295] de la Fuente-Fernandez R, Stoessl AJ. The placebo effect in Parkinson's disease. Trends Neurosci 2002;25:302–6. doi:10.1016/s0166-2236(02)02181-1.

[296] Hinz A, Ernst J, Glaesmer H, Brähler E, Rauscher FG, Petrowski K, et al. Frequency of somatic symptoms in the general population: Normative values for the Patient Health Questionnaire-15 (PHQ-15). J Psychosom Res 2017;96:27–31. doi:10.1016/j.jpsychores.2016.12.017.

[297] Herman T, Shema-shiratzky S, Arie L, Giladi N, Hausdorff JM. Depressive symptoms may increase the risk of the future development of freezing of gait in patients with Parkinson's disease: Findings from a 5-year prospective study. Park Relat Disord 2018. doi:10.1016/j.parkreldis.2018.09.013.

[298] Spitzer RL, Kroenke K, Williams JBW, Löwe B. A Brief Measure for Assessing Generalized Anxiety Disorder. Arch Intern Med 2006;166:1092. doi:10.1001/archinte.166.10.1092.

[299] Beard C, Björgvinsson T. Beyond generalized anxiety disorder: Psychometric properties of the GAD-7 in a heterogeneous psychiatric sample. J Anxiety Disord 2014;28:547–52. doi:10.1016/j.janxdis.2014.06.002.

[300] Carrozzino D, Bech P, Patierno C, Onofrj M, Morberg BM, Thomas A, et al. Somatization in Parkinson's Disease: A systematic review. Prog Neuro-Psychopharmacology Biol Psychiatry 2017;78:18–26. doi:10.1016/j.pnpbp.2017.05.011.

[301] Cosci F, Fava GA. The clinical inadequacy of the DSM-5 classification of somatic symptom and related disorders: An alternative trans-diagnostic model. CNS Spectr 2016;21:310–7. doi:10.1017/S1092852915000760.

[302] Bugalho P, Da Silva JA, Cargaleiro I, Serra M, Neto B. Psychiatric symptoms screening in the early stages of Parkinson's disease. J Neurol 2012;259:124–31. doi:10.1007/s00415-011-6140-8.

[303] Gallagher DA, Schrag A. Psychosis, apathy, depression and anxiety in Parkinson's disease. Neurobiol Dis 2012;46:581–9. doi:10.1016/j.nbd.2011.12.041.

[304] Carod-Artal FJ, Martinez-Martin P. Independent validation of the Non motor Symptoms Scale for Parkinson's disease in Brazilian patients. Park Relat Disord 2013;19:115–9. doi:10.1016/j.parkreldis.2012.08.008.

[305] Horváth K, Aschermann Z, Kovács M, Makkos A, Harmat M, Janszky J, et al. Minimal clinically important differences for the experiences of daily living parts of movement disorder society–sponsored unified Parkinson's disease rating scale. Mov Disord 2017;32:789–93. doi:10.1002/mds.26960.

[306] Becker H, Roberts G, Voelmeck W. Explanations for improvement in both experimental and control groups. West J Nurs Res 2003;25:746–55. doi:10.1177/0193945903253002.

[307] Bello-Haas VD, Klassen L, Sheppard S, Metcalfe A. Psychometric properties of activity, self-efficacy and quality-of-life measures in individuals with Parkinson's disease. Physiother Canada 2011;63:47–57. doi:10.3138/ptc.2009-08.

[308] Luo N, Tan LCS, Zhao Y, Lau PN, Au WL, Li SC. Determination of the longitudinal validity and minimally important difference of the 8-item Parkinson's disease questionnaire (PDQ-8). Mov Disord 2009;24:183–7. doi:10.1002/mds.22240.

[309] Bucks RS, Cruise KE, Skinner TC, Loftus AM, Barker RA, Thomas MG. Coping processes and health-related quality of life in Parkinson's disease. Int J Geriatr Psychiatry 2011;26:247–55. doi:10.1002/gps.2520.

[310] Shulman LM. Apathy in patients with Parkinson's disease. Int Rev Psychiatry 2000;12:298–306. doi:10.1080/09540260020002523.

[311] Ryan RM, Patrick H, Deci EL, Williams GC. Facilitating health behaviour change and its maintenance : Interventions based on Self-Determination Theory. Eur Heal Psychol 2008;10:2–5.

[312] Malmivaara A. Benchmarking Controlled Trial-a novel concept covering all observational effectiveness studies. Ann Med 2015;47:332–40. doi:10.3109/07853890.2015.1027255.

[313] Deci EL, Ryan RM. Self-determination theory: A macrotheory of human motivation, development, and health. Can Psychol 2008;49:182–5. doi:10.1037/a0012801.

[314] Lenth R V. Some practical guidelines for effective sample size determination. Am Stat 2001;55:187–93. doi:10.1198/000313001317098149.

[315] Hoenig JM, Heisey DM. The abuse of power: The pervasive fallacy of power calculations for data analysis. Am Stat 2001;55:19–24. doi:10.1198/000313001300339897.

[316] Wade DT, Halligan PW. The biopsychosocial model of illness : a model whose time has come. Clin Rehabil 2017;31:995–1004. doi:10.1177/0269215517709890.

[317] Kusnanto H, Agustian D, Hilmanto D. Biopsychosocial model of illnesses in primary care: A hermeneutic literature review. J Fam Med Prim Care 2018;7:497–500. doi:10.4103/jfmpc.jfmpc_145_17.

[318] Kincses P, Kovács N, Karádi K, Kállai J. Critical issues of the biopsychosocial treatment of Parkinson's disease. Orv Hetil 2015;156:472–8. doi:10.1556/OH.2015.30109.

[319] Gibson G, Studies D. What can the treatment of Parkinson's disease learn from dementia care ; applying a bio- - social approach to Parkinson ' s disease. Int J Older People Nurs 2017;12:1–8. doi:10.1111/opn.12159.

ADDENDUMS

Presented in alphabetical order.

A. Addendum A: Activity-specific Balance Confidence Scale (ABC Scale)

This section is to assess your perceived balance confidence. The section consists of 16 questions. Each question will ask you to rate how confident you feel when doing specific activities, with 0 indication no confidence in your abilities and 100 indication completely confident in your abilities.

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

↓ No Confidence

↓ Completely Confident

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

B. Addendum B: Ethical Approval Notice

UNIVERSITEIT·STELLENBOSCH·UNIVERSITY
jou kennisvennoot • your knowledge partner

Approval Notice

Response to Modifications- (New Application)

11-May-2017
Atterbury, Elizabeth EM

Ethics Reference #: S16/10/232

Title: **Exploring therapeutic neurogenic tremors with exercise as a treatment for selective motor and non-motor Parkinson's disease symptoms**

Dear Ms Elizabeth Atterbury,

The **Response to Modifications** - ***(New Application)*** received on **06-Mar-2017**, was reviewed by members of **Health Research Ethics Committee 2** via Expedited review procedures on **11-May-2017** and was approved.
Please note the following information about your approved research protocol:

Protocol Approval Period: **11-May-2017 -10-May-2018**

Please remember to use your **protocol number** (**S16/10/232**) on any documents or correspondence with the HREC concerning your research protocol.

Please note that the HREC has the prerogative and authority to ask further questions, seek additional information, require further modifications, or monitor the conduct of your research and the consent process.

After Ethical Review:
Please note a template of the progress report is obtainable on www.sun.ac.za/rds and should be submitted to the Committee before the year has expired. The Committee will then consider the continuation of the project for a further year (if necessary). Annually a number of projects may be selected randomly for an external audit.
Translation of the consent document to the language applicable to the study participants should be submitted.

Federal Wide Assurance Number: 00001372
Institutional Review Board (IRB) Number: IRB0005239

The Health Research Ethics Committee complies with the SA National Health Act No.61 2003 as it pertains to health research and the United States Code of Federal Regulations Title 45 Part 46. This committee abides by the ethical norms and principles for research, established by the Declaration of Helsinki, the South African Medical Research Council Guidelines as well as the Guidelines for Ethical Research: Principles Structures and Processes 2004 (Department of Health).

Provincial and City of Cape Town Approval

Please note that for research at a primary or secondary healthcare facility permission must still be obtained from the relevant authorities (Western Cape Department of Health and/or City Health) to conduct the research as stated in the protocol. Contact persons are Ms Claudette Abrahams at Western Cape Department of Health (healthres@pgwc.gov.za Tel: +27 21 483 9907) and Dr Helene Visser at City Health (Helene.Visser@capetown.gov.za Tel:

C. Addendum C: Fact Sheet

Parkinson's disease (PD) is the **second most common neurodegenerative disease**

- PD is defined as a **idiopathic, chronic & progressive**
- PD brain does not produce sufficient dopamine. **Dopamine** is a neurotransmitter (brain communicator)
  - helps nerve cells communicate about **automatic movement**
  - ALSO helps controls reward and pleasure centres, & emotions
- **<u>Keep in mind:</u>**
  - **Balance, coordination & rigidity**
- Struggles with balance which impacts movement. Thus chair helps them to feel safe and maintain balance. Coordination problems leads to multi-facetted movements becoming a problem, thus remind them constantly of important factors. Rigidity in muscles leads to stiffness, thus be attentive and patient with certain movements.
  - **Expression (masked face) & Speech**
- Often they have a masked expression, thus you often cannot tell whether they are engaged in the conversation. Don't let it put you off. Treat them as any other person. Generously assume they are engaged in the conversation. Their speech is often affected as well → they often speak very slowly or softly. The more comfortable they get, the more their speech might improve.
  - **Fear of falling**
- Individuals are often afraid of falling, even though they would not voice their concern. Please be aware of it and try to ensure that they feel as safe as possible.
  - **Freezing of gait**
- Some PD individuals suffer from freezing of gait → the sensation of their feet being stuck to the floor. Individuals would know how to overcome their freezing episode, but sometimes they might need a hand of just place their hand on your shoulder. Just be aware that it does happen, just be patient and ask the participant what you can do to help.

<u>Non-motor symptoms:</u>
- Sleeping problems
- Cognitive decline/Dementia
- Depression & Anxiety
- Apathy (motivation)
- Pain & fatigue
- Incontinence
- Digestive problems
- Autonomic dysfunction

<u>Motor symptoms:</u>
- Tremor
- Rigidity
- Akinesia
- Postural instability
- Stooped posture
- Shuffling gait
- Freezing of gait
- Handwriting
- Speech
- Facial expression

D. Addendum D: Informed Consent Form

UNIVERSITEIT•STELLENBOSCH•UNIVERSITY
jou kennisvennoot • your knowledge partner

PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM

TITLE OF THE RESEARCH PROJECT:

Exploring relaxation exercise interventions as a treatment for selective motor and non-motor Parkinson's disease symptoms.

REFERENCE NUMBER: S16/10/232

PRINCIPAL INVESTIGATOR: Elizma Atterbury

ADDRESS: Movement lab, Sport Science Department, Stellenbosch University

CONTACT NUMBER: 072 95 22 567 or pdresearchstudy@gmail.com

You are invited to participate in a research study conducted by Elizma Atterbury (Main researcher, Biokineticist & PhD Student) and Dr Karen Welman (Study Leader & Biokineticist) from the Sport Science Department at Stellenbosch University. Please take some time to read the information presented here, which will explain the details of this project. You are welcome to ask the researcher or her supervisor any questions about this study if you need more clarity. It is very important that you are fully satisfied and that you clearly understand what this research entails and how you could be involved. Also, your participation is **entirely voluntary** and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do agree to take part.

