AN INVESTIGATION OF THE CONTRIBUTION OF AXIAL RIGIDITY TO TURNING DEFICITS IN INDIVIDUALS WITH PARKINSON'S DISEASE

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A thesis submitted in partial fulfilment of the

requirements of Liverpool John Moores University

for the degree of Doctor of Philosophy

July 2019

ABSTRACT

Difficulty in turning is prominent in individuals with Parkinson's disease (PD) and the resulting postural instability increases their risk of falling. Therefore, understanding the mechanisms underpinning turning deficits in PD is highly important for rehabilitation and fall prevention.

The first aim of this thesis was to clarify the mechanisms of increased fall risk during turning in PD by emulating: head and neck rigidity in healthy adults, and then observing the effects on eye movements and whole-body coordination while turning on the spot. The results revealed that experimentally inducing head and neck rigidity had multiple effects on eye movement characteristics, step amplitude, and total steps taken to complete the turn. The resultant behaviour was similar to that previously observed in individuals with PD.

The second aim of this thesis was to validate the use of Inertial Measurement Units (IMUs) in combination with mobile electrooculography (EOG) for measuring eye, head and whole body coordination during turning with a view to developing a methodology that could be used to assess the effects of exercise intervention on turning characteristics of PD patients in a clinical setting. The results showed excellent reliability when compared with measures obtained using a Vicon motion analysis system suggesting that IMUs provide a viable alternative to camera-based motion capture for accurately measuring turning behaviour.

The third aim of the study was to conduct a scoping review to determine whether exercise-based rehabilitation is effective in reducing axial rigidity in individuals with PD. Four out of eleven studies eligible for inclusion focused explicitly on exercise-based treatment for axial rigidity in individuals with PD. The results of the scoping review were used to design a modified exercise programme aimed at improving axial rigidity and turning dysfunction in individuals with PD.

The final aim was to carry out a pilot Randomized Control Trial to study the effects of a modified exercise programme on various markers of functional mobility and turning performance in PD patients; e.g., Unified Parkinson's Disease Rating Scale (UPDRS) functional reach test, step size, total steps and improvement in fall efficacy scale in individuals with PD. These preliminary results support the notion that targeting axial deficits may be an effective rehabilitation approach for improving mobility and reducing falls in PD.

Acknowledgements

Initially, this thesis can be succeeded by the attentive support and assistance from my beloved supervisor, Prof. Mark Hollands who has been allowed me the opportunity to do this PhD under his supervision. I would like to express my sincere gratitude and deepest appreciation for his excellent guidance, problem solving, invaluable suggestion, supervision, proofreading, gramma checking, editing and support throughout the development of my PhD thesis. His challenges, enthusiasm, and immense knowledge brought this work towards a completion. I would like to thank you for encouraging me to grow as a research scientist.

I am equally grateful also widely extends to Asst. Prof., Amornpan Ajjimaporn, my advisor from Thailand. Her guidance and helping about this thesis and inspiration are excellent. My equal thanks are also extends to Dr. Kristen Hollands, from University of Salford, Manchester, UK, her helping about scoping review are useful. Asst. Prof., Prachaya Srivanitchapoom (M.D.), Assoc. Prof. Jarugool Tretriluxana and Dr. Suweena Khacharoen to support throughout the project until completion in Thailand. Moreover, I would like to give special thanks to Dr. Rebecca Robins, Damrongsak Ruaisungnoen, Nattaporn Intawachirarat, and Thunyanoot Prasertsakul for providing MATLAB advice in my thesis.

My equal gratefulness also relevantly reaches to my parents for their countless financial and mental supports and I would like to express the impressive appreciation to my friends and all persons helping me in various ways.

Finally, this thesis was supported by Liverpool John Moores University Funding and Mahidol University's Academic Development Scholarship.

Fuengfa Khobkhun

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List of Abbreviations

PD	=	Parkinson's disease
IMUs	=	Inertial Measurement Units
FRT	=	Functional reach test
FES-I	=	Fall Efficacy Scale International
RPE	=	Borg's Ratings of Perceived Exertion
QOL	=	Quality of life
ADL	=	Activity daily of living
COM	=	Centre of mass
COP	=	Centre of pressure
BOS	=	Base of support
FOG	=	Freezing of gait
EG	=	Exercise group
CG	=	Control group
UPDRS	=	The Unified Parkinson's Disease Rating Scale
STN	=	Subthalamic nucleus
GP	=	Globus pallidus
CNS	=	Central nervous system
SMA	=	Supplementary motor area
APAs	=	Anticipatory postural adjustments
ROM	=	Range of motion

Chapter 1
General Introduction

During daily life activities, 35–45% of all steps are made during turning movements, indicating that turning is an essential part of goal-directed locomotion (Glaister *et al.*, 2007). Most individuals with Parkinson's Disease (PD) have difficulties turning around when standing or walking (Mak, Patla and Hui-Chan, 2008), which increases their risk of falling (Bloem *et al.*, 2001). Falls can lead to severe injuries, resulting in immobility and loss of independence, resulting in a reduction in patients' quality of life and high costs for both the patient and healthcare systems (Smania *et al.*, 2011). Therefore, understanding the key mechanisms of turning deficits in individuals with PD and designing interventions to improve turning dysfunction are crucial.

1.1. Background of PD

According to James Parkinson, who first described the disease, later known as Parkinson's disease (PD) (Jankovic and Tolosa, 2007), in 'An Essay on the Shaking Palsy' in 1817, PD is a movement disorder and the most common disease associated with progressive neurological brain diseases. The global incidence and prevalence of PD is approximately 4.5–12 cases per 100,000 population annually and 18–328 cases per 100,000 population, respectively (Tanner and Aston, 2000; de Lau and Breteler, 2006). Countries with a high proportion of elderly people tend to have a high prevalence of PD; with a ratio of males to females of 3:2 (Pringsheim *et al.*, 2014). Approximately 1% of the population over the age of 55 years are affected by PD and most of these patients either have familial PD or develop the disease due to a combination of genetic and

environmental factors (Tanner and Aston, 2000; de Lau and Breteler, 2006; Jankovic and Tolosa, 2007).

According to the main neuropathological findings, PD is characterised by the loss of dopaminergic neurons of the nigrostriatal pathway; this dopamine deficiency, in turn, leads to dysfunction in the nucleus of the basal ganglia and the brainstem (Jankovic and Tolosa, 2007). The four main clinical symptoms of PD are: resting tremor, rigidity, bradykinesia and postural instability. The symptoms of PD can be categorised as either motor symptoms or non-motor symptoms (Jankovic and Tolosa, 2007). Motor symptoms include abnormalities in: speaking, writing, facial expression, gait, posture, decrease in the coordination of movement, impairment of balance, muscular fatigue and impairment of fine movement (Jankovic and Tolosa, 2007). Non-motor symptoms include autonomic nervous system dysfunction, behavioural, mental and emotional problems, impairment of cognition, perception and sensation and sleep disturbance. As the disease progresses, depression, amnesia and, eventually, dementia are found to affect approximately 30–50% of individuals with PD (Jankovic and Tolosa, 2007).

The stages of PD can be categorised in more detail by using the modified Hoehn and Yahr staging scale (Table 1-1), which is a standard staging system used to describe patient populations enrolled in clinical trials of interventions (Jankovic and Tolosa, 2007).

Table 1-1. The modified Hoehn and Yahr staging scale.

Stage	Symptoms
0	No signs of disease.
1	Unilateral symptoms only.
1.5	Unilateral and axial involvement.
2	Bilateral symptoms. No impairment of balance.
2.5	Mild bilateral disease with recovery on pull test.
3	Balance impairment. Mild to moderate disease. Physically independent.
4	Severe disability, but still able to walk or stand unassisted.
5	Needing a wheelchair or bedridden unless assisted.

1.2 Management of PD

The management of PD can be divided into three categories: pharmacological, surgical and non-pharmacological.

1.2.1 Pharmacological management

Pharmacological approaches should be considered depending on the following factors: age-range of the individual with PD, motor and non-motor symptoms and severity of PD (Srivanitchapoom, Pitakpatapee and Suengtaworn, 2018). For managing motor symptoms in patients under the age of 60, if the degree of severity is moderate to severe, levodopa combination should be the first option to be considered. If the severity grade is mild,

levodopa sparing strategy, such as dopamine agonists, anticholinergics or type-B monoamine oxidase inhibitor, should be considered (Srivanitchapoom, Pitakpatapee and Suengtaworn, 2018). For patients over the age of 60, levodopa combination proves to be useful in all degrees of severity (Connolly and Lang, 2014). Advanced non-oral therapies, including a continuous subcutaneous infusion of apomorphine, continuous intestinal infusion of levodopa/carbidopa gel and deep brain stimulation surgery, should be considered for patients who have already exhibited motor complications, such as levodopa-induced dyskinesia or wearing off, as they can be hardly controlled by simply adjusting oral medications (Srivanitchapoom, Pitakpatapee and Suengtaworn, 2018).

1.2.2 Surgical management

Surgical management of PD began over 60 years ago, but its popularity decreased after the discovery of L-dopa and other medical treatments (Fang and Tolleson, 2017). In the last decade, deep brain stimulation (DBS) was discovered, and it has proven to be a safe and effective treatment for the symptoms of PD (Fang and Tolleson, 2017). However, prominent issues, such as better tailoring of anatomic targets in individuals with PD and adjusting DBS signal delivery, such as with low-frequency stimulation (Srivanitchapoom, Pitakpatapee and Suengtaworn, 2018), are still being researched. Additionally, potential side effects, such as intracerebral haemorrhage, dysarthria, behavioural and visual impairment, are still concerns that need to be further examined.

1.2.3 Non-pharmacological management

Coping with signs and symptoms of PD requires cooperation amongst physicians, patients and relatives. Understanding the disease, its progression, and the guidelines of its primary treatment will help patients receive appropriate treatment. For instance, PD in the early

stage may not require surgical procedures, but periodical monitoring of disease progression and an appropriate dose of medication will be needed (Morris, 2000).

Physiotherapy was the preferred treatment intervention for PD prior to the discovery of L-dopa therapy. Physiotherapy has been proven to control and alleviate symptoms of PD (Morris, 2000). The principles of physiotherapy for PD patients include understanding the disease pathology that leads to abnormal movements, assessing abnormalities in individuals, creating an appropriate treatment plan and implementing correction and treatment (Morris, 2000).

Previous studies have shown that combining medications and physiotherapy is more beneficial to PD patients than solely administering medications (Baatile *et al.*, 2000; Morris, 2000; de Goede *et al.*, 2001; Hirsch *et al.*, 2003; Pohl *et al.*, 2003). The main objectives of physiotherapy for individuals with PD are to maximise functional ability and minimise secondary complications through movement rehabilitation, imparting education and supporting the whole person. Furthermore, physiotherapy for PD focuses on posture, transfers, upper limb function, balance, gait, prevention of falls, improving physical capacity and activity; utilising cueing strategies, cognitive movement strategies and exercise to optimise the patient's independence, safety, and wellbeing, thereby enhancing quality of life (Tomlinson *et al.*, 2014). Therefore, it is likely that physiotherapy plays a major role in rehabilitating individuals with PD.

1.3 Turning function in normal individuals and individuals with PD

1.3.1 Normal turning coordination

1.3.1.1 Segment reorientation

Studies focussing on both on-the-spot and steering turns (i.e. changing the direction of walking) have shown a common stereotyped movement sequence. Turning is initiated by saccadic eye movements to shift gaze in the direction of travel followed by the rotation of the head, then the trunk and pelvis and, finally, the stepping movements of the feet (Hollands and Marple-Horvat, 2001; Hollands, Ziavra and Bronstein, 2004; Reed-Jones *et al.*, 2009a; Reed-Jones *et al.*, 2009b; Akram, Frank and Fraser, 2010; Chou and Lee, 2013). Although adults employ the same temporal sequence as younger adults, there are significant differences in the spatial characteristics of the turn; for instance, younger adults show larger head-on-trunk rotation than older adults (Baird and Van Emmerik, 2009). It has also been observed that older adults as well as individuals with neurological conditions, especially individuals with PD, employ en-bloc movement strategy while turning, which is characterised by reduced relative rotations between adjacent segments and near-simultaneous rotation initiation (Lohnes and Earhart, 2011). However, several researches have also reported typical sequential reorientation among these populations (Anastasopoulos *et al.*, 2011; Chou and Lee, 2013; Ahmad *et al.*, 2014; Ashburn *et al.*, 2014).

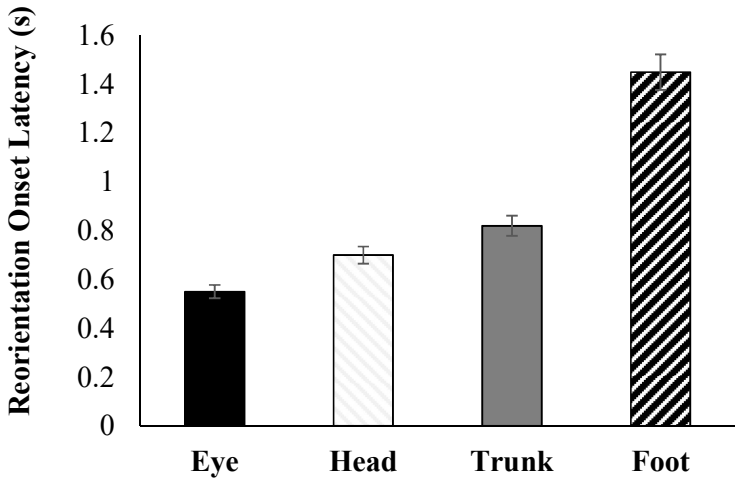


Figure 1-1: Recreated from (Hollands, Ziavra and Bronstein, 2004) and representing the timing of reorientation onset latency following a visual cue to turn 135º.

1.3.1.2 Anticipatory saccades and nystagmus

Prior to changing the direction of walking or making on-the-spot turns (Grasso *et al.*, 1998; Hollands and Marple-Horvat, 2001; Anastasopoulos *et al.*, 2009), healthy adults usually move their gaze in the new desired direction. Research on standing turns either explored turns to align with visual targets or turns to align with remembered locations and found that during memory-driven trials, where participants returned to the starting position following the visually-driven trials, participants used the same initiating eye movements as during visually-driven turns. However, axial segment reorientation was more en-bloc during memory-driven trials than during visually-driven trials, with the head and trunk rotation sometimes preceding eye movement (Anastasopoulos *et al.*, 2009). Akram et al. (2010) suggested that the en-bloc pattern of turning has also been replicated in healthy elderly people when turning with their eyes closed (Akram, Frank

and Chenouri, 2010). Therefore, it is clear that availability of vision can influence the eye, head and body coordination behaviour.

During large slow gaze shifts, such as those that occur during large body rotations to locations outside of the oculomotor range, individuals rarely generate single step gaze shifts. Instead, gaze reorientation is accomplished after the initial coordinated gaze shift, with the contribution of vestibular nystagmus until the new target is fixated.

Nystagmus can be divided into two phases: slow and fast phases (or quick phases). These phases normally act to irregularly shift and stabilise gaze on the environmental features of the turn. The slow phase stabilises gaze by compensating for head rotation and is driven by the Vestibule-Ocular-Reflex (VOR) (Barnes, 1979); however, the role that the fast phase anti-compensatory eye movements contribute to the coordination of turning behaviour is relatively undefined.

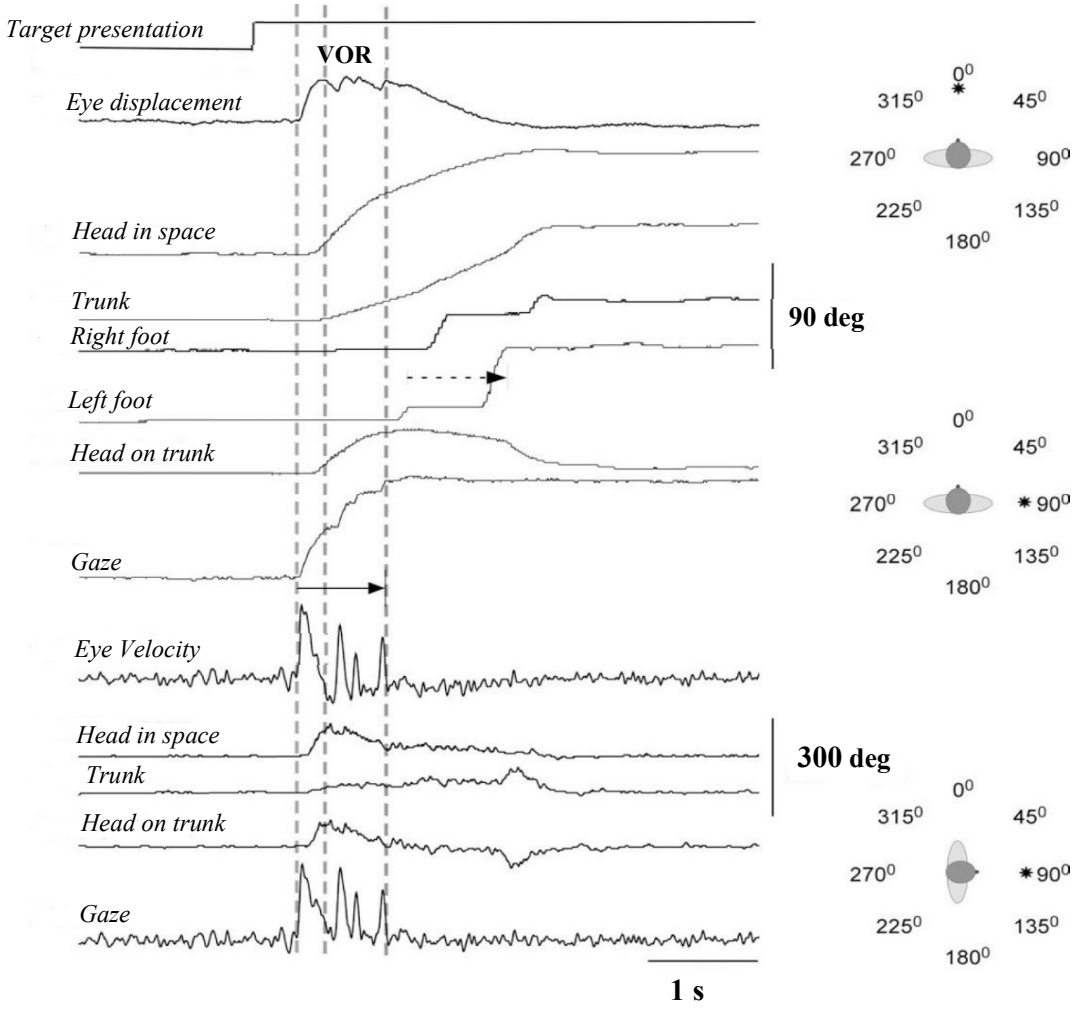


Figure 1-2: Reprinted from (Anastasopoulos *et al.*, 2011). An example of a visually guided whole-body turn to a target located at 90° turn to the right, demonstrating an initiating eye movement prior to head movement followed by nystagmus. The steep slope of the eye displacement curve in the positive direction indicates the fast phase of nystagmus while the more gradual descending slope after the peak indicates the slow phase of nystagmus, generated by VOR.

Anastasopoulos et al. (2015) found that characteristics of nystagmus during very fast turns differ significantly from those observed during turning at a natural speed. During natural, slower turns, single-step gaze shifts to eccentric targets only occurred in approximately 30% of the trials but, during fast turns, this occurred in 70% of the trials.

Examining the kinematic data showed that head velocity was significantly higher during single-step gaze shift trials than multi-step gaze transfers (Anastasopoulos *et al.*, 2015). However, the authors found that eye-in-orbit characteristics did not differ between single- and multi-step transfers and, therefore, it was proposed that head-in-space and eye-in-orbit movements may be controlled by separate mechanisms.

1.3.1.3 Anticipatory head movements

Head yaw typically leads trunk yaw by approximately 25° of rotation (Imai *et al.*, 2001) during walking and turning. Hollands et al. (2001) showed that if the head is immobilised with respect to the shoulders while walking and changing directions, the trunk reorients earlier than during normal head free turns (Hollands, Sorensen and Patla, 2001). This strategy is presumably used to maintain the anticipatory nature of gaze (eye direction in space). External perturbations to the head during turning can also affect subsequent segment reorientation; Vallis and Patla (2004) used a device fitted to the head to unexpectedly perturb it in the yaw direction during walking. It was found that when unexpected head perturbations occur in the direction of the turn one step prior to the turn, sequential segment orientation was preserved (Vallis and Patla, 2004). However, when the head was perturbed in the direction opposite the turn, the onset latency of each segment was delayed until the head oriented towards the travel path and the body segments rotated en-bloc. The authors found that sequential axial segment reorientation representing a 'steering synergy' could be automatically evoked following an unexpected head perturbation in the yaw direction. Moreover, they found that a subset of this synergy (trunk yaw and centre of mass translation in the mediolateral plane) was also released following voluntary head movements in the yaw direction (Vallis and Patla, 2004).

The anticipatory behaviour of the head during turning remains robust and consistent despite changes in curvature and walking velocity. Prévost et al. (2003) demonstrated that when walking speed is altered while making 90° turns around corners, head deviation occurs at approximately the same distance from the designated turn point regardless of walking speed. They concluded that head anticipatory orienting movements are used to obtain information about guidance of walking direction and this information is used to dynamically control gait during locomotion (Prevost *et al.*, 2003).

1.3.1.4 Stepping characteristics

It should be noted that turning requires a stepping action to maintain dynamic stability and control the characteristics the base of support (BOS) formed by the feet. Stepping actions are critical as they determine the width of the BOS to maintain balance. Hase and Stein (1999) categorised stepping strategies during turns in healthy adults into two types: spin turns and step turns (Hase and Stein, 1999). A spin turn is a strategy used to turn towards the stance limb to create a vertical axis of rotation; following this, the momentum of swing limb allows the body to rotate to the new direction while the ball of the foot of the stance limb acts as the BOS. Another stepping strategy of turning is the step turn. This strategy provides a wider BOS, as by using this strategy, an individual takes small steps to rotate. In addition, the step turn involves the use of small asymmetrical steps that slightly rotate both feet towards the new travel direction with each progressing step, thus maintaining a relatively wide BOS. During a spin turn, a small step is made by the non-turn foot, which results in both feet slightly rotating towards the new travel direction (Hong, Perlmutter and Earhart, 2009).

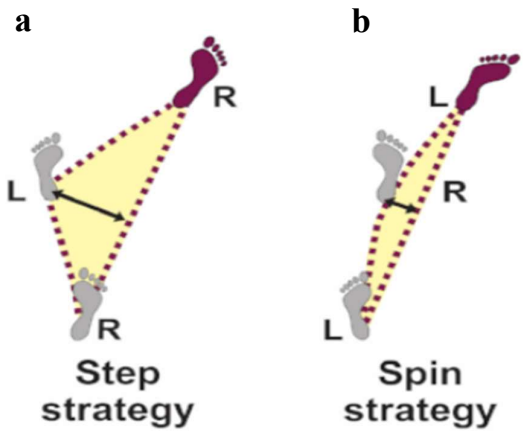


Figure 1-3: Reprinted from (David, 2017) **a)** the step turn (i.e. first turning step ipsilateral to the turning direction) and **b)** the spin turn (i.e. first turning step contralateral to the turning direction) during a right turn. The spin turn strategy results in a narrowing of the BOS and towards by momentum of swing limb, whereas the step turn strategy uses the step in the direction of the turn as the BOS is widened.

During walking turns, stride length decreases as the turn angle increases. During circular walking, gait becomes asymmetrical, and the stride length of the internal foot decreases in comparison to the stride length of the external foot (Hollands, Sorensen and Patla, 2001). Changes in the size of the BOS do not seem to have any significant effect on the reorientation of body segments according to the results of Paquette et al (2008), who used two types of turns, a 'step out' turn, which created a wider BOS, and a cross-over turn, which created a narrower BOS (Paquette *et al.*, 2008). Despite the challenge of a narrow BOS, the sequence of body reorientation remained the same between turn types; the main effect found was a slightly different reorientation between the older and younger participants, whereby COM displacement occurred before trunk roll in younger adults and after trunk roll in older adults. Older adults typically adopt the step turn strategy more often than the spin turn strategy when walking at their natural pace, suggesting that

maintaining a wider BOS becomes increasingly important with age (Paquette *et al.*, 2008). Ageing may also contribute to habits that decrease the BOS and challenge balance and stability. Older women have a tendency to bring their feet closer together, thus decreasing their BOS. Moreover, when making turns to unpredictable direction, they show more variance in foot positioning than their younger counterparts, regardless of the turn direction. Older women also use a small preparatory step in the anterior-posterior plane with the foot contralateral to the turn direction (Paquette *et al.*, 2008; Hong, Perlmutter and Earhart, 2009; Akram, Frank and Fraser, 2010).

1.3.2 Turning behaviour of individuals with PD

Individuals with PD turn a lot more slowly than healthy adults and exhibit differences in terms of the amplitude and timing of eye movements (Stack, Ashburn and Jupp, 2006; Anastasopoulos *et al.*, 2011; Lohnes and Earhart, 2011). Previous research has found that while turning, individuals with PD demonstrate a simultaneous rotation at the onset of axial segments, rather than a normal top-down sequence, and adopt a more en-bloc movement strategy (Huxham *et al.*, 2008). Although it is clear that individuals with PD show altered turning behaviour that puts them at a greater risk of falling (Haertner *et al.*, 2018), the mechanisms that underlie the turning problems have not yet been fully determined. Possible characteristics of PD that may contribute towards turning deficits include axial rigidity, bradykinesia (slowness of movements), shuffling gait, and altered vision and eye movement problems.

1.3.2.1 Possible mechanisms of turning dysfunction

1.3.2.1.1 Neck and trunk rigidity

Rigidity is one of the major manifestations of PD. A feeling of stiffness is the only symptom of rigidity that an individual experiences. As a clinical assessment, however, rigidity refers to the phenomenon of resistance to passive movement. Rigidity is also speed-independent – the faster the motion, the same the rigidity (Van Emmerik *et al.*, 1999; Mazzoni, Shabbott and Cortés, 2012; Baradaran *et al.*, 2013; Hulbert *et al.*, 2015); hence, those with PD tend to move slowly. Previous studies have reported that while only 27% of individuals with PD suffer from neck rigidity with unilateral involvement of the limbs, all people with PD suffer from rigidity in neck and trunk with bilateral involvement of the limbs (Cano-de-la-Cuerda *et al.*, 2011). Furthermore, Franzén et al. (2009) reported that neck and trunk muscle tone play an essential role in controlling postural balance, mobility and coordination (Franzén *et al.*, 2009). In PD patients, neck and trunk rigidity are highly related to poor turning performance, which results from compensatory hyperactivity in the extensor muscles to maintain posture. The increase in neck and trunk flexor tone results in the head moving beyond the neck, leading to increased neck extensor activity to prevent the head from falling forward. Moreover, neck and trunk rigidity in individuals with PD may result in altered spatial-temporal coordination of the axis, which is needed to maintain stability in axial body segments and lateral postural responses during turning (Smania *et al.*, 2011). For example, individuals with PD show significantly less variability in coordination between the pelvis and thorax during rotations from cycle to cycle across walking patterns and velocities compared to a healthy control group which may be partially explained by increased rigidity (Van Emmerik *et al.*, 1999). Research on bimanual movement coordination has shown that individuals with PD tend to find it more difficult to switch between coordination patterns, combine sequential movements and

perform simultaneous movements, such as in the coupling between head and neck movement, arm and leg movement or between the pelvis and thorax during locomotion. Importantly, pharmacologic treatment for PD patient appears to be ineffective to improve rigidity problems (Cano-de-la-Cuerda *et al.*, 2011; Tomlinson *et al.*, 2014). Due to the progressive nature of PD, axial rigidity will become increasingly problematic as the disease advances (Van Emmerik *et al.*, 1999).

1.3.2.1.2 Shuffling gait

The fast, frequent small stepping pattern that characterises PD gait results in an involuntary forward trunk lean that leads to a constant state of postural instability (Giladi *et al.*, 2001). Freezing of Gait (FOG) is a debilitating characteristic of gait in PD, potentially leading to patients having difficulty initiating walking or suddenly failing to continue moving forwards. As a result of rigidity, patients walk with shorter steps and cannot raise their feet as normal. Once they begin walking, the feet may appear dragged and glued to the ground, and shuffling gait disorder may set in. It has also been shown that individuals with PD who exhibit FOG show a reduced medial deviation and a forward shift of the COM while turning just before FOG episodes (Bengevoord *et al.*, 2016). It should be noted that reduction in medial COM deviation resulting from en-bloc turning may be responsible for incomplete weight shift to the inner side of the turning arc, resulting in more time, additional steps and increased toe clearance being required to complete a turn. Differences in the spatiotemporal characteristics of gait and balance impairments, the difficulties in changing head orientation and altered top-down coordination may all contribute to postural control turning problems (Bengevoord *et al.*, 2016). Therefore, it is likely that shuffling gait is one of the factors that put individuals with PD at a greater risk of losing balance and falling while turning (Bloem *et al.*, 2004).

1.3.2.1.3 Eye movement problems

Lohnes and Earhart (2011) provided evidence that impaired turning performance observed in individuals with PD can be partially explained by eye movement deficits. These deficits not only affect the eyes but also the coordination of eye movements with the associated movements of the head and body (Lohnes and Earhart, 2011). Indeed, the impairment of the top-down sequence is characterised by altered timing of segment rotations and smaller intersegmental rotations, which are accompanied by altered saccade timing or decreased saccade amplitude. In addition, eye-movement deficits are associated with axial segments being rotated in an en-bloc manner (Lohnes and Earhart, 2011). An en-bloc turning strategy may reduce the ability of individuals with PD to compensate for destabilisation, leading to a greater risk of instability. However, it is unclear whether the en-bloc turning strategy is widely used by older adults with PD and/or whether en-bloc leads to a greater risk of falling (Schlenstedt *et al.*, 2016). It should be noted that this study did not consider the relationships between rotation speed and eye and body segment characteristics and, therefore, it is not clear whether difference in eye movement is a causal factor or a by-product of turning dysfunction.

1.3.2.1.4 Bradykinesia

Bradykinesia is a movement impairment that involves slowness of movement. Slowness of body segment movements in response to a trigger suggests that a person will be less well prepared for negotiating mobility safely because they are less likely to detect an obstacle and step in time to initiate saving reactions, and thus more likely to trip or fall (Ashburn *et al.*, 2014). Slowed movement initiation is thought to result from altered of basal ganglia output needed to reinforce the cortical mechanisms that prepare and execute the commands to move (Berardelli *et al.*, 2001). Bradykinesia results in difficulty in controlling the sequential and simultaneous performance of movements (Mazzoni,

Shabbott and Cortés, 2012). Trunk rotation bradykinesia has been identified as a potential causal mechanism of altered eye, head and body coordination observed in individuals with PD during turning (Crenna *et al.*, 2007; Huxham *et al.*, 2008; Ashburn *et al.*, 2014). Moreover, previous studies have suggested that FOG is an extreme form of bradykinesia (often termed akinesia) and results in individuals being unable to continue walking forwards, especially while turning, leading them to fall (Mazzoni, Shabbott and Cortés, 2012).

1.3 Summary of key experimental papers relating to turning

As mentioned previously, several studies have investigated turning characteristics in both healthy adults and individuals with PD. A summary of experimental and measurement outcomes of several studies is presented in Table 1-2.

Table 1-2: Summary of experimental and measurement outcomes.

Study	Participants	Subject of Investigation	Results
Anastasopoulos et al. (2009) (Anastasopoulos *et al.*, 2009)	10 healthy people	A standing turn towards visually-cued locations, indicated by eight LED lights arranged circularly and spaced 45° apart, and memory-driven locations	Participants returned to the starting position during memory-driven trials, following the visually-cued trials. Participants initiated eye movements during the visually-cued turns. Axial segment reorientation during memory-driven turns was more simultaneous than during visually-cued turns.
Akram et al. (2010) (Akram, Frank and Fraser, 2010)	19 healthy older adults	A 90°-on-the-spot turn under eyes-open and eyes-closed conditions	In the eyes-open condition, older adults reoriented their head, shoulders and pelvis simultaneously. In the eyes-closed condition, the segment onset latencies were delayed and even more synchronous than with vision. Older adults typically used a step turn strategy to maintain balance.

Lohnes and Earhart, (2011) (Lohnes and Earhart, 2011)	- 23 individuals with PD with Hoehn and Yahr stages I–III - 19 controls	90° and 180° degrees in-place turns to the right and left	Individuals with PD demonstrated a greater number of saccades and exhibited differences in the initial fast phase velocity while turning as compared to the control group, suggesting that saccadic eye movement deficits affect whole-body coordination in people with PD.
Anastasopoulos et al. (2011) (Anastasopoulos *et al.*, 2011)	- 10 individuals with PD with Hoehn and Yahr stages I–II - 10 healthy older adults	A standing turns towards eight LEDs arranged circularly and spaced 45° apart that indicated targets of eccentricities up to 180°	Eye movement deficits in PD were found to be associated with a reduction in the extent to which the head leads the various axial segments to rotate in an en-bloc manner.

Yang et al. (2016) (Yang *et al.*, 2016)	- 13 individuals with PD with Hoehn and Yahr stages III - 12 age-matched healthy adults	Performing the Time Up and Go tests; recording with a 3D-motion capture analysis system	Individuals with PD rotated their head, thorax and pelvis simultaneously at a slower pace and with a greater number of steps than healthy adults. Individuals with PD had a smaller sagittal inclination angle but larger frontal inclination angle than the control group.
Ashburn et al. (2014) (Ashburn *et al.*, 2014)	- 31 individuals with PD with Hoehn and Yahr stages I-IV - 15 age-matched healthy adults	Performing on-the-spot turns while standing using visual cues and self-selected speed	Individuals with PD turned on-the-spot using their head, shoulders, eyes, thorax, pelvis and feet. Individuals with PD with Hoehn and Yahr stages III-IV had longer onset latency in response to the visual cue than individuals with PD with Hoehn and Yahr stages I-II and healthy control.

Vaugoyeau et al. (2003) (Vaugoyeau *et al.*, 2003)	- 10 individuals with PD - 5 age-matched control subjects	Performing a single diagonal step at 45° with- and without- re-orientation.	Compared to the control subjects, individuals with PD showed a lengthening of the postural phase, a decrease in step length and velocity and a reduction in horizontal forces. Postural preparation and coordination between posture and movement were found to impaired in people with PD.
Crenna et al. (2007) (Crenna *et al.*, 2007)	- 14 individuals with PD - 15 age-matched healthy adults	Two different tasks were tested: straight walking at a self-selected speed along a straight trajectory about 6m long and walking and turning while walking straight ahead for at least 2 m to perform a 90° left turn around a rod and continue walking in the new direction for at least 2 additional meters	Individuals with PD approached turns with a slower step and completed turning with a greater number of steps. The normal cranio-caudal sequence, whereby rotation of the head towards the intended direction of travel is followed by rotation of the trunk, was replaced by nearly simultaneous rotation of the head and trunk and decreased relative head excursion after the second turning step.

1.4 Summary

Turning performance requires whole-body coordination, complex coupling between posture and gait, and continuous and dynamic movement. It is clear that each of the aforementioned symptoms of PD, including head and neck rigidity, bradykinesia, shuffling gait and eye movement problems may contribute towards turning deficits and to the occurrence and frequency of falls in individuals with PD. However, the mechanisms that underlie the turning deficits in PD have not been fully determined. It remains unclear as to which characteristics of turning directly result from disease pathology and which indirectly result from altered behaviour, e.g. the extent to which altered eye movements and stepping characteristics are an indirect consequence of slow movement and the extent to which altered eye, head and body coordination is an indirect consequence of increased axial rigidity. Therefore, the following studies focused on investigating of the contribution of axial rigidity to turning deficits in PD to address the key mechanism and primary target for intervention.

1.4.1 Study 1 (Chapter 2) aimed to model the symptoms of axial rigidity and bradykinesia in young healthy adults and observe its effects on eye movement, body coordination and stepping characteristics. We predicted that the results would demonstrate which of the identified factors best explain the characteristics of individuals with PD while turning and which therefore should be the primary target of interventions for people with PD.

1.4.2 Study 2 (Chapter 3) aimed to validate the Inertial Measurement Units (IMUs) to determine whether they would be appropriate for measuring axial movement during turning. This study predicted to develop methodology capable of measuring eye, head and whole-body coordination in a clinical setting.

1.4.3 Study 3 (Chapter 4) details the findings of a systematic scoping review aimed at identifying effective exercise or physiotherapy treatments for reducing axial rigidity in PD patients (Chapter 5).