This study has been approved by the **Health Research Ethics Committee at Stellenbosch University** and will be conducted according to the ethical guidelines and principles of the international *Declaration of Helsinki*, South African Guidelines for *Good Clinical Practice* and the Medical Research Council (MRC) Ethical Guidelines for Research.

1. What is this research study all about?

- The research study will take place in a 70km radius from Stellenbosch University; thus locations that will be included is Stellenbosch Winelands, Helderberg area, Cape Town Metro, Northern suburbs of Cape Town, Southern suburbs of Cape Town and Paarl. From within these locations, one or more **exercise venues will be chosen** where the exercise classes will take place. This venue will be determined after recruitment of volunteers in order to make it as convenient for the participants as possible.
  - The **main aim** of this study is to investigate the effect of new relaxation exercise interventions on individuals with Parkinson's disease. To achieve this, we will see if these intervention therapies affect your motor symptoms, such as balance and mobility, as well as you non-motor symptoms, like depression, anxiety and sleep quality, as well as quality of life and disease severity. It is well known that daily stress has a huge impact on your body, physically and physiologically, and it can have far reaching effects in terms of poor sleeping, decreased mobility and ultimately poor quality of life. Exercise has been shown to be very beneficial for

individuals with Parkinson's disease. Therefore we will couple exercise and relaxation techniques together and investigate the possible effect it has on individuals' symptoms.

- All volunteers will be screened for the inclusion and exclusion criteria. The screening will take place telephonically, via email or at your house. After you have been screened and included in the study, the following procedures will be followed:

- The study contains **3 phases**. The whole study will run over **approximately 14 weeks** (possibly more for some) as depicted in the graph below. It is ideal to participate for the full intervention, but should you only be available for a portion of it, your participation will still be greatly beneficial and appreciated.

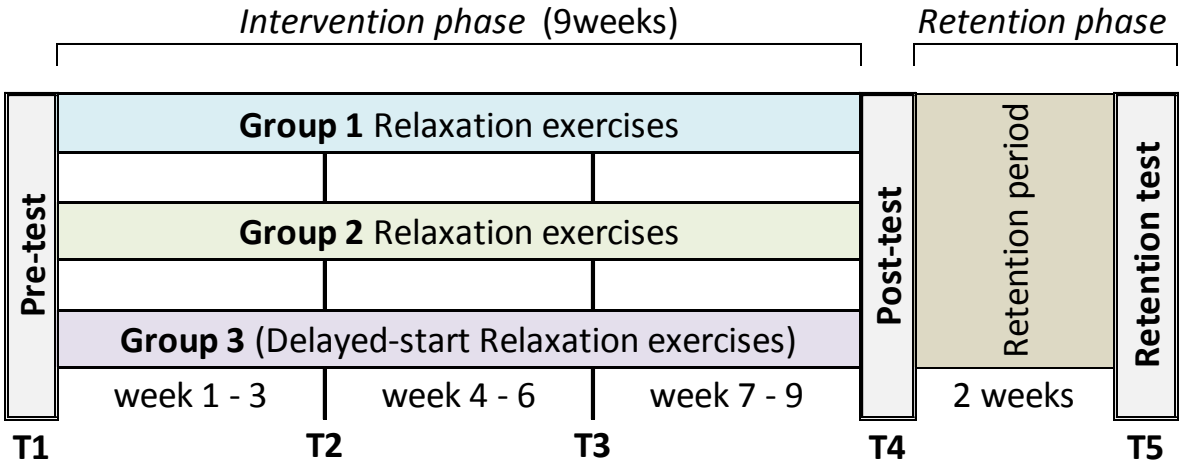
- Phase 1: Pre-Testing The pre-testing is to establish your own baseline readings before the intervention starts. This first testing will be slightly longer than other testing dates to follow. The testing procedure is very simple, as it will be repeated every 3 weeks during the 9 week intervention. There will be a total of 5 testing dates (see diagram below). More on the testing procedure in a section further in the document.

- Phase 2: Intervention Therapy period
  The intervention will run over a 9 week period. It will take place at the predetermined exercise venues, in a small group setting with a qualified therapist and possibly an assistant. The therapies to be used are body-based stress-relief and relaxation therapies and you will be **randomly assigned to 1 of 3 groups**. Two of the groups will start with the exercise intervention the week following the testing, whereas the third group will have a delayed start after the 9 week period. This delayed-start group is of great value to us because it allows us to monitor individuals' symptom fluctuation, while also circumventing logistical issues in terms of resources available.

  Therapies might include relaxation and breathing exercises, stretching, or a therapeutically-induced tremor. You will be required to complete **3 sessions per week**, but the therapies included are very safe and consist of easy exercises with a relaxation part that can be done at home. A session typically lasts between 30 – 60 minutes. During the first 2 weeks, you will see the therapist 3 times a week; this is to help you to become familiar with the therapy. Throughout weeks 3 to 6, you will see the therapist only twice and will be asked to complete 1 session in your own time at home. Finally, for the last 3 weeks, you will only see the therapist once and complete 2 sessions at home. The researchers would like to monitor your progress throughout the 9 weeks, and therefore you will be tested every 3 weeks. Phase 2 includes 3 testing dates. Additionally, participants will be asked to keep a sleep diary throughout the 9 week intervention.

  Phase 3: Post-testing and Retention period
  Phase 3, the final phase, consists of 4 weeks. During week 1, all post-testing will be done once the intervention therapies have been completed. For weeks 2 and 3, participants will be asked to **completely stop with the therapy**; the aim of this period is to investigate if any possible benefits obtained from the therapy sessions will last for 2 weeks after the last session. Finally, the participants will be tested for the last time in week 4 of the post-testing period. Once these retention tests are done, participants are welcome to continue using the therapies at home. **The third group (delayed-start group)** will start after the cessation of the post-testing with a 6 (possible 9) week intervention with the therapy that we have seen the greatest improvement in (more information will be communicated later).

- We know that **medication** plays a big role in the life of an individual with Parkinson's disease and it can have quite an effect on your performance. To accommodate for this fact, your tests will take place as close to the same time of day for every testing session. If there are any changes to your medication during the study, **please report** this as soon as you can to the researcher, as it influences the data we collect.



- **Note:** Your primary physician must approve you for exercise before you can take part in the intervention, and they should also confirm your diagnosis. You can do this on your next bi-annual appointment with your physician, if it is before the intervention phase starts. Or alternatively you can phone your doctor to get permission to participate and confirm your diagnosis, or you can give us permission to phone them on your behalf. Should your doctor deem it necessary to see you before permission is granted, the Sport Science Department of Stellenbosch University will cover the cost of the appointment.

2. What tests will I be subject to if I participate in this research?

- None of the tests will be invasive nor are they designed to cause you harm or discomfort.
- The testing procedure includes several questionnaires and a few physical tests. Testing procedure will last between 40 to 90 minutes.
- The questionnaires can be completed at home or filled in online. These questionnaires include assessing your disease severity, depressive moods, and perceived balance confidence. We will also ask you to complete a questionnaire to assess any non-motor symptoms you may experience, as well as your quality of life rating.
- The physical tests included will test your balance and your walking ability by challenging you in different ways, as well as you motor symptoms.
- The testing will be done either at your house or at the location where the exercises will take place.

3. What will your responsibilities be?

- Should you wish to participate in this study, your responsibility will be to participate in the testing dates communicated to you and be as honest and open with the researchers as possible. Furthermore, you will be asked to complete the intervention therapy which entails sessions with the therapist and completing certain session as home in your own time.
- In the case of any adverse events or other difficulties that might arise that could hamper your participation, it is your responsibility to inform the researchers so that they can make the necessary adjustments and arrangements to help you, where possible.

4. Will you benefit from taking part in this research?

- By participating in this research study, you are actively contributing to the pool of knowledge on Parkinson's disease. You will also gain more knowledge about your own current condition.

Personal benefits may include improvements in stress symptoms, leg strength, flexibility, mood, sleep, and quality of life.

- Working in a small group also offers the opportunity to meet new people, and the social aspect is seen as a big benefit for some individuals. Furthermore, after the study you will have gained knowledge about an exercise and relaxation therapy that is easy and safe to do at home.
- After every testing you will also receive a voucher for a specialized test or therapy. Details about the vouchers are discussed later in this document.
- Finally, once the study is finalised, you will also receive a report detailing your functional and disease status throughout the intervention period. This research has the potential to indicate new methods and therapies that should in the future be included in Parkinson's disease standard care.

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

- The risk for participating in this study in minimal. During the test, your balance will be challenged and could lead to some instability but throughout the testing procedure there will always be a chair behind you and a qualified researcher or research assistant at your side. All researchers and research assistants are first aiders and strict safety protocols are in place in case of an adverse event.
- The intervention therapies are very safe and you will be guided through all the exercises. Certain exercises will be modified for you if you do not feel comfortable with performing it. Some exercises will take place alongside a chair, however most of the session can be done seated or lying on the floor.
- The interventions might result in detox symptoms like light headaches or nausea, although it is not common, it carries minimal risk and it usually subsides quickly. Water will be supplied throughout the intervention. Additionally, some of the relaxation techniques might lead to heightened emotions. All the therapists are well equipped to handle any overwhelming feelings. A clinical psychologist forms part of the research team, should you wish to receive additional attention or if the researcher deems it necessary.
- Health and safety procedures are in place to deal with emergencies that may arise during the tests or intervention, i.e. a first aid kit, as well as the closest emergencies services to the exercise location.

6. If you do not agree or qualify to take part, what alternatives do you have?

- If you do not agree to participate in the full study for whatever reason, you can also opt to participating in the following ways: 1) you can participate in a small descriptive study to investigate walking with visual cues for individuals with Parkinson's disease, 2) you can opt to participate in a later leg of the study, or 3) if you are interested in exercising but cannot take part in the study at all, a set of 9 exercise DVD's can be made available to you. These DVD's contain an 8 week balance training programme that can easily be done at your house.

7. Who will have access to your medical records?

- All information that you share with the researchers will only be seen by the main researcher and supervisor. Information and records will be stored in a locked cabinet to which only the two abovementioned individuals will have access to. Furthermore for all publications of the research, the identity of participants will not be revealed and all data will be presented as group averages.

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

- This research study is covered by an insurance policy taken out by Stellenbosch University in the event that you suffer a bodily injury as a result of taking part in the study. Should any adverse events occur directly due to participating in this study, the insurers will be contacted to arrange for compensation for the expenses of any injury, where it is applicable. Participants

will be advised to contact Mr van Kerwel (wvankerwel@sun.ac.za) at Stellenbosch University for information on the issue of compensation and coverage of medical expenses in the event of a research-related injury. However the Sport Science Department will also cover the costs if Netcare (private ambulance service) is required and the person does not have their own medical aid. All researchers are qualified in Basic Life Support and the supervisor as well as the main researchers are qualified Biokineticists. A clinical psychologist is part of the research team to handle any emotional distress or results that might require further assistance.

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

- You will not receive any monetary compensation for participation in the study or for your transportation to and from the exercise venues. However, you will receive compensation for your time and effort. This will be in the form of a voucher of various services after the completion of each testing session. For each testing completed you will receive a selection of the following vouchers (valued between R250 – R600): 45min Massage, Balance assessment, Body composition analysis, Biokinetics assessment, Fitness assessment, Home exercise program, 3 individual Relaxation sessions, and gait analysis. These vouchers can be redeemed at the Sport Science Department, Stellenbosch University. These vouchers will be valid until end August 2018. There will be no costs involved for you if you do take part, except for transportation.

Is there anything else that you should know or do?

- You should inform your family practitioner or doctor that you are taking part in a research study.
- You can contact Miss Elizma Atterbury at 072 95 22 567 or Dr Karen Welman at 021 808 4733 if you have any further queries or encounter any problems.
- You can contact the Health Research Ethics Committee at 021-938 9207 if you have any concerns or complaints that have not been adequately addressed by the researcher.
- You will receive a copy of this information and consent form for your own records.

*****

Declaration by participant

By signing below, I …….. agree to take part in a research study entitled "Effect of relaxation exercises on motor and non-motor symptoms of individuals with Parkinson's disease".

I declare that:

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

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

....

Signature of participant **Signature of witness**

Declaration by investigator

I (name) …… declare that:

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

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

....

Signature of investigator **Signature of witness**

E. Addendum E: Intervention exercise routine

Summary of exercise routine and modifications

Exercise list:

1. Breathing
2. Ankle stretch
3. Calve raises
4. Posterior leg stretch
5. Inner thigh stretch
6. Hip and spine twist stretch
7. Wall sit
8. Butterfly pelvic bridge
9. Tremor
10. Integration / Relaxation

**How to get onto and up from the floor* (see description below exercise 10)

Set-up:

Yoga mat with sturdy chair. Bare feet or with socks on.

Pillows and blankets for comfort.

Principles of exercise therapy:

- Remain with the body, and give attention to sensations felt in the body during exercises.
- Nothing should hurt. Exercises should not cause pain. If it does, stop and revise exercise descriptions and either try another option, or do the exercise to a lesser extent (only to where it feel comfortable). Work within your own limit.
- Perform the exercises at a slow tempo to get full benefits of the stretches, and relaxation. This is also an important safety point.
- Remember to breathe and use your breathing throughout the session.

Exercises

Below each exercise is explained by giving the aim of the specific exercise, and also describing one or more options of how that aim can be achieved through exercise variations (numbered i – iii).

1. Breathing

AIM: Start the session with a calm heart and helps quiet the mind.

2. Ankle stretch

AIM: To stretch the ligaments on the side of the ankles

i. Single leg ankle stretch
ii. Double leg ankle stretch

3. Calve raises

AIM: To strengthen calves through fatiguing the muscles at the back of the lower leg.

i. Double leg calve raises
ii. Single leg calve raises

4. **Posterior leg stretch**

AIM: To stretch the whole posterior line on the leg – heel, though calves, hamstrings and even bum.

i. Double leg posterior leg stretch with chair
ii. Single leg posterior leg stretch with chair
iii. Single leg posterior leg stretch

5. **Inner thigh stretch**

AIM: to stretch the inner thighs, as well as hamstrings and back muscles.

i. Inner thigh stretch with chair
ii. Inner thigh stretch without chair

6. **Hip and spine twist stretch**

AIM: To stretch the front part of the hips and also to stretch the spine through a gentle twisting motion.

i. Gentle back bend with chair
ii. Gentle back bend without chair

7. **Wall sit**

AIM: To strengthen quadriceps through fatiguing the muscles at the front of the thighs.

8. **Butterfly pelvic bridge**

AIM: To strengthen the muscles in the lower back, bum and lower abdominal area through fatiguing the muscles through holding a pelvic bridge position.

9. **Tremor**

AIM: To activate the natural tremoring mechanism of the body to release tension from the body.

10. **Integration / Relaxation**

AIM: To give the body time to rest and relax.

**How to get onto and up from the floor*

How to get down:

1. Stand with chair in front. Back of the chair or seat can be facing knees, which ever preferred. Take a big step backwards.
2. Keeping weight on front leg. Slowly bend back leg and lower until knee touches the floor.
3. Using support from chair or floor, place both knees together.
4. Place both hands on the floor. Move the chair away if need be to stand comfortably on all fours.
5. Roll hips to whichever side preferred and place bum on ground.

How to get up:

1. Press up with the arms to become seated on the one hip.
2. Roll onto both knees with hands supporting on the floor – all fours position.
3. Using the support of the chair or floor, place one leg forward – foot flat on the ground.
4. Place body weight on front leg and use leg muscles and chair to push into a standing position.
5. Come up slowly and ensure to have balance before starting to walk.

DO NOT – let someone pull by the arms to help you upright. Rather let them give support at the trunk/ribs or underneath the arms.

F. Addendum F: Mini-BESTest

Mini-BESTest: Balance Evaluation Systems Test

ANTICIPATORY ***SUB SCORE:*** /6

1. SIT TO STAND
Instruction: *"Cross your arms across your chest. Try not to use your hands unless you must. Do not let your legs lean against the back of the chair when you stand. Please stand up now."*
(2) Normal: Comes to stand without use of hands and stabilizes independently.
(1) Moderate: Comes to stand WITH use of hands on first attempt.
(0) Severe: Unable to stand up from chair without assistance, OR needs several attempts with use of hands.

2. RISE TO TOES
Instruction: *"Place your feet shoulder width apart. Place your hands on your hips. Try to rise as high as you can onto your toes. I will count out loud to 3 seconds. Try to hold this pose for at least 3 seconds. Look straight ahead. Rise now."*
(2) Normal: Stable for 3 s with maximum height.
(1) Moderate: Heels up, but not full range (smaller than when holding hands), OR noticeable instability for 3 s.
(0) Severe: ≤ 3 s.

3. STAND ON ONE LEG
Instruction: "Look straight ahead. Keep your hands on your hips. Lift your leg off of the ground behind you without touching or resting your raised leg upon your other standing leg. Stay standing on one leg as long as you can. Look straight ahead. Lift now."

Left: *Time in Seconds Trial 1:_____Trial 2:_____*
(2) Normal: 20 s.
(1) Moderate: < 20 s.
(0) Severe: Unable.

Right: *Time in Seconds Trial 1:_____Trial 2:_____*
(2) Normal: 20 s.
(1) Moderate: < 20 s.
(0) Severe: Unable

To score each side separately use the trial with the longest time.
To calculate the sub-score and total score use the side [left or right] with the lowest numerical score [i.e. the worse side].

REACTIVE POSTURAL CONTROL ***SUB SCORE:*** /6

4. COMPENSATORY STEPPING CORRECTION- FORWARD
Instruction: "Stand with your feet shoulder width apart, arms at your sides. Lean forward against my hands beyond your forward limits. When I let go, do whatever is necessary, including taking a step, to avoid a fall."
(2) Normal: Recovers independently with a single, large step (second realignment step is allowed).
(1) Moderate: More than one step used to recover equilibrium.
(0) Severe: No step, OR would fall if not caught, OR falls spontaneously.

5. COMPENSATORY STEPPING CORRECTION- BACKWARD
Instruction: "Stand with your feet shoulder width apart, arms at your sides. Lean backward against my hands beyond your backward limits. When I let go, do whatever is necessary, including taking a step, to avoid a fall."
(2) Normal: Recovers independently with a single, large step.
(1) Moderate: More than one step used to recover equilibrium.
(0) Severe: No step, OR would fall if not caught, OR falls spontaneously.

6. COMPENSATORY STEPPING CORRECTION- LATERAL
Instruction: "Stand with your feet together, arms down at your sides. Lean into my hand beyond your sideways limit. When I let go, do whatever is necessary, including taking a step, to avoid a fall."

Left
(2) Normal: Recovers independently with 1 step (crossover or lateral OK).
(1) Moderate: Several steps to recover equilibrium.
(0) Severe: Falls, or cannot step.

Right
(2) Normal: Recovers independently with 1 step (crossover or lateral OK).
(1) Moderate: Several steps to recover equilibrium.
(0) Severe: Falls, or cannot step.

Use the side with the lowest score to calculate sub-score and total score.

SENSORY ORIENTATION ***SUB SCORE:*** /6

7. STANCE (FEET TOGETHER); EYES OPEN, FIRM SURFACE
Instruction: "Place your hands on your hips. Place your feet together until almost touching. Look straight ahead. Be as stable and still as possible, until I say stop."
Time in seconds:_____
(2) Normal: 30 s.
(1) Moderate: < 30 s.
(0) Severe: Unable.

8. STANCE (FEET TOGETHER); EYES CLOSED, FOAM SURFACE

Instruction: "Step onto the foam. Place your hands on your hips. Place your feet together until almost touching. Be as stable and still as possible, until I say stop. I will start timing when you close your eyes."

Time in seconds:_____

(2) Normal: 30 s.
(1) Moderate: < 30 s.
(0) Severe: Unable.

9. INCLINE- EYES CLOSED

Instruction: "Step onto the incline ramp. Please stand on the incline ramp with your toes toward the top. Place your feet shoulder width apart and have your arms down at your sides. I will start timing when you close your eyes."

Time in seconds:_____

(2) Normal: Stands independently 30 s and aligns with gravity.
(1) Moderate: Stands independently <30 s OR aligns with surface.
(0) Severe: Unable.

DYNAMIC GAIT ***SUB SCORE:*** /10

10. CHANGE IN GAIT SPEED

Instruction: "Begin walking at your normal speed, when I tell you 'fast', walk as fast as you can. When I say 'slow', walk very slowly."

(2) Normal: Significantly changes walking speed without imbalance.
(1) Moderate: Unable to change walking speed or signs of imbalance.
(0) Severe: Unable to achieve significant change in walking speed AND signs of imbalance.

11. WALK WITH HEAD TURNS – HORIZONTAL

Instruction: "Begin walking at your normal speed, when I say "right", turn your head and look to the right. When I say "left" turn your head and look to the left. Try to keep yourself walking in a straight line."

(2) Normal: performs head turns with no change in gait speed and good balance.
(1) Moderate: performs head turns with reduction in gait speed.
(0) Severe: performs head turns with imbalance.

12. WALK WITH PIVOT TURNS

Instruction: "Begin walking at your normal speed. When I tell you to 'turn and stop', turn as quickly as you can, face the opposite direction, and stop. After the turn, your feet should be close together."

(2) Normal: Turns with feet close FAST (≤ 3 steps) with good balance.
(1) Moderate: Turns with feet close SLOW (≥4 steps) with good balance.
(0) Severe: Cannot turn with feet close at any speed without imbalance.

13. STEP OVER OBSTACLES

Instruction: "Begin walking at your normal speed. When you get to the box, step over it, not around it and keep walking."

(2) Normal: Able to step over box with minimal change of gait speed and with good balance.
(1) Moderate: Steps over box but touches box OR displays cautious behavior by slowing gait.
(0) Severe: Unable to step over box OR steps around box.

14. TIMED UP & GO WITH DUAL TASK ***[3 METER WALK]***

Instruction TUG: "When I say 'Go', stand up from chair, walk at your normal speed across the tape on the floor, turn around, and come back to sit in the chair."