1.4.4 Study 4 (Chapter 5) describes the results of a pilot RCT which aimed to reduce axial rigidity and observe the effects on functional performance in individuals with PD.

The findings of this thesis will not only add to our understanding of these mechanisms but also demonstrate the feasibility of exercise interventions targeted at addressing the specific mechanism relevant to improve functional mobility and reduce the risk of falling in PD.

Chapter 2

Effects of axial rigidity and bradykinesia on whole-body coordination during standing turns

Abstract

Background: Difficulty in turning is prevalent in individuals with Parkinson's disease (PD) and the resulting postural instability increases the risk of falling. However, the underlying mechanisms of turning problems have not been fully determined. For example, it is unclear whether changes in the eye movements of individuals with PD during turning directly result from their neuropathology or indirectly from altered posture and turning characteristics. Therefore, this study aims to model axial rigidity and bradykinesia in young healthy adults and observe its effects on eye movements and whole-body coordination while turning on-the-spot.

Methods: Twelve healthy participants completed standing turns on level ground at 180 degrees. A Vicon motion system and a Bluegain electrooculography (EOG) system were used to record movement kinematics and measure horizontal eye movements, respectively. Participants were randomised to turn at one of three speeds, with or without increased head and neck rigidity (participants wore a head, neck and chest brace that restricted axial movement). Ten trials were recorded for each combination of experimental condition and turn direction, giving 60 trials in total. The effects of different conditions were assessed through repeated measures ANOVA.

Results: There was a significant main effect of turning speed ($P<0.001$) on the following dependent measures: onset latency of all segments, peak head-thorax angular separation, step angular displacement amplitude, step frequency and number of steps. Experimentally inducing head and neck rigidity had multiple significant effects ($P<0.001$) on eye

movement characteristics, head and whole-body coordination and stepping characteristics.

Conclusion: Our results suggest that increased head and neck rigidity and turning slowly results in altered eye movement, whole-body coordination and stepping behaviour consistent with previously documented differences exhibited by individuals with PD. Therefore, interventions aimed at reducing axial rigidity and bradykinesia may improve turning ability in this population.

2.1 Introduction

More than 50% of individuals with Parkinson's disease (PD) have difficulties turning during standing or walking (Mak, Patla and Hui-Chan, 2008). These turning disturbances are associated with increased risk of falling and which can lead to immobility and loss of independence, resulting in high costs for both the individual and health care systems (Bloem *et al.*, 2001; Haertner *et al.*, 2018). Therefore, identifying factors that result in altered patterns of turning is important for rehabilitation and fall prevention for individuals with PD. Previous research has shown that turning in healthy adults is a whole-body coordinated process characterised by a top-down sequence of body segments reorientation (Hollands, Ziavra and Bronstein, 2004; Mak, Patla and Hui-Chan, 2008). Prior to changing direction, healthy adults usually shift their gaze in the direction of the turn and this anticipatory gaze behaviour is believed to represent an important part of the eye, head and body coordinated process (Hollands, Ziavra and Bronstein, 2004; Anastasopoulos *et al.*, 2011). The timing and nature of eye movements and the characteristics of the relative rotation between body segments observed during turning is dependent on the speed and size of rotation and the visual context, i.e. whether participants are turning to a visual goal or to a remembered location (Ashburn *et al.*,

2014). These relationships are highly predictable and therefore it is clear that the eye, head and body are highly coordinated by the central nervous system (CNS). However, axial segmental coordination is disrupted in PD (Hong, Perlmutter and Earhart, 2009; Akram, Frank and Jog, 2013). During turning, previous research found that individuals with PD demonstrated a simultaneous rotation onset of the axial segments rather than the normal top-down sequence i.e. adopted an en-bloc movement strategy (Huxham *et al.*, 2008). This disrupted coordination of the axial segments may impede the pursuit of visual information to guide reorientation leading to postural instability during turning in PD (Hollands, Patla and Vickers, 2002).

The relationship between turning dysfunction in people with PD and falling is complex. It is believed to result from; a) postural reflex dysfunction, which is caused by axial rigidity; this results in altered spatial-temporal coordination of the axis, which is needed to maintain the stability of axial body segments and lateral postural responses during turning (Vaugoyeau *et al.*, 2006; Stack and Ashburn, 2008; Franzén *et al.*, 2009; Hong, Perlmutter and Earhart, 2009), b) bradykinesia; this results in difficulty controlling sequential and simultaneous movements (Berardelli *et al.*, 2001; Vaugoyeau *et al.*, 2003; Crenna *et al.*, 2007; Mak, Patla and Hui-Chan, 2008; Stack and Ashburn, 2008; Mazzoni, Shabbott and Cortés, 2012), c) sensory impairments such as deficits in eye movement with associated movements of the head and body (Lohnes and Earhart, 2011), and d) shuffling gait, which is characterised by abnormally small and frequent steps to maintain stability of centre of mass (COM) (Stack, Ashburn and Jupp, 2006; Crenna *et al.*, 2007; Bengevoord *et al.*, 2016). However, it remains unclear what characteristics of turning directly result from the disease pathology and what characteristics results indirectly from altered behaviour.

The proposed study primarily aims to model the symptoms of bradykinesia and axial rigidity in young healthy adults and observe its effects on eye movement, body coordination and stepping characteristics. We hypothesise that experimentally modelling axial rigidity and bradykinesia in young healthy adults will result in altered eye movement, intersegmental coordination and stepping characteristics similar to those previously observed in PD. The results will show which identified factor best explains altered turning characteristics in PD that are linked to falling risks and which, therefore, should be the primary target for intervention in individuals with PD.

2.2 Methods

2.2.1 Study design and participants

Twelve healthy young adults (5 males and 7 females, mean age 23.58±3.15 SD, mean weight 63.55±10.56 SD, and mean height 165.97±9.16 SD) participated in the experiment. All participants were asked to read a participant information sheet and sign an informed consent form approved by Liverpool John Moores Research Ethics Committee (REC) (Ref. no. 16/SPS/001). Participants were excluded if reporting any neurological or cognitive impairments, musculoskeletal problems such as fractures or severe pain.

2.2.2 Materials

Thirty-nine reflective spherical Vicon markers were attached on the bony prominences of the participants and tracked using a Bonita motion analysis system (Vicon, Oxford, UK) at a sampling frequency of 200Hz. The following body characteristics were measured using weighing scales, tape measures and Vernier callipers: body mass (kg), height (mm), limb length (mm), knee width (mm), ankle width (mm), shoulder off set (mm), elbow

width (mm), wrist width (mm), and hand thickness (mm) at both sides. A Bluegain Electrooculography (EOG) system (Cambridge Research System Ltd.) was used to record horizontal eye movements at a sampling frequency of 1000Hz. Two surface EOG electrodes were placed on the outer canthi of each eye and a reference electrode was placed in the centre of the forehead (Figure 2-1a). A LabVIEW programme was used to control the presentation of visual cues (described below) and synchronise the two data streams via a simultaneously marked time point within the EOG data acquisition software and Vicon Link analog input to Nexus motion data capture.

2.2.3 Turning protocol and data collection

Participants stood approximately 4 metres in front of a projector screen (2.74 x 3.66m. Cinefold Projection Sheet, Draper, Inc, Spiceland., Indiana, USA). Data were collected for twelve combinations of three experimental conditions as follows;

a. Participants either wore a head, neck and chest brace to model head and neck rigidity (Figure 2-1b) or head was unrestrained.
b. Participants were asked to turn at fast (1.5s), moderate (2s) and slow (3s) velocity to model bradykinesia as suggesting by literature for turning 180 degrees (Chou and Lee, 2013; Bengevoord *et al.*, 2016).
c. Participants turned either clockwise or counter-clockwise.

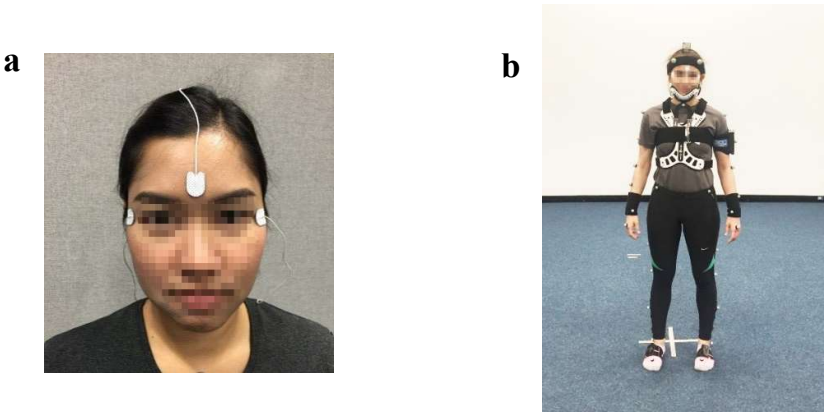


Figure 2-1: a For EOG setup, two electrodes were placed on the outer corners of the eyes and the reference electrode was placed on the centre of the forehead. **b** The participant wore a head, neck and chest brace.

Prior to each trial, a video was projected onto the screen showing an animation demonstrating the way participant should turn in accordance with one of the experimental conditions (Figure 2-2).

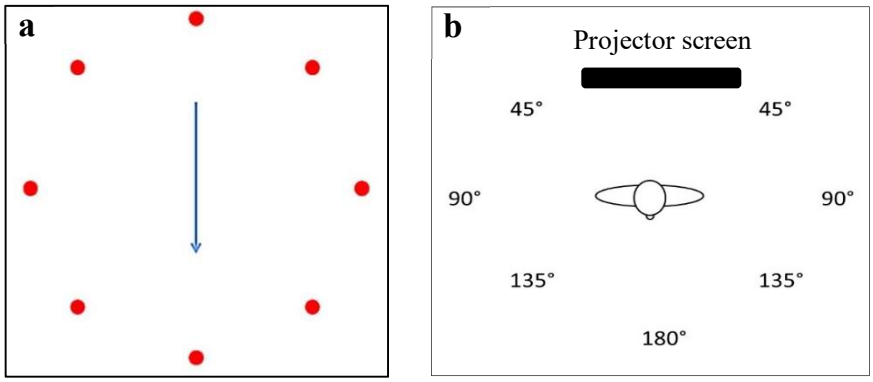


Figure 2-2: a) An example animation displayed to participants on the projector screen; b) participants completing standing turns on level ground through 180° and either to the left (counter-clockwise) or right (clockwise).

This was followed immediately by a visual cue to initiate the turn. Five trials were recorded for each experimental condition and for turns to both the left and right resulting in sixty trials total. Trials were organised into six blocks of 10 trials for each condition and counterbalanced across participants.

2.3 Data analysis

The Plug-In-Gait model (Vicon®, 2002) was used to determine angular displacement of the head, thorax, pelvis and left and right feet in the global reference frame. Kinematic data were passed through a dual low-pass fourth-order Butterworth filter using a cut-off frequency of 6Hz. The MATLAB (R2016a) programming environment was used to analyse all measures from the kinematic datasets, using the following as dependent variables:

1) Reorientation onset time of eye, head, trunk and feet and peak head-trunk separation as markers of axial segment coordination
2) Amplitude and velocity of yaw trajectory time-series from each body segment
3) Temporo-spatial stepping characteristics (step onset, step frequency, step size, and turn duration)

2.3.1 Axial segment reorientation

Displacement profiles were differentiated to yield velocity and acceleration profiles for each segment. The criteria used to determine the rotation onset for each segment as the earliest time point preceding segment displacement of 5° that was >0° with a velocity >0° s^{-1}. The end of rotation was determined as the first zero crossing in the velocity profile following the end of the segment rotation (Figure 2-3). The time-course of the turn trials varied in duration, and therefore, time-normalised profiles were created for the axial segments using the onset and offset latencies from the axial segments (i.e., the head,

thorax, and pelvis). The earliest onset latency (typically the head yaw onset latency) and the final axial offset latency were chosen for the normalisation procedure. Normalisation was performed using a customised MATLAB function, which increased each time series to a length of 1000 data points (i.e. longer than all individual time series) and interpolated the missing data points. Normalisation was performed in this way, so that the segments could be compared to each other over the whole course of all axial segment rotation. Using the normalised axial segment profiles, angular separation profiles were obtained from subtracting one profile from another, resulting in head–thorax, head–pelvis, and thorax–pelvis profiles. Turn speed was defined as peak head yaw velocity during the turn. Peak head velocity was chosen, since it was clearly definable and showed a consistent bell-shaped profile.

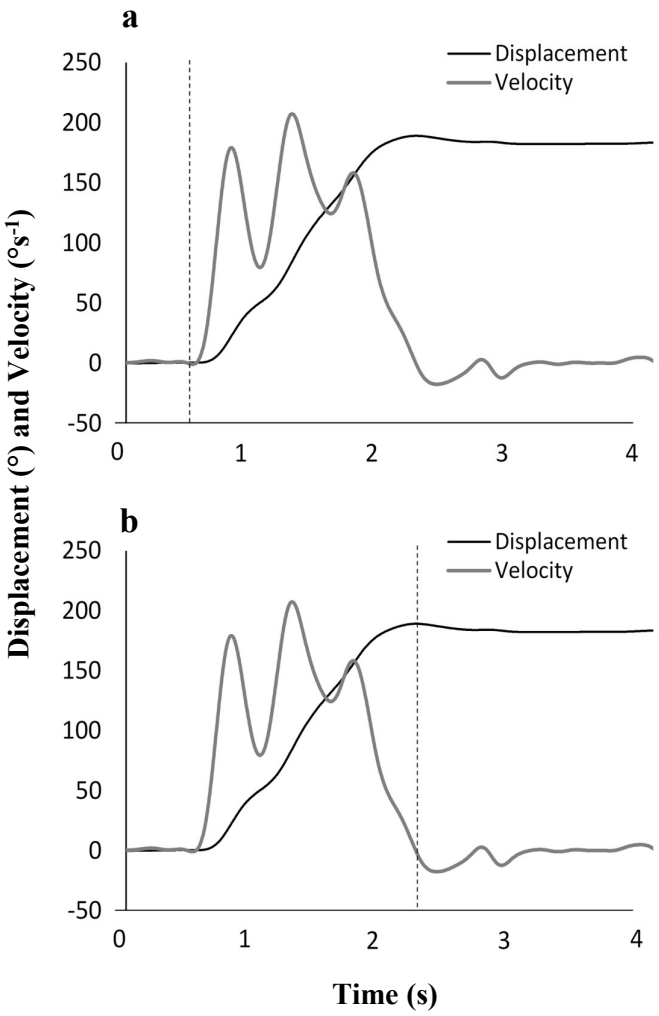


Figure 2-3: a) A time point fitting the onset criteria were viewed concurrently with displacement (black line) and velocity (blue line) profiles and determined as the onset latency for all segments. b) A time point end determination was the first time after the sustained rotation below $0^{\circ}s^{-1}$ as the end of segment rotation.

2.3.2 Step analysis

Individual steps were analysed and step onsets defined by: 1) a positive zero-crossing preceding and 2) a negative zero crossing following, a velocity value that reached 15% of the maximum angular foot yaw velocity. Each step onset was then determined as the first frame of the step interval with a velocity greater than or equal to $30^{\circ}s^{-1}$. Following the peak velocity of the individual step, step end time was signified by the first frame being less than $30^{\circ}s^{-1}$. Thereafter, Individual step size, placement amplitude, step velocity and step acceleration were determined from step onset to step end (Figure 2-4).

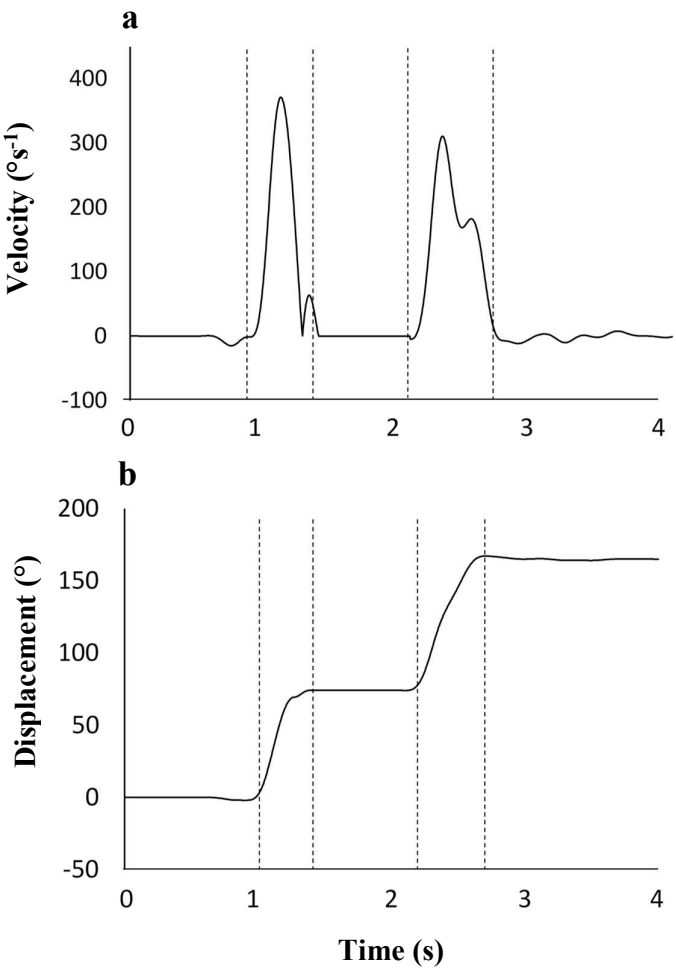


Figure 2-4: a) Step intervals velocity determination were shown by the dashed black lines to the left and right of each peak. b) Step onset (red dashed lines) and end time point determination (purple dashed line) that followed the peak velocity within each step interval.

2.3.3 Electrooculography

EOG calibration was performed before data collection. The participant was required to fixate a point on the screen directly in front of them and make slow sinusoidal head movements in the yaw plane (around vertical axis). Eye position and head position data were temporally aligned and a portion of the data between a peak and a trough of the sinusoidal pattern was selected for calibration analysis. A linear regression model was used to generate an equation which was used to convert EOG values measured in mV, to angular displacement of the head in degrees (°). Bespoke MATLAB (R2016a) scripts were used to obtain all measures from the EOG dataset. All EOG data was low-pass filtered using a fourth-order Butterworth filter with a 30Hz cut-off frequency. Differentiation of the eye displacement profile was performed to calculate angular velocity and acceleration profiles (Robins and Hollands, 2017).

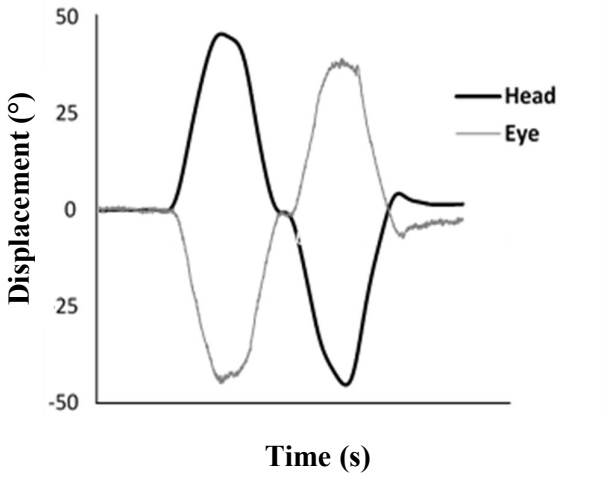


Figure 2-5: EOG Calibration. The participant was required to fixate a point and make sinusoidal head movements in the yaw plane. Eye position and head position data were temporally lined up and a portion of the data between a peak and a trough was selected for regression. In this representative example, VOR gain is near unity (i.e. the velocity of the eye and head are approximately equal and opposite), showing that the displacement of the eye will be approximately equal (and opposite) to the displacement of the head.

For fast phase determination, EOG data was inspected alongside head onset and end times, prior to analysis. To eliminate saccades and fixations that occurred prior to, and following, the turn, lower and upper limits were manually determined. From this selection of the data, nystagmus fast phases were determined using time intervals beginning with positive zero crossings and ending with negative zero crossings. Moreover, eccentric eye positions at fast phase onset and end were determined and all individual fast phase amplitudes, velocities and accelerations were gained from fast phase onset to fast phase end time.

2.4 Statistical analysis

The statistical package SPSS (23.0) was used for all statistical procedures. Repeated measures ANOVA were performed to assess the effects of our conditions on the following outcome measures:

1) Reorientation onset time of eye, head, trunk and feet and peak head-trunk separation as markers of axial segment coordination
2) Amplitude and velocity of yaw trajectory time-series from each body segment
3) Amplitude, frequency and velocity of eye movements
4) Temporo – spatial stepping characteristics (step onset, step frequency, step size, and turn duration)

A 2 x 2 x 3 repeated-measures ANOVA was performed on kinematics and eye movement variables with direction (left or right), condition (normal or rigidity) and speed (fast, moderate or slow) as repeated measure factors. Statistical significance was set at $P<0.05$. Bonferroni corrections were used for multiple comparisons.

2.5 Results

2.5.1 Segment onset latencies

Onset segment reorientation began with the eyes followed by the rotation of the head, trunk and pelvis and, finally, the leading and trailing foot; this sequence was preserved for each turning speed and turning condition (Figure 2-6).

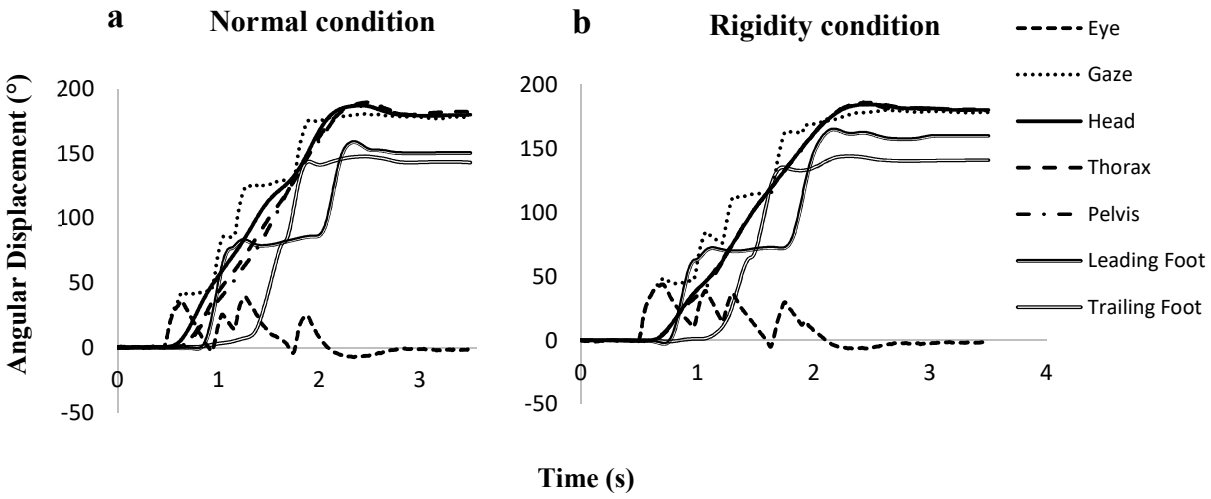


Figure 2-6: Turn displacement raw data from one trial at moderate speed for **a,** the normal condition, and **b**, the rigidity condition. Both traces clearly show that the gaze leads the other body segments throughout the majority of the 180° turn. In both conditions normal condition, segment reorientation began with the eye, followed by the rotation of axial segments (head, trunk and pelvis) and, finally, the leading and trailing foot.

There was a significant main effect of turn speed on mean onset latency for all segments (eye: $F_{(2, 22)} = 5.21$, $P<0.005$, $\eta_p^2 = 0.321$; head: $F_{(2, 22)} = 40.40$, $P<0.001$, $\eta_p^2 = 0.786$; thorax: $F_{(2, 22)} = 46.53$, $P<0.001$, $\eta_p^2 = 0.809$; pelvis: $F_{(2, 22)} = 46.04$, $P<0.001$, $\eta_p^2 = 0.807$; leading foot: $F_{(2, 22)} = 43.25$, $P<0.001$, $\eta_p^2 = 0.847$; trailing foot: $F_{(2, 22)} = 83.91$, $P<0.001$, $\eta_p^2 = 0.868$). Onset latencies were shortest during fast speed trials and longest during slow

speed trials for all turn conditions (Figure 2-7). There was no significant main effect of rigidity or interactions between speed and rigidity conditions for any segment onset latency.

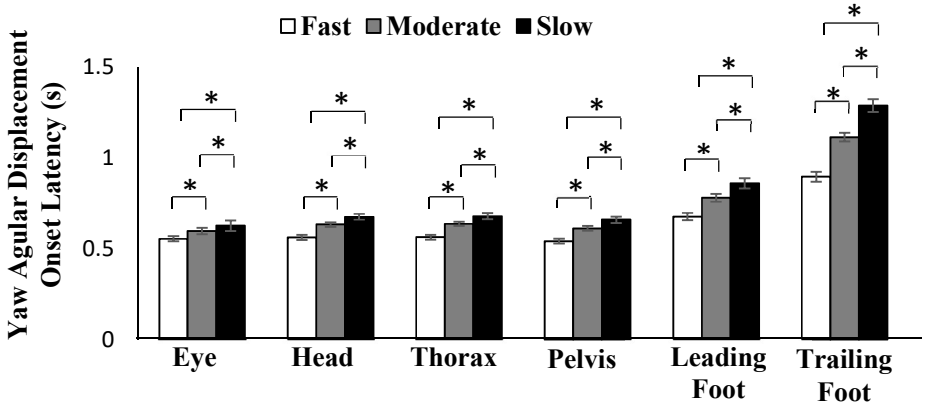


Figure 2-7: Bar graph showing the mean onset latencies with turning speed. There was a significant main effect of speed condition on the timing of rotation onset for all segments.

(* - significant)

2.5.2 Intersegmental relationships

There was a significant main effect of turning condition on peak head-thorax angular separation ($F_{(1, 11)} = 56.54$, $P<0.001$, $\eta_p^2 = 0.837$) and peak head-pelvic angular separation ($F_{(1, 11)} = 41.77$, $P<0.001$, $\eta_p^2 = 0.729$) (Figure 2-8) demonstrating that our rigidity condition was successful in restricting head rotation with respect to the upper body.

There was a significant interaction between turn speed and turn condition on peak head–-thorax angular separation ($F_{(2, 22)} = 13.42$, $P<0.001$, $\eta_p^2 = 0.582$) and peak head–pelvic angular separation ($F_{(2, 22)} = 7.13$, $P<0.005$, $\eta_p^2 = 0.427$) showing that peak segmental

separation increased with an increase in turn speed but only under the normal head unrestrained condition.

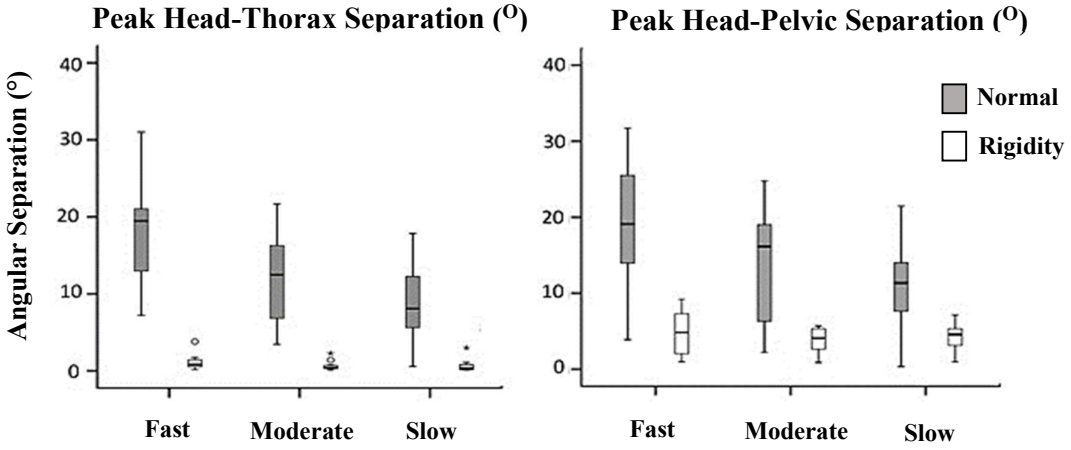


Figure 2-8: The effects of turning speed on mean peak head–thorax angular separation and peak head–pelvis angular separation under both conditions. A box and whiskers plots diagram has been used to illustrate the median peak head–thorax angular separation and peak head–pelvic angular separation.

In addition, Figure 2-9 shows the regression analysis between peak head yaw velocity and peak head–thorax angular segment separation, which revealed the existence of significant positive relationships between the head and thorax under normal condition (R^2 = 0.45, P<0.005).

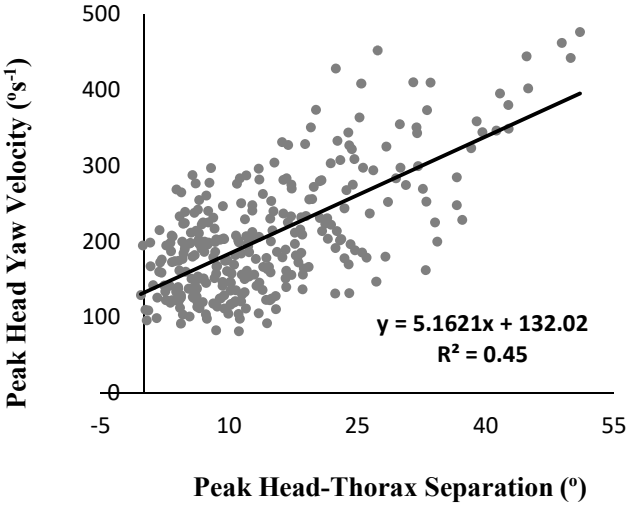


Figure 2-9: Scatterplot showing the results of regression analyses between peak head yaw velocity and maximum head-thorax angular separation. During the normal condition, a significant positive correlation between peak head yaw velocity and the head-thorax separation was found ($R^2 = 0.45$, $P<0.005$).

2.5.3 Turn speed characteristics

The mean of turn speed characteristics for fast turns were 101.30 ± 12.20 $°s^{-1}$ in normal condition and 108.40 ± 16.05 $°s^{-1}$ in rigidity condition, for moderate turns were 73.94 ± 5.08 $°s^{-1}$ in normal condition and 75.37 ± 6.20 $°s^{-1}$ in rigidity condition, and finally, for slow turns were 55.14 ± 3.16 $°s^{-1}$ in normal condition and 58.80 ± 3.22 $°s^{-1}$ in rigidity condition.

2.5.4 Fast phase characteristics

There was a significant main effect of turn condition on initial fast phase amplitude ($F_{(1, 11)} = 11.15$, $P<0.05$, $\eta_p^2 = 0.503$) and velocity ($F_{(1, 11)} = 8.52$, $P<0.05$, $\eta_p^2 = 0.437$) (Figure 2-10a and 2-10b, respectively). There were no main effects of turn speed or interaction

between turn speed and condition. Furthermore, there was no effect of turn speed or rigidity condition on initial gaze shift amplitude (sum of eye plus head rotation) (Figure 2-10c).

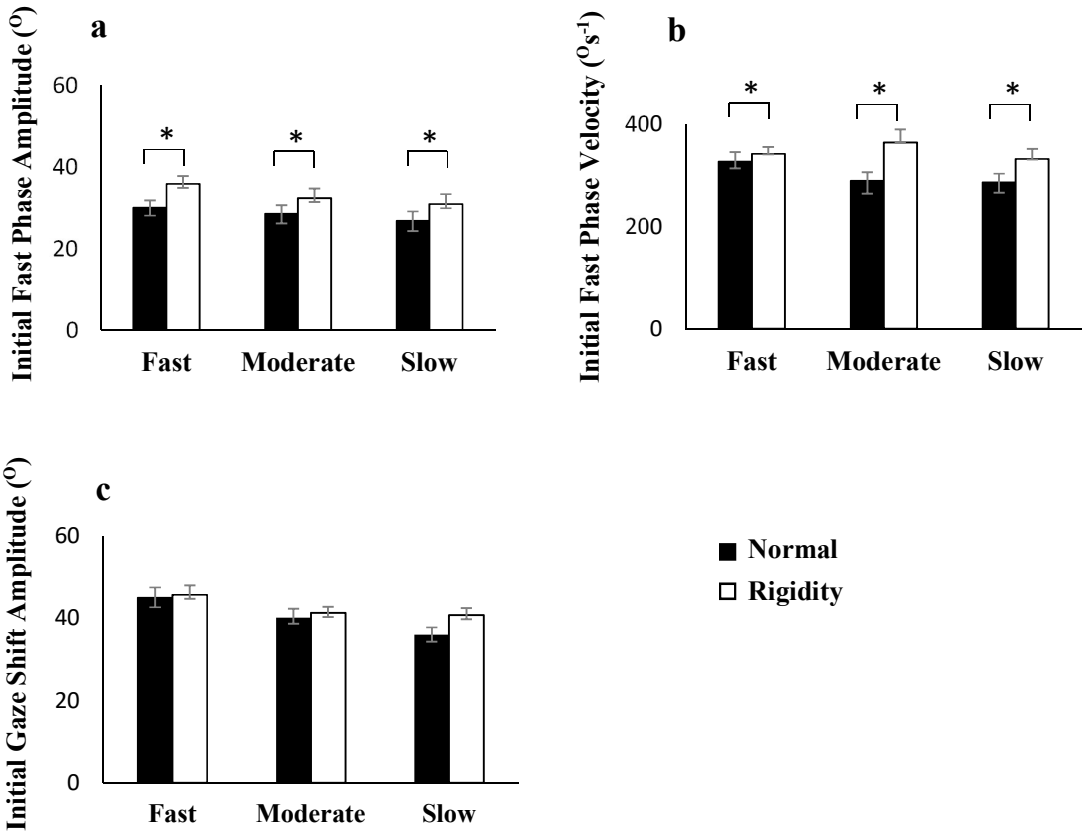


Figure 2-10: Experimentally inducing neck rigidity had multiple effects on eye movement characteristics.

The peak fast phase velocity was analysed as a function of fast phase amplitude for both normal and rigidity conditions (Figure 2-11a and 2-11b). All amplitudes were included in the analysis which was similar to the methodology used by Robins et al. (2017) (23). Similar strengths of relationships between peak fast phase velocity and fast phase

amplitude were observed under both normal and rigidity condition correlation ($R^2 = 0.28$, $P<0.001$) than the rigidity condition ($R^2 = 0.26$, $P<0.001$).

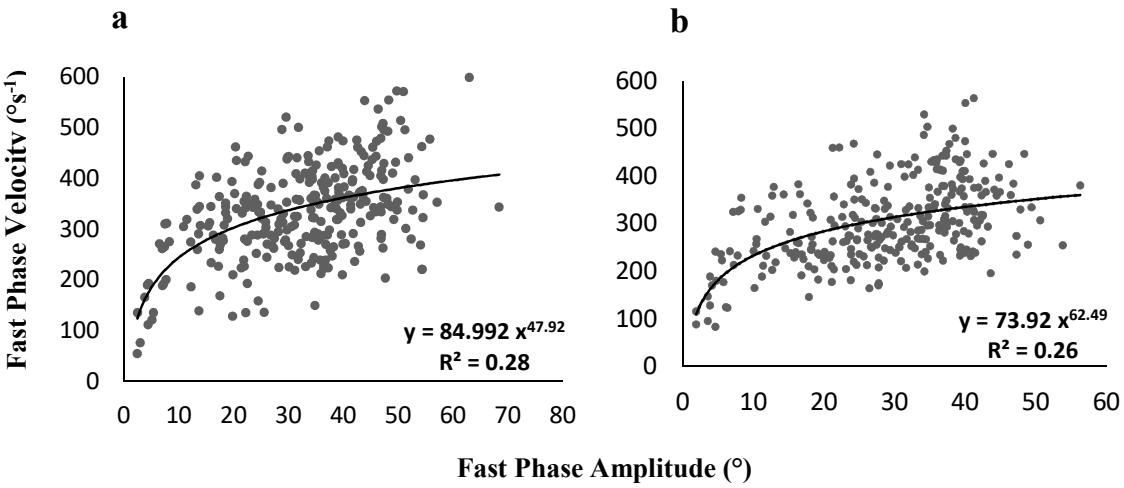


Figure 2-11: Main sequence plots for nystagmus fast phases under normal (a) and rigidity conditions (b). The relationship between fast phase amplitude and fast phase velocity under normal condition was similar to that observed under the rigidity condition.

Table 2-1: Mean and standard deviations for initial and maximum/peak fast phase characteristics as well as fast phase frequency measurements.

		Normal	Rigidity
Initial Fast Phase	Fast	30.03 ± 8.12	35.84 ± 7.58
Amplitude (°)*	Moderate	28.50 ± 7.36	32.38 ± 9.84
	Slow	26.73 ± 9.65	30.87 ± 10.05
Maximum Fast Phase	Fast	33.50 ± 6.79	39.01 ± 8.12
Amplitude (°)*	Moderate	32.91 ± 6.78	37.88 ± 6.65
	Slow	32.56 ± 6.23	37.07 ± 6.51
Initial Fast Phase	Fast	326.56 ± 73.20	342.09 ± 86.84
Velocity ($°s^{-1}$) *	Moderate	289.00 ± 60.53	364.40 ± 89.04
	Slow	286.09 ± 60.00	331.64 ± 67.92
Peak Fast Phase	Fast	376.31 ± 61.46	439.36 ± 68.07
Velocity ($°s^{-1}$)*	Moderate	386.63 ± 62.58	482.79 ± 85.34
	Slow	376.26 ± 61.45	445.94 ± 68.10
Initial Fast Phase	Fast	24092.91 ± 6870.43	24956.90 ± 7054.87
Acceleration ($°s^{-2}$)*	Moderate	22920.26 ± 5060.79	28393.01 ± 2306.89
	Slow	21573.93 ± 5348.74	24721.91 ± 6871.42
Peak Fast Phase	Fast	34789.74 ± 10181.57	40330.56 ± 11099.85
Acceleration ($°s^{-2}$)*	Moderate	36177.76 ± 8025.85	45028.68 ± 11746.45
	Slow	32935.47 ± 7534.10	38602.93 ± 9557.79
Number of Fast	Fast	3.10 ± 0.90	3.20 ± 0.71
Phases (N)**	Moderate	4.70 ± 1.42	4.90 ± 0.98
	Slow	6.57 ± 2.33	6.05 ± 1.96
Nystagmus Fast Phase	Fast	2.15 ± 0.60	2.32 ± 0.68
Frequency (Hz)	Moderate	2.30 ± 0.68	2.49 ± 0.70
	Slow	2.45 ± 0.69	2.38 ± 0.68

*significant main effect of turn condition, and

** significant main effect of turn speed on eye movement characteristics ($P<0.005$)

2.5.5 Stepping characteristics

The average step size defined as the yaw rotation of the foot during the swing phase was calculated for each step during the turn. There was a significant main effect of turn speed on step size ($F_{(2, 22)} = 27.31$, $P<0.001$, $\eta_p^2 = 0.713$) and total number of steps taken to turn ($F_{(2, 22)} = 31.49$, $P<0.001$, $\eta_p^2 = 0.481$) (Figure 2-12a and 2-12b). Furthermore, there were a significant main effect of turn condition on step size ($F_{(1, 11)} = 5.77$, $P<0.005$, $\eta_p^2 = 0.344$) and total steps ($F_{(1, 11)} = 27.54$, $P<0.005$, $\eta_p^2 = 0.741$). No interaction effects found between turn speed and turn condition.

Post hoc pairwise comparisons revealed that the effects of turn speed were limited to step size, and there were significantly decreased differences between fast and moderate speeds ($P= 0.001$), fast and slow speeds ($P=0.001$) and moderate and slow speeds ($P=0.011$). Significant effects of turn conditions were limited to the step size and there were significantly smaller of step size ($P=0.035$) on rigidity condition compared to normal condition.

In addition, post hoc tests showed the effects of turn speed were limited to total steps, and there were significant differences between fast and moderate speeds ($P<0.001$), fast and slow speeds ($P<0.001$) and moderate and slow speeds ($P=0.011$), which showed that more steps were made during slow turns than during fast turns and more steps while making moderate turns than while making fast turns. Modelling head and neck rigidity caused significant differences between turn conditions ($P=0.025$).

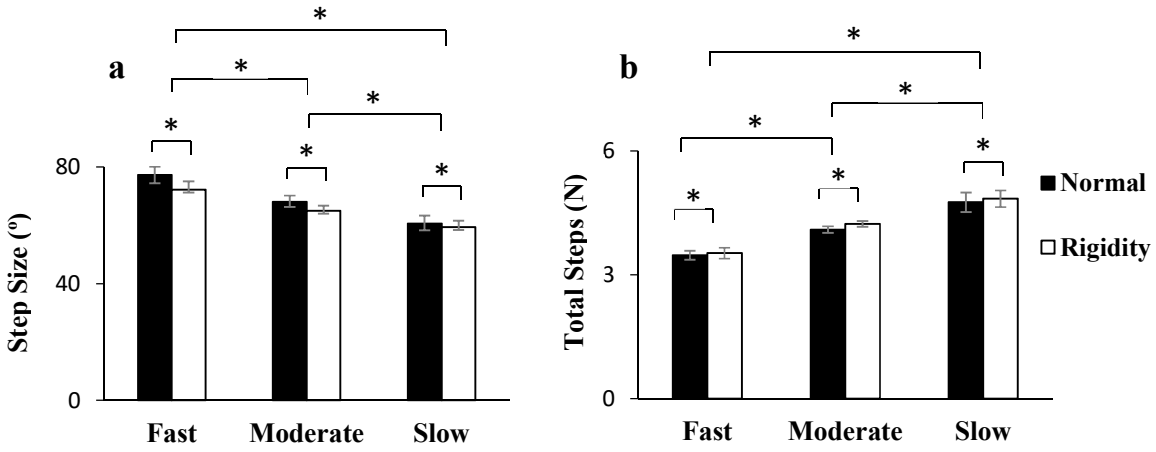


Figure 2-12: The effect of turn speed on **a)** step size and **b**) the total number of steps taken to turn.

There was a main effect of turn speed ($F_{(2, 22)} = 32.66$, $P<0.001$) and a main effect of turn condition ($F_{(1, 11)} = 9.23$, $P<0.005$) on step frequency calculated for each turn as the number of steps taken divided by stepping duration; modelling axial rigidity resulted in significantly increased stepping frequency for all turn speeds (Figure 2-13).

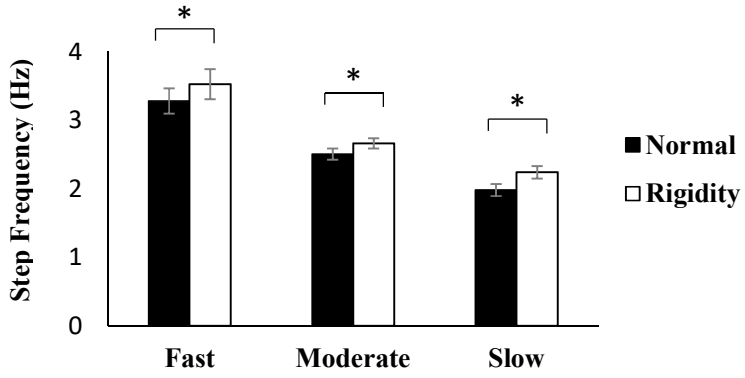


Figure 2-13: The effects of rigidity condition on stepping frequency for all turn speeds.

2.6 Discussion

The aim of the study was to expand our understanding of the mechanisms responsible for increased risk of falling while turning in people with PD by emulating the following: a) head and neck rigidity and b) bradykinesia in healthy adults. This is the first study to examine the effects of modelling axial rigidity and turning speed on eye, head and whole body coordination during standing turns. In line with our hypotheses, we found that both turning slowly and modelling axial rigidity, by restricting head on body movement, resulted in altered eye movement, whole-body coordination and stepping characteristics compatible with behaviour previously observed in individuals with PD. We discuss our findings in the context of previous studies of eye, head and body coordination during turning in individuals with PD.

2.6.1 Effects of manipulating turning speed

The first aim of the study was to examine the effects of turning speed on eye, head and whole body coordination during turning in healthy adults with a view to gaining insight into the contribution of bradykinesia to turning characteristics of individuals with PD.

There was a significant main effect of turning speed on the following dependent measures: reorientation onset latency of eye, head thorax and feet, peak head-thorax angular separation, step angular displacement amplitude, step frequency and number of steps.

2.6.1.1 Reorientation onset latencies

Several previous studies have documented that, when visually cued to turn, individuals with PD take longer to initiate axial segment rotation than neurotypical control

participants and suggested that bradykinesia could account for these differences (Vaugoyeau *et al.*, 2003; Mak, Patla and Hui-Chan, 2008; Stack and Ashburn, 2008; Akram, Frank and Jog, 2013; Ashburn *et al.*, 2014). The current results from healthy participants asked to turn at different speeds are in line with these findings; segment reorientation began with the eyes followed by the rotation of the head, trunk and pelvis and, finally, the leading and trailing foot. It is noteworthy that onset latencies were shortest during fast speed trials and longest during slow speed trials for all segments. Our current findings support the suggestion that turning slowly can account for the documented differences in the timing of rotation initiation in individuals with PD.

2.6.1.2 Peak head-thorax angular separation

Although traditionally lack of differences in the timing of axial segment reorientation onset have been used to characterize turning as en-bloc (Ashburn *et al.*, 2014), measuring the rotation of the head with respect to the upper body during the duration of the turn gives a more complete description of which body segments lead which during the turning motion (Crenna *et al.*, 2007; Hong, Perlmutter and Earhart, 2009; Anastasopoulos *et al.*, 2011). Our results clearly show that the head is rotated in advance of the body by up to around 20 degrees on average during fast turns but this reduces to around 10 degrees during slow turns. Furthermore we have showed that the extent of peak head-thorax separation is a linear function of peak head yaw velocity; a proxy of turning speed (Figure 2-8). This is consistent with the results of Robins and Hollands (2018) who showed a somewhat similar relationship in participants turning with a more limited range of turning speeds (Robins and Hollands, 2017).

These results demonstrate that turning slowly due to generalized bradykinesia may also contribute towards the en-bloc nature of head and body posture in PD patients.

2.6.1.3 Stepping characteristics

Slow turning was associated with smaller and more frequent steps; characteristics that are also commonly described in individuals with PD (Stack, Ashburn and Jupp, 2006; Hong, Perlmutter and Earhart, 2009; Anastasopoulos *et al.*, 2011; Lohnes and Earhart, 2011). During walking, individuals with PD generally take rapid, short steps which presumably serve to constrain COM excursions within the reduced base of support formed by keeping the feet closer together, resulting in a shuffling gait disorder. Stack et al. (2006) showed that individuals with PD who had difficulty in turning took more number of steps compared to those who reported no problems in turning, suggesting that shuffling gait may represent a strategy to compensate for actual or perceived instability (Stack, Ashburn and Jupp, 2006). Our results suggest that small, frequent steps may also be partially explained by a generalized effect of simply moving slowly.

2.6.2 Effects of modelling axial rigidity

The second aim of the study was to examine the possible contribution of axial rigidity to the turning problems of PD patients by experimentally restricting head on body rotations in healthy adults and observing the effects on eye, head and whole-body coordination.

It is important to note that restricting head on body rotation had no significant effect on the mean turning speed in any of the required turn speed conditions (Figure 2-10). Therefore, we can rule out the possibility that changes to eye, head and body coordination and stepping characteristics are an in indirect consequence of changes to turn speed.

2.6.2.1 Eye movement characteristics

Irrespective of our experimental manipulations, we found that, on average, the eyes led rotation of all other segments (Figure 2-6). Strikingly, the first gaze (eye in reorientation in space) shift amplitude was preserved in the head restrained condition by increasing amplitude of first saccadic eye movement (Figure 2-11). Considering the finding that the eye movement initiation preceded that of all other segments this suggests that during the initiation of turning eye and head movements are programmed together in order to shift gaze to a desired eccentric location. It maybe that this gaze shift serves to provide a visual anchor that is used to guide balance during the destabilizing initiation of postural reorganization at the onset of the turning movement. Gaze anchoring on salient environmental features via combined head rotations and saccadic eye movements is likely similar to the alternating saccade and fixation strategy employed during manual reaches (Neggers and Bekkering, 2001; Rand, 2014), precision stepping (Hollands *et al.*, 1995; Hollands and Marple-Horvat, 2001), and obstacle crossing (Patla, 1997). Gaze anchoring could presumably be used to provide the head with intermittent stabilised reference point during rotation which may explain why the size and frequency of fast phases is altered when vision is removed (Robins and Hollands, 2017).

2.6.2.2 Stepping characteristics

The effects of modelling axial rigidity were to reduce step amplitude and increase the number and frequency of steps (Figure 2-13). These changes to stepping characteristics are consistent with those observed in individuals with PD (Stack, Ashburn and Jupp, 2006; Crenna *et al.*, 2007; Stack and Ashburn, 2008; Hong, Perlmutter and Earhart, 2009; Anastasopoulos *et al.*, 2011; Lohnes and Earhart, 2011). It is possible that reducing the degrees of freedom of rotation of axial body segments alters the ability to accelerate and control the COM which is needed to make large stepping movements (Hong, Perlmutter

and Earhart, 2009). Previous study also suggests that although taking many small steps may result in freezing episodes (Stack and Ashburn, 2008), it may be beneficial in order to preserve postural stability and maintain COM in a wider base of support throughout the turn.

Robins and Hollands (2017) showed that fixing gaze with respect to the head in healthy young participants also resulted in reduced stepping frequency (Robins and Hollands, 2017). However, it is noteworthy that peak head-thorax separation was also reduced which raises the possibility that altered stepping may have been an indirect consequence of restricting head on body rotations rather than effects of changes in gaze per se.

It is, perhaps, interesting to note that activation of neck proprioceptive signals, as induced by prolonged neck muscle vibration or tonic head deviation, has a strong influence on gait trajectory orientation (Ivanenko, Grasso and Lacquaniti, 2000; Bove *et al.*, 2001; Bove, Courtine and Schieppati, 2002) suggesting that that turning can be driven by proprioceptive drive from neck muscle spindle 1a afferents.

In combination, these studies support a role of head on trunk rotation in driving turning (Bove *et al.*, 2001; Bove, Courtine and Schieppati, 2002). These results raise the possibility that reduced head on trunk rotation due to axial rigidity in individuals with PD, and associated reduction in proprioceptive drive from neck muscle spindles, may contribute towards altered stepping patterns e.g. reduced amplitude and increased frequency of stepping movements.

The current study sought to expand understanding of the mechanisms responsible for increased fall risk during turning in PD by emulating axial rigidity and bradykinesia in healthy adults. We have modelled the peripheral symptoms, which result from CNS dysfunction caused by PD. Our results suggest that one of the mechanisms of turning dysfunction is a by-product of slow turning speed due to pathologically induced bradykinesia (in the case of PD) and individual capacity behaviour or choice (for example, balance ability, muscle coordination and self-confidence). Therefore, it seems more likely that bradykinesia is responsible for the observed behaviour in healthy young adults. The slow turning in PD resulting from bradykinesia results in difficulty in performing activities in patients' daily lives, especially turning or sequential movements, and leads to the inability to start and stop movement, leading to falls. This adaptive strategy allows a better and slower control of movement, as proposed in a general theory of bradykinesia, which is considered to be a compensatory strategy to reduce the variability of motor performance.

Furthermore, experimentally inducing head and neck rigidity resulted in reduced step amplitude and an increase in the number and frequency of steps. The head restrained condition may reduce intersegmental coordination producing an en-bloc presentation and reduced segment rotation amy result in changing stepping characteristics to maintain balance and stability during the turn. In addition, this is the first study to demonstrate that restraining head and neck movement alters fast phase characteristics during standing turns. These results are relevant to reported disturbances in eye characteristics of individuals with PD during turning. Lohnes and Earhart (2011) reported that people with PD exhibit a greater number of saccades during turning and show differences in initial fast phase amplitude and velocity, compared to a control group (Lohnes and Earhart, 2011). They suggested that saccadic eye movement dysfunction due to PD

neuropathology may explain these changes. Our results show that the same trends in eye movement characteristics of people with PD, as those observed by these authors, can be evoked by modelling axial rigidity inn healthy participants. Therefore, it it is possible that rigidity is responsible for the observed eye movement behaviour.

2.7. Conclusion

The current study suggests that experimentally inducing head and neck rigidity contributes to previously-documented PD-related differences in eye movement, whole-body coordination and stepping behaviour during turning. Furthermore, turning slowly results in altered whole-body coordination and stepping behaviour consistent with those exhibited by PD patients. Therefore, interventions aimed at reducing axial rigidity and bradykinesia may prove effective in improving the turning ability of individuals with PD.

Chapter 3

Can we accurately measure axial segment coordination during turning using Inertial Measurement Units (IMUs)?

3.1 Introduction

Three dimensional motion analysis is one of the most important investigative methods to study human locomotion functions, such as changing direction and turning on the spot (Andriacchi and Alexander, 2000). In both clinical and research settings, objective measurements of spatiotemporal parameters of body movement are needed to identify movement impairments or evaluate the effects of therapeutic interventions. Investigating abnormal movement patterns provides useful information that aids in clinical decision-making. This information also plays a role during the follow-up stage for patients by helping determine the effectiveness of a particular exercise or treatment intervention (Suciu *et al.*, 2016). For example, there is a consensus among physiotherapist that performing movement analysis is beneficial for rehabilitation in individuals with PD; this includes analysis of functional mobility, pre- and post-rehabilitation planning and follow up (de Bruin *et al.*, 2012).

Camera-based 3D motion analysis systems (such as the Vicon motion analysis system) are the gold standard laboratory tool for analysis of human movements with a high degree of accuracy (Smania *et al.*, 2011; de Bruin *et al.*, 2012). However, the required cameras, force platforms and software programmes are expensive, time-consuming and require skilled technicians and a large measurement volume. Therefore, using such equipment in a clinical setting is prohibitive. Also, it is not clear to what extent data collected in a laboratory environment is representative of natural performance in daily life (Hartmann

et al., 2009). In recent years, inertial measurement units (IMUs) have been shown to be a viable alternative monitoring solution to assess movement in clinical and research settings (Picerno, Cereatti and Cappozzo, 2008; Picerno, 2017). These sensors are housed in small boxes that can be attached to different body segments and provide linear acceleration and Euler angle measurements. They also have low power requirements and allow continuous measurements outside the laboratory environment in real-life contexts (de Bruin *et al.*, 2012). However, the validity of IMUs for studying axial segment coordination during turning has not been examined. The aim of this study is to validate the use of IMUs to examine turning characteristics in healthy participants by comparing collected data to data generated by a Vicon motion analysis system. The results will allow us to determine whether IMU devices could be used in isolation to gather accurate data from individuals with PD within a real-life context in a clinical setting**.**

3.2 Method

3.2.1 Participants

Six healthy participants (three male and three female, 23.3±3.7 years, 66.98±13.55 kg, and 168.5±8.5 cm in height) participated in the experiment. Participants were asked to wear a sleeveless shirt and close-fitting trousers.

Figure 3-1: The participant was attached with markers and IMUs.

The data collection protocol was similar to that used in study 1. Prior to each trial, a video was projected onto a screen showing an animation indicating the way the participant should turn. Data from healthy participants turning were analysed under each of the three condition speeds: (1) fast speed (1.5s), (2) moderate speed (2s), and (3) slow speed (3s). Ten trials were recorded for each experimental condition and for turns to both the left and right resulting in thirty trials total per each participant.

3.2.2 Data acquisition

Vicon markers were tracked using a Bonita motion analysis system (Vicon, Oxford, UK) at a sampling frequency of 200 Hz. The Plug-In-Gait model (Vicon®, 2002) was used to calculate joint kinematics, 39 reflective spherical markers were attached on the bony prominences of the participants and anthropometric data were measured.

The four-IMU sensors (x-Inertial Measurement Units, x-io Technologies, LTD., UK) were attached on the following body segments including: centre of the forehead, middle thorax, the centre of left foot and right foot. The IMU devices collected data at a sampling frequency of 256 Hz to record the angular displacements of body segments in real time.

The IMU sensor was designed to be small. Its host of on-board sensors, algorithms, configurable auxiliary port and real-time communication via USB or Bluetooth make it both a powerful sensor and controller. In addition, IMU devices incorporate algorithms that provide estimates of the sensor's orientation with respect to a global, fixed coordinate system. This orientation can be represented by the Euler angles in the local segment as well as by the estimates of sensor orientations that require the use of magnetometer measurements with a common global reference frame. In terms of producing data, the source IMU allows the researcher to configure all internal IMU settings and view sensor data in real-time and export data from an on-board SD card to a software such as MATLAB and Microsoft Excel.

3.3 Data processing and data analysis

For data processing, the data from the IMU devices were subsampled to 200 Hz, which corresponded to the sampling rate of the Vicon data. The two angular displacement time-series data streams were temporally aligned using a MATLAB (R2016b) programming environment that used the cross-correlation function (xcorr). This function calculated the time lag between the two data streams that corresponded to a maximum correlation coefficient. The correlation coefficients for displacement, velocity, and acceleration profiles with the newly aligned data were calculated.

The MATLAB (R2016a) programming environment was then used to separate and analyse all measures from the kinematic datasets.

3.3.1 Head and thorax data processing

Displacement and velocity profiles were used to compare the Vicon data and the IMU data. Head and thorax data from two datasets were passed through a dual low-pass 4th-order Butterworth filter using a cut-off frequency of 6Hz. Displacement profiles were differentiated to yield velocity and acceleration profiles for each segment.

3.3.2 Step analysis

The foot data were passed through a dual low-pass 4th-order Butterworth filter using a cut-off frequency of 10Hz. An interval for each step was defined as the positive zero crossing preceding and the negative zero crossing following, a velocity which surpassed a threshold of 15% of the maximum step velocity. Each step onset was then determined as the first frame of the step interval with a velocity greater than or equal to $30^{\circ}s^{-1}$. Following the peak velocity of the individual step, step end-time was defined as the first frame at which velocity fell below $30^{\circ}s^{-1}$. Thereafter, individual step size, number of step, step frequency and step duration were determined from step onset to step end.

3.4 Statistical analysis

The statistical package SPSS (23.0) was used for all statistical procedures. Bland–Altman plots were used to describe the agreement between the two measurement techniques by constructing limits of agreement. These statistical limits were calculated using the mean and standard deviations (SD) of the differences between the Vicon and IMU data (Bland and Altman, 1999). Intraclass correlation coefficient (ICC) was used as an index of reliability to estimate the population variances based on the variability between the Vicon and IMU data. The ICC demonstrates a value from zero (which implies no agreement) to one (which implies perfect agreement). Furthermore, paired t-tests were used to compare

the means of all axial segment movement parameters and stepping parameters obtained using the two systems that included: reorientation onset of head, thorax and feet, head and thorax end-time, peak head yaw velocity, peak head-thorax angular separation, total step, turn duration, step frequency. All mean values are presented with SD unless stated otherwise. The Bonferroni correction was applied for the 12 t-tests, which resulted in a corrected alpha of $P<0.016$.

3.5 Results

An example of the raw angular displacement and velocity waveforms obtained during a turning trial in moderate speed and turned to the right is shown in Figure 3-2. The displacement and velocity time series of the head and the feet measured from the two systems closely resemble each other, but small differences are evident in the thorax plots. This observation is consistent for all trials under all speed conditions.

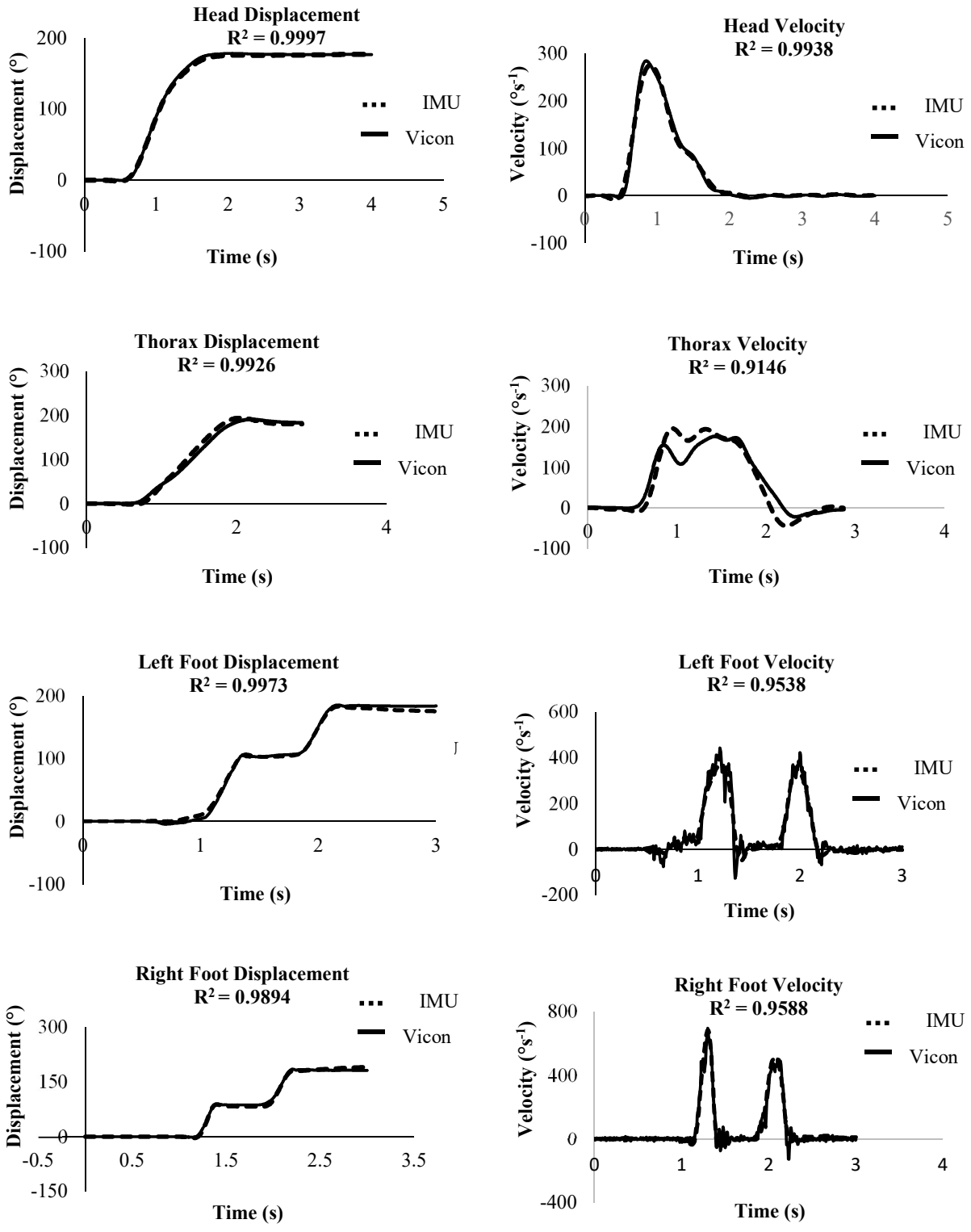


Figure 3-2: Examples of angular displacement and velocity collected during one trial. Solid lines represent data collected by Vicon motion system and dotted lines by IMUs sensors.

The similarity between the waveforms measured by the Vicon motion and IMUs during the experiment in all speed conditions is shown in Table 3-1 and Table 3-2.

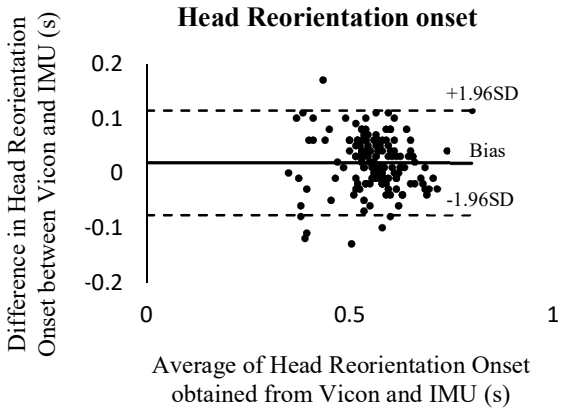
Table 3-1: Demonstrates the R^2, the gradient of graph (m) and the y intercept (c) of the regression best fit line comparing the displacement profiles of the two datasets.

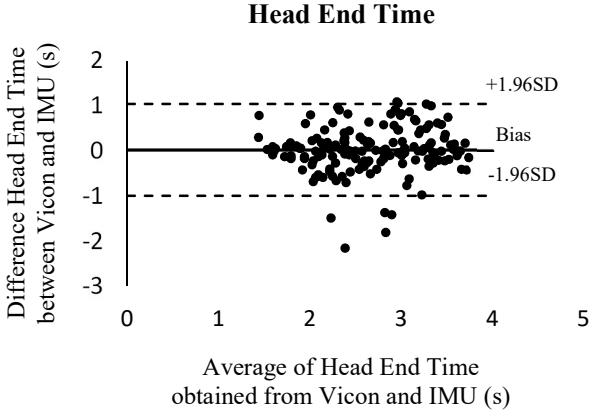
Segments	R^2 of the displacement	m of the equation of straight line of the displacement	c of the equation of straight line of the displacement
Head	0.999	1.021	-0.078
Thorax	0.983	0.978	3.009
Lt. Foot	0.997	0.924	0.509
Rt. Foot	0.992	0.954	1.226

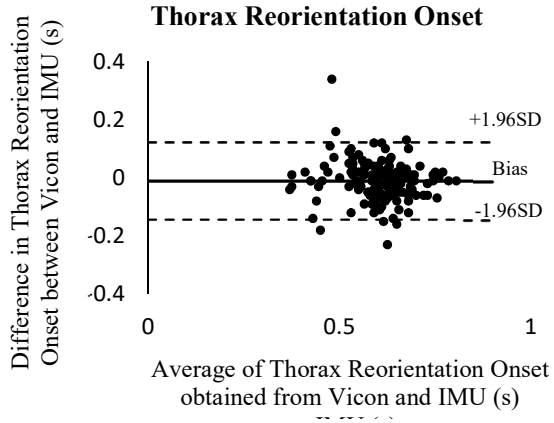
Table 3-2: Demonstrates the R^2, the gradient of graph (m) and the y intercept (c) of the regression best fit lines comparing the velocity profiles between two datasets.

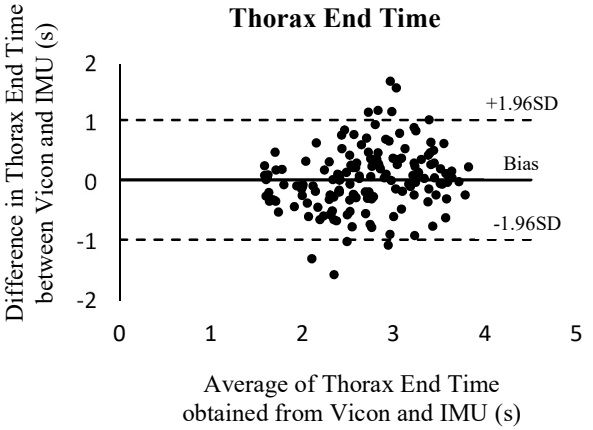
Segment	R^2 of the velocity	m of the equation of straight line of the velocity	c of the equation of straight line of the velocity
Head	0.968	1.018	0.0732
Thorax	0.777	0.685	15.589
Lt. Foot	0.884	0.848	1.473
Rt. Foot	0.856	0.805	3.010

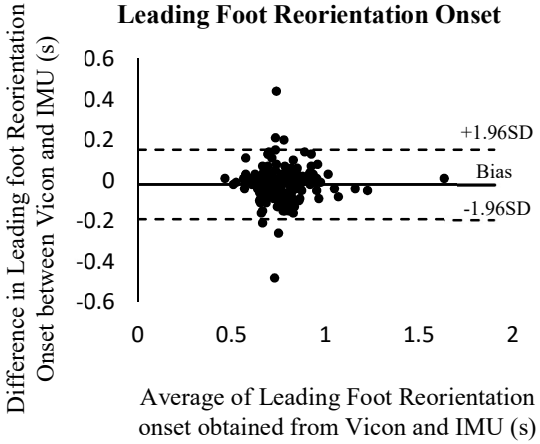
The Bland–Altman plots show the assumptions of normality of differences and the limits of agreement, which were calculated to be ± 1.96 times the SD of the differences between both the systems. The resulting graph in Figure 3-3 is a scatter plot XY graph in which the Y-axis shows the difference between the Vicon and IMU data while the X-axis represents the average of these measures. In other words, the difference between the measurements of the two data sets is plotted against the mean of the two measurements. Bland–Altman recommended that 95% of the data points should lie within ± 1.96 SD of the mean difference (Giavarina, 2015). In the results, all axial segment movement parameters show no heteroscedasticity.

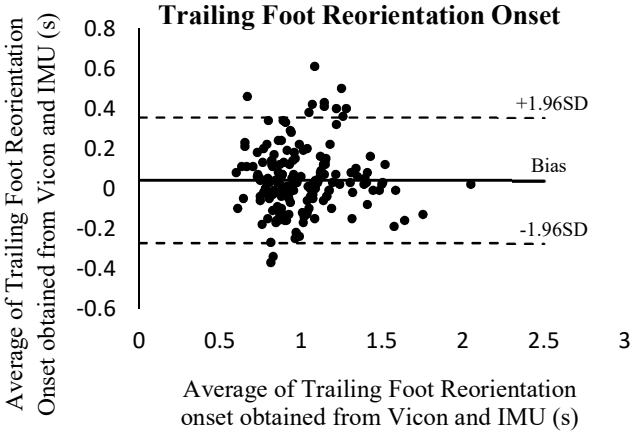

Head Reorientation onset
Difference in Head Reorientation Onset between Vicon and IMU (s)
+1.96SD
Bias
-1.96SD
Average of Head Reorientation Onset obtained from Vicon and IMU (s)


Head End Time
Difference Head End Time between Vicon and IMU (s)
+1.96SD
Bias
-1.96SD
Average of Head End Time obtained from Vicon and IMU (s)


Thorax Reorientation Onset
Difference in Thorax Reorientation Onset between Vicon and IMU (s)
+1.96SD
Bias
-1.96SD
Average of Thorax Reorientation Onset obtained from Vicon and IMU (s)


Thorax End Time
Difference in Thorax End Time between Vicon and IMU (s)
+1.96SD
Bias
-1.96SD
Average of Thorax End Time obtained from Vicon and IMU (s)


Leading Foot Reorientation Onset
Difference in Leading foot Reorientation Onset between Vicon and IMU (s)
+1.96SD
Bias
-1.96SD
Average of Leading Foot Reorientation onset obtained from Vicon and IMU (s)


Trailing Foot Reorientation Onset
Average of Trailing Foot Reorientation Onset obtained from Vicon and IMU (s)
+1.96SD
Bias
-1.96SD
Average of Trailing Foot Reorientation onset obtained from Vicon and IMU (s)

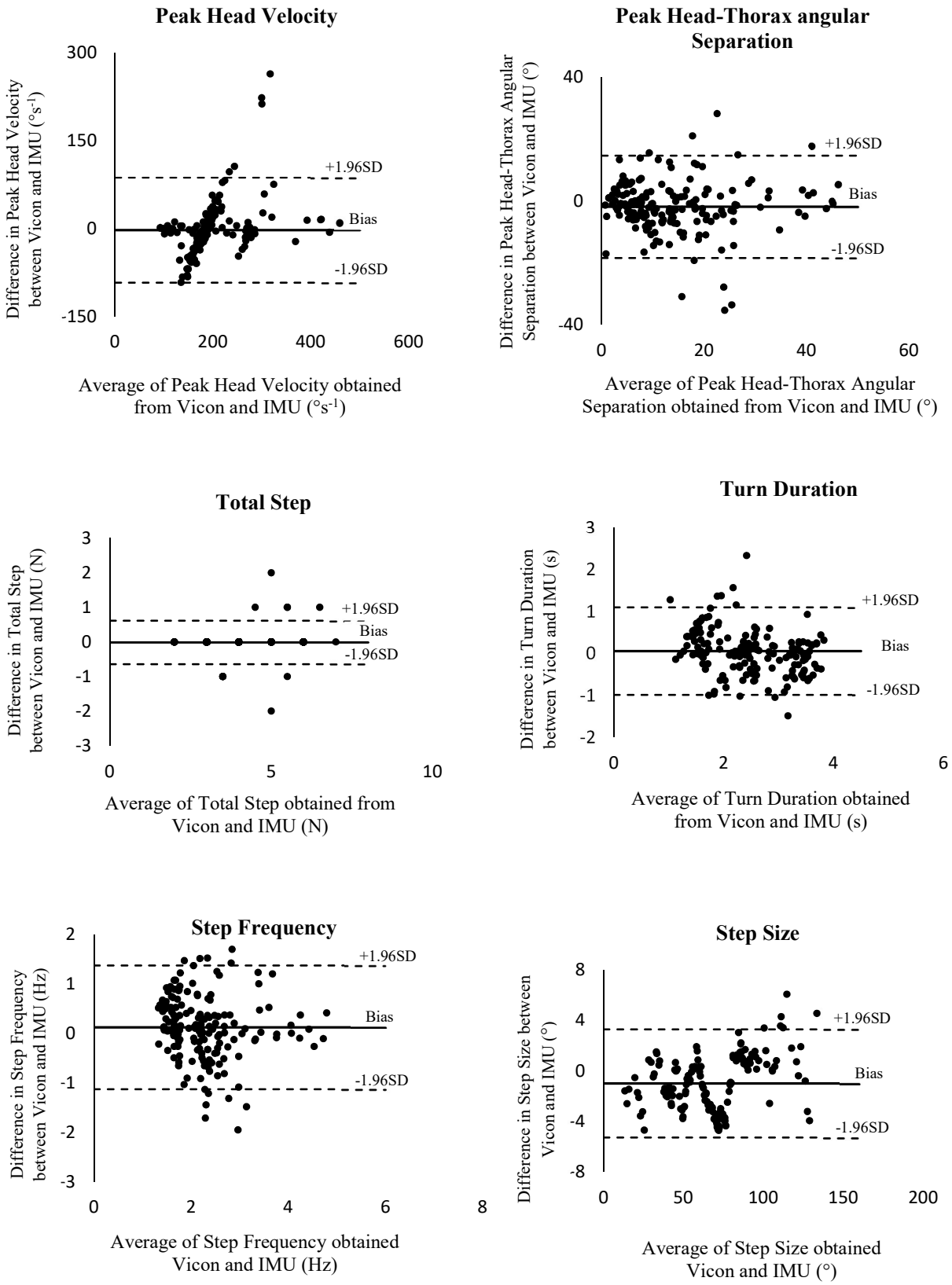


Figure 3-3: Bland–Altman plots for all variables. **Solid line** systematic bias (mean); *dash lines* limits of agreement.