Instruction TUG with Dual Task: "Count backwards by threes starting at ___. When I say 'Go', stand up from chair, walk at your normal speed across the tape on the floor, turn around, and come back to sit in the chair. Continue counting backwards the entire time."

TUG:_____seconds; Dual Task TUG:_____seconds

(2) Normal: No noticeable change in sitting, standing or walking while backward counting when compared to TUG without Dual Task.
(1) Moderate: Dual Task affects either counting OR walking (>10%) when compared to the TUG without Dual Task.
(0) Severe: Stops counting while walking OR stops walking while counting.

When scoring item 14, if subject's gait speed slows more than 10% between the TUG without and with a Dual Task the score should be decreased by a point.

TOTAL SCORE: _____/28

Mini-BESTest Instructions

Subject Conditions: Subject should be tested with flat-heeled shoes OR shoes and socks off.
Equipment: Temper® foam (also called T-foam™ 4 inches thick, medium density T41 firmness rating), chair without arm rests or wheels, incline ramp, stopwatch, a box (9" height) and a 3 meter distance measured out and marked on the floor with tape [from chair].
Scoring: The test has a maximum score of **28** points from **14 items** that are each scored from 0-2.
"0" indicates the lowest level of function and "2" the highest level of function.
If a subject must use an assistive device for an item, score that item one category lower.
If a subject requires physical assistance to perform an item, score "0" for that item.
For **Item 3** (stand on one leg) and **Item 6** (compensatory stepping-lateral) only include the score for one side (the worse score).
For **Item 3** (stand on one leg) select the best time of the 2 trials [from a given side] for the score.
For **Item 14** (timed up & go with dual task) if a person's gait slows greater than 10% between the TUG without and with a dual task then the score should be decreased by a point.

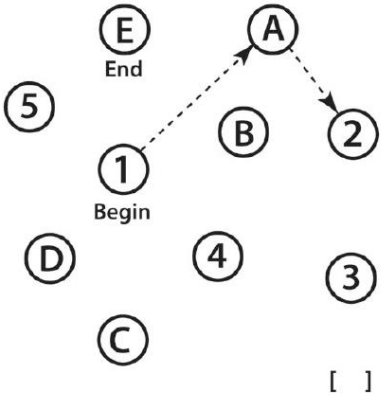
1. SIT TO STAND	Note the initiation of the movement, and the use of the subject's hands on the seat of the chair, the thighs, or the thrusting of the arms forward.
2. RISE TO TOES	Allow the subject two attempts. Score the best attempt. (If you suspect that subject is using less than full height, ask the subject to rise up while holding the examiners' hands.) Make sure the subject looks at a non-moving target 4-12 feet away.
3. STAND ON ONE LEG	Allow the subject two attempts and record the times. Record the number of seconds the subject can hold up to a maximum of 20 seconds. Stop timing when the subject moves hands off of hips or puts a foot down. Make sure the subject looks at a non-moving target 4-12 feet ahead. Repeat on other side.
4. COMPENSATORY STEPPING CORRECTION-FORWARD	Stand in front of the subject with one hand on each shoulder and ask the subject to lean forward (Make sure there is room for them to step forward). Require the subject to lean until the subject's shoulders and hips are in front of toes. After you feel the subject's body weight in your hands, very suddenly release your support. The test must elicit a step. NOTE: Be prepared to catch subject.
5. COMPENSATORY STEPPING CORRECTION - BACKWARD	Stand behind the subject with one hand on each scapula and ask the subject to lean backward (Make sure there is room for the subject to step backward.) Require the subject to lean until their shoulders and hips are in back of their heels. After you feel the subject's body weight in your hands, very suddenly release your support. Test must elicit a step. NOTE: Be prepared to catch subject.
6. COMPENSATORY STEPPING CORRECTION- LATERAL	Stand to the side of the subject, place one hand on the side of the subject's pelvis, and have the subject lean their whole body into your hands. Require the subject to lean until the midline of the pelvis is over the right (or left) foot and then suddenly release your hold. NOTE: Be prepared to catch subject.
7. STANCE (FEET TOGETHER); EYES OPEN, FIRM SURFACE	Record the time the subject was able to stand with feet together up to a maximum of 30 seconds. Make sure subject looks at a non-moving target 4-12 feet away.
8. STANCE (FEET TOGETHER); EYES CLOSED, FOAM SURFACE	Use medium density Temper® foam, 4 inches thick. Assist subject in stepping onto foam. Record the time the subject was able to stand in each condition to a maximum of 30 seconds. Have the subject step off of the foam between trials. Flip the foam over between each trial to ensure the foam has retained its shape.
9. INCLINE EYES CLOSED	Aid the subject onto the ramp. Once the subject closes eyes, begin timing and record time. Note if there is excessive sway.
10. CHANGE IN SPEED	Allow the subject to take 3-5 steps at normal speed, and then say "fast". After 3-5 fast steps, say "slow". Allow 3-5 slow steps before the subject stops walking.
11. WALK WITH HEAD TURNS-HORIZONTAL	Allow the subject to reach normal speed, and give the commands "right, left" every 3-5 steps. Score if you see a problem in either direction. If subject has severe cervical restrictions allow combined head and trunk movements.
12. WALK WITH PIVOT TURNS	Demonstrate a pivot turn. Once the subject is walking at normal speed, say "turn and stop." Count the number of steps from "turn" until the subject is stable. Imbalance may be indicated by wide stance, extra stepping or trunk motion.
13. STEP OVER OBSTACLES	Place the box (9 inches or 23 cm height) 10 feet away from where the subject will begin walking. Two shoeboxes taped together works well to create this apparatus.
14. TIMED UP & GO WITH DUAL TASK	*Use the TUG time to determine the effects of dual tasking. The subject should walk a 3 meter distance.* *TUG:* Have the subject sitting with the subject's back against the chair. The subject will be timed from the moment you say "Go" until the subject returns to sitting. Stop timing when the subject's buttocks hit the chair bottom and the subject's back is against the chair. The chair should be firm without arms. *TUG With Dual Task*: While sitting determine how fast and accurately the subject can count backwards by threes starting from a number between 100-90. Then, ask the subject to count from a different number and after a few numbers say "Go". Time the subject from the moment you say "Go" until the subject returns to the sitting position. Score dual task as affecting counting or walking if speed slows (>10%) from TUG and or new signs of imbalance.

G. Addendum G: Montreal Cognitive Assessment (MoCA)

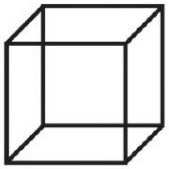
MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

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

VISUOSPATIAL / EXECUTIVE



Copy cube



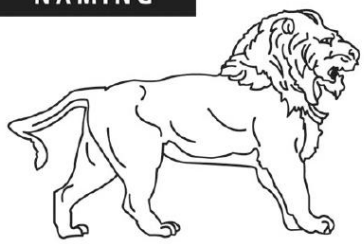
[ ] [ ]

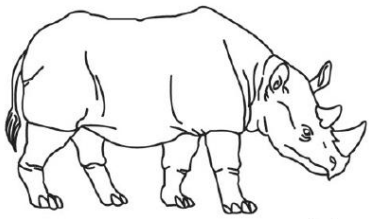
Draw CLOCK (Ten past eleven)
(3 points)

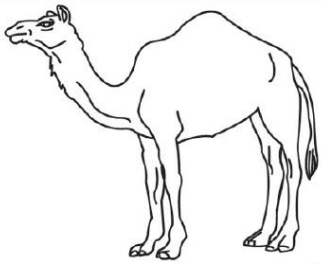
[ ] Contour [ ] Numbers [ ] Hands

POINTS ___/5

NAMING







[ ] [ ] [ ]

___/3

MEMORY Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. 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 **www.mocatest.org** Normal ≥ 26 / 30

TOTAL ___/30
Add 1 point if ≤ 12 yr edu

Administered by: _____

H. Addendum H: Non-motor symptoms Questionnaire (NMSQuest)

PD NMS QUESTIONNAIRE

Name: ..... Date: ..... Age: .....

Centre ID: Male ☐ Female ☐

NON-MOVEMENT PROBLEMS IN PARKINSON'S

The movement symptoms of Parkinson's are well known. However, other problems can sometimes occur as part of the condition or its treatment. It is important that the doctor knows about these, particularly if they are troublesome for you.

A range of problems is listed below. Please tick the box 'Yes' if you have experienced it **during the past month.** The doctor or nurse may ask you some questions to help decide. If you have **not** experienced the problem in the past month tick the 'No' box. You should answer 'No' even if you have had the problem in the past but not in the past month.

Have you experienced any of the following in the last month?

	Yes	No
1. Dribbling of saliva during the daytime	☐	☐
2. Loss or change in your ability to taste or smell	☐	☐
3. Difficulty swallowing food or drink or problems with choking	☐	☐
4. Vomiting or feelings of sickness (nausea)	☐	☐
5. Constipation (less than 3 bowel movements a week) or having to strain to pass a stool (faeces)	☐	☐
6. Bowel (fecal) incontinence	☐	☐
7. Feeling that your bowel emptying is incomplete after having been to the toilet	☐	☐
8. A sense of urgency to pass urine makes you rush to the toilet	☐	☐
9. Getting up regularly at night to pass urine	☐	☐
10. Unexplained pains (not due to known conditions such as arthritis)	☐	☐
11. Unexplained change in weight (not due to change in diet)	☐	☐
12. Problems remembering things that have happened recently or forgetting to do things	☐	☐
13. Loss of interest in what is happening around you or doing things	☐	☐
14. Seeing or hearing things that you know or are told are not there	☐	☐
15. Difficulty concentrating or staying focussed	☐	☐
16. Feeling sad, 'low' or 'blue'	☐	☐
17. Feeling anxious, frightened or panicky	☐	☐
18. Feeling less interested in sex or more interested in sex	☐	☐
19. Finding it difficult to have sex when you try	☐	☐
20. Feeling light headed, dizzy or weak standing from sitting or lying	☐	☐
21. Falling	☐	☐
22. Finding it difficult to stay awake during activities such as working, driving or eating	☐	☐
23. Difficulty getting to sleep at night or staying asleep at night	☐	☐
24. Intense, vivid dreams or frightening dreams	☐	☐
25. Talking or moving about in your sleep as if you are 'acting' out a dream	☐	☐
26. Unpleasant sensations in your legs at night or while resting, and a feeling that you need to move	☐	☐
27. Swelling of your legs	☐	☐
28. Excessive sweating	☐	☐
29. Double vision	☐	☐
30. Believing things are happening to you that other people say are not true	☐	☐

All the information you supply through this form will be treated with confidence and will only be used for the purpose for which it has been collected. Information supplied will be used for monitoring purposes. Your personal data will be processed and held in accordance with the Data Protection Act 1998.

Developed and validated by the International PD Non Motor Group
For information contact: susanne.tluk@uhl.nhs.uk or alison.forbes@uhl.nhs.uk

I. Addendum I: Non-Motor Symptom Scale (NMSS)

Non-Motor Symptom assessment scale for Parkinson's Disease

Patient ID No: _____ **Initials:** _____ **Age:** _____

Symptoms assessed over the last month. Each symptom scored with respect to:

Severity: 0 = None, 1 = Mild: symptoms present but causes little distress or disturbance to patient;
2 = Moderate: some distress or disturbance to patient; 3 = Severe: major source of distress or disturbance to patient.

Frequency: 1 = Rarely (<1/wk); 2 = Often (1/wk); 3 = Frequent (several times per week);
4 = Very Frequent (daily or all the time).

Domains will be weighed differentially. Yes/ No answers are not included in final frequency x severity calculation.
(Bracketed text in questions within the scale is included as an explanatory aid).

	Severity	Frequency	Frequency x Severity
Domain 1: Cardiovascular including falls			
1. Does the patient experience light-headedness, dizziness, weakness on standing from sitting or lying position?	☐	☐	☐
2. Does the patient fall because of fainting or blacking out?	☐	☐	☐
SCORE:			☐
Domain 2: Sleep/fatigue			
3. Does the patient doze off or fall asleep unintentionally during daytime activities? (For example, during conversation, during mealtimes, or while watching television or reading).	☐	☐	☐
4. Does fatigue (tiredness) or lack of energy (not slowness) limit the patient's daytime activities?	☐	☐	☐
5. Does the patient have difficulties falling or staying asleep?	☐	☐	☐
6. Does the patient experience an urge to move the legs or restlessness in legs that improves with movement when he/she is sitting or lying down inactive?	☐	☐	☐
SCORE:			☐
Domain 3: Mood/cognition			
7. Has the patient lost interest in his/her surroundings?	☐	☐	☐
8. Has the patient lost interest in doing things or lack motivation to start new activities?	☐	☐	☐
9. Does the patient feel nervous, worried or frightened for no apparent reason?	☐	☐	☐
10. Does the patient seem sad or depressed or has he/she reported such feelings?	☐	☐	☐
11. Does the patient have flat moods without the normal "highs" and " lows"?	☐	☐	☐
12. Does the patient have difficulty in experiencing pleasure from their usual activities or report that they lack pleasure?	☐	☐	☐
SCORE:			☐
Domain 4: Perceptual problems/hallucinations			
13. Does the patient indicate that he/she sees things that are not there?	☐	☐	☐
14. Does the patient have beliefs that you know are not true? (For example, about being harmed, being robbed or being unfaithful)	☐	☐	☐
15. Does the patient experience double vision? (2 separate real objects and not blurred vision)	☐	☐	☐
SCORE:			☐

	Severity	Frequency	Frequency x Severity
Domain 5: Attention/memory			
16. Does the patient have problems sustaining concentration during activities? (For example, reading or having a conversation)	☐	☐	☐
17. Does the patient forget things that he/she has been told a short time ago or events that happened in the last few days?	☐	☐	☐
18. Does the patient forget to do things? (For example, take tablets or turn off domestic appliances?)	☐	☐	☐
SCORE:			☐
Domain 6: Gastrointestinal tract			
19. Does the patient dribble saliva during the day?	☐	☐	☐
20. Does the patient have difficulty swallowing?	☐	☐	☐
21. Does the patient suffer from constipation? (Bowel action less than three times weekly)	☐	☐	☐
SCORE:			☐
Domain 7: Urinary			
22. Does the patient have difficulty holding urine? (Urgency)	☐	☐	☐
23. Does the patient have to void within 2 hours of last voiding? (Frequency)	☐	☐	☐
24. Does the patient have to get up regularly at night to pass urine? (Nocturia)	☐	☐	☐
SCORE:			☐
Domain 8: Sexual function			
25. Does the patient have altered interest in sex? (Very much increased or decreased, please underline)	☐	☐	☐
26. Does the patient have problems having sex?	☐	☐	☐
SCORE:			☐
Domain 9: Miscellaneous			
27. Does the patient suffer from pain not explained by other known conditions? (Is it related to intake of drugs and is it relieved by antiparkinson drugs?)	☐	☐	☐
28. Does the patient report a change in ability to taste or smell?	☐	☐	☐
29. Does the patient report a recent change in weight (not related to dieting)?	☐	☐	☐
30. Does the patient experience excessive sweating (not related to hot weather)?	☐	☐	☐
SCORE:			☐
TOTAL SCORE:			☐

Developed by the International Parkinson's Disease Non-Motor Group.
Contacts: ray.chaudhuri@uhl.nhs.uk or alison.forbes@uhl.nhs.uk

J. Addendum J: Parkinson's Disease Quality of Life Questionnaire 8 (PDQ-8)

Parkinson's Disease Quality of Life Questionnaire (PDQ-8)

Due to having Parkinson's disease,
how often during the last month have you…

*Please **tick one box** for each question*

		Never	Occasionally	Sometimes	Often	Always or cannot do at all
1.	Had difficulty getting around in public?	☐	☐	☐	☐	☐
2.	Had difficulty dressing yourself?	☐	☐	☐	☐	☐
3.	Felt depressed?	☐	☐	☐	☐	☐
4.	Had problems with your close personal relationships?	☐	☐	☐	☐	☐
5.	Had problems with your concentration, e.g. when reading or watching TV?	☐	☐	☐	☐	☐
6.	Felt unable to communicate with people properly?	☐	☐	☐	☐	☐
7.	Had painful muscle cramps or spasms?	☐	☐	☐	☐	☐
8.	Felt embarrassed in public due to having Parkinson's disease?	☐	☐	☐	☐	☐

Please check that you have ***ticked one box for each question***.

Thank you for completing the questionnaire.

K. Addendum K: Patent Health Questionnaire – Somatisation-Anxiety-Depression-Symptoms (PHQ –SADS)

PATIENT HEALTH QUESTIONNAIRE (PHQ-SADS)

This questionnaire is an important part of providing you with the best health care possible. Your answers will help in understanding problems that you may have. Please answer every question to the best of your ability

A. During the last 4 weeks, how much have you been bothered by any of the following problems?		Not bothered (0)	Bothered a little (1)	Bothered a lot (2)
1.	Stomach pain	☐	☐	☐
2.	Back pain	☐	☐	☐
3.	Pain in your arms, legs, or joints (knees, hips, etc.)	☐	☐	☐
4.	Feeling tired or having little energy	☐	☐	☐
5.	Trouble falling or staying asleep, or sleeping too much	☐	☐	☐
6.	Menstrual cramps or other problems with your periods	☐	☐	☐
7.	Pain or problems during sexual intercourse	☐	☐	☐
8.	Headaches	☐	☐	☐
9.	Chest pain	☐	☐	☐
10.	Dizziness	☐	☐	☐
11.	Fainting spells	☐	☐	☐
12.	Feeling your heart pound or race	☐	☐	☐
13.	Shortness of breath	☐	☐	☐
14.	Constipation, loose bowels, or diarrhea	☐	☐	☐
15.	Nausea, gas, or indigestion	☐	☐	☐

PHQ-15 Score ☐ = _____ + _____

B. Over the last 2 weeks, how often have you been bothered by any of the following problems?		Not at all (0)	Several days (1)	More than half the days (2)	Nearly every day (3)
1.	Feeling nervous anxiety or on edge	☐	☐	☐	☐
2.	Not being able to stop or control worrying	☐	☐	☐	☐
3.	Worrying too much about different things	☐	☐	☐	☐
4.	Trouble relaxing	☐	☐	☐	☐
5.	Being so restless that it is hard to sit still	☐	☐	☐	☐
6.	Becoming easily annoyed or irritable	☐	☐	☐	☐
7.	Feeling afraid as if something awful might happen	☐	☐	☐	☐

GAD-7 Score ☐ = _____+_____+_____

C. Questions about anxiety attacks.

	NO	YES
a. In the last 4 weeks, have you had an anxiety attack ↓ suddenly feeling fear or panic?.....	☐	☐
If you checked "NO", go to question D.		
b. Has this ever happened before?.....	☐	☐
c. Do some of these attacks come suddenly out of the blue ↓ that is, in situations where you don't expect to be nervous or uncomfortable?.....	☐	☐
d. Do these attacks bother you a lot or are you worried about having another attack?.....	☐	☐
e. During your last bad anxiety attack, did you have symptoms like shortness of breath, sweating, or your heart racing, pounding or skipping?.....	☐	☐

D. Over the last 2 weeks, how often have you been bothered by any of the following problems?

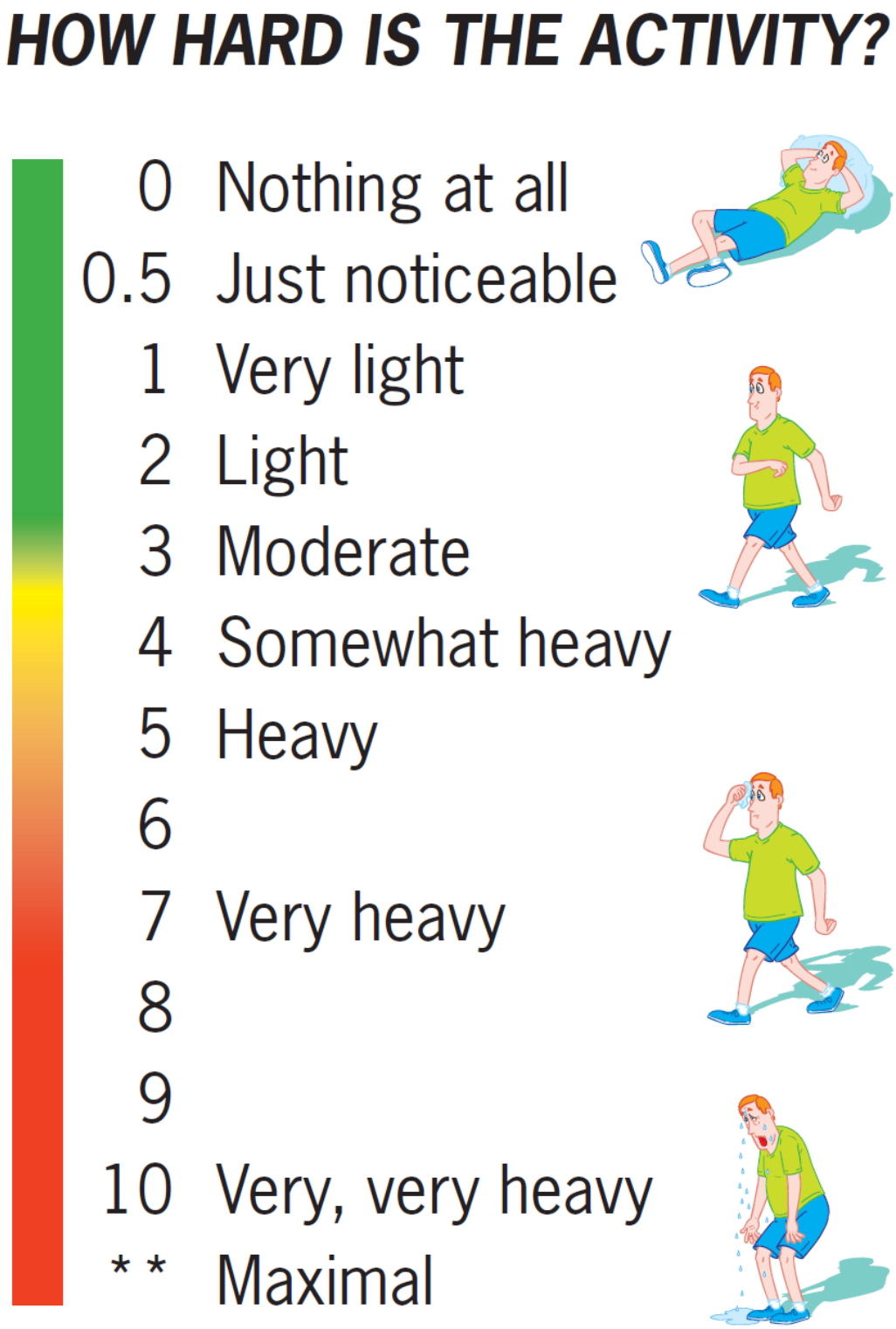
	Not at all (0)	Several days (1)	More than half the days (2)	Nearly every day (3)
1. Little interest or pleasure in doing things.....	☐	☐	☐	☐
2. Feeling down, depressed, or hopeless.....	☐	☐	☐	☐
3. Trouble falling or staying asleep, or sleeping too much.....	☐	☐	☐	☐
4. Feeling tired or having little energy.....	☐	☐	☐	☐
5. Poor appetite or overeating.....	☐	☐	☐	☐
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down.....	☐	☐	☐	☐
7. Trouble concentrating on things, such as reading the newspaper or watching television.....	☐	☐	☐	☐
8. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual.....	☐	☐	☐	☐
9. Thoughts that you would be beter off dead of or hurting yourself in some way.....	☐	☐	☐	☐