Table 3-3 presents the variables for the two systems for averaged values across 180 trials of each variable. The levels of agreement between the two systems were excellent for all variables (ICC between 0.80 and 0.98). However, there were small but significant differences between the two systems in head reorientation onset (P<0.016).

Table 3-3: The validity of Vicon motion system and the Inertial Measurement Unit (IMU) for all variables.

Variables	**Vicon (mean ±SD)**	**IMU (mean ±SD)**	**$ICC_{(2,4)}$**	**95% CI**	***P-value***
Head reorientation onset (s)	0.56 ± 0.07	0.55 ± 0.08	0.87	0.80-0.92	0.01*
Thorax reorientation onset (s)	0.59 ± 0.08	0.60 ± 0.09	0.82	0.75-0.87	0.046
Leading foot reorientation onset (s)	0.77 ± 0.14	0.79 ± 0.14	0.89	0.85-0.92	0.030
Trailing foot reorientation onset (s)	1.03 ± 0.25	0.99 ± 0.25	0.88	0.83-0.91	0.047
Head end time (s)	2.68 ± 0.66	2.66 ± 0.62	0.80	0.73-0.86	0.579
Thorax end time (s)	2.71 ± 0.68	2.66 ± 0.57	0.80	0.72-0.85	0.240
Peak head Yaw velocity ($°s^{-1}$)	193.93 ± 76.54	197.13 ± 59.36	0.88	0.83-0.91	0.357
Peak head-thorax angular separation (°)	13.17 ± 11.02	15.05 ± 11.17	0.83	0.76-0.81	0.040
Total steps (N)	4.04 ± 1.02	4.05 ± 0.98	0.97	0.96-0.98	0.639
Turn duration (s)	2.55 ± 0.71	2.54 ± 0.88	0.88	0.83-0.91	0.151
Step frequency (Hz)	2.32 ± 0.74	2.20 ± 0.83	0.80	0.73-0.85	0.141
Step size (°)	68.93 ± 26.44	69.00 ± 25.72	0.88	0.901-0.96	0.888

*significantly different from the Vicon system

3.6 Discussion

The aim of this study was to validate the use of IMUs for measuring axial segmental coordination during turning in healthy participants by comparing collected data to data generated by a camera-based Vicon motion capture system. The IMUs produced accurate measurements of displacement and velocity profiles of the head and the feet as compared to the Vicon system, which was demonstrated by very high ICC values during all three speeds of turning.

The Bland–Altman plots in Figure 3-3 demonstrate that the limits of agreement are a narrow range of values for all axial segment movement parameters. In addition, there is a small range of variability around the mean constant of the parameters, including head, thorax and feet reorientation onset and end time, peak head-thorax angular separation, turn duration and step frequency. It may be concluded from the results of the Bland–Altman plots and the high levels of agreement (ICC between 0.80 and 0.98) in the 180 trials of standing turns that the two systems produce equivalent measurements of axial segment movement parameters (Bland and Altman, 1999; Hartmann *et al.*, 2009). However, there were small but significant differences between the two systems in some variables, such as head reorientation onset. Several factors may have contributed to these results. First, differently defined markers or position calculations between the two systems could explain the differences in displacement (Brennan *et al.*, 2011). For recordings using the Vicon system, reflection markers were placed on the body segments of the subject at anatomical landmarks consistent with the Plug-in-gait model. The 3D positions of these markers were recorded at 200Hz by an optical tracking system with ten cameras. Furthermore, The Plug-In-Gait model (Vicon®, 2002) was used to determine angular displacement of the head, thorax and right feet in the global reference frame. On

the other hand, we attached the IMU sensors directly to the head and thorax as well as the feet and collected data at a sampling rate of 260 Hz. Therefore, the difference between the data processing methodology of the two systems might have resulted in the differences in measures of displacement. Second, variation of the position of IMU sensors could explain the differences in measured axial movement parameters; for example, the limitation of places to attach the IMU sensors at the thorax region meant that the IMUs had to be placed in a vertical orientation. In contrast, we put IMUs in a horizontal position on the head and feet, corresponding to the original calibration axes. The attachment between the IMU and the axial body segment might not have been firm and resulted in the tilting of the IMU, thereby interfering with measurements of yaw Euler angles. In addition, the IMU positioned over the trunk might have been tilted due to postural alignment, lumbar lordosis of the subject and inaccuracy in the positioning of the instrument (Hartmann *et al.*, 2009). However, a previous study (Brennan *et al.*, 2011) has shown that the contribution is relatively small in comparison to the error caused by the anatomical frame discrepancy between the systems. The study quantified the accuracy of inertial sensors in 3D anatomical joint angle measurement with respect to an instrumented gimbal. The gimbal rotated about three axes and directly measured the angles in the knee joint coordinate system recommended by the International Society of Biomechanics. Through the use of sensor attachment devices physically fixed to the gimbal, the joint angle estimation error, which occurs due to the inaccuracy of the sensor attachment matrix, was essentially eliminated, leaving only error due to the inertial sensors. The angle estimation errors are smaller than those reported previously in human gait studies, which suggest that the sensor attachment is also a significant source of error in the inertial sensors measurement. As mentioned above, these factors can be perceived as limitations of the estimations of the data productivity of IMUs.

In summary, the aim of this study was to validate the use of IMUs to measure axial movement parameters during turning. Although the results demonstrated significant differences from Vicon system in some parameters, the differences were very small (less than a degree of angular displacement or a few milliseconds in timing of segment onset) and the results of ICC showed excellent agreement for all axial movement parameters. Therefore, we can conclude that IMUs are appropriate for studying the effects of intervention on turning behaviour. Indeed, the benefit of monitoring turning characteristics with small sensors that have low power requirements, such as IMUs, is that the clinician can determine axial segment behaviour, and effectiveness of rehabilitation outside of the laboratory. Therefore, IMU sensors should be incorporated into rehabilitation strategies to measure turning characteristics especially in PD patients, stroke patients and older adults.

Chapter 4

Effectiveness of exercise-based rehabilitation for the treatment of axial rigidity in individuals with Parkinson's disease: *A Scoping Review*

Abstract

Background: The benefits of physiotherapy for improving movement performance and quality of life in people with Parkinson's disease (PD) are well-established. However, the mechanism behind these improvements remains unclear. Understanding how physiotherapy treatments work will inform the design more effective, individually tailored and cost-efficient interventions. Axial rigidity is a common symptom of PD and is believed to contribute towards mobility problems including side lying to sitting, balancing, turning, walking and leads to an increased risk of falling. Furthermore, it is possible that the positive effects of physiotherapy on functional performance in PD patients might partially be due to reductions in axial rigidity. Therefore, a scoping review was conducted to determine whether there is sufficient high-quality evidence to investigate whether improvements in function due to exercise-based rehabilitation may be associated with reduced axial rigidity.

Methods and analysis: The following databases were searched systematically: Cochrane Library, Physiotherapy Evidence Database (PEDro), Scopus, Web of Science and PubMed. Articles comparing the effects of exercise-based treatment as an experimental intervention with a non-physiotherapy intervention as the control were described using the synthesis method**.**

Results: Four out of the eleven studies eligible for inclusion focussed explicitly on exercise-based treatment for axial rigidity in individuals with PD. Two studies hinted at the beneficial results of exercise in improving axial rigidity as evidenced by an improvement in the Unified Parkinson's Disease Rating Scale (UPDRS), axial rotation,

spinal flexibility and motion of the neck and trunk. Furthermore, three other studies provided evidence for improvement of functional problems related to axial rigidity.

Conclusion: This review evinces insufficient high-quality evidence to determine whether improvements in function due to exercise-based treatment are associated with reduced axial rigidity. Further research is required to explore the relationship between the benefits of exercise-based interventions on functional mobility and improvements in axial rigidity in people with PD.

4.1 Introduction

Parkinson's disease (PD) is a neurodegenerative movement disorder, which is most common among the elderly (Guttman, Kish and Furukawa, 2003). Dopaminergic medication is the first management strategy used to alleviate symptoms of PD, but it cannot eliminate the motor problems entirely and may lead to partial deterioration of movement functions and participation in activities of daily living (ADL) (Tomlinson *et al.*, 2012). Given the limitations of dopaminergic medication, physiotherapy is usually recommended for alleviating symptoms and coping with motor control problems (Tomlinson *et al.*, 2012; Ajimsha *et al.*, 2014). Physiotherapy has been proven to be beneficial for individuals with PD in terms of mobility and transfers, posture, upper limb function, strengthening, balance, gait and functional performance. This can be achieved by wide range of techniques including treadmill training, exercising, cueing strategies, cognitive movement strategies, dancing and martial arts to optimise the patient's independence, safety and well-being, thereby decreasing the risk of falling and enhancing quality of life (QOL) (Dibble *et al.*, 2006; Luessi *et al.*, 2012; Tomlinson *et al.*, 2014; Cheng *et al.*, 2016; Stozek *et al.*, 2016; Godi *et al.*, 2017; Spildooren *et al.*, 2017).

Previous research, as mentioned above, has reported that physiotherapy has positive effects, and there is an increasing amount of evidence to show that exercise alleviates the PD patients' motor symptoms (Fisher *et al.*, 2008; Schenkman *et al.*, 2012; Tomlinson *et al.*, 2012; Petzinger *et al.*, 2013; Tomlinson *et al.*, 2014). However, the mechanisms through which exercise may improve motor performance are unclear. Understanding how physiotherapy treatment works is important, as it will facilitate the designing of more effective and cost-efficient interventions. It might, especially, be useful in the case of reducing axial rigidity in this population.

The most visible symptom with respect to clinical manifestation of PD, is axial rigidity, which causes patients to experience difficulty while changing their movements (Schenkman *et al.*, 1998; Schaafsma *et al.*, 2003; Huxham *et al.*, 2008; Mazzoni, Shabbott and Cortés, 2012). Franzén et al. in 2009 reported that the tone of the neck and trunk muscles plays an essential role in controlling postural balance, mobility and coordination (Franzén *et al.*, 2009; Franzen *et al.*, 2012). Corresponding to this finding is the evidence that suggests that the loss of axial mobility might contribute to functional limitations, such as while moving from a supine to a sitting position or reaching and turning while standing, for individuals with PD (Schenkman *et al.*, 2001). Indeed, it has been suggested that axial rigidity is likely to contribute to the risk of falling among PD patients, as discussed above (Schenkman *et al.*, 1998; Schenkman *et al.*, 2001; Franzén *et al.*, 2009; Mazzoni, Shabbott and Cortés, 2012; Schenkman *et al.*, 2012; Stozek *et al.*, 2016).

It can be concluded from the results of the aforemtioned studies that it is possible that the positive effects of physiotherapy on functional performance in PD patients might be partially due to reduction in axial rigidity. However, a comprehensive review of physiotherapy intervention associated with axial rigidity in PD patients is needed to help

researchers better understand common approaches and guide the translation of research to clinical settings. A scoping approach offers feasible means of collecting and synthesising a wide range of evidence to achieve this, which is particularly useful for bringing together evidence from heterogeneous sources (Mitchell and Catanzaro, 1987; Schenkman *et al.*, 1998; Reuter *et al.*, 1999; Morris, 2000; Shumway-Cook and Woollacott, 2001; Fisher *et al.*, 2008; Hong and Earhart, 2008; Luessi *et al.*, 2012; Petzinger *et al.*, 2013; Tomlinson *et al.*, 2014). Therefore, this scoping review was conducted to determine whether there is sufficient high-quality evidence to investigate the current literature, as exercise-based rehabilitation might be associated with reducing axial rigidity in individuals with PD.

4.2 Materials and Methods

The objectives of this scoping review were to identify, understand, summarise and disseminate findings from a broad body of literature about the effects of exercise on reducing axial rigidity in individuals with PD. The protocol of this scoping review was based on the framework outlined by Arksey and O'Malley (Arksey and O'Malley, 2005). The methodology included five steps, which have been listed as follows: (1) identifying the research question, (2) identifying studies relevant to the research question, (3) selecting studies, (4) charting of information and data within the included studies and (5) collecting, summarising and reporting the results.

4.2.1 Step 1: Identifying the research question

The research question that guided this scoping review was "Is exercise-based rehabilitation effective for the treatment of axial rigidity in people with Parkinson's disease?" To formulate a structure for the research question, the PICOT method was

employed to address the search strategy design (Riva *et al.*, 2012). The population was "idiopathic PD stage 1 to 4 by Hoehn and Yahr staging scale" (Jankovic and Tolosa, 2007), as defined by study authors. For the intervention, "exercised-based rehabilitation" was defined as activity that is planned, structured, repetitive and purposive for improvement of axial rigidity problems, and the control group was defined as "usual care, education or medication only", i.e. not receiving any physiotherapy. The outcome was "rigidity outcomes", defined as those relating to rigidity including both clinical and laboratory outcomes, i.e. UPDRS rigidity items, flexibility, range of motion and functional axial movement tasks. The time frame adopted was "literature from 1970 to 2017".

4.2.2 Step 2: Identifying relevant studies

To ensure a comprehensive search of the literature, the following licensed databases were searched for peer-reviewed articles: Cochrane Central Register of Controlled Studies (CENTRAL) (*The Cochrane Library*; last searched November 2017), PubMed (1970 to November 2017), PEDro (1971 to November 2017), Scopus (last search November 2017), Web of Science (1991 to November 2017). Hand searching was included for more relevant citations to ensure conducting a comprehensive search.

In the next step, the keywords were identified based on the review of the relevant literature and ultimately the three authors' (FK, MH, KH) consensus. The keywords probed three main categories: (1) Parkinson's disease, (2) physiotherapy or intervention or exercise or rehabilitation or physical therapy and (3) rigidity or stiffness or rotation or flexibility or range of motion.

4.2.3 Step 3: Study selection and identification

After completing all database searches, the citations were compiled and entered into EndNote X7.7.1 bibliographic manager, where duplicate citations were removed. From the search results, two review authors (FK and MH) independently read the titles and screened the abstracts of potentially relevant studies. They eliminated obviously irrelevant studies, with the full paper being obtained if the abstract did not provide sufficient information to determine eligibility for inclusion in the review. Based on our inclusion criteria (participants, type of interventions, outcome and comparator), two review authors independently categorised these studies as "relevant", "irrelevant" or "possibly relevant". If there was any disagreement, it was resolved by referring to a third review author (KH). Furthermore, authors of potentially eligible studies were contacted for further information if the details of their study were unclear.

4.2.4 Step 4: Charting the information and data

Two review authors (FK and MH) independently assessed the eligible papers or abstracts for study details and outcome data. These were then validated through discussion, and any discrepancies were resolved by consensus. Study details were recorded on a standard study description form, which included the following: authors, year of publication, source of origin, aims, sample size, methodology, intervention type and comparator, concept, duration of the intervention and eligibility criteria. The outcome data that was extracted included data on UPDRS, especially Part III motor evaluation, including rigidity items, axial range of motion, flexibility outcomes, functional reach test, functional axial rotation test and turning and gait characteristics related to axial movement performance. Additionally, authors of any eligible unpublished studies were contacted to ask if further details and data for their study could be provided.

4.2.5 Step 5: Collating, summarising and reporting

Following data extraction, a narrative synthesis was conducted to describe the articles. Overall, an exercise-based rehabilitation focussing on reducing axial rigidity, met the criteria that was used to identify, summarise and disseminate the research findings (e.g. exercise programmes, type of exercise and duration of exercise).

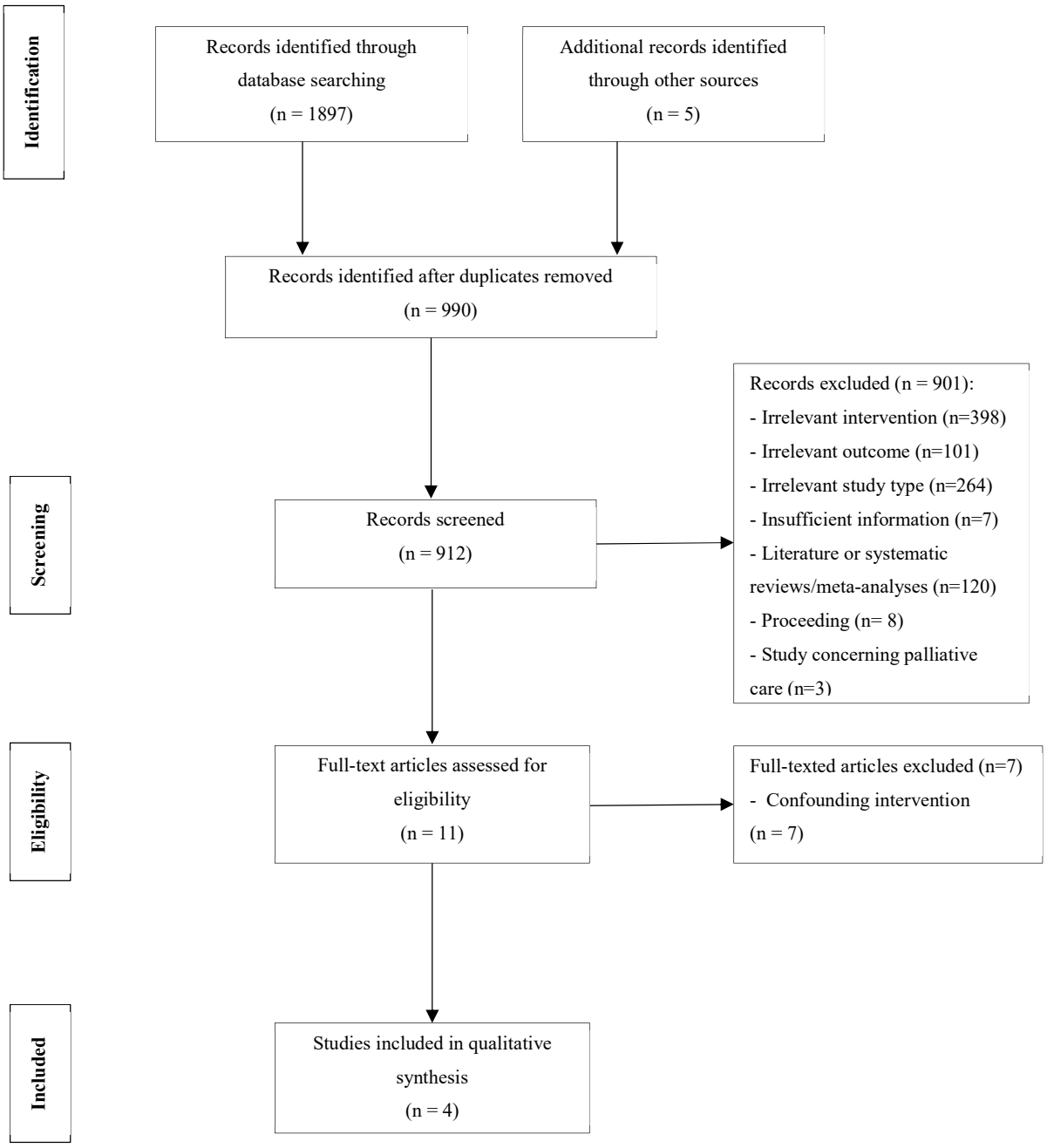


Figure 4-1: Study PRISMA flow diagram for the scoping process

4.3 Results

A total of 1902 results were retrieved from all sources. Duplicates were then removed (n = 990), yielding 912 records for eligibility screening. Following this, the abstracts of each study were screened, resulting in the exclusion of 896 papers. Eleven articles were read in full and assessed for eligibility, and an additional seven were excluded from this scoping review as the participants had received confounding intervention and been involved in a multidisciplinary intervention. Therefore, only four studies were available for inclusion in this review (see Figure 4-1).

4.3.1 Study design

Four papers published between 1998 and 2016 were included in the scoping review (see Table 4-1 for a summary). Out of these four, two papers described randomised controlled trials (RCTs) (Schenkman *et al.*, 1998; Ni, Mooney and Signorile, 2016) and the other two described studies with a parallel group design (Bartolo *et al.*, 2010; Ni, Mooney and Signorile, 2016; Stozek *et al.*, 2016). These studies were conducted in the United States (n = 2), Italy (n = 1) and Poland (n = 1).

Three studies involved participants who were diagnosed with PD by a neurologist. Two of these studies targeted participants with mild to moderate PD (Hoehn and Yahr 1.5-3), and only one study included participants with severe PD (Hoehn and Yahr 4).

The number of participants in each of the four papers ranged from 27 to 61 (17–29 men, 10–32 women), and their age ranged from 55 to 85. The Hoehn & Yahr stage ranged from 1.5 to 4. The duration of the interventions ranged from 4 weeks to 12 weeks.

4.3.2 Type of intervention

Schenkman et al. (1998) compared the effects of an axial mobility exercise programme with a control group who received usual care. They studied 51 participants (Schenkman *et al.*, 1998), and the study design was a randomised controlled trial. The treatment sessions were conducted over a period of 10 weeks, and there were 30 sessions. The exercise programme was based on the concept that improved muscle length and coordination can be achieved when people are taught to move in a relaxed manner, with the appropriation of the muscle group.

Bartolo et al. (2010) compared the effects of a rehabilitation programme with a control group who received medication (Bartolo *et al.*, 2010). They studied 22 participants and used a parallel group design. The treatment sessions consisted of individual 90-minute daily sessions and were conducted over a period of four weeks. The rehabilitation programme included cardiovascular warm-up activities (10 minutes), stretching exercises (15 minutes), strengthening exercises in a functional context (15 minutes), overground gait training (20 minutes), balance training (15 minutes) and relaxation exercises (15 minutes).

Stozek et al. (2016) studied 61 participants (Stozek *et al.*, 2016). The study employed a parallel group design, and the participants were randomly allocated into two groups – the rehabilitation or control with usual care. The treatment sessions lasted for four weeks and consisted of 28 therapy sessions. Each session lasted for two hours with breaks and was held twice per day during the first two weeks. During the two consecutive weeks, the sessions were conducted thrice a week, with one session per day. The intervention was conducted with small groups of patients with the rehabilitation programme focussing on improving balance, postural stability, walking and performance of ADL. It consisted of

relaxation exercises, respiratory (breathing) exercises, range of motion and stretching exercises, exercises of trunk rotation in various body positions, mobility exercises and functional training, postural re-education, balance exercises, gait training, music and elements of dance, speech therapy and exercises of facial expression as well as education.

Ni et al. (2016) compared the effects of power yoga exercises with a control group with usual care. The study involved 26 participants and employed a parallel group design. The treatment sessions were an hour per session and were held over 12 weeks, twice per week. The specially designed power yoga program (YOGA) involved yoga practice using the Vinyasa style, which incorporates vigorous, fitness-based positions. Power yoga was designed to improve movement speed, muscle strength and power specific to PD-related decrements. Furthermore, strength, power, flexibility and balance were addressed by stabilising body extremities and strengthening core muscles through the YOGA intervention.

Table 4-1. Description of included articles.

Author (year)	Study location	Population Studied	Interventions
Schenkman et al. (1998) (Schenkman *et al.*, 1998)	Duke University Medical Center, Durham, North Carolina, USA	- 23 participants in the exercise group and 23 in the control group - Participants' mean age was 70.6 years (exercise) and 71.2 years (control) - % of females 21.7 (exercise) and 31.4 (control) - Hoehn and Yahr stage 2-3	- Exercise: The standardised programme includes a series of exercises divided into seven graduated stages. The exercises begin in the supine position and progress to standing. - Duration of exercise: 10 weeks. - Control: usual care.

Bartolo et al. (2010) (Bartolo *et al.*, 2010)	The ‘‘C. Mondino Institute of Neurology’’, University of Pavia, Italy	- 22 participants in the exercise group and 22 in the control group - Participants’ mean age was 71.9 years (exercise) and 72.2 years (control) - Male/female 12/10 (exercise) and 12/10 (control) - Hoehn and Yahr stage 1/2/3/4: 7/8/7/0 (exercise) and 8/7/7/0 (control)	- Exercise each session included cardiovascular warm-up activities (10 minutes), stretching exercises (15 minutes), strengthening exercises in a functional context (15 minutes), overground gait training (20 minutes), balance training (15 minutes), and relaxation exercises (15 minutes) - Duration of exercise: 4 weeks. - Control: matched with the patients in the study group for age, disease duration and disease severity were usual care.

Stozek et al. (2016) (Stozek *et al.*, 2016)	- The Movement Disorder Clinic, Department of Neurology, University Hospital in Cracow, Poland. - Department of Clinical Rehabilitation, University School of Physical Education, Cracow, Poland	- 30 participants in the exercise group and 31 in the control group. - Participants' mean age was 64 years (exercise) and 67 years (control) - Male/female 13/17 (exercise) and 16/15 (control) - Hoehn and Yahr stage 2.3 (exercise) and 2.3 (control)	- The exercise programme consisted of relaxation exercises, respiratory (breathing) exercises, range of motion and stretching exercises, exercises of trunk rotation in various body positions, mobility exercises and functional training, postural re-education, balance exercises, gait training, music and elements of dance, speech therapy and exercises of facial expression as well as education. - Duration of exercise: 4 weeks. - Control: usual care

Ni et al. (2016) (Ni, Mooney and Signorile, 2016)	Laboratory of Neuromuscular Research and Active Aging, University of Miami, USA	- 15 participants in the power yoga programme group (YOGA) and 12 in the control group - Participants' mean age was 71 years (YOGA) and 75 years (control) - Male/female 11/4 (YOGA) and 6/6 (control) - Hoehn and Yahr stage 2.2 (YOGA) and 2.1 (control)	- The power yoga programme (YOGA) was a specially designed for PD to improve movement speed, muscle strength and power. - Duration of exercise: 12 weeks. - Control: usual care with education.

4.3.3 Effects of intervention on outcomes

From the description of the objectives, outcome and intervention in Tables 4-1 and 4-2, it can be seen that all studies described the type of exercise, exercise programmes, duration of exercise and session of exercise used. The categories presented below are those of the effectiveness of exercise intervention on the relevant outcomes. It should be noted that the focus is on reducing axial rigidity that might be associated with improving functional mobility, as per the inclusion and exclusion criteria provided by exercise-based rehabilitation.

The study by Schenkman et al. (1998) (Schenkman *et al.*, 1998) measured the primary outcomes (functional axial rotation (FAR), functional reach (FR) and supine to stand), secondary analysis outcomes (range of motion and spine configuration) and physical performance (stand to supine position, 360-degree turns with and without step, 6-minute walk and 10-metre walk) as part of an exercise programme in the early and mid-stages of PD. The results demonstrated that only FAR and FR in outcome variables were significantly different when the exercise group was compared with a control group (P=0.39). In addition, three of the physical performance measures improved significantly for the 45 subjects ($P \leq 0.05$). To provide more detail, the time to complete a 360-degree turn without a step decreased by almost one second (P=0.036) with a reduction of one step to complete the turn *(*P=0.010), and the time required to complete supine to standing position decreased significantly (P=0.033) when the exercise group and the control group were compared at the end of 10 weeks.

Bartolo et al. (2010) (Bartolo *et al.*, 2010) assessed trunk range of motion during two movement tasks – trunk flexion and lateral bending – which was calculated from the upright standing posture. Trunk posture and motion were evaluated using motion

analysis. The variables were characterised by the degree of trunk flexion, inclination and rotation. The results showed that, in the upright condition, the exercise group and the control group showed a combination of forward flexion, inclination and rotation of the trunk. There was a significant difference in trunk flexion (P<0.01) and trunk inclination (P<0.01) between the exercise group and the control group at the end of the study.

Stozek et al. (2016) (Stozek *et al.*, 2016) investigated the balance (pastor test and tandem test), gait (10-metre walk and 360 degree turn), motor functions (e.g. standing up from sitting, standing up from lying position, lying down on mat, supine to side lying, and supine to prone) and the range of spinal rotation in the lumbar and thoracolumbar. After four weeks, the results showed a significant difference in balance (P=0.001), gait assessment, both 10-metre walk (P=0.001) and 360-degree turn (P=0.003), and motor performance of all activities (P=0.001) between the rehabilitation group and the control group. In addition, there was also a significant difference between the two groups in terms of spinal rotation in the lumbar and thoracolumbar (P=0.001).

Ni et al. (2016) (Ni, Mooney and Signorile, 2016) evaluated the outcomes of bradykinesia, rigidity, muscle strength and power, and quality of life through the Parkinson's Disease Questionnaire (PDQ-39). The results showed that the yoga group produced a significant 2.6 point decrease in rigidity score and a large effect size compared to the control group (g = -0.64, P= 0.001). Additionally, the yoga group showed better scores in PDQ-39 in the mobility domain and sum scores for the post-test compared to the pre-test, and significant differences were also seen in mobility (g = −0.82, P=0.025), ADL (g = −0.46, P=0.035) and the sum score (g = −0.70, p = 0.016) between the yoga and control group after training.

Table 4-2. Articles addressing intervention needs and evidence of their intervention.

Author (year)	Study Objective	Outcome measures	Main findings
Schenkman et al. (1998) (Schenkman *et al.*, 1998)	To improve spinal flexibility and the physical performance of individuals with PD, particularly those in the early and mid-stage of the disease.	- Primary outcomes included FAR, FR and supine position to and from standing. - Outcome measures used in the exploratory analyses were cervical range of motion, lumber range of motion, spine configuration, extremity range of motion, turning while standing, six-minute walk and ten-metre walk.	The exercises learned in each stage were continued throughout the programme, with progressively higher-level activities being added. Improvements in axial mobility and physical performance can be achieved with a 10-week exercise programme for individuals in the early and mid-stage of PD.

Bartolo et al. (2010) (Bartolo *et al.*, 2010)	To analyse quantitatively changes in trunk posture and motion recorded after a trunk-specific rehabilitation treatment of a sample of individuals with PD.	- Clinical evaluation: UPDRS motor items and Hoehn and Yahr stage. - Motion analysis was conducted using a 6-camera optoelectronic system (ELITE, BTS Engineering, Milan, Italy) to measure kinematic of the trunk in two conditions 1) flexion, inclination and rotation values in the erect standing posture; 2) ranges of trunk flexion and inclination during trunk movements.	Identification of PD affected by lateral trunk flexion is important for both therapeutic and prognostic purposes. An intensive 4-week rehabilitation programme, specifically, can significantly improve trunk flexibility and mobility clinical status.

Stozek et al. (2016) (Stozek *et al.*, 2016)	To assess the effects of a rehabilitation program on balance, gait, motor performance and trunk rotation in individuals with PD.	- Balance test: Tandem stance and Pastor test - Gait assessment with turning - Physical performance test - Spinal axial rotation was measured with a tape measure, following to the Pavelka method.	The four-week rehabilitation training was focussed on various exercises that improve balance, postural stability, walking and performance of ADL mobility, balance and gait exercises. The positive effects supported that PD patients need rehabilitation.
Ni et al. (2016) (Ni, Mooney and Signorile, 2016)	To evaluate the effects of a specially designed power yoga program (YOGA) on bradykinesia, rigidity, muscular performance and quality of life in older individuals with PD.	- UPDRS motor score - One repetition maximums (1RM) - Peak powers on biceps curl, chest press, leg press, hip abduction and seated calf -Parkinson's disease questionnaire (PDQ-39).	Three months of a specially designed power yoga programme was able to reduce bradykinesia and rigidity, increase muscle strength and power and improve self-reported quality of life in PD patients.

4.4 Discussion

The purpose of this scoping review was to identify exercise-based interventions that have been used to reduce axial rigidity in individuals with PD as well as to summarise the findings. In accordance with the aims of this scoping review, the inclusion and exclusion criteria were deliberately very broad (Arksey and O'Malley, 2005). This discussion compares the findings from various types of exercise and their outcomes. Additionally, limitations as well as implications for the development of exercise-based interventions or rehabilitation to reduce axial rigidity in PD patients are discussed.

A substantial number of randomised and non-randomised controlled trials of exercise-based rehabilitation to reduce axial rigidity in individuals with PD have been published. However, only four articles met the inclusion criteria for this review. Most studies involved participants with mild to moderate PD, and only one study involved participants with severe PD. Axial rigidity is a common problem in PD patients; thus, including these types of participants can help determine the effectiveness of exercise on this population. Most studies included outcomes that either directly measured rigidity or were based on clinicians' reports on rigidity or physical performance parameters (such as UPDRS, especially rigidity items, flexibility outcome, range of motion, balance, gait outcomes, turning outcomes and QOL outcomes). The exercise group in only one study showed improvement in UPDRS for the rigidity item (Ni, Mooney and Signorile, 2016). An improvement in flexibility was shown in two out of four studies (Schenkman *et al.*, 1998; Stozek *et al.*, 2016), and an increase in range of motion was highlighted by two out of four studies (Schenkman *et al.*, 1998; Bartolo *et al.*, 2010). Three out of four studies show the effects of interventions on improving the general functions or physical performance

of PD patients e.g. gait pattern, mobility and reducing the risk of falls (Schenkman *et al.*, 1998; Ni, Mooney and Signorile, 2016; Stozek *et al.*, 2016).

Typically, individuals with PD have problems with axial rigidity and revert to more primitive movement patterns, which lack many of the automatic postural adjustments and whole-body coordination characteristics that accompany simple activities, such as supine to standing, getting up from sitting or turning over in bed (Morris, 2000; Shumway-Cook and Woollacott, 2001). To deal with this problem, individuals with PD are systematically taught strategies of physical performance during each stage of the exercise programme, which focusses on improving impairment and mobility. Repetitive practice of these preferred strategies, with structured commands, were used to enhance incorporation of these strategies into daily activities to overcome motor planning deficits associated with PD (Schenkman *et al.*, 1998; Morris, 2000; Shumway-Cook and Woollacott, 2001). Furthermore, the interventions were targeted at maximising functional exercise, improving gait patterns, maintaining or increasing independent mobility and reducing the risk of falls.