PHQ-9 Score ☐ = _____+_____+ _____

E. If you checked off any problems on this questionnaire, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult
☐	☐	☐	☐

L. Addendum L: Rate of Perceived Exertion (RPE) Scale



M. Addendum M: Recruitment Flyer

CALLING ALL POTENTIAL PARTICIPANTS!

Can relaxation exercises improve motor and non-motor symptoms for individuals with Parkinson's disease?

Stellenbosch University is investigating the effects of relaxation exercises on Parkinson's disease symptoms.

- ✓ *Have you been diagnosed with Parkinson's disease?*
- ✓ *Are you able to execute dynamic balance activities (i.e. walking or getting up from a chair)?*
- ✓ *Do you live within a ±70km radius of Stellenbosch?*
- ✓ *Speak English or Afrikaans as your mother tongue?*

Participation includes:

- Free 9 week relaxation exercise program
- 8 testing dates to assess selective motor and non-motor symptoms
- Receive a Movement Laboratory voucher (valued at R350 each) for each testing

If you, a friend or family member are interested in participating contact:

Elizma Atterbury

☎ 072 95 22 567 | ✉ pdresearchstudy@gmail.com

Or ☎ 021 808 4733 | ✉ usmovementlab@outlook.com

Movement Laboratories
STELLENBOSCH UNIVERSITY

UNIVERSITEIT·STELLENBOSCH·UNIVERSITY
jou kennisvennoot · your knowledge partner

Ethics number: S16/10/232

Movement Laboratories
STELLENBOSCH UNIVERSITY

N. Addendum N: Research Screening Form

Personal Information	
Name and surname:	
Date of birth:	
Age:	
Gender:	☐ Male ☐ Female
Contact details: *(please indicate preferred contact method with a *)*	
➔ Telephone number:	
➔ Email address:	
Physical address:	
Years of education and occupation (if retired, state previous):	
Home language:	
Are you going away anytime between June 2017 and November 2017? If yes, please state dates.	
Parkinson's disease information:	
When were you diagnosed with Parkinson's disease?	
Which side is most affected? ☐ Right ☐ Left ☐ Both	
Current medication, and duration of use:	
Any adverse effects of medication? If yes, please elaborate.	
What is you most dominant symptom and to what degree does it affect your quality of life?	
On a scale of 1 to 10 how able are you to execute dynamic balance activities, such as getting up from a chair, walking and climbing stairs (with 1 indicating no problem and 10 indicating you cannot execute the above mentioned activities)?	
Who is your doctor? Please provide his/her contact details.	
Would you be able to get approval from your doctor to participate in this study? If not, would you mind if we contact him/her?	
Caregiver information:	
Do you require the assistance of a caregiver for daily tasks?	
☐ Yes ☐ No ☐ Sometimes	
Who is your caregiver?	
What is your relationship to your caregiver?	
How much time do you spend with your caregiver?	
Would your caregiver like to attend the exercises as well?	
Physical activity information:	
How many times per week do you participate in physical activity or exercise?	
What is the total duration spent on physical activity or exercise per week (in minutes)?	
What type of physical activities or exercise do you participate in per week?	
Do you do housework and / or gardening? If yes, please elaborate on household chores:	
Do you participate in any leisure time activities? If yes, please elaborate on these activities:	

Health Screening

1. Do you have a history of any of the following?	2. Do you have a recent history of, or currently have, any joint / muscle injuries or pain?
☐ Angina /Chest pains	☐ Neck
☐ Breathing problems / difficulties / shortness of breath	☐ Upper back
☐ Cancer	☐ Lower back
☐ Coronary thrombosis	☐ Hip
☐ Diabetes	☐ Thigh
☐ Edema / swelling of ankles	☐ Knee
☐ Fainting or dizziness	☐ Lower leg
☐ Heart attack	☐ Ankle
☐ High blood pressure	☐ Foot (drop)
☐ High cholesterol	☐ Shoulder
☐ Intermittent claudication	☐ Elbow
☐ Known heart murmur	☐ Wrist or hand
☐ Leaking valve	☐ Other (please specify):
☐ Low blood pressure	
☐ Lung disease	
☐ Narrowing arteries	**3. Has your doctor previously indicated any other conditions that we should know of? And please elaborate on any of the conditions ticked above.**
☐ Other heart condition or disease	
Pain/ discomfort in chest, neck, jaw, arms	
☐ Palpitations	
☐ Recent operation	
☐ Rheumatic fever	
☐ Seizures	
☐ Stroke	
Unusual fatigue	
☐ Cognitive difficulties / dementia	
☐ Other (please indicate): Colonoscopy, Gastroscopy, Drop foot	

Addendum O: Talk topics

Topics are discussed before the session for about 5 minutes. You don't have to relay the info word-for-word, you can make it your own. You can leave out some information and explain it very simplistically. Please don't go off topic or add information. Discuss the topics in the order below; there is one topic per session. Only the last session do not have a topic; this time is often used to complete a quick form.

1. Introduction
2. Exercises
3. Stress and Trauma
4. Anatomy of stress
5. Fight or flight
6. Physiology of stress
7. Brain & stress
8. Bell Curve of stress
9. "Safe enough" environment
10. Self-regulation
11. Resilience
12. Mindfulness
13. Stress management
14. Breathing and HRV
15. Sleep
16. Boundaries
17. Conclude (forms)

---

1. Introduction

You will be doing a therapy that is theorized to naturally release stress and tension from the body. I won't be telling you the name of the therapy, because I do not want you get a preconceived idea about how the therapy should go or what benefit you should expect to experience. I would like you to remain open-minded during the therapy and curiously observe the effects in your body.

This therapy is said to work on the basis that stress (whether it is constant low grade stress or a traumatic event) is stored in the body, and we as human have almost "lost" the way we should naturally release stress. This therapy's aim is to teach and reactivate that mechanism speculated to release stress and return the body to calmer state.

We approach our sessions with simple principles. And since we want you to relax fully, we want to be very upfront and clear on these principles. Think of lying on a hammock – if you doubt how tightly it is bound at the ends, you will not relax fully. Thus we will emphasize our principles as a way to figuratively tighten the ends of the hammock so that you can trust the environment and relax completely.

These principles are:

1. Non-judgement zone → Reserve any judge for yourself and for other participants. There are very little right or wrong that you can do during session, so do not judge others or yourself. The therapist will help you if you struggle. Each person should work within their own ability.
2. Complete confidentiality → we handle any information with the utmost of confidentiality. The same applies for any information shared during sessions. Please do not discuss information shared with other people outside the group, and handle the info with care.

3. Be presently curious about your body → Don't compare your body or movements to others; each person has their own process. Rather just be curious in your body. Observe different sensation without placing a label immediately on it.

2. Exercises

No topic. Take time with exercises. Emphasize certain aspects:

- Many research supports the notion that there is a BODY/MIND/BRAIN continuum. Thus, we would like the body and brain (mind) to be present without pre-conceived ideas.
- Exercises: nothing should hurt. Work within you own limits.
- After care: be kind to your body afterwards. Drink lots of water!

3. Stress and Trauma

Stress is a part of day-to-day living. Not all stress experiences are harmful. It is also the process that makes you motivated, that prepares you for action, whether it is danger or even proposing to the love of your life (heart racing, digestive problems, feeling jittery).

Good: Eustress (mild to moderate stress) can act as a motivator and energizer.

Bad: Distress (higher levels of stress) can result in medical or social problems. Often this stress is tolerable and we can handle them in small amounts.

Ugly: Toxic-side of stress. Trauma (accumulation of stress or an event)

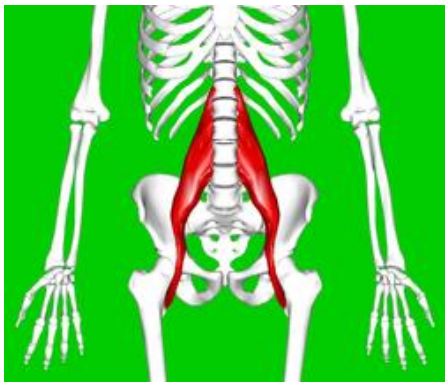
Both are essential to life → Need to be motivated, help deliver on our ambitions. Through distress or trauma we often forge long-lasting relationships and build social support structures.

What is the difference between stress and trauma?

As far as the body is concerned there is no difference. Both minor stress (eg hearing bad news) and major trauma (eg car accident) send the same chemicals into the blood stream to deal with the situation. We will discuss those chemicals next week.

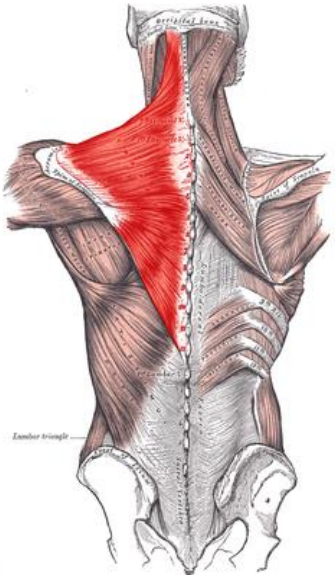
- Definition of trauma:
  A disturbing event that occurs in a condition of helplessness
- It can be an event or accumulative
- Types of trauma: Hard or soft
- **The body does not know the difference**

4. Anatomy of stress



When your body experiences a stressful situation, certain muscles are activated to perform a fight or flight or freeze response. The first and primary muscles that are activated are the psoas muscles and the trapezius (or traps) muscles.

The psoas muscle is a very important muscle complex. The psoas joins the upper body and the lower body, the axial to the appendicular skeleton, the inside to the outside, and the back to the front. Your psoas muscles stabilize your trunk and spine during movement and sitting; they form part of your hip flexors, which helps you to walk and are also responsible for forward trunk flexion. The psoas muscles support your internal organs and work like hydraulic pumps allowing blood and lymph to be pushed in and out of your cells.



Your **psoas muscles** are vital not only to your structural well-being, but also to your psychological well-being **because of their connection to your breath**. **Here's why:** There are two tendons for the diaphragm that extend down and connect to the spine alongside where the psoas muscles attach. These connections between the psoas muscle and the diaphragm literally connect your ability to walk and breathe, and also how you respond to fear and excitement. In other words, your psoas has a direct influence on your fight or flight response, and visa versa. During prolonged periods of stress, your psoas is constantly contracted.

The traps are big diamond shape muscles that originate from the base of the skull toward the shoulders and ends towards the middle of the back. It is responsible for shoulder and spine stabilization, and also work to perform shoulder movements.

Depending on the intensity of stressful situation, the muscles in the body are activated to perform the following responses:

Flight: Run away

Fight: Punch or kick

Freeze: Pull into the fetal position

These muscles stay activated as long as the stressful situation is still there.

5. Fight or flight

Previously we chatted about the body and muscles reacting to a fight or flight or freeze situation. Today we will discuss this neutral response of your body more; let's first talk about your nervous system:

Firstly you have a central and peripheral nervous system (NS). The central NS includes your brain and spinal cord. The peripheral NS includes ALL the nerves that branch out from the spinal cord. The peripheral NS has 2 branches: Somatic NS which regulates all your deliberate and voluntary movements (picking up a glass for example); and the autonomic NS which regulates all the involuntary movements and actions happening in the body – heartbeat, breathing rate, digestions, stress response, swallowing, facial expressions, etc. This autonomic NS is then further branched into 2: The Sympathetic and parasympathetic NS. These two NS work alternatively to one another. Meaning when the one NS is activated, the other one is dormant. Both are not activated

simultaneously. The system are antagonist of each other. These two NS are also referred to as the fight/flight/freeze system and the rest & digest system.

When your body perceives that you are in danger, may it be confronted with bear or perhaps have a difficult conversation with someone, the sympathetic or fight/flight/freeze response is activated. This is what we experience as a stress response – like previously discussed, it is not all bad. It makes you motivated and energized and prepares you for action. With animals, they will prefer to run away (flight), if that is not possible they will attack (fight), and if they are overpowered, they will "play dead" (freeze). Humans have the same response, whoever we have an extra step beforehand→ negotiate or talk our way out. If the situation does not go away, we will run away or withdraw (flight), if that is not possible we will defend ourselves (fight), and if the situation is too much, our bodies will disconnect and we experience feeling numb (freeze).

These are all natural responses. And naturally after the danger have subsided and we perceive the situation to be safe enough, the fight/flight/response is deactivated and the rest & digest system is promoted. The body needs this system to be activated to promote healthy digestion, muscles relaxation, good quality of sleep, improved reasoning → this is also the time our body integrates the experience ensure that we react smarter in the next situation.

However, often we find ourselves in situations where the "safe enough" signal occurs infrequently and thus our fight/flight/freeze response remains activated → the psoas muscle is one of the "switches". Tight psoas muscles send signal to the brain that there is still present danger and thus remains activated. Thus we lose out on all the good things that happen during rest & digest phase, and we remain tense, anxious, and unable to relax or sleep well. It can lead to depression.

6. Physiology of stress

The main chemical that affects our physiology during a stress response is Adrenaline. Or at least that is one of the major ones. In reality there is a multitude of hormones and chemical signals that are released during stressful situations. But how does it work?

Your body is an amazing machine and react within seconds, and it starts with your brain. Even before you are aware that you might be in danger, your fast-thinking brain has already assessed the situation. Your hypothalamus is an area in the brain that can determine a dangerous situation, if the hypothalamus is activated it sends signals to several body parts to release hormones which prepares you for actions.

Adrenaline and cortisol are the two major hormones. Among many other functions, cortisol help make more sugar available in the bloodstream to ensure there is enough energy to take action. Adrenaline helps to prepare the muscles for action. It also increase your heartrate and breathing rate, and increase your body temperature (thus perspiration). These hormones selectively "switch off" other systems in the body that might take up unnecessary energy during a stress response – such as the digestive, immune, secretion and reproductive systems.

This "off-switch" is amazing to help the body to get away from danger, and is only supposed to be a short-term and immediate solution. However if were remain in high-stress situation, adrenaline and cortisol and wreak havoc in the body because of other systems not functioning properly. Thus long term stressful situations have a big influence on our digestion, blood-sugar control, and even immune response. Hence why stressed individuals often get sick compared to more relaxed individuals.

Another important and interesting factor is to what extent your perception of your stress response plays a roll. For example imagine being in love and having to speak in front of a hall full of people. In both situations your body will experience a stress response, but with being in love your experience the increased heart rate and "butterflies' in your stomach as a positive experience. Research has shown this positive perception is actually good you're your heart health. Whereas the perception that the stress response is harmful, actually causes the arteries to react in a different way, and thus results in the stress response to be negative. So being aware of your perception of stress might be a very useful a healthy tool.

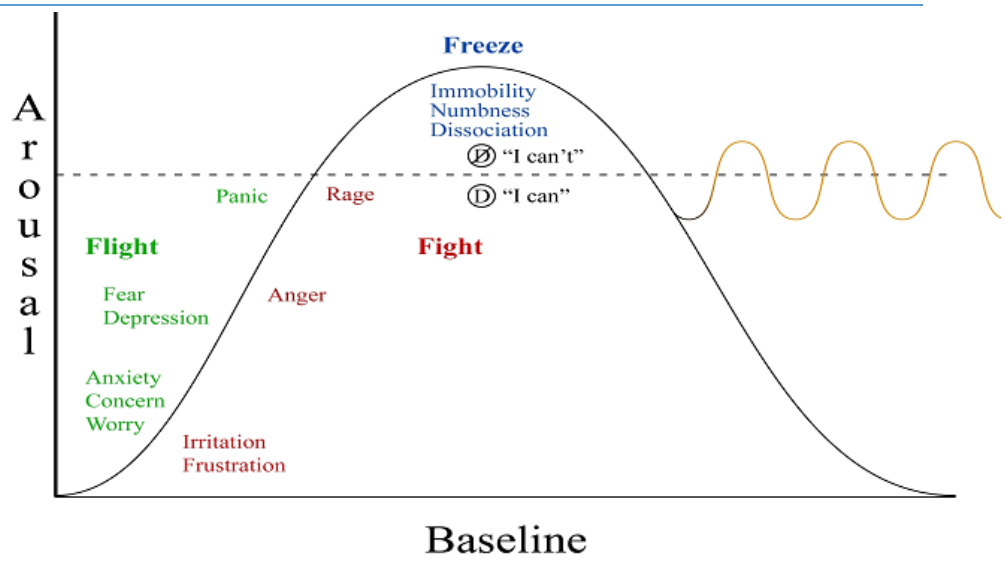
7. Brain & stress

Thanks to modern day technology and brain imaging tools we can examine images of the brain. Thus it is now understood that the brain is constantly rewiring itself according to the messages received from the body. There is an interactive dance in the entire system between body and brain (mind) that is now widely accepted as the BODY/MIND/BRAIN continuum.
According to research theories, our brain actually consists of 3 distinct neurocomputers → triune brain theory.

- **R-Brain – Reptilian brain (brainstem)**
  - Instinctual
  - Respiration
  - Heart rate
  - Blood pressure
  - Temperature
- **M-Brain – Mid-brain or mammalian brain (limbic system)**
  - Feeding
  - Fighting
  - Fear
  - Fornication
- **N-Brain – Neurocortex or primate brain**
  - Rational
  - Creative
  - Spiritual
  - Imagination
  - Belief systems

Stressful situation can influence what part of this triune brain we use. Depending of the intensity of the stressful situation, the N-brain can shut down. Thus our rational thinking, creativity and logic goes out the door when we are stressed. That's why we often struggle to think of smart solution during a stressful period or we become forgetful.

8. Bell Curve of stress



This is how stress in your body works and how it builds up. I going to use a story to explain this curve to you:

Imagine a busy mom receiving a phone call from the school asking her to come in immediately – there is an issue with her son. At this stage she might be feeling frustrated for being called in, but also concerned because it sounded like a serious issue. So on her way to the school her mind is racing. As she gets to the school, she sees

there is an ambulance. Without even getting out of the car, the school principle instructs her to follow the ambulance to the hospital. Her son is in the back and require medical attention. At this stage she is very anxious and fearful about that's going on. The principle only said that her son was involved in an accident, and she is fearing for her son's life. As she enters the hospital, she just see her son being rolled into the emergency operating room and now she is in panic mode. Overcome by this high intensity emotion, she goes into freeze mode – meaning she dissociates from this strong emotion. Her body is still experiencing all high stress responses, but she is disconnect from the emotion and thus experience to be numb. Now she is in a state to calmly phone her husband and inform him of what happened, she can have a conversation with the nurses and give the medical aid details, etc.

I am sure we have all had a similar experience before and can relate to this build-up of emotion. This important part of this curve is that we often forget that we have to get down the way we got up there. As a natural part of the body dealing with situations like this, is that we experience the same emotion that got us in the frozen of dissociated state in the first place. Thus part of coming down the curve and coming out of this "frozen" state, is to experience those panic emotions again. This is how the body processes this experience. It is uncomfortable, unnerving and unpleasant but it is often short-lived. The body is trying to complete the cycle. Often we do not want to experience this and thus think that being "frozen" is a better place to live our lives from. But the body cannot stay there either, and thus often we get stuck fluctuating between intense emotions and dissociating from these emotions, as we seek methods to keep us in a frozen state. That's where addiction comes from – any form of addiction including addiction to food, television, smoking, sleeping, etc.

9. "Safe enough" environment

Relaxation depends largely on the environment that you find yourself in. For the body to experience relaxation at its best, it requires an environment that it deems "safe enough". Linking back to the chat we had about the nervous systems that can pick-up when you are in danger or when you are safe, and activate the appropriate nervous system. Thus during session we aim to create an environment where your nervous system can activate the "rest & digest" system.

There is a theory that our nervous systems can pick up on one another. Perhaps you have had an experience like that where a certain person's presence makes you feel anxious because they are anxious; or the opposite, perhaps being around a person who is very calm has calmed your own emotions. So in the sessions the therapists' main job is to be a calm, grounding and calming nervous system. Perhaps you have struggled to achieve the same success when doing the sessions at home. It might be that the environment is not as calm. However some individuals actually prefer doing the session on their own and may find that they are able to experience a greater level of relaxation. That is also perfectly normal.

Take care doing the sessions at home, and make sure to create an environment that makes you feel at ease. Sometimes it might be necessary to tell your spouse to give you an hour to do the session without interruptions. Maybe you should take the phone off the hook or your cell phone on silent. Put on some nice music if you prefer, etc. etc. Be kind to yourself and ensure you set-up the environment correct for your session.

Also keep this concept in mind when interacting with people and what effect might have on you mood. Or even what effect you might have on someone else's mood. It is good to be aware of this, so you can act according to you best interest.

10. Self-regulation

Self-regulation is an important part of being human. Your body self-regulates by sleeping, socially we decide to join a group or rather spend time alone, physically we regulate by doing hard labour or exercise and having a rest day and emotionally we self-regulate our emotions. Our brains and nervous systems also self-regulate by

activating and deactivation our fight-flight response and thoughts impacts on our thoughts. We are not just mammals following our basic instinct, we have various levels of our being that we need to attend to.