Of the four studies that were selected for this scoping review, the study by Schenkman et al. (Schenkman *et al.*, 1998) discovered that four weeks of flexibility, balance and functional exercises were most beneficial in improving overall functional abilities. This exercise programme was designed to improve spinal flexibility, coordinated movement as well as balance and function despite rigidity, bradykinesia and motor planning deficits in PD patients. Furthermore, the second study by Ni et al. showed that if a 12-week controlled study of yoga is applied twice per week, it can significantly reduce rigidity and bradykinesia scores in UPDRS (Ni, Mooney and Signorile, 2016). Yoga exercises have been found to improve health-related QOL in individuals by improving gait function and

diminishing the fear of falling. It has also been suggested that a long-term yoga programme may affect psychological sections and cognitive impairment; however, this needs further investigation. Stozek et al. (Stozek *et al.*, 2016) found that a rehabilitation programme, focussing on mobility, balance and gait, can improve motor functions in terms of analysed balance and gait parameters. It can also improve a range of trunk rotations in individuals with PD. However, this study did not address the mechanism of this programme. However, from the previous study, it can be assumed that this specific training focusses on problems that PD patients face when learning movements but, under repeated movement training, individuals with PD can memorise their movements and, hence, eradicate these problems (Shumway-Cook and Woollacott, 2001). Finally, the study by Bartolo et al. (Bartolo *et al.*, 2010) aimed to reduce rigidity and improve flexibility and mobility of the trunk. Their main finding indicates that a four-week specific rehabilitation treatment can lead to significant improvements in both axial posture and trunk mobility, and these changes are associated with a reduction in UPDRS motor score, indicating an improvement in clinical status. Unfortunately, this study did not evaluate the functional mobility associated with the main findings. This could again be attributed to the lack of evidence, as the review included a limited number of studies. Thus, the nature and reporting of studies are likely to provide challenges for therapists aiming to implement interventions into clinical practice. One problem is the general lack of terms of rigidity variable in the systematic review which conducted by Timlinson et al. (2012). The authors aimed to examine the effectiveness of 'different types of physiotherapy' to improve functional ability for individuals with PD and compare with individuals with PD with 'no intervention' whereas our scoping review is focused only on exercise to reduce axial rigidity and improve turning ability. Twenty-nine studies were identified for systematic review. These included 14 studies on exercise for PD patients to improve gait outcomes, functional mobility, and balance outcomes, collect data on falls, clinician-rated

impairment, and disability measures and QOL outcomes (Tomlinson *et al.*, 2012). The first observation made from this study is that the authors identified more studies than our scoping review, as they included patients undergoing active treatment as well as all physiotherapy treatment techniques, and the second observation is that they included all outcomes. The last observation from the same study is that none of the reviewed studies included interventions to improve axial rigidity or address rigidity problems associated with functional mobility in individuals with PD. Thus, it is clear that there is little evidence to support the effectiveness of exercise to reduce axial rigidity.

The strength of this scoping review is that it provides initial steps of investigation of improvements in functional ability may be associated with reduced axial rigidity. Prudence is necessary when recommending exercise interventions to reduce axial rigidity in individuals with PD, as the mechanism through which these improvements can be achieved remains unclear. Thus, it is necessary to provide some foundational information to develop a novel, evidence-based exercise-based intervention for axial rigidity in individuals with PD.

4.5 Knowlegde gaps and future recommendations

There is still a need for well-designed, large-scale studies to evaluate the benefits of exercise or interventions for reducing axial rigidity. The summary of the advantages and disadvantages of each study identified through this scoping review is as follows:

Author	Advantage	Disadvantage
Schenkman et al. (1998)	The programme directly improved axial mobility and functional ability	- Long-term intervention - No measure of falls and UPDRS at the end of the intervention - Made clinical assessment only
Bartolo et al. (2010)	- General exercises - Using motion analysis	- Focus only trunk movement - No clinical measurement relevant to turning and falls
Stozek et al. (2016)	- Various exercises	- Exercise training under therapist in all sessions
Ni et al. (2016)	- Yoga programme can reduce axial rigidity and bradykinesia	- No functional outcome measurement

Therefore, further research is needed to develop exercise intervention to ameliorate the axial postural rigidity in the neck, trunk, and pelvis that would lead to enhancement in whole-body coordination. Further, the effects of treatment need to be monitored by kinematic measurements during the completion of functional movement. Such monitoring is important because of the potential importance of the resultant data in clinical and research settings. For this purpose, the exercise programme that was selected to be analysed in this study was adapted from Schenkman et al. (1998). The exercise programme by this author that was based on the concept that muscle length and

coordination can be achieved when participants are taught to move in a relaxed manner, with the participation of appropriate muscle groups. Additionally, this work demonstrated that the programme is based on eight principles. First, the design of this programme enhances the participation of the appropriate synergistic muscles. Second, slow movements and gentle diaphragmatic breathing relaxation are used to promote the range of motion but do not force stretching. Third, the axial structures are emphasised for relaxation and mobility. Fourth, isolated efficient movement of the axial structure can be learned in supported positions. Fifth, the exercises become increasingly complex by increasing the number of segments and decreasing the amount of support. Sixth, each stage of the exercise programme builds on previous stages to enhance relaxation and retain an optimal range of motion in all segments. Seventh, functional training is incorporated with each stage so that participants learn to incorporate the movement strategies into normal daily activities. Last, participants learn to perform the exercises independently so that they can continue them as part of their daily routine once the formal training sessions are completed (Schenkman *et al.*, 1998). Thus, it is likely that the modified programme of Schenkman et al. (1998) can be reduced axial rigidity and improve functions in individuals with PD.

In addition, recommendation for future researches are needed to determine which combinations of exercises (e.g. axial mobility, general flexibility and strengthening, sensory cueing, cardiovascular conditioning and behavioural modification) are most effective in combination with pharmacological interventions for restoring or preserving functional ability across a spectrum of required activities for individuals in the early and midstages of PD. Quantitative measurement of outcomes can be considered a useful tool for formulating an accurate functional prognosis, establishing specific rehabilitation objectives and monitoring improvements of motor impairments and the effects of

pharmacological and rehabilitation interventions in PD patients. The benefits of exercise are most likely to depend on continued participation in the exercise regimen long after formal training has been completed. Investigations are needed to determine the characteristics of individuals who are most likely to consistently engage in the exercise programme and to assess the long-term outcome for those who do so.

4.6 Conclusion

The findings of this scoping review indicate that there is insufficient high-quality evidence to determine whether improvements in function due to exercise-based rehabilitation are associated with reduced axial rigidity in individuals with PD. This advocates the need for high-quality research to determine which exercise or physiotherapy intervention may be beneficial to this population and help guide physiotherapists on how to deliver this.

Chapter 5

Effects of a modified exercise programme for improving axial rigidity and turning dysfunction in individuals with Parkinson's disease

Abstract

Background and aim: Axial rigidity is a common symptom of Parkinson's disease (PD) which contributes to mobility problems and leads to increased risk of falls. Axial deficits negatively affect the ability to turn resulting in altered segment co-ordination and timing. Previous studies have shown that pharmacological treatment of rigidity in PD patients is ineffective in improving coordination problems during turning. Therefore, alternative rehabilitation approaches are needed. Specific design of multi-modal treatment strategies in rehabilitation, focusing on the axial deficits, might improve turning performance in this population (Hulbert *et al.*, 2015). This pilot randomised controlled trial (RCT) study investigated the effects of using a modified exercise programme on improving axial rigidity and turning dysfunction in individuals with PD.

Methodology*:* Twenty-two individuals with PD were randomly divided into two groups: exercise (EG) (n = 11) and control groups (CG) (n = 11). Both groups continued their earlier medical treatment and had stable medical status. Participants' severity levels and motor abilities were assessed using the Modified Hoehn and Yahr scale and the Unified Parkinson's Disease-Rating Scale (UPDRS). Turning kinematics were recorded using Inertial Measurement Units (IMUs) while participants performed a 180° standing turn on level ground. Eye movements were measured using a BlueGain electrooculography system. Clinical outcomes were assessed by the Functional Reach Test Scale (FRT), Fall Efficacy Scale International (FES-I), and Borg**'**s Ratings of Perceived Exertion Scale **(**REP**)**. An animation on a video screen was played immediately before each trial to show

the direction that participants should turn. Trial order was randomised for each participant. Ten trials were recorded in total.

The exercise programme targeting improvement in symptoms of axial rigidity in individuals with PD was identified from a scoping review (Schenkman *et al.*, 1998). The exercise programme included: correct posture, stretching, deep breathing, rotation of axial segments training in supine, side lying, prone lying, sitting, and standing positions, balance training and task-specific of turning training. The participants in the exercise group received individual training from the physiotherapist in nine- sessions spread over four weeks. The intensity of the exercises was chosen by the physiotherapist investigator. For the first two weeks, participants were scheduled to exercise three times per week. During week three, the participants exercised twice per week and then exercised once per week during the last week of training. When the exercise group did not partake in the exercise programme, they performed and recorded their daily exercise programme at home during the four-week period, in a diary. The participants in the control group received only medication and were asked to record their daily activities in a diary during the four-week period. Mixed analysis of variance (ANOVA) was used to compare the variables between and within groups.

Results: There were no significant differences between the EG and CG in the baseline comparisons of any variables. The EG had a significant after training reduction in total UPDRS score, UPDRS motor score, UPDRS rigidity score, FES-I, onset latency of body segments, total number of steps and step duration. Following training, the EG group also showed significantly increases in turn speed, FRT and step size.

Conclusion: The modified exercise programme utilised in the present study had positive effects on clinical outcomes and improved turning performance in individuals with PD.

These preliminary results support the notion that targeting axial deficits might be an effective rehabilitation approach for improving mobility and reducing falls in PD.

5.1 Introduction

Parkinson's disease (PD) is a neurodegenerative movement disorder that commonly affects the elderly (Guttman, Kish and Furukawa, 2003). PD is caused by the loss of dopamine (DA) due to the degeneration of substantia nigra pars compacta (SNpc) dopaminergic neurons, which leads to functional changes in the nucleus of the basal ganglia and in the nucleus of the brainstem. The clinical diagnosis of PD includes detecting symptoms such as bradykinesia, rigidity, resting tremor and postural instability (Jankovic and Tolosa, 2007). PD results in a decline in movement function, which limits mobility and activities of daily of living (ADL), thereby increasing the incidence of falls and, consequently, leading to disability and decrease in quality of life (QOL) (Jankovic and Tolosa, 2007).

Axial deficits are characterised by segmental rigidity resulting in reduced segment rotation and altered segment co-ordination and timing. Axial rigidity is controlled by different neuronal circuits than those that control appendicular rigidity and abnormally elevated axial rigidity contributes to many mobility problems, including difficulty in terms of side-lying to sitting, maintaining balance and walking. High axial rigidity also affects the ability to turn, which limits ADL and may increase the risk of falling (Schenkman *et al.*, 1998; Schaafsma *et al.*, 2003; Huxham *et al.*, 2008; Mazzoni, Shabbott and Cortés, 2012). Studies on healthy individuals have shown that, during turning, the eyes are first moved in the direction of the turn, followed by the head, trunk, pelvis and the feet (Hollands, Ziavra and Bronstein, 2004; Anastasopoulos *et al.*, 2011). Individuals

with PD turn a lot more slowly than healthy adults and exhibit differences in terms of the amplitude and timing of eye movements (Stack, Ashburn and Jupp, 2006; Chou and Lee, 2013). They also tend to move all segments of their body together rather than in a top-down sequence and exhibit a shuffling walking style, which involves taking small but frequent steps while turning (Lohnes and Earhart, 2011; Ashburn *et al.*, 2014). Individuals with PD are also less stable when they turn, which puts them at a greater risk of falling (Stack, Ashburn and Jupp, 2006).

Currently, the management of PD symptoms are aimed at recovering functional status, thus improving both clinical disability and quality of life (QOL) (Pacchetti *et al.*, 2000). Dopaminergic medication is the first strategy that is used to alleviate PD symptoms, but evidence has suggested that pharmacological treatment of rigidity in PD patients appears to be less effective at improving coordination problems during axial body movements than the inclusion of rehabilitation as an adjuvant intervention to pharmacological and neurosurgical treatments (Cano-de-la-Cuerda *et al.*, 2011; Tomlinson *et al.*, 2012). To cope with the problem of rigidity, exercise physiotherapy has shown promise and has been recommended for neuro-rehabilitation of PD patients (Schenkman *et al.*, 1998; Schenkman *et al.*, 2012; Tomlinson *et al.*, 2012; Ajimsha *et al.*, 2014; Shujaat, Soomro and Khan, 2014; Ni, Mooney and Signorile, 2016). However, there is a general lack of evidence in terms of the effects of exercise or physiotherapy on rigidity in systematic reviews (2). Timlinson et al. (2013) conducted a systematic review of 29 studies, examining the effectiveness of physiotherapy, which included 14 studies on exercise for PD patients to improve gait outcomes, functional mobility and balance outcomes, provision data on falls, clinician-rated impairment and disability measures and QOL outcomes (Tomlinson *et al.*, 2012). None of the reviewed studies included interventions to improve axial rigidity or address rigidity problems associated with functional mobility

in individuals with PD. To address the gap in the literature, we conducted a scoping review to determine the effects of exercise-based rehabilitation to reduce axial rigidity and improve functional performance in individuals with PD (Khobkhun *et al.*, 2018b). We found that four out of eleven studies eligible for inclusion focused explicitly on exercise-based treatments for axial rigidity in PD patients. Two studies found the beneficial results of exercise in improving axial rigidity as evidenced by: improvement in the Unified Parkinson's Disease Rating Scale (UPDRS), axial rotation range, spinal flexibility and motion of the neck and trunk. Three further studies provided evidence for improvement of functional problems related to axial rigidity. We concluded that further research is required to explore the relationship between the benefits of exercise-based interventions on functional mobility and improvements in axial rigidity in individuals with PD.

The present study was designed to determine the effects of a 4-week modified exercise programme on axial rigidity and turning dysfunction in individuals with PD at the stages of 1.5 to 3 as assessed by the modified Hoehn and Yahr scale. Previous studies have reported that these early stages of PD commonly lead to axial rigidity and affect the spinal range of motion of PD patient (Schenkman *et al.*, 1998). Thus, giving rehabilitation to individuals with PD at the stages of 1.5 to 3 could yield better results (Schenkman *et al.*, 2001; Vaugoyeau *et al.*, 2003). Furthermore, the exercise programme in this study was modified from an axial mobility programme designed by Schenkman et al. (1998) (Schenkman *et al.*, 1998). They used this intervention programme for rehabilitation over 10 weeks in community-dwelling older individuals with early- and mid-stage PD and demonstrated significant differences in functional axial rotation, functional reach and steps during 360-degree turns in the PD group compared to the usual care. Therefore, the present study modified the programme by selecting specific elements of exercises that

focus on improving axial rigidity and turning dysfunction for individuals with early and mid-stage PD; the contents of the exercise programme were then approved by PD experts (FK, PS and SK). We applied an auditory cue in this programme and investigated the effects of exercise on axial rigidity and turning 180 degrees using standard devices such as the initial measurement unit (IMUs) and electrooculography (EOG) to measure kinematic and eye movement, respectively. Finally, we also measured the clinical outcomes associated with axial rigidity and falls in order to evaluate the improvements made in the programme, as suggested by a previous study (Schenkman *et al.*, 1998).

5.2 Methods

5.2.1 Participants

Participants included individuals who were diagnosed with idiopathic PD by a neurologist. They were recruited from the Movement Disorder Clinic, Division of Neurology, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand. The participants were randomly divided into two groups: the exercise group (EG) and control group (CG). All participants were asked to sign an informed consent form, which was approved by the Ethical Committee of Mahidol University Institutional Review Board, Mahidol University, Thailand (MU- CIRB 2017/ 181. 1210) . The Clinical Trial Registration Number was NCT03473834.

The inclusion criteria were: 1) clinically diagnosed with PD stages 1. 5 to 3 as assessed by the modified Hoehn and Yahr scale, 2) age between 50 and 75 years, 3) taking PD medication regularly for at least a month, 4) no signs of wearing-off phenomenon, 5) able

to walk independently without any assistive device and 6) able to follow commands and instructions.

The exclusion criteria were: 1) clinically diagnosed with dementia or other neurological or cardiopulmonary diseases, 2) musculoskeletal problems that could influence the test performance, 3) high blood pressure (more than 140/90 mmHg), 4) haemodialysis, and 5) visual problems that could not be corrected with lenses or glasses. Table 5- 1 demonstrates that no statistically significant differences were found between groups in terms of characteristics of the participants at the baseline assessment.

Table 5-1. Comparison of baseline characteristics of the participant of the exercise (EG) and control (CG) groups.

Variables	**EG (n=11)**	**CG (n=11)**	***P*-Value[a]**
	mean ± SD	**mean ± SD**	
Gender (male/female)	4/7	7/4	-
Age (years)	67.45 ± 5.26	65.73 ± 5.92	0.910
Hoehn and Yahr Scale	2.32 ± 0.46	2.32 ± 0.46	1.00
Body Mass Index (BMI) (kg/m^2)	23.32 ± 2.79	23.65 ± 4.68	0.114
PD onset (years)	6.24 ± 3.35	6.96 ± 3.81	0.640

5.2.2 Experimental procedures

The study was conducted at the College of Sports Science and Technology (CSST) and Postural Control and Balance Laboratory, Faculty of Physical Therapy, Mahidol University. Individuals with PD who met the inclusion and exclusion criteria were invited to participate in the study. All participants were rated for disease state using the Unified Parkinson's Disease Rating Scale (UPDRS). Turning kinematics and eye movement characteristics were assessed using Inertial Measurement Units (IMUs) and a Bluegain

wireless electrooculography system, respectively. Clinical abilities were assessed using: the Functional Reach Test Scale (FRT), Fall Efficacy Scale International (FES-I), and Borg's Ratings of Perceived Exertion Scale **(**REP**).** The participants in EG group were assessed for all parameters at 3 time points; 1) at the baseline (week 0), 2) intermediate (week 2) and 3) post- (week 4) training; whereas, the participants in CG group were assessed at only 2 time points; at the baseline (at week 0) and post- (at week 4) training.

5.2.2.1 Turning kinematic and stepping characteristics assessment

Turning kinematics and stepping characteristics were recorded while participants performed a turn on level ground through 180° in a standing position. As shown in Figure 5-1, the participants were instrumented with IMU devices on: the centre of the head, middle thorax, and the centre of left foot and right foot.

Figure 5-1: Position of IMUs attachment on body segments.

5.2.2.2 Eye movement assessments

Eye movements were measured using a BlueGain wireless electrooculography system (Cambridge Research System Ltd.) Two skin surface electrodes were placed on the outer canthi of the eyes and a reference electrode was placed on the centre of the forehead (Robins and Hollands, 2017).

Prior to each trial, an animated video was played to demonstrate the way we wanted the participants to turn, and they were asked to turn as fast as they comfortably could. The animation was immediately followed by a visual cue to initiate the turn as the same in chapter 2. A LabVIEW programme was used to control the visual cue and mark the time point within the EOG data capture software. Trials were recorded for turns to both the left and right (randomly presented), resulting in a total of 10 trials (Figure 5-2).

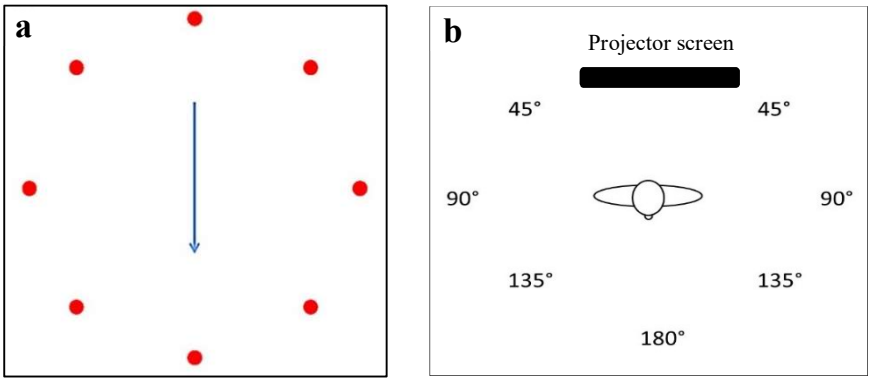


Figure 5-2: a) An animation on the video screen; **b**) participants completing standing turns on level ground through 180° and either to the left or right.

5.2.2.3 Clinical ability assessments

Clinical abilities were assessed using the Functional Reach Test Scale (FRT), Fall Efficacy Scale International (FES-I), and Borg's Ratings of Perceived Exertion Scale (REP).

FRT is a clinical measurement, which is usually used to detect postural and balance control in the standing position (Demura and Yamada, 2007). The equipment includes a scale measurement in inches, which was attached on a wall at the height of the acromion for each participant (Weiner *et al.*, 1992). To conduct measurements using FRT, the researcher explained the aim and experimental procedures of this measurement to participants. Secondly, participants were asked to stand with their dominant arm at 90 degrees of shoulder flexion. Following this, the participants were instructed to reach out as far forward as possible along the scale measurement without taking a step while the researcher recorded the value on the scale (Figure 5-3).

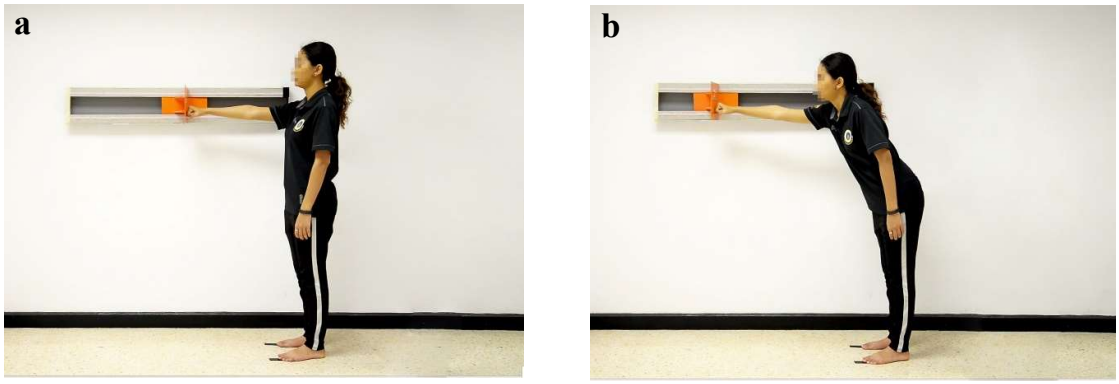


Figure 5-3: Functional reach test, (**a**) starting position and (**b**) terminal position.

Additionally, questionnaires that were included the FES-I and REP scale were used in this protocol. The FES-I is a questionnaire that assesses the fear of falling (Dewan and

MacDermid, 2014). This is a 16-item questionnaire which was developed by the Prevention of Falls Network Europe group (ProFaNE) to augment content covered by the original 10-item Fall Efficacy Scale (FES). However, the present study used the Thai FES-I for this assessment, which was translated from the original English FES-I and, as validated by Thiamwong, Ladda (2011), is reliable in terms of assessing fear of falling among Thai older adults (Thiamwong, 2011; Thiamwong and Suwanno, 2014). Participants were asked to rate the 16 items of the questionnaire on a four-point Likert scale depending on their concerns about the possibility of falling when performing 16 activities. The total score was 64; a higher score would indicate a greater fear of falling.

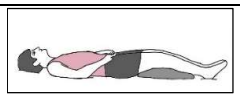
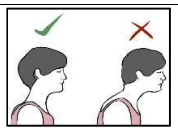
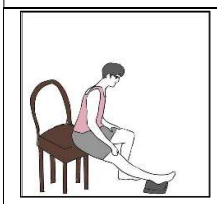
The RPE scale is widely utilised to monitor and quantify an individual's perception of effort during exercise; it is frequently used in clinical exercise testing. According to Penko et al. (2017), the RPE scale has become increasingly important because aerobic exercise is beneficial for individuals with mild to moderate PD (Penko *et al.*, 2017). The modified category-ratio scale (0 to 10 scale) allows participants to subjectively rate their level of exertion during exercise or exercise testing; a higher score indicates a greater effort.

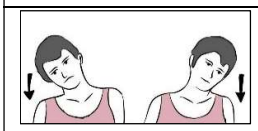
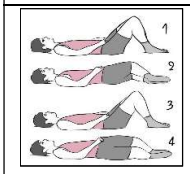
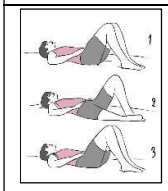
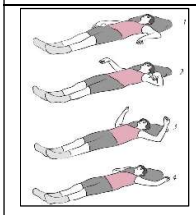
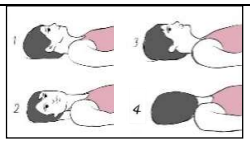
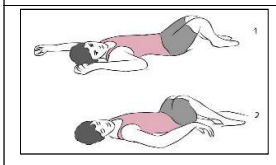
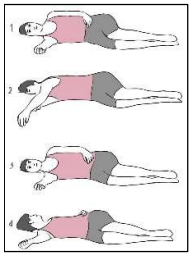
5.2.3 The modified exercise programme

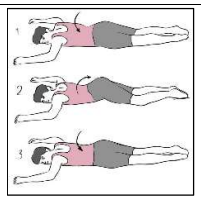
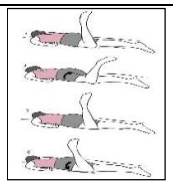
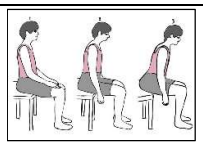
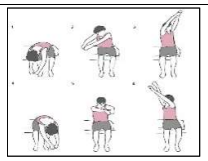
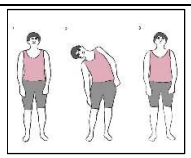
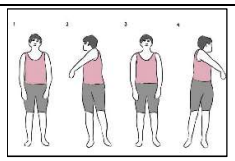
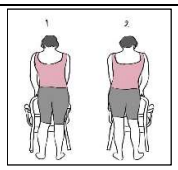
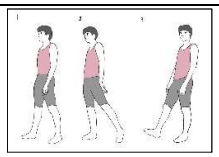
The modified exercise programme included the following exercises: deep breathing and correcting the posture, stretching, axial segments rotation training in supine, side lying, prone lying, sitting and standing positions, balance training and task-specific turning training (Table 5–2). For each aspect of the training, the participants performed exercises following the auditory cue of a metronome beat. Moreover, the difficulty level of the training was increased over the intervention. The participants were required to perform each of the abovementioned exercises to their maximum potential and receive the

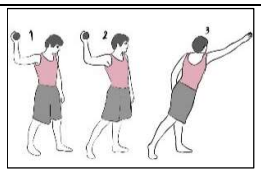
perceptual feedback with relaxation (i.e., how do you feel after exerting to your maximum potential?). The week before the participants were to participate in the programme, they, along with their caregivers, were asked to attend a workshop on the exercise programme wherein how they should go about the programme was explained to them. Following this, they were asked to repeat the exercises in a step-by-step manner. This process was repeated in the participants' homes as well. The EG received a modified programme for 15 sessions, comprising 9 sessions under supervision by a physiotherapist at the clinic and 6 unsupervised, at-home sessions within a 4-week period. When the participants were not attending the exercise programme, they recorded the daily exercises they performed at home for four weeks in a diary (Appendix 1). For the CG, they were instructed to continue medication with their routine activities throughout the course of the study. The researcher called participants once a week to check their compliance with the study protocol.

Table 5-2. Details a modified exercise program in one session.

Exercise form	**Purpose**	**Posture**	**Exercise content**
1. Deep breathing exercise and correcting posture (5 minutes)	To increase vital capacity and relaxation		Breathe slowly and deeply. Repeat three times, or until participant feel relaxed.
	To correct neck and trunk posture		
2. Stretching (15 minutes)	To relax and increase flexibility		Stretch each muscle group and hold for 20 - 30 seconds, with three repetitions
2.1. Hamstring stretching			

			per leg or until muscle relax.
2.2. Calf muscles stretching			
2.3. Neck muscles stretching			
3. Segmental rotation (45 minutes)	To increase flexibility and mobility of segmental body segment		Repeat ten times on each side.
3.1 Supine lying position 3.1.1. Double hip rotation			
3.1.2. Single hip rotation			
3.1.3. Shoulder rotation			
3.1.4. Neck rotation			
3.1.5. Combine movement in supine			
3.2 Side lying position - Reach and roll			Repeat ten times on each side

3.3 Prone lying position 3.3.1. Prone pelvic rotation			Repeat ten times on each side
3.3.2. Prone hip rotation			
3.4 Sitting position 3.4.1. Forward lean			Repeat ten times on each side.
3.4.2. Pelvic clock			
3.4.3. Trunk rotation			
3.4.4. Diagonal back extension			
3.5 Standing position 3.5.1. Side bends			Repeat ten times on each side.
3.5.2. Body twits			
3.5.3. Hip tilts			
3.5.4. Stand ‘rock’			

4. Recreational movements (5 minutes)	To increase balance and to challenge movement		Repeat ten times on each side.
5. Task specific turning training (10 minutes)	To increase balance and improve turning task		Repeat five to ten times on each side.
6. Deep breathing or stretching exercises until participant feel relaxed			

5.3 Data Processing

5.3.1 Kinematics analysis

IMU sensors were used to determine the angular displacement of the head, thorax and left and right feet in the global reference frame. At the beginning of the recording session, all IMU sensors and EOG recordings were triggered at the same time using the following procedure. The participants would sit on a chair with their eyes open and fixate on a target reference. Then, the chair would be rotated three or four times back and forth in both directions. The two data streams generated were synchronised using a clean eye signal and a clear sinusoidal of vestibulo-ocular-reflex (VOR) of a horizontal EOG trace that could be matched up to the IMU yaw angular displacement traces.

Kinematic data were passed through a dual fourth-order Butterworth low pass filter using a cut-off frequency of 6Hz. The MATLAB (R2017b) programming environment was used to analyse all measures from the kinematic datasets. To yield velocity and acceleration profiles for each segment, the displacement profiles were differentiated. The criteria used to determine the rotation onset for each segment as the earliest time point

preceding segment displacement of 5° was >0° with a velocity >0° s^{-1}. The end of rotation was determined as the first zero crossing in the velocity profile, following the end of the segment rotation.

As the time-course of the turn trials varied in duration, time-normalised profiles were created for the axial segments by using the onset and offset latencies from the head and thorax. For the normalisation procedure, the earliest onset latency (typically the head yaw onset latency) and the final axial offset latency were chosen. Normalisation was performed using a customised MATLAB function, which not only increased each time series to a length of 1000 data points (i.e., longer than all individual time series) but also interpolated the missing data points. It was chosen to perform normalisation in this way to facilitate comparing segments to each other over the course of all axial segment rotations. Using the normalised axial segment profiles, angular separation profiles were obtained from subtracting one profile from another, which resulted in head-thorax profiles.

Individual steps were analysed and step onsets were defined according to the following: 1) a positive zero-crossing preceding and 2) a negative zero crossing, following a velocity value that reached 15% of the maximum angular foot yaw velocity. Each step onset was then determined as the first frame of the step interval with a velocity greater than or equal to $30^{\circ}s^{-1}$. Following the peak velocity of the individual step, step end time was signified by the first frame being less than $30^{\circ}s^{-1}$. Thereafter, individual step size, placement amplitude, step velocity and step acceleration were determined from step onset to step end.

5.3.2 Electrooculography analysis

Before beginning data collection, EOG calibration was performed. The participant was required to fixate a point on a projector screen that was placed directly in front of them and make slow sinusoidal head movements in the yaw plane. Eye position and head position data were temporally aligned, and a portion of the data between a peak and a trough (in which the velocity of the eye and head were equal and opposite) was selected for calibration analysis. A linear regression model was used to determine the linear relationship (straight line equation) between EOG amplitude (measured in mV) to and head yaw rotation (°). Acustomised MATLAB (R2017b) was used to obtain all measures from the EOG dataset. All EOG data was filtered using a fourth- order Butterworth low pass filter with a 30Hz cut- off frequency. The eye displacement time series was differentiated to calculate angular velocity and acceleration profiles.

For fast phase determination, the EOG data was inspected alongside head onset and end times prior to analysis. To eliminate saccades and fixations that occurred before and after the turn, sections of data between the start and end of the turn were manually determined. From this selection of data, nystagmus fast phases were determined using time intervals that began with positive zero crossings and ended with negative zero crossings.

Time intervals were defined as nystagmus fast phases when the change in amplitude was ≥1.5° and the velocity was ≥30 $°s^{-1}$. Thereafter, the time of the positive zero crossing was deemed to be the onset, and the time of the negative crossing was determined as the end of the individual fast phase.

Eccentric eye positions at both the fast phase onset and end were determined, and all individual fast phase amplitudes, velocities and accelerations were obtained from the data between fast phase onset and fast phase end time.

5.4 Statistical analysis

The statistical package SPSS (24.0) was used for all statistical procedures. All data were reported as a mean ± SD. The mean change from each variable was calculated by change in scores or measures i.e. (week 4 – week 0 scores) between the baseline and post-assessments. Independent t-tests were performed to compare the means and differences of each dependent variable between the two groups.

Mixed analysis of variance (ANOVA) was used to compare the variables between groups and within groups (the baseline, intermediate and post-assessments in the EG group and the baseline and post-assessments in the CG group). The statistical significance was set at $P<0.05$. Bonferroni corrections were used for multiple comparisons.

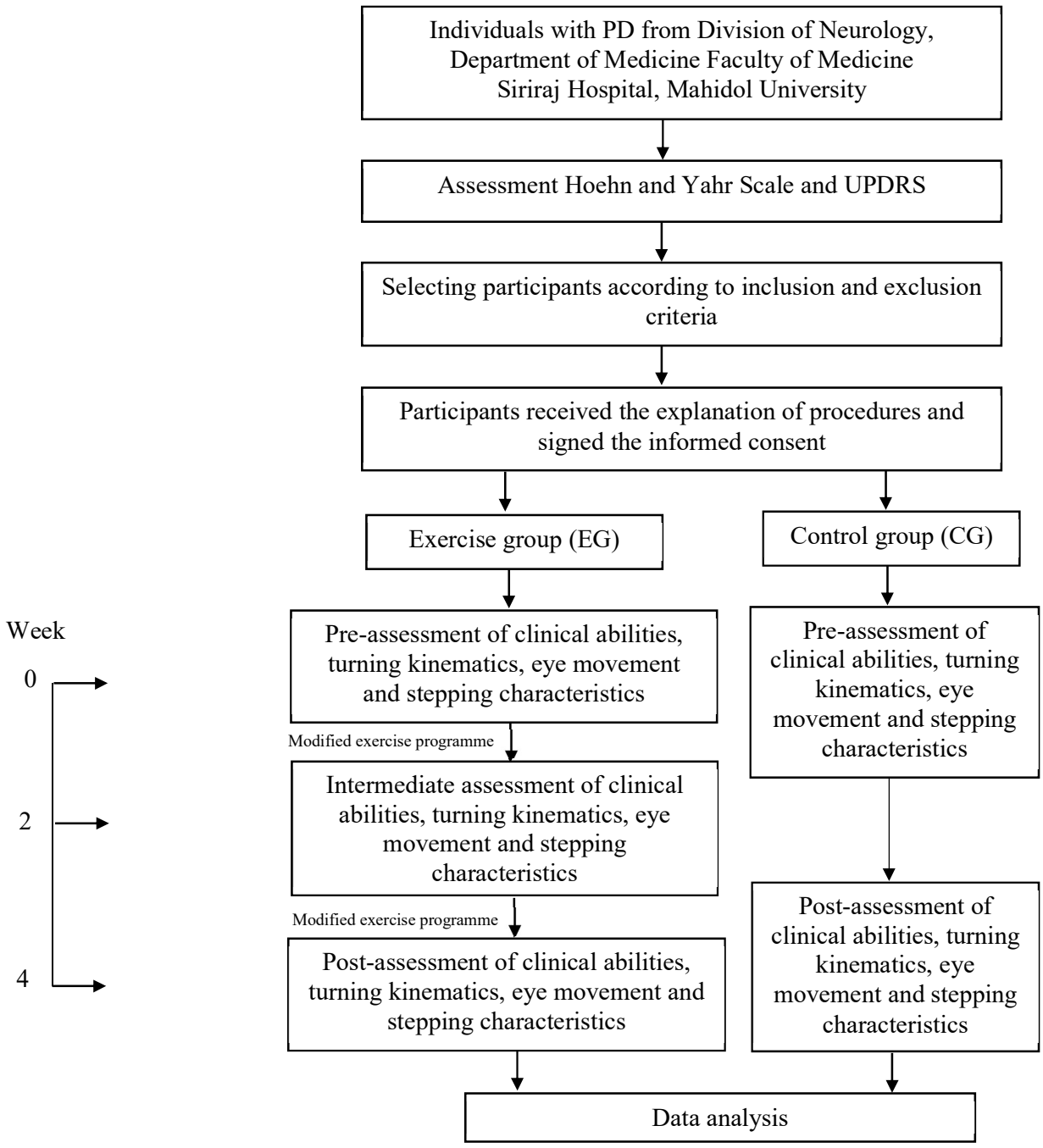


Figure 5-4: Flowchart of showing experimental protocol timeline.

5.5 Results

5.5.1 Clinical ability variables, turning kinematics, eye movements and stepping characteristics at the baseline assessment of the exercise (EG) and control (CG) groups

Table 5-3 demonstrates that no statistically significant differences were found between groups in terms of clinical ability variables, turning kinematics, eye movement and stepping characteristics of the participants at the baseline assessment.