During the sessions, self-regulation is often encouraged → as much as you need it, for whichever reason – you're tired, you feel overwhelmed, you need a break, you just want to stop. The self-regulation of the autonomic nervous system (ANS) has increasingly been recognized as an important factor in several psychological and physiological problems. Clinical problems such as PTSD, anxiety based disorders including simple phobias, mood disorders, eating disorders and some learning disorders such as ADHD are all characterized by ANS dysregulation (Josephs, & Zettl, TTB II, 2001; Perry, 1999; Scaer, R., 2001; Van der Kolk, et al., 1996).

Persistent dysregulation compels many individuals to seek various means for controlling or numbing the activation. Their inevitable failure to effectively regulate their system is believed to be the driving force behind addictive behaviours such as alcoholism and drug use or forms of distraction such as hyperactivity, aggression self-mutilation and/or avoidance behaviours (Josephs, & Zettl, TTB III, 2001; Van der Kolk, B., 1989).

11. Resilience

Resilience is that ineffable quality that allows some people to be knocked down by life and come back stronger than ever. We often take a militaristic, "tough" approach to resilience and grit. We imagine a soldier slogging through the mud, a boxer going one more round, or a football player picking himself up off the turf for one more play. We believe that the longer we tough it out, the tougher we are, and therefore the more successful we will be. However, this entire conception is scientifically inaccurate.

The very lack of a recovery period is dramatically holding back our collective ability to be resilient and successful. Research has found that there is a direct correlation between lack of recovery and increased incidence of health and safety problems.

Psychologists have identified some of the factors that make someone resilient, among them a positive attitude, optimism, the ability to regulate emotions, and the ability to see failure as a form of helpful feedback. Even after misfortune, resilient people are blessed with such an outlook that they are able to change course and soldier on.

The key to resilience is trying really hard, then stopping, recovering, and then trying again. This conclusion is based on biology. Homeostasis is a fundamental biological concept describing the ability of the brain to continuously restore and sustain well-being. Positive neuroscientist Brent Furl from Texas A&M University coined the term "homeostatic value" to describe the value that certain actions have for creating equilibrium, and thus wellbeing, in the body. When the body is out of alignment from overworking, we waste a vast amount of mental and physical resources trying to return to balance before we can move forward.

12. Mindfulness

- Mindfulness encompasses both internal processes and external environments.
- Mindfulness is being aware of your thoughts, emotions and physical sensations in the present moment.
- With practice, mindfulness cultivates the possibility of freeing yourself of reactive, habitual patterns of thinking, feeling and acting.
- Mindfulness promotes balance, choice, wisdom and acceptance of what is.

Kabat-Zinn's definition:
Mindfulness means paying attention in a particular way: on purpose, in the present moment, and non-judgmentally.

Try not to view everything through the lens of the past, because then we compare. Even though that comparison is handy when in a life-threatening situation, constant comparison forces you to make assumptions that are often wrong or misleading.
If you view everything through the lens of the future, then you will create expectation. Our brains are made to make predictions based of experiences, however in our modern society we are bombarded with expectations of how aspects of your life should go. If those expectations are not met, we are disappointed and become unhappy.
Kabat-Zinn delineates seven foundations of mindfulness practice:

- **Non-judging**—being aware of judging and reaction to inner and outer experiences;
- **Patience**—understanding and accepting that sometimes things must unfold in their own time;
- **Beginner's mind**—seeing everything as if for the first time;
- **Trust**—taking responsibility for being yourself and learning to listen to and trust your own being;
- **Non-striving**—realizing that there is no goal other than for you to be yourself;
- **Acceptance**—seeing things as they actually are in the present; and
- **Letting go**—releasing thoughts, feelings, and situations that the mind seems to want to hold on to (Kabat-Zinn, 1990).

13. Stress management

Stress, like we have discussed, is a global issue. High-stress jobs or situations have high mortality rates linked to it. Often people are advised to avoid stress as much as possible. Even though that is good advice in terms of aspects that you can control, most often in life the aspects that we cannot control results in greater stress, and sometimes trauma. Therefore avoiding stress is not the best solution → the better option is learning how to manage stress.

Remember lower stress levels are good since chronic ongoing stress, and permanent low grade tension, leads to illness and disease. By doing relaxation exercises you can aid the body to return to a balanced state.

Because we as humans are ineffective in managing our stress levels of discharging excess stress, we build it up in our body. Think of your body as a cup. A stressful or traumatic event might fill your cup completely in one go, or your cup might become fuller slowly overtime. Our bodies are at a vulnerable place when our cups are almost full and even more so when it spills over (referring to either becoming sick, or losing your temper or saying something you don't mean). Therefore by participating in active stress relief you are able to slowly and systematically empty your cup. So every time you participate in a stress-relieving activity you are placing yourself in a better position → with a half full cup you have a lot more room to think and act before your cup spills over.

Hopefully after this intervention you have the tools to help you with stress management. Tools like:

- Being aware of your stress levels
- Not connecting stress immediately to something bad, but rather your body preparing you for action
- Stretching exercises
- Neurogenic tremor **[RELAXTION GROUP: DO NOT MENTION THIS]**
- Breathing techniques (which will be discussed in next session)

14. Breathing and HRV

Your breathing and your heart rate is linked. If the one goes up, the other one goes up. Your body (brainstem to be more specific) controls breathing automatically. However we can also choose how to breathe (when we are aware of it). Thus you can consciously sit and start breathing faster, and after a minute you will realize that your heartrate has increased as well. Similarly this occurs when you breathe slower. A slower heart rate is often a sign of a strong heart, but this recent research they have found that heart rate variability (HRV) is a

greater indicator of heart health. HRV have been linked to anxiety and heart disease. HRV is a measurement of how much each heartbeat differs from another. If you have high HRV, it indicates that your heart is not beating with a regular tempo. A low HRV indicates that your heartbeats are very consistent and the heart is contracting rhythmically, which is very good.

Thus it is of great importance to note that you have the power to change your HRV whenever you feel the need to, just simply by breathing correctly. When you are stressed, your breathing and HR is affected and your HRV goes up. This irregular beat acts as a messenger to your brain that you are in danger, and often causes that your rational thinking part of your brain is switched off. So through conscious breathing you can alter your brain function.

Here are 3 tips to help you breathe better:

1. Rhythm – is providing better quality fuel for the brain

2. Smoothness – the rhythm of breathing must be done in an even fashion, not staccato

→ Through the nose!

3. Location of attention– is recommended to the centre of the chest.

→ Reverts away from head noises

➔ Returns awareness of the emotion level.

15. Sleep

Sleep is as necessary to health as food and water. During sleep your body is busy repairing muscles and other tissues, replace aging or dead cells, etc. Sleep also gives the brain a chance to organize and archive memories (Dreams are thought by some to be part of this process). And it also lowers your energy consumption.

If you do not get enough sleep, your body builds up a sleep debt. And the sleep debt can only be repaid by sleep. The average person needs between 8-9hours of sleep. Children and adolescents need more sleep. As adults, our sleep need does not change as we age. Teach yourself to sleep less, but not to need less sleep!

All living things (people, animals, even plants) have a circadian or ± 24-hour rhythm. It affects when we feel sleepy and alert. This circadian rhythm plays a role in our feeding patterns, alertness, core body temperature, brain wave activity, hormone production, regulation blood sugar, urine production, cell regeneration.

There are many hormones that are secreted while you sleep. Growth hormone is secreted at night and that why children need more sleep. Children who grow up being constantly sleep deprived, actually have stunted growth. Another one of these hormones are melatonin, which only gets secreted in darkness. Melatonin plays a roles in your digestive system as well as your immune system. So in the evenings, the blue light from your TV or smart phone can actually stop the production of melatonin. So try to avoid bright screens before bed to help you sleep better.

16. Boundaries

Boundaries distinguish each individual's "territory," the place where personal responsibility begins and ends. The self is the only area over which an individual has any control.

Because you set the limits, you are personally responsible for protecting yourself. You are responsible for your feelings, your values, your behaviour, your thoughts, choices, insights, beliefs, limits – everything! Your duty to yourself is to take care of yourself and not allow others to trespass. This includes cultivating your ability to say "no," to others even if your actions disappoint them or hurt them. The good news is that since you are

responsible for yourself, other adults are responsible for themselves. Always! They have to deal with your limits. You have to deal with theirs. People have a real hard time with this concept.

Common Boundary Questions:

- Isn't it selfish to set limits with others?
- How can I set limits and still be a "good" person?
- Why do I feel guilty when I try to set limits?

Let's take them in order:

Isn't it selfish to set limits? No, no, no. In fact, it is destructive not to set limits. Who will take care of you if you don't? Who knows more about what you need, or don't need, than you do? It is unfortunate that the word "selfish" has such a bad connotation. Perhaps we need to think in terms of "self-caring." Then we may more appropriately ask, "Isn't it self-caring to set limits?" You bet!

How can I set limits and still be a "good" person? How can you not? By the way, what is a "good" person? (The word I prefer is "integrity.") How do you feel when you've been sooo good that you have been taken advantage of? Do you hide your angry, resentful feelings, smile and pretend – often even to yourself – that all is OK? Or, do you let your anger out on the next poor soul who crosses your path? How can you possibly feel good about yourself if you carry so much luggage?

Why do I feel guilty when I try to set limits? Because you are well-trained to believe that it is your responsibility not to disappoint others, to please, protect, "make" them like you, etc. There are cognitive techniques that can effectively help stamp out irrational guilt.
Not all guilt is irrational. Each situation needs to be examined. What is the individual's underlying motivation?

---

17. Conclude (forms)

O. Addendum P: Turn-It-In report

turnitin

Digital Receipt: 14% similarity

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

The first page of your submissions is displayed below.

Submission author:	Karen Welman on behalf of EM Atterbury
Assignment title:	Turnitin (No Repository) Part 3 (Mo...EM
Submission title:	Atterbury PhD
File name:	3903_EM_Atterbur...0
File size:	
Page count:	97
Word count:	45,087
Character count:	243,909
Submission date:	23-Oct-2018 08:04AM (UTC+0200)
Submission ID:	1025128824

Exploring therapeutic neurogenic tremors with exercise as a treatment for selective motor and non-motor Parkinson's disease symptoms

Not you, we, they but I

You teased, you laughed, you called me names
I absorbed, I internalized it
I believed it for years
But with my hands balled in fists;
I shake it off, I shake it off

We played, we loved,
We grew deeper into our hearts
as you fur turned grey
Through my mistake and godly timing, you left
I left
My body froze, my thoughts grew dark
But with my feet dancing and arms wrapped around;
I shake it off, I shake it off

They entered, uninvited, unwelcome, unrecognizable
They took more than belonged
They shook more than foundations
I picked up my armour
I nurtured the wounded
But with chest trembling and silent shouts;
I shake it off, I shake it off

I experienced, I felt, I remember
Times of sadness and shame
Moments of fear and pain
Lifetimes of doubt
But with my whole being wanting, willing,
Waiting to be unburdened
I shake it off, I shake it off

You cannot hold me captive
if I compassionately hold myself
I choose the way forward, the way to freedom
Unconditionally I choose myself.