Table 5-3. Mean differences between the exercise (EG) and control (CG) groups at the baseline assessment.

Variables	**EG (n=11)**	**CG (n=11)**	***P*-Value[a]**
	mean ± SD	**mean ± SD**	
Clinical ability variables			
UPDRS Total Score(score)	37.36 ± 7.34	37.64 ± 7.68	0.933
UPDRS Motor Score (score)	22.91 ± 4.87	21.00 ± 4.31	0.342
UPDRS Rigidity Score (score)	2.09 ± 0.70	1.73 ± 0.65	0.220
FRT (inch)	7.55 ± 1.73	7.34 ± 1.98	0.627
FES-I (score)	32.45 ± 7.13	31.09 ± 5.74	0.794
RPE (score)	4.36 ± 1.12	3.64 ± 0.81	0.096
Turning kinematics			
Head onset (s)	0.72 ± 0.13	0.61 ± 0.22	0.199
Thorax onset (s)	0.74 ± 0.15	0.73 ± 0.35	0.947
Eye onset (s)	0.79 ± 0.17	0.72 ± 0.21	0.453
Leading foot onset (s)	1.02 ± 0.22	0.91 ± 0.32	0.323
Trailing foot onset (s)	1.52 ± 0.22	1.42 ± 0.32	0.421
Peak head-thorax separation (º)	17.69 ± 6.75	20.02 ± 9.00	0.500
Turn speed ($^{o}s^{-1}$)	55.74 ± 17.39	54.24 ± 12.59	0.819

Eye movement characteristics			
First fast phase amplitude (º)	18.53 ± 9.22	17.62 ± 7.03	0.797
First fast phase velocity ($°s^{-1}$)	220.07 ± 60.61	239.49 ± 85	0.544
First fast phase acceleration ($°s^{-2}$)	22290.52 ± 10756.32	25912.38 ± 18660.26	0.583
Maximum fast phase amplitude (º)	27.10 ± 8.09	23.59 ± 7.54	0.305
Peak fast phase velocity ($°s^{-1}$)	323.10 ± 70.55	337.99 ± 125.14	0.735
Peak fast phase acceleration ($°s^{-2}$)	33666.83 ± 12327.01	42699.35 ± 29603.42	0.361
Number of fast phase (n)	7.65 ± 2.67	9.49 ± 3.76	0.203
Nystagmus fast phase frequency (n)	2.12 ± 0.30	2.33 ± 0.59	0.315
Stepping characteristics			
Total step (n)	6.51 ± 4.48	6.74 ± 3.19	0.892
Step duration (s)	3.62 ± 1.50	3.52 ± 0.95	0.846
Step Frequency (n)	1.82 ± 0.39	1.88 ± 0.43	0.727
Step size (º)	65.78 ± 18.96	61.55 ± 21.37	0.629

[a] = *P*-value from an independent t-test

5.5.2 Clinical ability variables, turning kinematics, eye movement and stepping characteristics at post- assessment of the exercise (EG) and control (CG) groups

Results of the experiment demonstrated differences between groups in terms of mean change from the baseline (Table 5-4). The differences between each variable of both groups demonstrated that the modified exercise programme used in this study had a significant impact ($P<0.05$) on the clinical ability by improving the UPDRS total score, UPDRS motor score, UPDRS rigidity score, FES-I and RPE, and FRT. There was a significant effect of training on turning kinematics characterised by a decrease in the head, eye and the feet onset latencies. There was also a significant effect of training on eye movement characteristics demonstrated as increased peak fast phase velocity and number of fast phase, and on stepping characteristics by increasing turn speed, step duration and step size at baseline assessment between the EG and CG groups.

Table 5-4. Mean differences between the exercise (EG) and control (CG) groups at post-assessment.

Variables	EG (n=11)	CG (n=11)	*P*-Value[a]
	Mean ± SD	Mean ± SD	
Clinical ability variables			
UPDRS Total Score	-5.91 ± 2.51*	1.27 ± 1.62	*P*<0.0001
UPDRS Motor Score	-3.91 ± 3.08*	0.55 ± 0.69	*P*<0.0001
UPDRS Rigidity Score	-0.91 ± 0.70*	0	*P*<0.0001
FRT (inch)	1.48 ± 1.31*	-0.98 ± 0.91	*P*<0.0001
FES-I (score)	-6.18 ± 4.56*	1.55 ± 2.54	*P*<0.0001
RPE (score)	-1.82 ± 1.08*	0.09 ± 0.54	*P*<0.0001
Turning kinematics			
Head onset (s)	-0.16 ± 0.15*	0.16 ± 0.23	0.001
Thorax onset (s)	-0.17 ± 0.16	0.03 ± 0.39	0.126
Eye onset (s)	-0.14 ± 0.19*	0.11 ± 0.21	0.009
Leading foot onset (s)	-0.21 ± 0.32*	0.15 ± 0.23	0.006
Trailing foot onset (s)	-0.26 ± 0.38*	0.18 ± 0.28	0.006
Peak head-thorax separation (º)	2.71 ± 7.38	-2.02 ± 4.06	0.077
Turn speed ($^{o}s^{-1}$)	11.23 ± 10.98*	-0.24 ± 10.81	0.023
Eye movement characteristics			
First fast phase amplitude (º)	5.46 ± 11.38	0.69 ± 5.04	0.219
First fast phase velocity ($°s^{-1}$)	-10.83 ± 52.71	9.01 ± 45.12	0.354
First fast phase acceleration ($°s^{-2}$)	-5186.33 ± 12791.59	2600.52 ± 7756.53	0.100
Maximum fast phase amplitude (º)	2.13 ± 9.58	0.96 ± 3.63	0.710
Peak fast phase velocity ($°s^{-1}$)	-39.63 ± 62.08	20.77 ± 37.68	0.110
Peak fast phase acceleration ($°s^{-2}$)	-7931.90 ± 15524.20	2417.58 ± 7146.52	0.058
Number of fast phase (n)	-1.93 ± 2.05*	0.08 ± 1.29	0.013
Nystagmus fast phase frequency (n)	-0.11 ± 0.40	-0.17 ± 0.39	0.725

Stepping characteristics			
Total step (n)	-1.65 ± 3.39	0.33 ± 1.43	0.090
Step duration (s)	-0.87 ± 1.23*	0.18 ± 0.55	0.018
Step Frequency (n)	0.09 ± 0.27	-0.01 ± 0.30	0.440
Step size **(º)**	7.99 ± 7.63*	-0.70 ± 5.32	0.006

* = significant differences from CG groups, $P<0.05$ from independent t-test.

5.5.3 Clinical ability variables, turning kinematics, eye movement and stepping characteristics at the baseline, intermediate and post- assessments of the exercise group

Significant differences ($P<0.05$) were found between the baseline, intermediate and post-assessments of the EG. The results showed that the UPDRS total score, UPDRS motor score, UPDRS rigidity score and head and thorax onset latency of the exercise group decreased significantly ($P<0.05$), whereas the FRT, FES-I, RPE and step size between the baseline and intermediate assessments increased significantly ($P<0.05$) (Table 5-5).

Table 5-5. Mean differences between intermediate assessment and post-assessments in exercise group (EG) compared to baseline.

Variables	**At intermediate**	**At post-**	***P*-Value[a]**
	Mean ± SD	**Mean ± SD**	
Clinical ability variables			
UPDRS Total Score*	-3.73 ± 2.65	-5.91 ± 2.51	P=0.007
UPDRS Motor Score*	-2.64 ± 2.38	-3.91 ± 3.08	P=0.121
UPDRS Rigidity Score*	-0.55 ± 0.52	-0.91 ± 0.70	P=0.114
Peak head-thorax separation **(º)**	-2.13 ± 6.63	2.71 ± 7.38	P=0.139
Turn speed ($^{o}s^{-1}$)*	1-1.72 ± 10.48	11.23 ± 10.98	P=1.000
FRT (inch)*	1.86 ± 1.85	1.48 ± 1.31	P=1.000
FES-I (score)	-4.73 ± 3.41	-6.18 ± 4.56	P=0.544

RPE (score)*	-1.55 ± 0.93	-1.82 ± 1.08	*P*=0.576
Turning kinematics			
Eye onset (s)	-0.14 ± 0.14	-0.14 ± 0.19	*P*=1.000
Head onset (s)*	-0.13± 0.15	-0.16 ± 0.15	*P*=0.583
Thorax onset (s)*	-0.11 ± 0.09	-0.17 ± 0.16	*P*=1.000
Leading foot onset (s)	-0.15 ± 0.32	-0.21 ± 0.32	*P*=0.540
Trailing foot onset (s)	-0.20 ± 0.34	-0.26 ± 0.38	*P*=0.954
Peak head-thorax separation (º)	-2.13 ± 6.63	2.71 ± 7.38	*P*=0.139
Turn speed ($^{o}s^{-1}$)*	11.72 ± 10.48	11.23 ± 10.98	*P*=1.000
Eye movement characteristics			
First fast phase amplitude (º)	3.43 ± 12.72	5.46 ± 11.38	*P*=0.656
First fast phase velocity ($°s^{-1}$)	-16.49 ± 65.54	-10.83 ± 52.71	*P*=1.000
First fast phase acceleration ($°s^{-2}$)	-6286.54 ± 9800.57	-5186.33 ± 12791.59	*P*=1.000
Maximum fast phase amplitude (º)	0.28 ± 10.16	2.13 ± 9.58	*P*=0.817
Peak fast phase velocity ($°s^{-1}$)	-37.31 ± 64.10	-39.63 ± 62.08	*P*=1.000
Peak fast phase acceleration ($°s^{-2}$)	-8044.59 ± 10829.86	-7931.90 ± 15524.20	*P*=1.000
Number of fast phase (n)	-1.72 ± 1.73	-1.93 ± 2.05	*P*=1.000
Nystagmus fast phase frequency (n)	-0.22 ± 0.32	-0.11 ± 0.40	*P*=1.000
Stepping characteristics			
Total step (n)	-1.26 ± 2.37	-1.65 ± 3.39	*P*=0.752
Step duration (s)	-0.82 ± 0.97	-0.87 ± 1.23	*P*=1.000
Step Frequency (n)	0.13 ± 0.20	0.09 ± 0.27	*P*=0.959
Step size (º)*	7.11 ± 5.43	7.99 ± 7.63	*P*=1.000

[a] = *P*-value from mixed ANOVA

* = significant differences between the baseline and intermediate assessments

5.5.4 Effects of a 4-week modified exercise programme on clinical abilities

With respect to UPDRS variables, significant differences ($P<0.0001$) were found in the mean change from the baseline at post-assessment in terms of UPDRS total scores, UPDRS motor scores and UPDRS rigidity scores between groups (Table 5-4).

Mixed ANOVA was applied to analyse the UPDRS variables. There was a significant group-time interaction for the UPDRS total score ($F_{(1, 20)} = 63.68$, $P<0.001$, $\eta_p^2 = 0.761$), UPDRS motor score ($F_{(1, 20)} = 21.91$, $P<0.001$, $\eta_p^2 = 0.532$) and UPDRS rigidity score ($F_{(1, 20)} = 18.52$, $P<0.001$, $\eta_p^2 = 0.481$) (Figure 5-5 (a-c)), demonstrating that the UPDRS variables decreased when compare the EG and the CG at post-assessment on completion of a 4-week training programme. Furthermore, there was a significant main effect of time assessment within the EG on UPDRS total scores ($F_{(2, 20)} = 35.77$, $P<0.001$, $\eta_p^2 = 0.570$), UPDRS motor scores ($F_{(2, 20)} = 14.29$, $P<0.001$, $\eta_p^2 = 0.348$), and UPDRS rigidity scores ($F_{(2, 20)} = 13.57$, $P<0.001$, $\eta_p^2 = 0.481$). Furthermore, post-hoc analysis revealed that there was a significant decrease ($P<0.05$) in UPDRS total scores among the baseline, intermediate and post-assessments, UPDRS motor scores between the baseline and intermediate assessments and the baseline and post-assessments, and UPDRS rigidity scores between the baseline and intermediate assessments and the baseline and post-assessments within the EG (Figure 5-5 (d-f)).

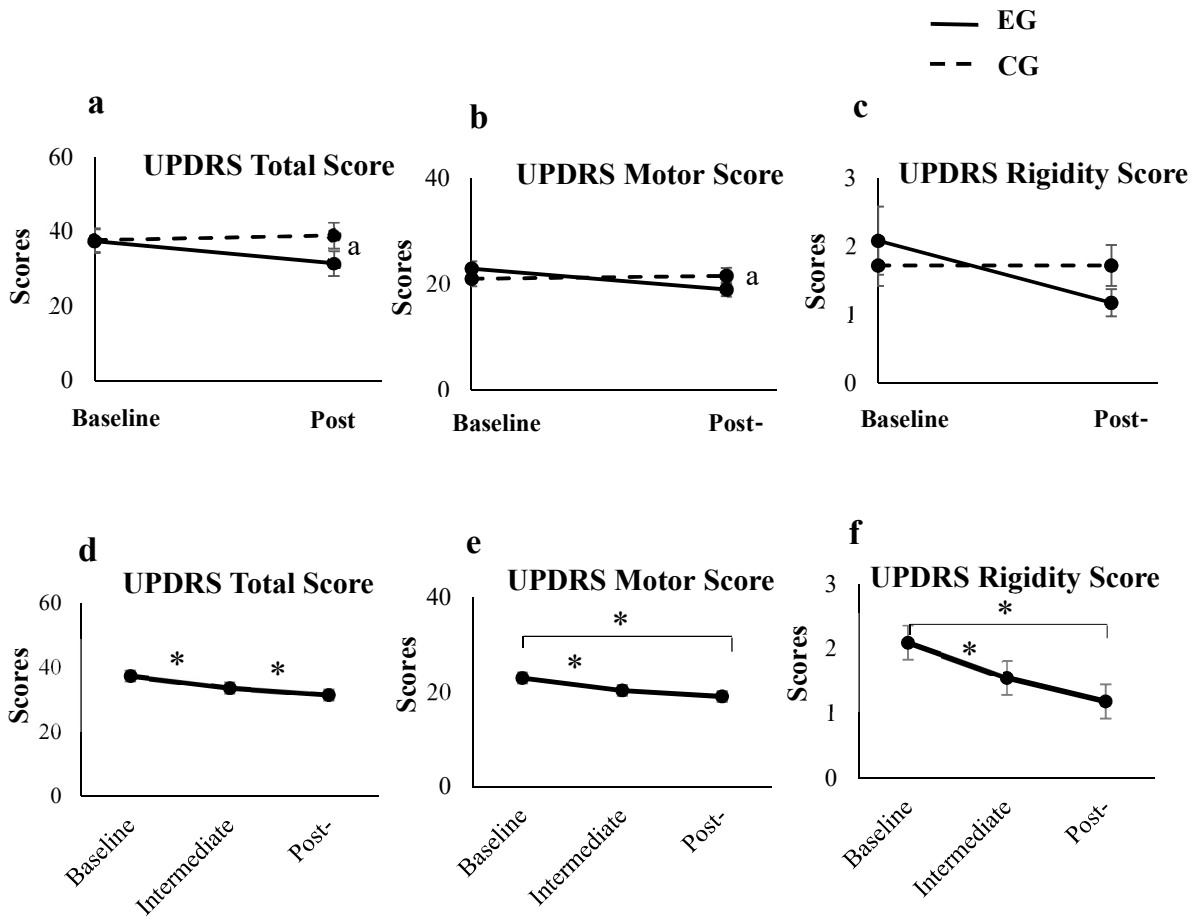


Figure 5-5: a-c Comparison of UPDRS variables of the EG and CG groups at the baseline and post-assessments and **d-f** within the exercise group (n=11 for each group).

[a] = significant differences from CG.

* = significant differences within the EG.

A significant group-time interaction was found for FRT ($F_{(1, 20)}$ = 26.19, P<0.001, η_p^2 = 0.567), FES-I ($F_{(1, 20)}$ = 24.12, P<0.001, η_p^2 = 0.547) and RPE ($F_{(1, 20)}$ = 26.16, P<0.001, η_p^2 = 0.567) (Figure 5-6 (a-c)) when compare the EG to the CG at post-assessment. Furthermore, mixed ANOVA found a significant main effect of time assessment within the EG on FRT ($F_{(2, 20)}$ = 9.30, P<0.001, η_p^2 = 0.053), FES-I ($F_{(2, 20)}$ = 15.79, P<0.001, η_p^2 = 0.303) and RPE ($F_{(2, 20)}$ = 25.85, P<0.001, η_p^2 = 0.615) (Figure 5-6 (a-c)). Post-hoc

tests revealed that there was a significant increase (P<0.05) in FRT between the baseline assessments and post-assessments (Figure 5-6a), whereas there was a significant decrease (P<0.05) in FES-I (Figure 5-6b) and RPE (Figure 5-6c) between the baseline and intermediate assessments and between the baseline and post-assessments.

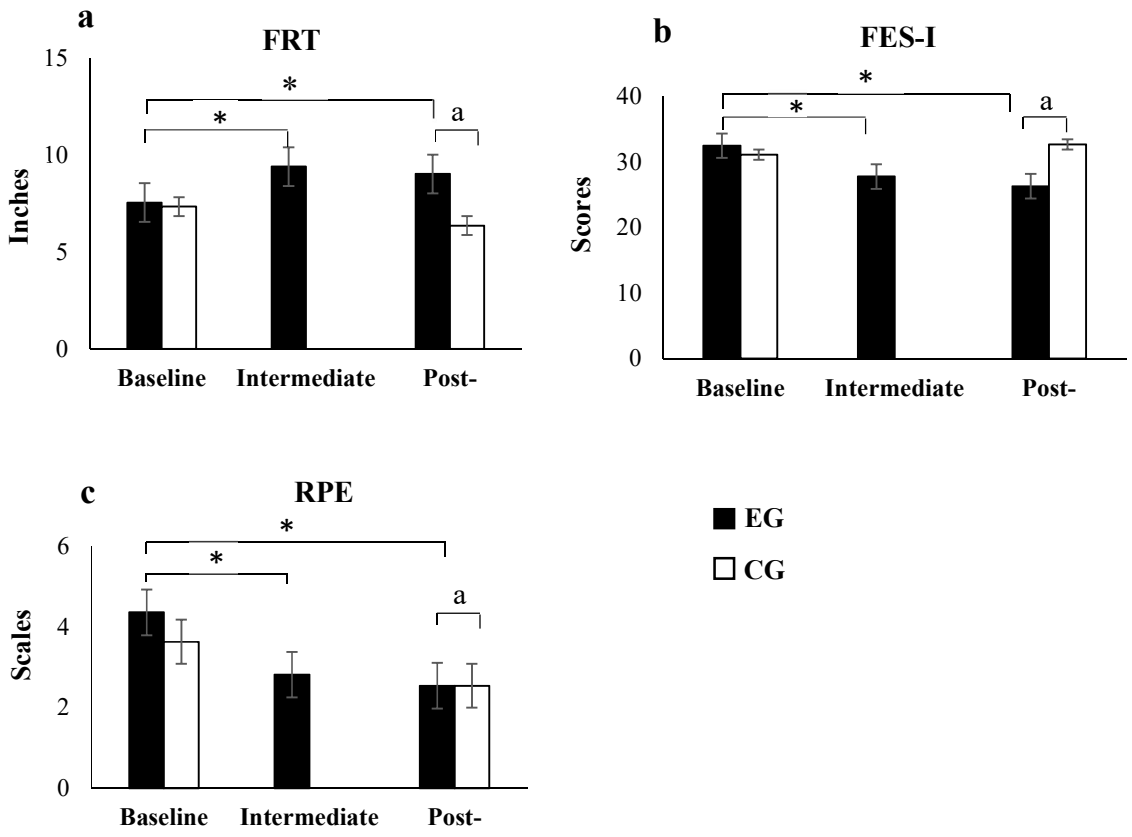


Figure 5-6: Comparison of **a)** FRT, **b)** FES-I and **c)** RPE at the baseline and post-assessments of the control groups and at the baseline, intermediate and post-assessments of the exercise groups (n=11 for each group).

[a] = significant differences from CG.

* = significant differences within the EG.

5.5.5 Effects of a 4-week the modified exercise programme on turning kinematics

5.5.5.1 Segment onset latency

The raw data traces of the EG between the baseline assessment **(a)** and post-assessment conditions **(b)** are shown in Figure 5-7.

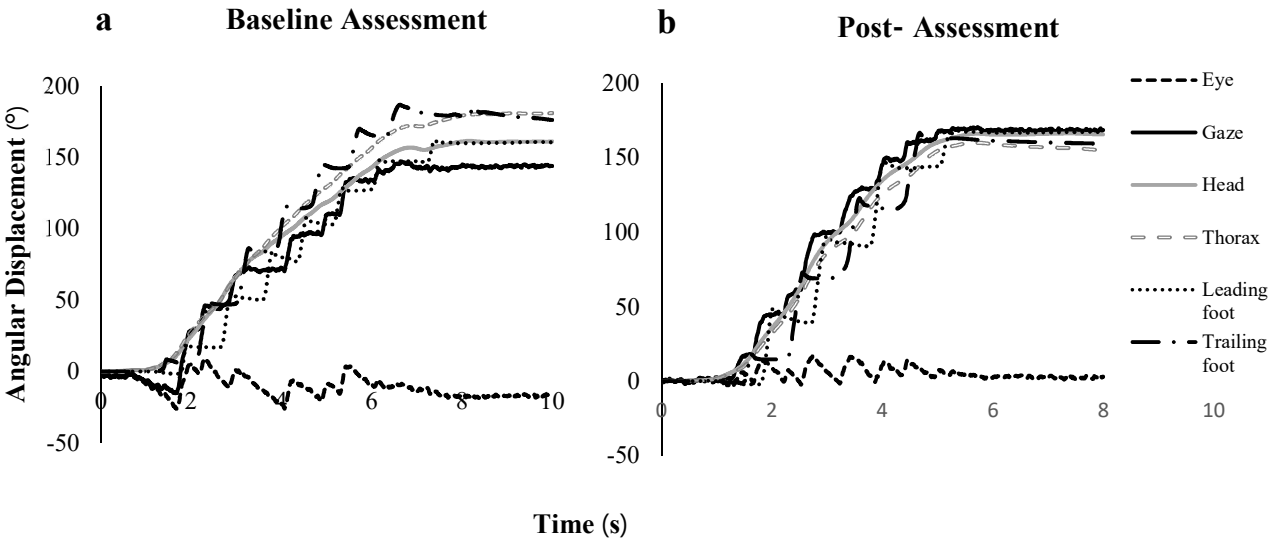


Figure 5-7: Representative displacement traces for **(a)** one baseline assessment trial of 180 degrees and **(b)** one post-assessment trial of 180 degrees in the EG (n=11).

In the baseline assessment, the nystagmus (eye trace) is prominent and exhibits the typical saw-tooth pattern. The nystagmus remains evident during post-assessment. During baseline assessment, the order of the onset of segment reorientation began with the head, followed by the eye, the trunk and, finally, the leading and trailing foot. However, gaze leads the other body segments throughout the majority of the turn. All participants in both groups were found to display similar behaviour.

Mixed ANOVA found no main or interaction effects of group-time between groups at post-assessment. However, there was a significant decrease ($P<0.05$) in the head and the thorax onset latencies between the baseline and intermediate assessments and the baseline assessments and post-assessments in the EG (Figure 5-8a). Segment reorientation began with rotation of the head followed by the eye, the trunk and, finally, the leading and trailing foot in the EG, whereas the order of segment reorientation began with rotation of the eye, followed by the head, the trunk and, finally, the leading and trailing foot in the CG group (Figure 5-8b). These results demonstrated that PD participants in both groups reoriented their whole-body segments simultaneously during turning, rather than a normal top-down sequence, and adopted to a more en-bloc movement strategy.

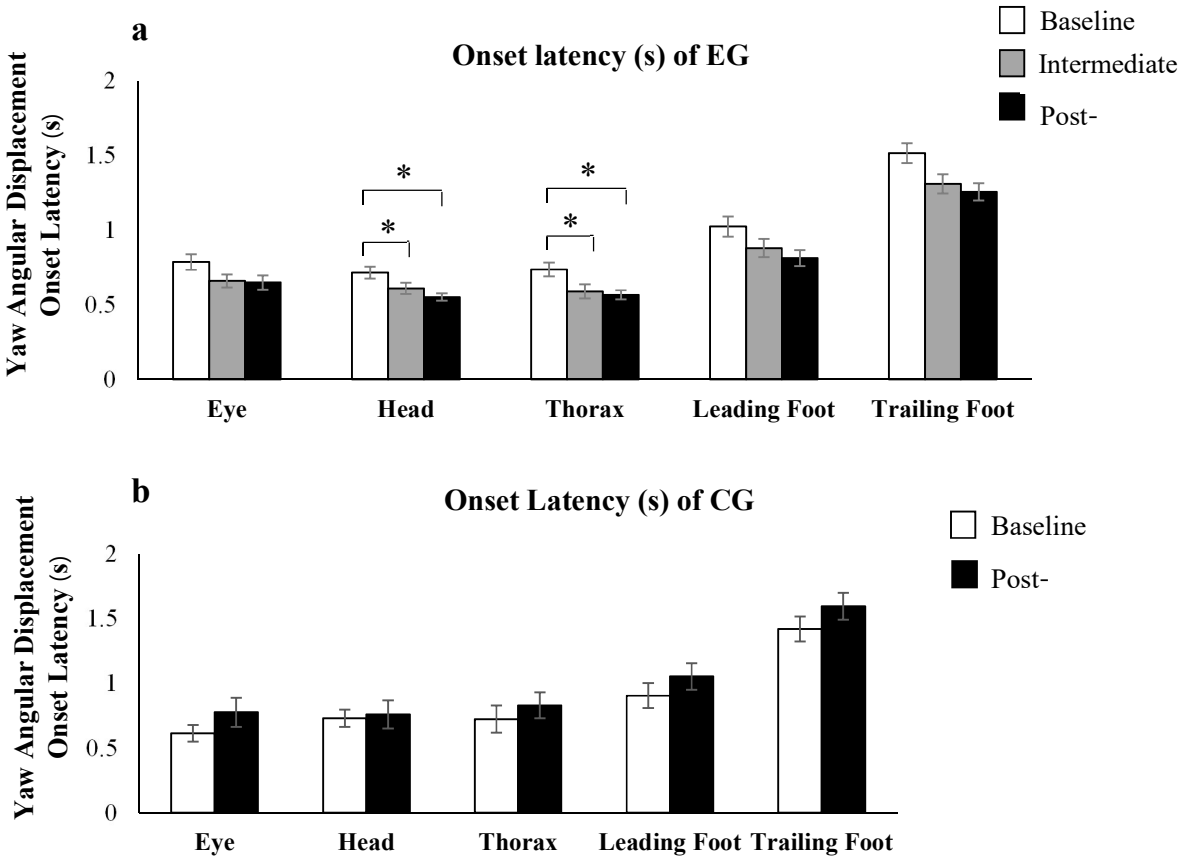


Figure 5-8: Bar graph showing the mean onset latencies of the baseline and post-assessments of the exercise (EG) **(a)** and control (CG) **(b)** groups. The initiation of reorientation of the body segments was en-bloc in all assessments in both groups. However, there was no statistically significant difference in the timing of the onset of rotation of all segments between groups.

* = significant differences within the EG.

5.5.5.2 Intersegmental relationship

Mixed ANOVA revealed no significant difference in the mean change of peak head-thorax angular separation during post-assessment between the groups (Table 5-4). There were no main or interaction effects of group-time on peak head-thorax angular separation between the groups in any assessments. Furthermore, there was no effect of time assessments on peak head-thorax angular separation within the groups (Figure 5-9).

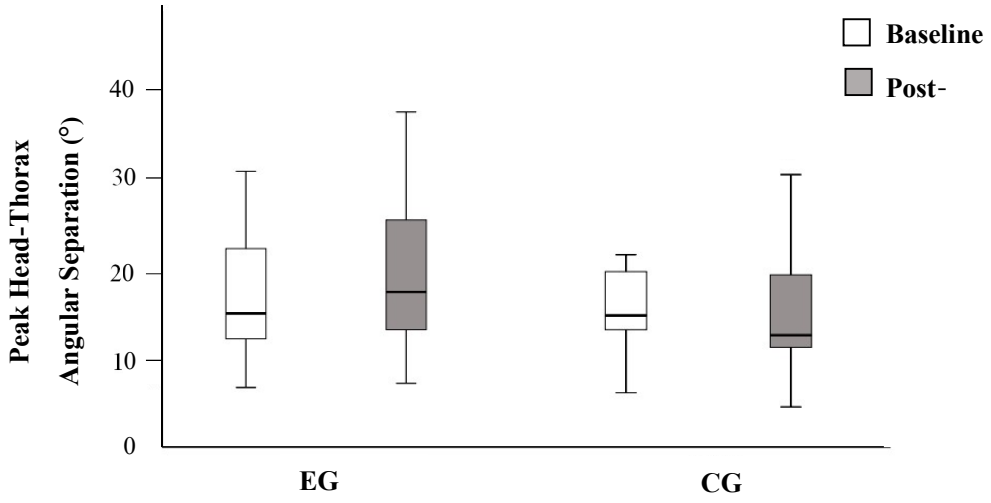


Figure 5-9: This figure compares the mean peak head-thorax angular separation at baseline and post-assessments between the groups. A box and whisker plot diagram has been used to illustrate the median peak head-thorax angular separation. No significant differences were observed during assessments in the exercise group (EG), as compared to the control group (CG).

5.5.6 Effects of a 4 -week modified exercise programme on eye movement characteristics

Mixed ANOVA revealed no main or interaction effects of group-time for fast phase characteristics in the baseline and post-assessments between and within groups (Figure 5-10). Furthermore, the means for the fast phase amplitude and velocity characteristics were calculated, as shown in Table 5-6.

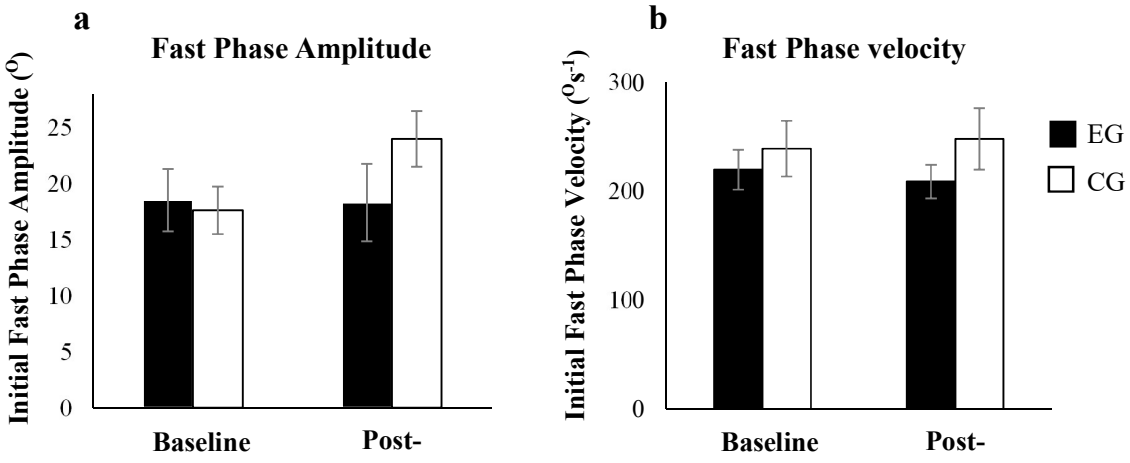


Figure 5-10: There was no significant difference in the baseline and post-assessments within and between groups in terms of **a)** fast phase amplitude and **b)** fast phase velocity.

Table 5-6: Mean and standard deviations between the exercise (EG) and control (CG) groups for the initial and maximum/peak fast phase characteristics as well as fast phase frequency (Data represent in mean ± SD).

Variables	Baseline assessment		***P*-Value**	Post- assessment		***P*-Value**
	EG	CG		EG	CG	
Initial Fast Phase Amplitude **(°)**	18.53 ± 9.22	17.62 ± 7.03	0.797	18.32 ± 8.24	23.99 ± 11.44	0.197
Initial Fast Phase Velocity **(°s-^{1})**	220.07 ± 60.61	239.49 ± 85	0.544	209.24 ± 51.43	248.50 ± 93.48	0.237
Maximum Fast Phase Amplitude **(°)**	22290.52 ± 10756.32	25912.38 ± 18660.26	0.583	17104.19 ± 6371.23	28512.90 ± 25174.63	0.161
Initial Fast Phase Acceleration **(°s^{-2})**	27.10 ± 8.09	23.59 ± 7.54	0.305	29.23 ± 10.39	24.56 ± 8.19	0.255
Peak Fast Phase Velocity **(°s^{-1})**	323.10 ± 70.55	337.99 ± 125.14	0.735	283.47 ± 61.89	358.76 ± 133.68	0.106
Peak Fast Phase Acceleration **(°s^{-2})**	33666.83 ± 12327.01	42699.35 ± 29603.42	0.736	25734.93 ± 7314.37	45116.92 ± 32862.01	0.071
Number of Fast Phases **(**N**)**	7.65 ± 2.67	9.49 ± 3.76	0.361	5.73 ± 1.08[a]	9.56 ± 4.40	0.011
Nystagmus Fast Phase Frequency **(**Hz**)**	2.12 ± 0.30	2.33 ± 0.59	0.203	2.01 ± 0.37	2.16 ± 0.49	0.438

[a] = significant differences from CG.

5.5.7 Effects of a 4 -week modified exercise programme on stepping characteristics

The comparison of step size during the baseline and post-assessments and the differences between the EG and CG are presented in Figure 5-11.

Mixed ANOVA revealed that a significant group-time interaction was found for step size ($F_{(1, 20)}$ = 9.6, P<0.05, η_p^2 = 0.324)Furthermore, a significant main effect of time . assessment was found forstep size ($F_{(2, 20)}$ = 11.6, P<0.05, η_p^2 = 0.252) within the EG. Post hoc pairwise comparisons revealed that the effects of time assessment on step size occurred in the EG and were limited to between the baseline and intermediate assessment (P=0.014) and between the baseline and post- assessments (P=0.018). However, the CG demonstrated no difference in step size during post-assessment compared to the baseline assessment.

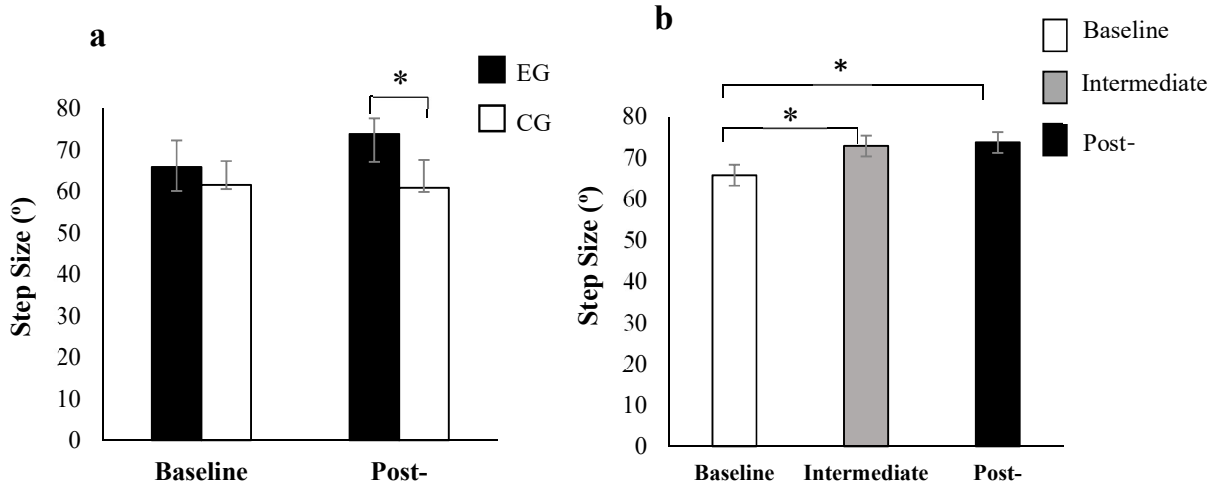


Figure 5-11: These figures show significant differences (P<0.05) in **a)** step size between groups and **b)** step size within the exercise group (EG).

The comparison of total step, step duration and step frequency during baseline and post-assessments and the differences between the EG and CG groups are presented in Table 5-4 and Figure 5-12. Mixed ANOVA showed a significant group-time interaction for total step count ($F_{(1, 20)} = 3.18$, $P<0.05$, $\eta_p^2 = 0.137$) and step duration ($F_{(1, 20)} = 6.54$, $P<0.05$, $\eta_p^2 = 0.246$) (Figure 5-12), demonstrating that total step count and step duration were decreased when comparing between groups at post-assessment on completion of a 4-week training programme. There were no main or interaction effects of time assessments within groups on total step count and step duration. In addition, there were no main or interaction effects of group and time between groups and no effect of time assessments within groups for step frequency.

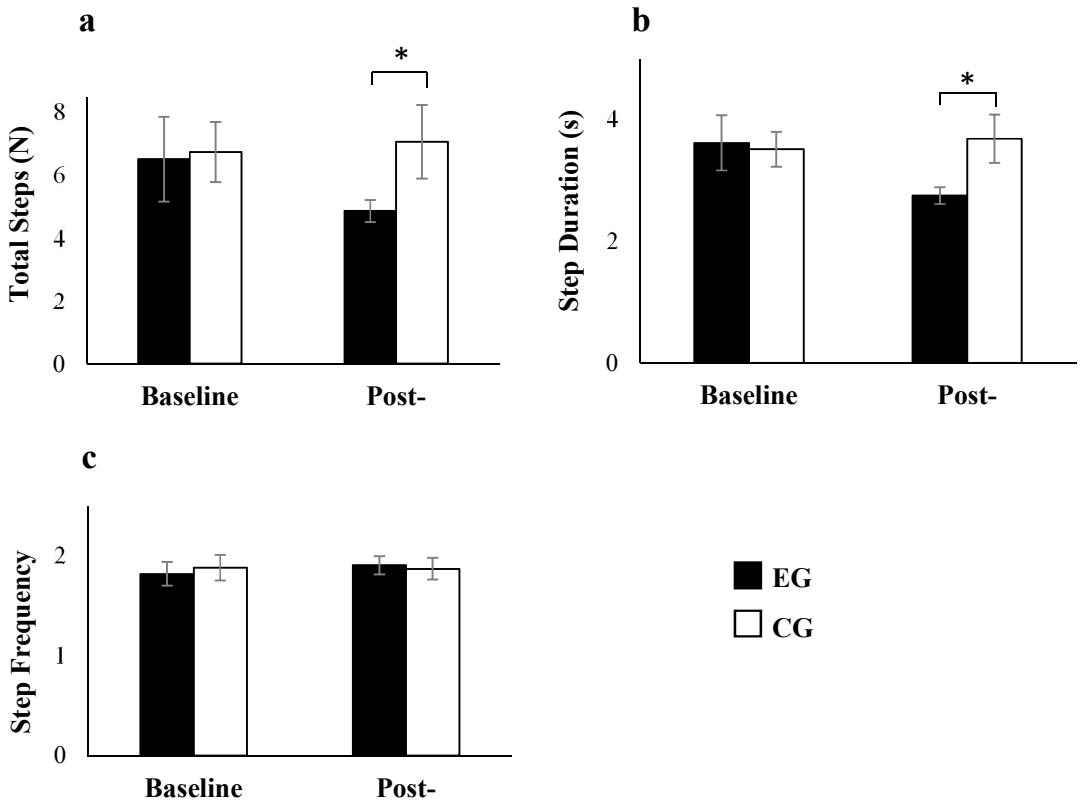


Figure 5-12: Comparison of **a)** total steps, **b)** step duration and **c)** step frequency in the exercise (EG) and the control (CG) groups during baseline and post-assessments.

Finally, mixed ANOVA revealed a significant group-time interaction for turn speed ($F_{(1, 20)} = 6.10$, $P<0.05$, $\eta_p^2 = 0.234$), demonstrating that the EG turn with increased speed when comparing between groups at post-assessment on completing a 4-week training programme (Figure 5-13). There was a significant main effect of time assessment within the EG on turn speed ($F_{(2, 20)} = 7.69$, $P<0.05$, $\eta_p^2 = 0.219$). Post hoc pairwise comparisons revealed that the effects of time assessment on step size occurred in the EG and were limited to between the baseline and intermediate assessments ($P=0.012$) and between the baseline and post-assessments ($P=0.021$). There were no main or interaction effects within the CG.

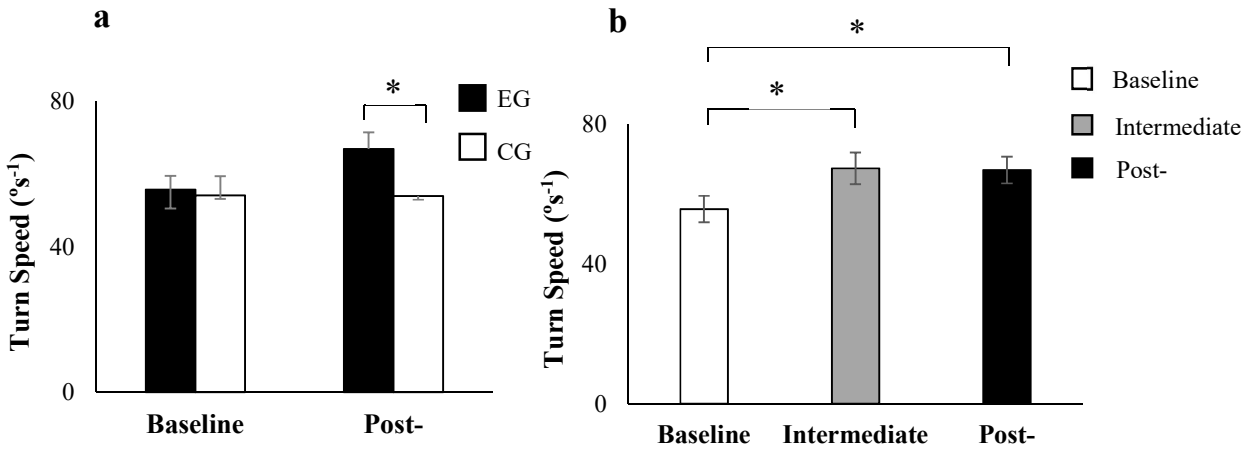


Figure 5-13: These figures show significant differences ($P<0.05$) in **a)** turn speed between groups and **b)** turn speed within the exercise group (EG).

5.5.8 Report of activities daily of living during a 4-week period

During the four-week modified exercise programme of the present study, five participants in the EG did not perform the modified exercises at home during the first week (as noted from the diary records). Thus, the researcher had to call and remind those patients and

their caregivers to participate. From further conversations with participants of this group, it was apparent that all participants felt less stiffness and an improvement in movement during the one- month exercise period. Before participated in the research, three participants experienced problems while performing activities outside their home. However, after participating in the exercise programme, they were able to do housework and perform activities outside their home, such as going out for dinner and shopping at the market.

From the CG's diaries, it was discovered that five participants exercised regularly and performed some activities such as going to the shopping centre, doing housework, and watering plants. Another two participants were frequently in the sitting and lying- down position. However, five participants were found not to keep diary records and, when the researcher called, they said that they only stayed at home and did not perform any activities. No participant reported falls during the one-month period.

5.6 Discussion

The aim of the study was to investigate the effects of using a modified exercise programme on improving axial rigidity and turning dysfunction in individuals with PD. This is the first study to examine the effects of this type of exercise on eye, head and whole-body coordination during standing turns. Our results show that the exercise programme improved functional performance in terms of analysed clinical abilities, turning characteristics and stepping characteristics.

5.6.1 Effects of a 4-week modified exercise programme on clinical abilities

Our results demonstrate a reduction in PD symptoms as measured by the UPDRS total scores, motor score and rigidity score (Figure 5-5). These findings are consistent with previous studies that indicated improvement of UPDRS, especially in UPDRS in motor subscale after participation in an exercise programme (Tomlinson *et al.*, 2012; Tomlinson *et al.*, 2014; Dashtipour *et al.*, 2015; Ni, Mooney and Signorile, 2016). Several brain regions are involved in the generation of movements in PD: basal ganglia circuits, limbic structures, cortical motor circuits, thalamus, and dopaminergic neurons pathways (Petzinger *et al.*, 2013). A possible explanation for improvements in functional scores may be related to facilitating the activity of dopaminergic neurons in motor areas, thereby improving motor function, balance and reducing motor symptoms such as rigidity and bradykinesia (Patti *et al.*, 1996). Ni et al. (2016) found that a yoga programme can also significantly reduce UPDRS motor symptoms and UPDRS rigidity (Ni, Mooney and Signorile, 2016). The authors concluded that yoga is dependent on the brain circuitry involved in motor planning and movement execution. Another possible explanation may be related to the motor learning that the patient expereienced during our exercise programme. For example, the benefits of increased movement amplitude and speed in rotation or turning practice appear to transfer to increased amplitude and speed of finger and foot tapping (Petzinger *et al.*, 2013).

Our results show that the FRT significantly increased in the exercise group compared to the control group after completing the 4-week programme (Figure 5-6a). Furthermore, results within the group comparison of the EG showed a continuous increase from baseline assessment to intermediate assessment to post-assessment. Therefore, it can be postulated that the rotation of axial segments training and balance training in our

programme reduced axial rigidity, contributed to an increase in mobility, and improved coordination and postural stability, leading to better dynamic balance control and an improvement in the distance achieved in the FRT (Weiner *et al.*, 1992; Demura and Yamada, 2007). This is supported by the study of Schenkman et al.(2001), who revealed that individuals with PD who showed increased spinal flexibility, as measured by the FRT, also showed improvement in postural control and balance (Schenkman, Morey and Kuchibhatla, 2000).

The EG exhibited a decrease in the fear of falling as measured by the FES-I over the baseline, intermediate and post-assessments compared to the CG (Figure 5-6b). Moreover, most participants indicated greater confidence in participating in outside activities following the exercise programme. A previous study investigated the effect of an exercise intervention on reducing falls in PD (Protas *et al.*, 2005). It revealed the benefit of a fully supervised 8-week programme of treadmill gait and step perturbation training in PD. Patients in the exercise group showed a substantial reduction in the rate of falling and an improvement in gait and dynamic balance parameters. Similarly, Ashburn et al. (2009) investigated a 6-week programme in which patients were trained at home to learn strategies to prevent falls and performed a range of movement, muscle strengthening, balance training and walking exercises, whereas the CG received usual care. The results showed a consistent trend towards lower rates of falling and significantly lower rates of repeated near falls (Ashburn *et al.*, 2007). Taken together, our results and those of previous studies suggest that the fear of falling in PD can be reduced by an exercise intervention. These improvements may be useful in preserving independence in PD.

The RPE scales in the EG was reported to be 5/10 during baseline assessment, indicating that the participants perceived the workload as a soft-hard (mild to moderate intensity) level (Figure 5-6c). However, the participants in this study had no previous experience in any rehabilitation programmes. Furthermore, we obtained an improvement in RPE scores from the beginning to the end of the programme. The RPE scales in the EG continuously improved from 5/10 in the first week to 3/10 in the fourth week. Therefore, these results suggest that the intensity used in our programme can be safely utilised for starting rehabilitation in individuals with early to moderate PD and that the exercises become even more tolerable after training.

5.6.2 Effects of a 4-week modified exercise programme on turning kinematics

This study is the first to investigate the effects of a modified exercise programme on axial rigidity and turning dysfunction. With respect to turning outcomes, we investigated the onset of segment reorientation and intersegmental relationships. For the onset latencies of the body segment, the results show that only the head and the thorax onset latencies significantly decreased ($P<0.05$) when compare the baseline to the intermediate assessments and the baseline to the post-assessments in the EG. On average, the angular displacement profiles of segment reorientation began with the head, followed by the reorientation of the trunk or eyes, and, finally, the feet (see Figure 5-8). In the EG, only the mean onset of latency for the head and the thorax statistically decreased during post-assessment when compared to the baseline assessment. Our results from the previous study (Khobkhun *et al.*, 2018a) as well as the current study show that faster turning (as increased in turn speed) is associated with reduced onset times. It seems that the relative timing sequence is initiated sooner for faster turns. This supports the notion that the body segments are not controlled independently by the CNS, but rather are programmed as a

sequence released earlier or later depending on the required speed of the turning movement. This interpretation is consistent with the proposal that turning is controlled as a CNS control synergy (Hollands, Ziavra and Bronstein, 2004) which can be defined as a specific motor pattern that is a component of a central motor programme for human movement. This motor pattern can be adapted to control similar motor tasks, reducing the complexity of motor planning and reducing the reliance on sensory feedback.

There were no significant differences in the peak head-thorax angular separation either between or within groups (Figure 5-9). This may be due to the en-bloc turning strategy, which is related to intersegmental coordination deficits in PD. Therefore, the exercise could be adapted to include more specific training to improve intersegmental relationship in PD which may lead to en-bloc pattern improvement during turning. However, Bartolo et al. (2010) observed a significant increase in the range of trunk flexion and lateral bending after a 4-week rehabilitation programme. They also found an improvement in posture, a decrease in trunk lateral flexion and more inclination in the standing position in patients with PD (Bartolo *et al.*, 2010). However, PD is also found to be associated with loss of flexibility and altered posture. The authors suggested that a lack of spinal flexibility may contribute to difficulty in maintaining balance and may cause physical limitations for individuals with PD. According to Stieger et al. (1996) impairment of axial intersegmental movement is a common cause of disability in PD patients, which may indicate that segment angular separation is restricted in PD (Steiger, Thompson and Marsden, 1996).

5.6.3 Effects of a 4-week modified exercise programme on eye movement characteristics

The only effects of our intervention on eye movements was a significant difference in the number of fast phases during post-assessment between groups and within the EG (Figure 5-10). These results can be explained by the change in turn speed increased speed in the exercise group during post-assessment. This is supported by the finding that fast phase frequency was relatively constant. Lohnes and Earhart (2011) previously reported that PD patients exhibited a greater number of saccades during turning and showed differences in initial fast phase velocity (Lohnes and Earhart, 2011). They suggested that saccadic eye movement dysfunction due to PD neuropathology may explain these changes. However, our results in a previous experiment show the same trends in eye movement characteristics of PD observed by these authors can be evoked by asking healthy participants to turn slowly (Khobkhun *et al.*, 2018a).

5.6.4 Effects of a 4-week modified exercise programme on stepping characteristics

The last observation in our results was that the stepping characteristics, such as step size, total steps, step duration, step frequency and also turn speed, improved after a 4-week exercise programme in the EG **(**Table 5-4, Figures 5-11, Figure 5-12 and Figure 5-13**)**. This improvement in stepping characteristics may be due to the stretching exercise, segment rotational training and task-specific turning training. First, our stretching exercise included stretching of hamstring muscles, calf muscles and neck muscles to enhance muscle readiness and flexibility and facilitate movement initiation. Rawson et al. (2019) found that stretching exercise twice a week, for 12 weeks can lead to improvement in backward walking in PD. The author suggested that this may be due to

the fact that the stretching was designed to increase spinal flexibility and improve mobility, leading to enhanced flexibility and freedom of movement (Rawson *et al.*, 2019). The positive effects of stretching on improving stepping outcomes are also supported by Behm et al. (2004). They found that stretching of lower limb muscles can change the mechanical output, the afferent limb muscle responses and proprioception, which would be expected to affect the ability to adapt effectively in stability challenges. They also found that stretching exercise induced improvement in reaction time and movement time in step initiation (Behm *et al.*, 2004). They suggested that these improvements may relate to the balance disturbance mechanism. Postural control and balance involves the interaction of automatic postural and voluntary motor commands. Automatic postural responses are modulated by trunk and leg inputs and anticipatory postural adjustments which are controlled by the CNS. Therefore, stretching exercise may improve anticipatory postural adjustments and voluntary responses of trunk and limb muscles in challenging postural control and balance during turning. Cristopoliski et al. (2009) found that stretching the hip and calf muscle can improve temporo-spatial gait in the elderly (Cristopoliski *et al.*, 2009). After the stretching protocol, the experimental group had more increased range of motion of the hip joint and increased step length compared to the control group. Our own results also demonstrate that stretching exercises led to an improvement not only in behavioural performance, but also in dynamic balance during turning (the improvement of FRT).

It is noteworthy that the PD patients who underwent a modified 4-week exercise programme demonstrated a significant improvement in clinical abilities (UPDRS total scores, UPDRS motor scores, UPDRS rigidity score, FRT, FES-I and RPE), displaying kinematic outcomes (segment onset latency, intersegmental relationships) and stepping characteristics (step size, total step and step duration). In the EG, the differences between

the FRT and RPE results in the baseline and intermediate assessments and UPDRS in rigidity score in the intermediate and post-assessments were noted.

Regarding the effect of exercise in the EG, a reducing of axial rigidity (by a decrease in the UPDRS rigidity score and increase in FRT) may change the capability of a participant in this group, which may be inferred from a relative improvement in performance as a result of practice or experience. In addition, a reduction in axial rigidity may result in the transfer effect of turning performance (improvement in turning kinematics and stepping characteristics). These results suggest that the modified exercise programme could reduce axial rigidity, leading to an improvement in the whole-body rotation of the body segments. Axial body segment coordination is a key contributor to turning adaptations and improvement in its control may result in a reduction in the number of falls experienced by individuals with PD.

5.7 Conclusion

The present study found that a modified exercise programme which focused on axial mobility had positive effects on the ability of PD patients to turn around by decreasing rigidity (as evidenced by reduced UPRS and increased FRT). Improvements were characterised by a reduction in the time taken to initiate the turn and larger, faster and less frequent steps. UPDRS scores, turning speed and RPE were also improved after training. This programme also reduced the fear of falling (as evidenced by reduction in FES-I scores). From these preliminary results it can be concluded that a 4-week modified exercise programme which focuses on axial deficits can be prescribed as an effective intervention approach for improving mobility and reducing falls in PD.

Chapter 6
General Discussion

6.1 The main aims of this thesis were to:

1) To elucidate the role of axial rigidity in changes to eye, head and whole-body coordination and turning dysfunction of individuals with Parkinson's disease (PD) by experimentally inducing axial rigidity in healthy individuals and observing the effects of eye, head and whole-body coordination during turning (study 1).

2) To develop methodology capable of measuring eye, head and whole-body coordination in a clinical setting (study 2).

3) To identify effective exercise or physiotherapy treatments for reducing axial rigidity in PD patients (study 3 – scoping review).

4) To design and implement a pilot RCT utilising an exercise-based intervention to reduce axial rigidity and observe the effects on functional performance in individuals with PD (study 4).

6.2 Summary of findings

1) Experimentally modelling axial rigidity and bradykinesia resulted in altered eye movement, whole body coordination and stepping characteristics compatible with behaviour previously observed in individuals with PD. Modelling axial rigidity led to increased initial fast phase amplitude and velocity, number of step and step frequency and decrease in step amplitude. Turning slowly led to increased reorientation onset latency of body segments, decrease in peak head-thorax angular separation and increase in step angular displacement amplitude, step frequency and number of steps.

2) IMU devices produced accurate measures of axial segmental coordination during turning as demonstrated by an excellent agreement of the ICC values, when compared to the Vicon system.

3) The scoping review identified that there is insufficient evidence to determine whether improvements in functional mobility due to exercise-based rehabilitation are associated with reduced axial rigidity in individuals with PD.

4) The modified exercise programme aimed at reducing axial rigidity had positive effects on clinical outcomes and improved turning performance in individuals with PD. These results support the proposal that targeting axial deficits might be an effective rehabilitation approach for improving mobility and reducing falls in PD.

6.3 Extent of effects of modelling axial rigidity

6.3.1 Inter-segmental coordination

Axial rigidity can be defined as the stiffness of the axial structures of the body, i.e. the head, neck, trunk and pelvis, resulting in axial rotation deficits and turning difficulties experienced by individuals with PD (Mak, Patla and Hui-Chan, 2008; Akram, Frank and Fraser, 2010; Ashburn *et al.*, 2014; Hulbert *et al.*, 2015). We elucidated the role of axial rigidity by using a head, neck and chest brace to limit the movement of participants' head and neck and studying the effects on their turning characteristics.

6.3.2 Eye movement characteristics

Our findings demonstrated that experimentally inducing head and neck rigidity altered the characteristics of eye movement, specifically, the first gaze shift amplitude was preserved by increasing the first fast phase amplitude. Furthermore, the initiation of eye movement preceded all other segments. A gaze anchoring mechanism could explain the

spatial characteristics of the first fast phase in the modelling rigidity condition. Gaze anchoring may be implemented by using a gaze shift to fixate environmental features ahead of the turn. The consistent finding is that gaze precedes head rotation to a desired eccentric location during the majority of the turn (Hollands *et al.*, 1995; Patla, 1997; Hollands and Marple-Horvat, 2001; Neggers and Bekkering, 2001; Rand, 2014). As stated in Chapter 2 gaze shifts may provide a visual anchor that is used to guide balance during the destabilising postural reorganisation that occurs at every step throughout the turn. This is similar to findings by Rand (2014), who demonstrated that the alternating saccade and fixation strategy are employed during manual reaches, for example, initiation of a saccade to the target often precedes that of hand movement and gaze anchoring in which the gaze is fixated on the reach target until the hand movement is completed (Rand, 2014). Similar intermittent gaze anchoring strategies have also been demonstrated in precision stepping tasks. If eye and stepping movements are organized as part of a centrally coordinated synergy then the characteristics of nystagmus during turning on the spot may be modulated by this central process (Hollands and Marple-Horvat, 2001).

A study by Anastasopoulos et al. (2011) investigated gaze shifting behaviour during turning in PD patients. Participants made coordinated eye-head-body gaze shifts from an LED positioned at 0° in an array of LEDs, to one of the seven eccentric locations (±45, ±90, ±135, and 180 degrees) (Anastasopoulos *et al.*, 2011). The investigators measured the number of gaze shifts participants used to foveate the target LED and found that while PD patients were less able to make single gaze shifts than control subjects, the relative contribution of the eye to the coordinated gaze shift was much higher than that of healthy adults, whose head-on-trunk and eye-in-orbit rotation contributed relatively equally to the gaze shift. It appears that, in the absence of signals from active head-on-trunk movements, the eye movement is increased to achieve gaze anticipation. This study demonstrated that

for individuals with PD who have axial rigidity and are less able to make head-on-trunk rotations than healthy adults, their eye movements would need to precede the movement in the direction of the body's motion. Taken together, our results and the previous study suggest that in the absence of signals from active head-on-trunk movements, the movement is increased to maintain the size of gaze shifts.

6.3.3 Stepping characteristics

Experimentally inducing head and neck rigidity reduced step amplitude and increased the number and frequency of steps. These results may be due to two reasons: (1) reduced head-on-trunk rotation and (2) associated reduction in the proprioceptive drive from neck muscle spindles.

6.3.3.1 En-bloc turning consequences

The head restrained condition may alter the intersegment coordination, producing an en-bloc presentation, resulting in changing stepping characteristics to maintain balance and stability during the turn. Our results support that reducing head-on-trunk rotation affects the stepping characteristics that are responsible for the required ability to maintain balance during the turns. These results are consistent with a previous study observed in individuals with PD (Stack, Ashburn and Jupp, 2006; Crenna *et al.*, 2007; Stack and Ashburn, 2008; Hong, Perlmutter and Earhart, 2009; Anastasopoulos *et al.*, 2011; Lohnes and Earhart, 2011). Mak et al. (2008) reported that a reduction of axial rotation results in a narrower turn step in PD patients compared to healthy adults (Mak, Patla and Hui-Chan, 2008). The authors noted the narrow step could have resulted from the inadequate force used to accelerate the COM towards the direction of the turn, with a resultant destabilisation effect and adaptation in step strategy. Akram et al. (2013) demonstrated that a reduction of segment rotation during on-the-spot turns in PD patient resulted in an

increase in the total number of steps taken to complete the turns, possibly due a delay in segment reorientation initiation and reduced turning velocity (Akram, Frank and Jog, 2013). Previous research also suggests that although taking many small steps may result in freezing episodes, it may be beneficial in order to preserve postural stability and maintain COM in a wider base of support throughout the turn (Stack and Ashburn, 2008).

6.3.3.2 Neck proprioception contributions

Modelling head and neck rigidity may affect the integration of information sent from neck proprioceptors, which are normally interpreted in frames of reference derived from cutaneous, visual and vestibular signals, giving rise to a coherent body scheme for posture (including equilibrium maintenance) as well as for movement (Bove *et al.*, 2001). Based on postural studies, one might expect that the vibration of neck muscles could also affect locomotion, since posture and locomotion control the position of the COM to maintain a dynamic body balance (Ivanenko, Grasso and Lacquaniti, 2000; Bove *et al.*, 2001). Consequently, changes to neck muscle proprioception resulting from reduced head on trunk rotation might result in a distorted internal representation of the body configuration. As a result, the internal representation of the body centre of mass might be inaccurate. In order to restore the dynamic equilibrium in the context of this distorted representation, compensatory movements may be generated, resulting in altered postural control. The proprioception input from the neck is not only integrated into the control of stance, but also in turning locomotion. Previous studies have reported that stepping on-the-spot was affected by static head inclination and neck torsion (Bove, Courtine and Schieppati, 2002). Ivanenko et al. (2000) showed that if the head is horizontally turned or the eyes are laterally rotated, the vibration of dorsal neck muscles during stepping-in-place causes stepping in the direction of the naso-occipital axis or of the gaze, respectively (Ivanenko, Grasso and Lacquaniti, 2000). Activation of neck proprioceptive signals, as induced by a

prolonged neck muscle vibration or tonic head deviation, has a strong influence on gait trajectory orientation (Ivanenko, Grasso and Lacquaniti, 2000; Bove *et al.*, 2001; Bove, Courtine and Schieppati, 2002). It is possible that the CNS interprets neck muscle vibration as actual head rotation, and that this is sufficient to elicit turning behaviour. A reduction in the proprioceptive drive from neck muscle spindles due to neck rigidity may contribute towards altered stepping patterns, for example, reducing the amplitude and increasing the step frequency.

6.4 Implementation of IMUs

The results from this study indicate that IMUs can accurately measure axial movement parameters during turning in healthy participants (ICC between 0.80 and 0.98) when compared with measurements from a Vicon system).

As stated in Chapter 2, laboratory-based movement analysis techniques are time-consuming, expensive and require a large measurement volume and technical expertise. The results suggested that IMU devices could be used in isolation to gather accurate data from individuals with PD within a real-life context. Furthermore, IMUs can directly measure temporo-spatial parameters of gait that could be used during daily clinical assessments of gait and postural control. Individuals with PD who turn during standing or walking often freeze and/or fall down; asking a patient to execute a turn in the clinic does not often fully reveal their impairment. The advantages of continuous monitoring of mobility with small sensors and low power requirements, such as IMUs, allow characterisation of fluctuations across the day and week, response to medications and other interventions and the influence of real-world distractions and complex environments (Horak, King and Mancini, 2015). In our study, using IMU devices in the

laboratory can provide the real characteristics of turning performance. We predict that therapists can use IMUs to evaluate the turning performance of PD continuously during daily activities for a more ecological and realistic understanding of patients' mobility in the world. Physiotherapists can also incorporate movement monitors to provide real-time feedback to improve motor learning and motor performance, both during a regular training session. With technology becoming increasingly accessible and pervasive, therapists need to critically evaluate the advantages and limitations of implementing emerging technologies, such as IMU, into their clinical practice. Therefore, mobility assessment in the home and community provides important information for the clinician and patient to determine fall risk, disease progression, the effectiveness of rehabilitation and potential benefits of preventative intervention. In this study, we show that the investigation of turning at different speeds with IMUs is feasible for individuals with PD.

6.5 Results of the scoping review

The aims of the scoping review were to identify effective exercise-based treatments for reducing axial rigidity in PD patients. In accordance with the aims of a scoping review the criteria were deliberately kept very broad (Arksey and O'Malley, 2005). However, only four articles met the inclusion criteria. The participants in the studies included those with mild to severe PD. Most studies included outcomes that either directly measured rigidity or were based on clinicians' reports on rigidity or physical performance parameters. The exercise group in only one study showed improvement in the UPDRS for the rigidity score (Ni, Mooney and Signorile, 2016). An improvement in flexibility was shown in two studies (Schenkman *et al.*, 1998; Stozek *et al.*, 2016), and an increase in range in motion (ROM) outcome was highlighted by two studies (Schenkman *et al.*, 1998; Bartolo *et al.*, 2010). In addition to the positive effects on axial rigidity, three out

of four of the included studies also showed positive effects of interventions on improving general functional performance of PD patients (mobility, gait pattern, and a reduction in the risk of falls) (Schenkman *et al.*, 1998; Ni, Mooney and Signorile, 2016; Stozek *et al.*, 2016).

As stated in Chapter 4, the paucity of evidence for the effects of physiotherapy on axial rigidity identified in the present study is consistent with previous systematic reviews (Tomlinson *et al.*, 2012; Tomlinson *et al.*, 2014). It may be that since our study set the PICOT criteria for inclusion to cover only exercise-based treatment in comparison with a usual care group that the inferences, which can be drawn from this evidence, are limited. In future work, a scoping review study could be made to develop the criteria to expand another aspect of reducing axial rigidity associated with functional mobility. This could be done through exercise-based treatment, which could then be compared with other physiotherapy techniques. Another consideration is that individuals with PD may benefit in improvement of axial rigidity from a multi-disciplinary approach. Some literature suggests that levodopa therapy and deep brain stimulation is beneficial in improving axial rigidity (Schenkman and Butler, 1989). Furthermore, the mechanism of axial rigidity is controlled by neuronal circuits that differ from the ones which control appendicular rigidity. An understanding of the mechanism of axial rigidity and its direct and indirect effects is unclear and makes it difficult to identify appropriate strategies and physiotherapy approaches for addressing this problem. Schenkman and Butler (1989) proposed that it is unlikely that physiotherapy intervention can permanently reverse the rigidity, which is a direct result of nervous system pathology (Schenkman and Butler, 1989). There is still a need for well-designed, large-scale studies to evaluate the benefits of exercise or interventions in terms of reducing axial rigidity. Further research is needed to develop exercise interventions that could focus on the programme of restoration or

maintenance of axial mobility with special emphasis on type, duration and detail of exercise for PD patients.

6.6 The possible mechanism of a modified exercise programme

The experiment described in chapter 5 aimed to design and implement a pilot RCT, utilising an exercise-based intervention to reduce axial rigidity and observe the effects on functional performance in individuals with PD. Common problems that PD patients face include: a stooped posture, axial rigidity or stiffness, segmental coordination deficits, slowness of movement, and postural control and balance disturbance; thus, these were the major targets of the selected programme. These impairments affect an individual's functional performance in terms of turning ability. We attempted to develop an exercise programme focussed on reducing axial rigidity and improving turning. To achieve this we modified an exercise program identified in our scoping review (Schenkman *et al.*, 1998). One session of the programme comprised deep breathing and postural correction, stretching exercises, segment rotation training in supine, side lying, prone lying and standing positions, balance training and task-specific turning training

Results of this pilot RCT demonstrated that the exercise group (EG) had a significant (P<0.05) improvement in clinical abilities and turning kinematic outcomes after training for a 4-week modified exercise programme by reduction in total UPDRS score, UPDRS motor score, UPDRS rigidity score, FES-I, onset latency of body segment reorientation, and total number of steps and step duration during turns compared to the control group (CG). Following the training, the EG group also showed significantly (P<0.05) increases in: turn speed, FRT and step size compared to the CG.

6.6.1 Motor learning

The improvement of the aforementioned outcomes may be due to the stretching exercise, segment rotational training and task-specific turning training effects on reducing axial rigidity. Reducing axial rigidity would lead to an increase in spinal flexibility and axial mobility and improved coordination and postural stability, leading to better dynamic balance control and an improvement in the spatio-temporal movement of axial segments. Specific brain regions are involved in the generation of movements: basal ganglia circuits, cortical motor circuits, thalamus and neurons pathways. Also, turning on-the-spot involves anticipatory postural adjustments (APAs). Consequently, APAs are controlled by neural circuits, including the supplementary motor area (SMA) of the cortex and basal ganglia and are organised subcortically with the pontomedullary reticular formation involved in posture control through the brain stem–spinal pathways (Kanekar and Aruin, 2015; Lin, Creath and Rogers, 2016). APAs are generated prior to an intentional motor action and are produced in preparation for a predictable external perturbation (Lin, Creath and Rogers, 2016). While APAs are acquired based on previous experiences, they are also capable of short-term adaptation in response to immediate environmental changes (Kanekar and Aruin, 2015; Lin, Creath and Rogers, 2016). As a result, the onset latency of whole-body responses is thought to be linked to APA and the cortical command for the initiation of turning movement (Lin, Creath and Rogers, 2016).

Task-specific training is one of the concepts of motor learning and may induce cellular or/and molecular changes to form either short-term and/or long-term memory. The ability to carry out these changes is called “plasticity” (Shumway-Cook and Woollacott, 2001). The formation processes of short-term memory include: 1) changes in the excitation-secretion coupling at the presynaptic level through phosphorylation and Ca2+ influx; 2) Ca2+ influx at the postsynaptic level and increased neurotransmitter release (Petzinger *et*

al., 2007; Fisher *et al.*, 2008; Petzinger *et al.*, 2013). If short-term memory is reinforced, it will be transformed to be long-term memory. The sustained stimulation leads to persistent activation of the protein kinase A (PKA) and MAP kinase Erk (MAPK) pathways (Petzinger *et al.*, 2013). These changes express proteins involved in protein synthesis, axon growth, synaptic structure and function in related neural circuits. Therefore, this motor learning process may be evoked by our task-specific training and improve short-term memory in individuals with PD.

6.6.2 Brain and neural connectivity

The basal ganglia play a critical role in triggering a sequential movement in a smooth manner with proper coordination. PD which is characterised by the loss of dopaminergic neurons of the nigrostriatal pathway and dysfunction in the nucleus of the basal ganglia and the brainstem, have an impaired ability to internally cue movement for adjusting smoothness and coordinating movement. Therefore, auditory and visual cues are recommended for intervention while exercising to improve mobility in PD. The influence of cues on motor performance in PD has been explained by the activation of an alternative neural circuit (Willems *et al.*, 2007). Lateral pathways are relatively more active in externally cued motor performance than medial pathways in automatic motor control. There are studies on individuals with PD employing exercises that change the neural connections between brain areas. Fisher et al. (2013) investigated that an 8-week program of treadmill exercise was accompanied by an increase in dopaminergic neurons binding potential within the dorsal striatum of individuals with early stage PD (Fisher *et al.*, 2013). Further evidence was observed by Alberts and colleagues in 2009 who used functional magnetic resonance imaging (fMRI) to show that utilising forced cycling, combining cognitive engagement in PD, can increase connectivity between cortico-subcortical regions involved in automatic control (Ridgel, Vitek and Alberts, 2009).

In conclusion, this thesis is the first study to investigate the effects of exercise intervention to reduce axial rigidity and observe the effects on turning performance in PD. Our results show that a modified exercise program can improve functional mobility, which may result from cortical control due to the increased connectivity in neural control involving the supplementary motor area (SMA) and basal ganglia in PD.

6.6.3 Extent of effects of exercise on eye movements

Regarding eye movement outcomes, our findings demonstrated that a modified programme only improved number of fast phases. This could be due to the fact that PD patients who participated in our study did not have impairment of eye movements. Therefore, keeping this explanation in mind, any research aimed at investigating the effects of their exercise on eye movements, should have the inclusion criteria for eye movement impairment and combining eye movement rehabilitation with exercise programme to extend the benefit of turning characteristics in PD .

In summary, we found that a 4-week period of our programme could improve both axial rigidity and turning characteristics in individuals with PD. Previous studies have demonstrated that beneficial effects of exercise on PD patients require a training period of approximately 4 to 12 weeks (Schenkman *et al.*, 1998; Ellis *et al.*, 2005; Willems *et al.*, 2007; Yousefi *et al.*, 2009; Bartolo *et al.*, 2010; Schenkman *et al.*, 2012; Morrone *et al.*, 2016; Ni, Mooney and Signorile, 2016; Hulbert *et al.*, 2017). For example, Bartolo et al. (2010) indicated that an intensive 4-week rehabilitation programme could significantly improve trunk flexibility and clinical mobility status (Bartolo *et al.*, 2010). Likewise, Stozek et al. (2016) indicated that a 4-week rehabilitation training programme that focusses on various exercises can improve balance, postural stability, walking and performance in terms of ADL mobility, balance and gait exercises (Stozek *et al.*, 2016).

Dibble et al. *(*2007*)* suggested that strengthening and balancing exercises over 8-week had been shown to improve stride length and balance in PD patients (Dibble *et al.*, 2006). Additionally, Scandialis et al. (2001) found that muscle strength and functional capacity in walking are improved after training the leg muscles for 8 weeks (Scandalis *et al.*, 2001). Ni et al. (2016) compare the effects for a power yoga group with those for a control group over 12 weeks. This yoga programme improved movement speed, muscle strength and power, specific to PD-related decrements (Ni, Mooney and Signorile, 2016). The differences in the time spent on training could depend on the details of the training programme, stage of the disease and outcome measurements. However, the results of our study indicated that a programme lasting four weeks is sufficient to improve both the axial rigidity problem and turning characteristics in individuals with PD.

6.7 Limitations and future direction

6.7.1 Limitation of study 1

The head, neck and chest brace used in study 1 used to model axial rigidity in PD only restrained the head and neck. We did not attempt to model the deficit, which might occur at the pelvic segment. Previous findings reported that the decreased head on pelvis rotation may affect the ability of turning in PD (Spildooren *et al.*, 2013). Further work is recommended that uses head-neck-trunk and pelvis restraint, which would more accurately model the axial rigidity in PD. Furthermore, it is important to investigate eye movement, whole-body coordination, balance and posture during walking turns to assess the similarities and differences observed during on-the-spot turns. This approach would further our understanding of the mechanisms that underlie turning problems and risk of falls in PD.

6.7.2 Limitation of study 2

In our study in which we validated the use of IMUs to examine turning characteristics, the four IMU sensors available were attached to the centre of the forehead, middle thorax, the centre of the left foot and right foot. If we had had access to additional sensors, we would also have attached a unit to the pelvis. Another limitation in the current study was the fact that the position of IMU over the thorax may have been tilted because of poor postural alignment or thorax curve of the subject, which led to noise in thorax data. We solved this issue by designing a box to hold the IMU in such a way as to avoid tilting which we used in study 3. The pilot data obtained was better than when the IMU was attached to the thorax directly.

6.7.3 Clinical implication

The future studies could clarify distinctions between turns, which occur during starting from a static posture or ongoing locomotion. When beginning a turn from quiet stance, anticipatory postural adjustments, biomechanics and sensory mechanisms are likely to be different from those which occur during ongoing walking. Secondly, other parameters should be considered to investigate turning performance, such as muscle activity (Hong, Perlmutter and Earhart, 2009) and brain activity (Fisher *et al.*, 2008; Fisher *et al.*, 2013), to expand our understanding of turning mechanisms. This information would make the researcher concerned about the muscle and brain activity changes underlying turning investigation. The clinicians could use this information for informing the design of rehabilitation strategies and specific training programmes that could influence both the muscle activity and neural connections in individuals with PD.

Another consideration of this thesis was that the assessor of the last study was not blind, and this may have affected the evaluation of the outcomes. Furthermore, we did not

investigate the effects of the modified exercise programme during the long term and follow-up period. Future investigations with longer training and follow-up period are recommended. In terms of medication, exercise training and measurement sessions featured participants under "on" medication state; future research is needed to examine and compare the effect of exercise on PD patients in their "off" state. Consequently, the paradigm of rehabilitation should be targeted on reducing axial rigidity associated with improving turning performance.

Last, further studies should investigate other factors involved during the exercise programme, such as eye movement training, behavioural modification, or cognitive training, which may be more effective and more advantageous for individuals with PD. Also, further research to assess the long-term effects of exercise on turning performance and investigation using a greater number of participants is necessary.

6.8 Summary and conclusions

The work described in this thesis has provided evidence that segmental reorientation, intersegmental coordination, fast phase characteristics and stepping behaviour are systematically altered by changes in both experimentally modelling axial rigidity and bradykinesia and in individuals with PD. We have validated IMU devices as a viable alternative to using video-based motion capture for measuring coordination of axial segments during turning in clinical settings. Furthermore, our scoping review indicated there is insufficient evidence to determine whether improvements in function due to exercise-based rehabilitation are associated with reduced axial rigidity in individuals with PD. Therefore, we modified and adopted an exercise programme identified in our scoping review and found that this programme had a positive effect on various markers of

functional abilities and improved turning performance in individuals with PD. These preliminary results support the notion that targeting axial deficiencies may be an effective rehabilitation approach for improving mobility and reducing falls in those with PD.

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Appendices

Appendix 1. A scoping review and rational for Chapter 4

A scoping review refers to a scoping study, rapid review, or mapping review, is considered the first step towards successful research literature (Arksey and O'Malley, 2005). A scoping review involves mapping relevant literature on a particular topic to access a variety of data. It is a review process that aims to sort a large collection of information on the basis of its relevance to a particular field of interest. In other words, a scoping review is a review that is carried out with the aim of 'mapping research concepts that underpin a research area' (Peters *et al.*, 2015). There are various methods of carrying out a research review of the literature such as meta-analyses, narrative reviews, traditional literature reviews, rapid reviews, systematic reviews, structured reviews, and research syntheses. Among these research reviews, systematic reviews are the most adept with researchers. However, systematic reviews and scoping reviews could be viewed as opposite sides of the same coin. If anything, a scoping review should be the parent review carried out by a researcher before they proceed to carry out a systematic review.

Although scoping reviews and systematic reviews are similar in that they both use rigorous and transparent methods iteratively, they also differ in certain aspects (Pham *et al.*, 2014). One of the differences is that whilst a systematic review is centred on a well-defined question with a predefined study design, a scoping review focuses on wide topics that have a variety of applicable study designs (Arksey and O'Malley, 2005). Second, whereas systematic reviews attempt to answer the research question by assessing a narrow range of quality materials, scoping reviews do not analyse the materials based on any specific research question or quality (Arksey and O'Malley, 2005).

The number of scoping reviews published since 2009, especially in the health and social sciences sector, has expanded dramatically, mainly because of the benefits of conducting a scoping review (Pham *et al.*, 2014). First, scoping reviews help the researcher to analyse the degree, array and nature of previous research in a particular field of interest. It is useful to create an overview of what other researchers have done. Scoping reviews also aid in the process of analysing the feasibility, relevance and cost of undertaking a systematic review. In addition, a scoping review helps to summarise and disseminate research findings to make it easier for stakeholders to gain an overview of the research content. Finally, scoping reviews suggest areas where more research should be done in order to strengthen the existing literature. The methodology of a scoping review is including as follows:

Step 1: Identify the research question

From the onset, it is vital that the research question is identified because it provides the following guideline for which the strategies used in the scope review. The research question helps to define the parameters and to analyse the implications of such parameters on the quality of the results (Arksey and O'Malley, 2005). The research question must capture the objective of the scoping review. For instance, the research question in the article 'A Scoping Review for Scoping Reviews' was: 'What are the characteristics and range of methodologies used in scoping reviews in the literature?' (Pham *et al.*, 2014). The objective of this study was to analyse the features and methodologies used in other scoping studies.

Step 2: Identifying relevant studies

This process involves identifying as much material as possible that could be relevant to the research question. The researcher may obtain such material from various sources such as the reference list of relevant journals or books, electronic databases, search engines, or existing networks of relevant organisations and conferences. The researcher must determine the criteria under which material is selected. The criteria may include language, date, subject and methodology, amongst others.

Step 3: Study selection

Sorting potential sources is necessary to eliminate those that are irrelevant to the rapid review's research question (Arksey and O'Malley, 2005). To conduct adequate sorting, the researcher must first determine the criteria under which relevant sources will be accepted. These criteria will help the researcher to establish consistency in their decision making. Moreover, the inclusion criteria may include the study design, the experimental group, or control group in each piece of research material. The researcher will then use the criteria to create a list of materials relevant to the research question.

Step 4: Charting the data

The purpose of charting or representing the data is to create a summary of the information gathered in the previous step. Well-represented data will culminate in a good analysis and comparison of the materials obtained. The researcher must decide how to represent the information obtained in the primary studies and how to effectively compare different interventions (Arksey and O'Malley, 2005). For instance, the data may be entered into a Microsoft Excel spreadsheet. After, the data can be used to plot a graph using software tools in Microsoft Excel.

Step 5: Collating, summarising and reporting the data

A prior scoping review must be conclusive and must achieve the objectives set out in step 1. Therefore, the final steps in conducting a scoping review are to analyse, summarise and draw conclusions on the findings of the study (Arksey and O'Malley, 2005). Whilst a systematic review may synthesise a new view with regard to the data entered, a scoping review does not attempt to make any interpretation of the quality of evidence provided in the various materials. The sole purpose of a scoping review is to create a summary of the findings. A good review will include a narrative review of the nature, degree and distribution of the material discovered in step 3. This may include various factors of comparison such as the methods applied, care recipient groups, caregivers, or measures of effectiveness.

- **The mechanism of rigidity**

With regard to the primary aim of the first part of this study, the most visible symptom of clinical manifestation of PD is axial rigidity, which causes patients to experience difficulty while changing their movements (Griffin *et al.*, 2011; Mazzoni, Shabbott and Cortés, 2012; Ajimsha *et al.*, 2014). As stated in Franzén et al. (2009), rigidity is one of the major manifestations of PD. The only symptom caused by rigidity is a feeling of stiffness (Franzén *et al.*, 2009). As a clinical assessment, however, rigidity refers to the phenomenon of increased resistance within the passive range of motion of muscle. Rigidity can be categorised into two types: lead-pipe rigidity, where resistance remains uniform, constant and smooth, and cogwheel rigidity, where a tremor is imposed upon the increased tone (Rodriguez-Oroz *et al.*, 2009).

The underlying mechanism of rigidity in PD and how it responds to dopaminergic medication is poorly understood, making it difficult to explain by simply using the classic model of basal ganglia pathophysiology (Rodriguez-Oroz *et al.*, 2009). The basic explanation of basal ganglia activity in PD suggests that increased neuronal activity in the subthalamic nucleus (STN) and internal globus pallidus (GP) and its resultant inhibition of thalamocortical projections should result in decreased muscle activation and reduced response to stretching (Mazzoni, Shabbott and Cortés, 2012; Baradaran *et al.*, 2013). Furthermore, it has been suggested that contributions from the spinal cord and its relevance to brain stem, including higher cortical circuits, all been have an important role in the pathophysiology of rigidity (Hong, Perlmutter and Earhart, 2007). Reflex responses could be one potential mechanism; these responses increase in excitability in long loop reflex pathways. Rapid passive stretching of a contracting muscle leads to responses at different latencies. In PD, a longer latency response is associated with transcortical involvement. It has been hypothesised that if this transcortical loop become hyperactive, then the enhanced response to stretching may appear as rigidity in a clinical setting. Another hypothesis suggests that inappropriate commands from one or several descending spinal pathways can cause malfunctions in the short reflex pathways at the spinal level (Baradaran *et al.*, 2013). However, clinical observations may suggest an alternate explanation. This hints that a systems-level, distributed brain network may significantly contribute to the mechanism of rigidity in PD.

In clinical observation, individuals with PD may complain of stiffness or functional difficulties in general. However, it should be noted that rigidity is a sign detected by a clinician rather than a symptom described by a patient. Neck rigidity becomes more prominent with disease duration and is well correlated with the severity of the disease (Jankovic and Tolosa, 2007; Cohen *et al.*, 2015). Furthermore, axial rigidity, in terms of

restricted spinal and axial mobility in individuals with PD, affects both the axial structures and the extremities. There is some evidence to suggest that axial flexibility is correlated with the physical performance of activity daily of living (ADL) in healthy adults, such as moving from a supine to a sitting position or reaching and turning while standing (Schenkman *et al.*, 2001). Therefore, it has been suggested that loss of axial mobility may functionally limit individuals with PD (Schenkman *et al.*, 2001). Correspondingly, Franzén et al. (2009), reported that neck and trunk muscle tone plays an essential role in controlling postural balance, mobility and coordination (Franzén *et al.*, 2009). Additionally, an increase in neck and trunk flexor tone results in the head moving ahead of the neck, leading to increased neck extensor activity to prevent the head from falling forward. Furthermore, rigidity in individuals with PD may result in altered spatial-temporal coordination of the axis that is needed to control the stability of axial body segments and lateral postural responses while changing direction (Smania *et al.*, 2011). Indeed, it has been suggested that the presence of axial rigidity is likely to contribute to the risk of falling; it may also decrease the quality of life (QOL) of individuals with PD, as discussed above.

- **Physiotherapy in PD**

Currently, the modern management of PD is directed towards recovering functional status to improve both clinical disability and QOL (Pacchetti *et al.*, 2000). Dopaminergic medication is the first strategy that is used to alleviate PD symptoms, but it cannot eliminate the problems and may lead to deterioration, in part, of movement functions and participation (Tomlinson *et al.*, 2012). To cope with motor control problem, physiotherapy has shown promise in the treatment of PD (Tomlinson *et al.*, 2012; Ajimsha *et al.*, 2014). Importantly, the physiotherapist is a member of the multidisciplinary approach team and strives to maximise functional ability and minimise

secondary complications through movement rehabilitation within a context of education and support for individuals with PD, and this rehabilitation treatment is usually prescribed along with medical treatment (Morris, 2000; Tomlinson *et al.*, 2012).

Physiotherapy is also targeted at delaying problems with motor control, especially, gait, posture and balance (autogenic). Several techniques of physiotherapy (e.g., general physiotherapy, treadmill training and cueing) have been recommended for individuals with PD (Tomlinson *et al.*, 2012). Exercise is the most recommended form of physiotherapy to failure neuro-rehabilitation in individuals with PD (Tomlinson *et al.*, 2012; Petzinger *et al.*, 2013). Exercise is a subcategory of physical activity that is planned, structured, repetitive and purposive for improving or maintaining the condition of any part of the body (Petzinger *et al.*, 2013). In terms of PD, there has been a major interest in utilising exercise, as it incorporates many aspects of practice that are important for goal-directed motor skill learning. These elements comprise repetition, intensity and challenge which, together with skill training, lead to improvement of motor performance.

Several studies on physiotherapy in the management of motor impairment and functional performance in individuals with PD have proven it to be beneficial. It has also been reported that physiotherapy improves the motor performance and QOL of individuals with PD. Dibble et al. (2007) have suggested that strengthening and balancing exercises can be helpful in managing stride length and balance in individuals with PD (Dibble *et al.*, 2006). Exercise and motor training have also been indicated to improve balance, as balance impairments lead to high morbidity in individuals with PD (Allen *et al.*, 2010; Allen *et al.*, 2011). Azulay et al. (2006) assessed the effect of visual cues on gait training in individuals with PD. The results showed that the spatial and temporal variables of gait improved (Azulay, Mesure and Blin, 2006). Previous research that examined the use treadmill exercise has also shown that if individuals with mild to moderate stages of PD

exercise, it improves postural stability, joint excursion, gait rhythmicity and gait performance (Herman *et al.*, 2007). Similarly, Ellis et al. (2005), investigated the effects of a physical therapy programme on 68 individuals with PD (Ellis *et al.*, 2005). The exercise programme included cardiovascular warm-up, stretching, functional training, gait training, balance training and relaxation. Pre- and post- exercise were evaluated using the Sickness Impact Profile (SIP-68) and an evaluation form that was concerned with functional status and comfortable walking speed; the form was filled using a Unified Parkinson Disease Rating Scale (UPDRS). It was found that the exercise group who participated in the exercise programme for 6 weeks showed greater improvement in functional status and QOL than the control group who did not exercise. Additionally, Scandialis et al. (2001) found that muscle strength and functional capacity of walking improved after individuals underwent leg-muscle training for 8 weeks (Scandalis *et al.*, 2001b). The exercise programme included warm-up, stretching, breathing exercise and gait training, which proved to be useful for individuals with PD as a measure to control the disease's progression (Turnbull, 1992). Furthermore, other complementary strategies, including Tai Chi, boxing, dancing and yoga, have also been reported to address movement deficits to improve dynamic postural control, cognition and coordination as well as reduce the risk of falling in individuals with PD (Hackney *et al.*, 2007; Combs *et al.*, 2011; Duncan and Earhart, 2012; Hashimoto *et al.*, 2015).

Inferring from the information provided in the previous section, it is possible that the positive effects of physiotherapy on functional performance of individuals with PD may be due, in part, to reductions in axial rigidity. To help researchers better understand common approaches and to guide the translation of research to a clinical setting, there is a need for a comprehensive systematic review. Therefore, the second part of this study will conduct a scoping review to determine whether there is sufficient high-quality

evidence to investigate whether exercise-based rehabilitation is associated with a reduction in axial rigidity in individuals with PD.

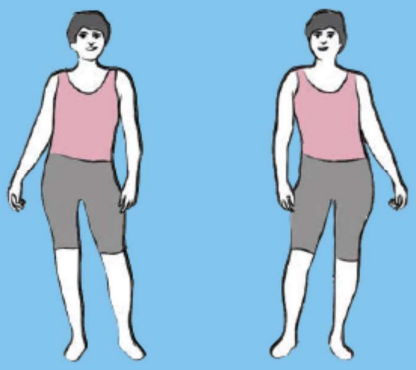
Appendix 2. Booklet for the exercise group

โปรแกรมออกกำลังกาย

ในงานวิจัยเรื่องผลการตอบสนองการฝึกออกกำลังกาย
แบบประยุกต์ต่อความเกร็งแกนกลางลำตัว
และทักษะการหมุนตัวในผู้ป่วยพาร์กินสัน

ผู้เขียน
เฟื่องฟ้า ขอบคุณ

ที่ปรึกษา
ผศ.ดร.อมรพันธ์ อัจจิมาพร
Dr. Mark Hollands
รศ.ดร.จารุกูล ตรีไตรลักษณะ
นายแพทย์ปรัชญา ศรีภูมิวานิช
ดร.สุวีณา ค้าเจริญ (ที่ปรึกษาพิเศษ)



*หมายเหตุ โปรแกรมการออกกำลังกายนี้ยังอยู่ในกระบวนการทำวิจัย
ยังไม่อนุญาตนำไปเผยแพร่ต่อสาธารณชน

การยืดกล้ามเนื้อก่อนออกกำลังกายตามโปรแกรม

ท่านต้องยืดก่อนเริ่มโปรแกรมทุกครั้ง

1. ยืดกล้ามเนื้อต้นขาด้านหลัง

ท่าเริ่ม: นั่งบนเก้าอี้หรือเตียงเตี้ย เหยียดขาขวาตรง ส้นเท้าวางบนพื้น

ท่ายืด: ยืดลำตัวตรง และพยายามเหยียดขาขวาให้ตรง จากนั้นค่อย ๆ โน้มตัวไปข้างหน้าในขณะที่ลำตัวยืดตรง ท่านจะรู้สึกว่ากล้ามเนื้อต้นขาด้านหลังถูกยืด ทำค้างไว้ ประมาณ 30 วินาที จากนั้นพัก ทำ 3 ครั้ง และเปลี่ยนไปทำที่ขาข้างซ้ายอีก 3 ครั้ง

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2. ยืดกล้ามเนื้อน่องด้านหลัง

ท่าเริ่ม: ยืนหลังตรง ก้าวขาซ้ายไปข้างหน้า 1 ก้าว มือแตะกำแพง

ท่ายืด: ค่อย ๆ โน้มตัวไปข้างหน้า ในขณะที่หลังตรง และส้นเท้าขวาสัมผัสพื้น จนรู้สึกว่าบริเวณด้านหลังน่องขวาถูกยืด ทำค้างไว้ครั้งละ 20-30 วินาที จนครบ 3 ครั้ง แล้วเปลี่ยนเป็นข้างซ้าย

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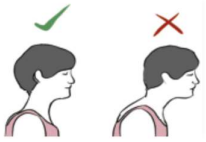
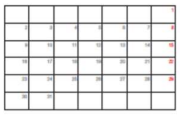
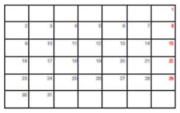
3. ยืดกล้ามเนื้อคอ

3ก **ท่าเริ่ม:** นั่งบนเก้าอี้ ตัวตรง หลังตรง และเท้าวางราบบนพื้น ส่องกระจกหรือญาติคอยแนะนำให้ผู้ป่วย ปรับตำแหน่งของหูให้อยู่ในแนวเดียวกับไหล่ตามองตรง หน้าไม่ก้มหรือเงย





3ข **ท่าเอียงคอ:** นั่งบนเก้าอี้ ตัวตรง หลังตรง และเท้าวางราบบนพื้น ศีรษะอยู่ในแนวตรงแล้ว ให้ท่านค่อยๆ เอียงคอไปทางขวาช้าๆ โดยให้หูข้างขวาไปชิดไหล่ขวามากที่สุด จากนั้นเอียงคอกลับมาตำแหน่งเดิม และเปลี่ยนไปทำข้างซ้าย ทำ 3 รอบ



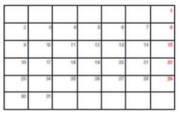
หลังจากยืดกล้ามเนื้อแล้ว ท่านเข้าสู่การออกกำลังกาย โดยให้ท่านทำจนรู้สึกผ่อนคลายทุกท่า และหากท่านได้ทำแล้ว ให้ท่านทำเครื่องหมายถูกในตารางทุกวัน หากท่านรู้สึกเหนื่อยหรือรู้สึกผิดปกติใดๆ ให้ท่านหยุดพักจนกว่าจะดีขึ้น

โปรแกรมการออกกำลังกายแบบประยุกต์มีดังนี้

1. การฝึกหายใจ

ท่าเริ่ม: นอนหงาย ใช้หมอนรองใต้ข้อเข่าได้หากต้องการ วางมือทั้งสองบริเวณหน้าท้อง

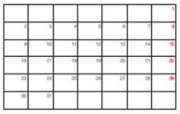
ท่าออกกำลังกาย: หายใจเข้าลึกๆ ทางจมูกให้ท้องป่องจนดันมือที่วางอยู่บนหน้าท้องขึ้น แล้วหายใจออกยาวๆ ช้าๆ ทางปาก จนท้องแฟบ มือที่วางอยู่จะเคลื่อนที่ลง ทำทั้งหมด 3 ครั้ง

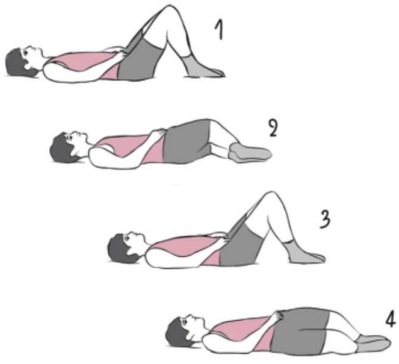


2. ฝึกหมุนกล้ามเนื้อลำตัวส่วนล่าง

ท่าเริ่ม: นอนหงายราบกับพื้น ชันเข่าขึ้น

ท่าออกกำลังกาย: จากนั้นให้บิดหมุนขาทั้งสองข้างไปทางขวาช้าๆ ให้มากที่สุดเท่าที่ทำได้แต่ต้องไม่ฝืนจนเกินไป จากนั้นค่อยๆ หมุนกลับ และหมุนไปทางซ้ายช้า ๆ เท่าที่ทำได้ (ท่านสามารถหมุนตามจังหวะเมโตรโนมตามที่นักกายภาพบำบัดแนะนำได้) หายใจเข้า-ออกลึกๆ ทำจนรู้สึกผ่อนคลาย

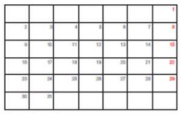


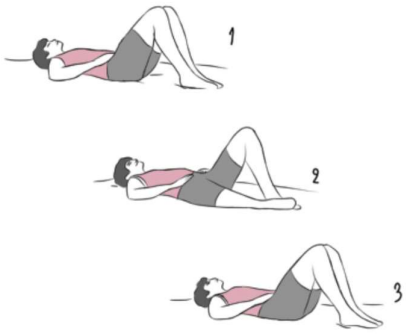


3. ฝึกหมุนกล้ามเนื้อสะโพก

ท่าเริ่ม: นอนหงายราบกับพื้น ชันเข่าขึ้น

ท่าออกกำลังกาย: จากนั้นหมุนแบะขาขวาช้าๆ จนกระทั่งด้านข้างของเข่าแตะพื้น จากนั้นค่อยๆ หมุนกลับ และทำซ้ำ 10 ครั้ง หรือจนรู้สึกผ่อนคลาย พักหายใจเข้า-ออก ผ่อนคลายและเปลี่ยนเป็นขาซ้ายทำเช่นเดียวกัน (ท่านสามารถหมุนตามจังหวะเมโตรโนมตามที่นักกายภาพบำบัดแนะนำได้)

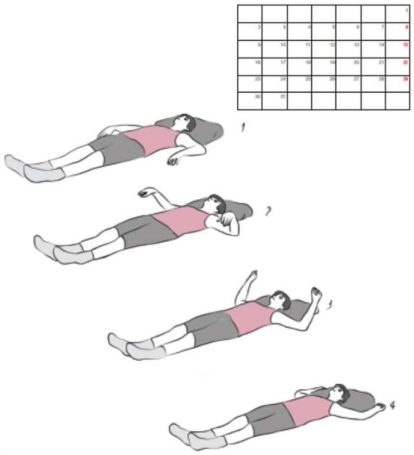




4. ฝึกหมุนแขน

ท่าเริ่ม: นอนหงายราบกับพื้น กางแขนออกทางด้านข้างและงอศอก 90 องศา คว่ำมือลงตามรูป

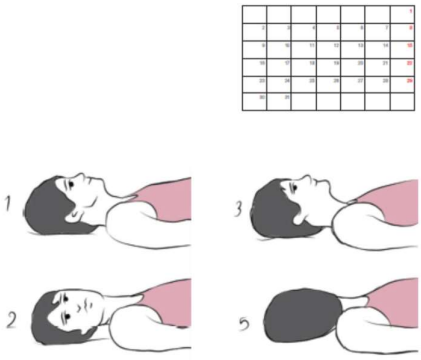
ท่าออกกำลังกาย: ค่อยๆบิดหมุนแขนทั้งสองข้างขึ้นไปทางศีรษะช้าๆ โดยแขนท่อนแขน และมือไปพร้อมๆ กันจนติดพื้น เท่าที่ทำได้ พยายามไม่ให้หัวไหล่ลอยขึ้นจากพื้น จากนั้นค่อยๆ หมุนกลับลงมาทางสะโพก เท่าที่ทำได้ (ท่านสามารถหมุนตามจังหวะเมโตรโนมตามที่นักกายภาพบำบัดแนะนำได้) หายใจเข้า-ออกลึกๆ ทำซ้ำ 10 ครั้งหรือจนรู้สึกผ่อนคลาย



5. ฝึกหมุนคอ

ท่าเริ่ม: ท่านนอนหงายราบกับพื้น ศีรษะและคอปล่อยสบายๆ ไม่ก้มหรือหงายจนเกินไป

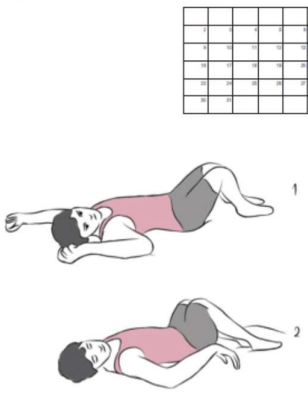
ท่าออกกำลังกาย: ตำแหน่งคออยู่ในแนวตรงแล้ว ให้ท่านค่อยๆ หันศีรษะไปทางขวาช้าๆ จากนั้นหันศีรษะกลับมาตำแหน่งเริ่มต้น และเปลี่ยนเป็นหันศีรษะไปทางด้านซ้ายเช่นเดียวกัน (ท่านสามารถหมุนตามจังหวะเมโตรโนมตามที่นักกายภาพบำบัดแนะนำได้) ทำจนรู้สึกผ่อนคลาย



6. ฝึกรวมท่าออกกำลังกายข้อ 1-5

ท่าเริ่ม: นอนหงายราบกับพื้น หน้าตรงผ่อนคลาย ชันเข่าขึ้น กางแขนออกวางราบข้างศีรษะ งอศอก 90 องศา

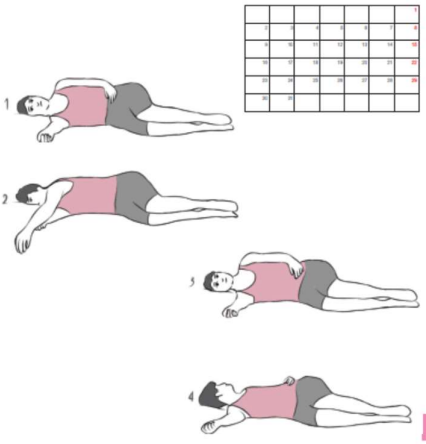
ท่าออกกำลังกาย: บิดหมุนแขนขึ้นไปทางศีรษะ หมุนคอมาทางขวา หมุนสะโพกและเข่าไปทางซ้าย จากนั้นกลับมาท่าตรง และเปลี่ยนเป็น หมุนแขนลงไปทางสะโพก หมุนคอมาทางซ้าย หมุนสะโพกและเข่าไปทางขวา (ท่านสามารถหมุนตามจังหวะเมโตรโนมตามที่นักกายภาพบำบัดแนะนำได้) ทำจนรู้สึกผ่อนคลาย



7. ฝึกการเอื้อมไปและกลับร่วมกลับการหมุนลำตัวส่วนบน

ท่าเริ่ม: นอนตะแคงขวา วางแขนขวาบนเตียงโดยยื่นแขนมาข้างหน้า แขนซ้ายอยู่บนลำตัว งอเข่างอสะโพก

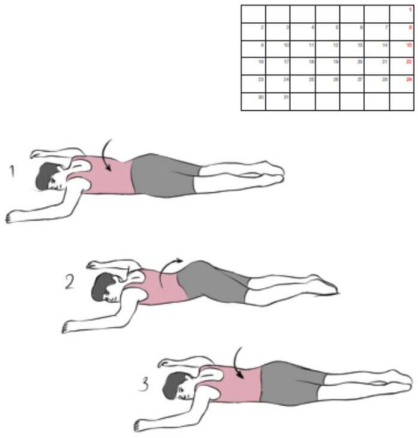
ท่าออกกำลังกาย: เอื้อมแขนซ้ายไปข้างหน้าและถอยกลับให้มากที่สุดเท่าที่จะทำได้ โดยหมุนลำตัวไปด้วยทั้งไปและกลับ เหยียดข้อศอกไปข้างหน้า และงอข้อศอกกลับ และพยายามให้สะโพกอยู่กับที่ ทำจนรู้สึกผ่อนคลาย และเปลี่ยนไปนอนตะแคงทับซ้าย ท่านเอื้อมแขนขวาไปข้างหน้าและถอยกลับให้มากที่สุดเท่าที่จะทำได้ โดยหมุนลำตัวไปด้วยทั้งไปและกลับ เหยียดข้อศอกไปข้างหน้า และงอข้อศอกกลับ (ท่านสามารถหมุนตามจังหวะเมโตรโนมตามที่นักกายภาพบำบัดแนะนำได้) ทำจนรู้สึกผ่อนคลาย



8. ฝึกหมุนเชิงกราน

ท่าเริ่ม: นอนคว่ำ

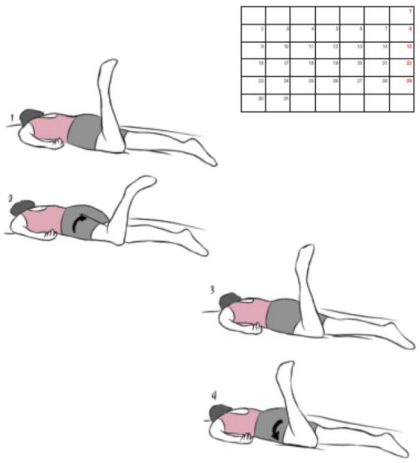
ท่าฝึก: หมุนเชิงกรานขวากดลงที่เตียงแบบเบาๆ **และช้าๆ** จากนั้นหมุนขึ้นโดยยกสะโพกขึ้นเล็กน้อย ทำซ้ำจนรู้สึกผ่อนคลาย จากนั้นสลับข้าง หมุนเชิงกรานซ้ายลง โดยกดลงที่เตียงแบบเบาๆ **และช้าๆ** จากนั้นหมุนขึ้นโดยยกสะโพกขึ้นเล็กน้อย ทำซ้ำจนรู้สึกผ่อนคลาย



9. ฝึกหมุนสะโพกท่านอนคว่ำ

ท่าเริ่ม: นอนคว่ำ งอเข่าข้างขวา เท้าชี้ขึ้น

ท่าฝึก: หมุนสะโพกขวาเข้าด้านใน สลับกับหมุนออกด้านนอก**ช้าๆ** ทำจนรู้สึกผ่อนคลาย จากนั้นสลับข้าง งอเข่าข้างซ้าย เท้าชี้ขึ้น หมุนสะโพกซ้ายเข้าด้านใน สลับกับหมุนออกด้านนอก**ช้าๆ** (ท่านสามารถหมุนตามจังหวะเมโตรโนมตามที่นักกายภาพบำบัดแนะนำได้) ทำจนรู้สึกผ่อนคลาย



10. การฝึกโน้มตัวไปข้างหน้าในท่านั่ง

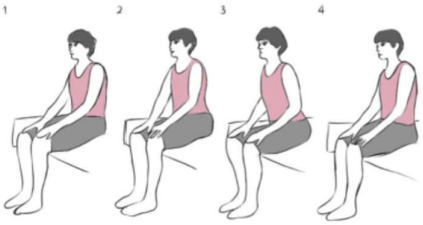
ท่าเริ่ม: ท่านนั่งบนเก้าอี้หรือเตียง โดยลำตัวตรง และวางเท้าติดกับพื้น

ท่าฝึก: หมุนสะโพกไปทางด้านหน้า โดยให้หลังส่วนเอวแอ่นเล็กน้อย โน้มตัวลงจนลำตัวถ่ายน้ำหนักและเคลื่อนมาที่ขา ท่านต้องแน่ใจว่าหลังส่วนเอวยังแอ่น และศีรษะยังตั้งตรงอยู่ (ท่านสามารถทำตามจังหวะเมโตรโนมตามที่นักกายภาพบำบัดแนะนำได้) ทำจนรู้สึกผ่อนคลาย

11. การฝึกหมุนสะโพกเป็นวงกลม

ท่าเริ่ม: นั่งบนเก้าอี้หรือเตียง โดยลำตัวตรง และวางเท้าวางราบกับพื้น

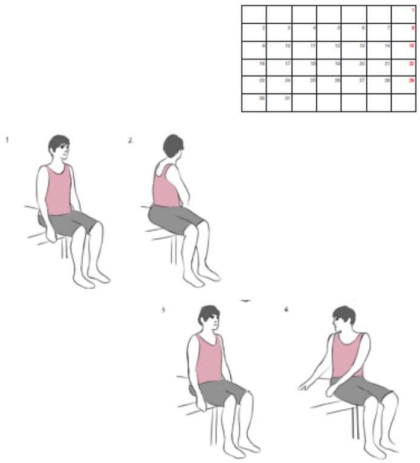
ท่าฝึก: ท่านค่อยๆ แอ่นหลังส่วนล่างเล็กน้อย ถ่ายน้ำหนักไปทางสะโพกขวา งอหลังส่วนล่าง ถ่ายน้ำหนักมาที่สะโพกซ้าย **ทำช้าๆ และพยายามให้ราบเรียบคล้ายๆ เล่น ฮูลาฮูป** จากนั้นเปลี่ยนเป็นหมุนไปอีกข้างทำตามและทวนเข็มนาฬิกา ทำจนรู้สึกผ่อนคลาย



12. การฝึกหมุนลำตัวท่านั่ง

ท่าเริ่ม: ท่านนั่งบนเก้าอี้หรือเตียง โดยลำตัวตรง และวางเท้าราบกับพื้น

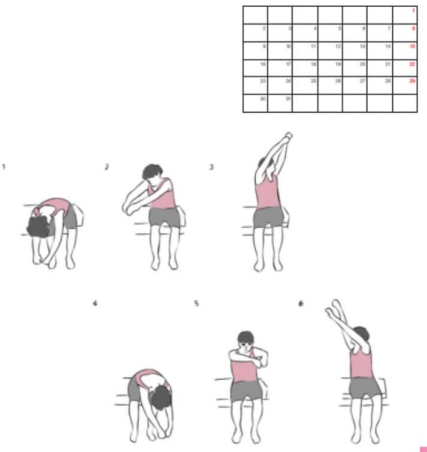
ท่าฝึก: หมุนลำตัวไปทางขวาให้ไกลที่สุด โดยก้นต้องติดพื้น จากนั้นค่อยๆ เปลี่ยนเป็นหมุนลำตัวไปทางซ้ายให้ไกลที่สุด โดยก้นต้องติดพื้นเช่นเดียวกัน (ท่านสามารถหมุนตามจังหวะเมโตรโนมตามที่นักกายภาพบำบัดแนะนำได้) ทำจนรู้สึกผ่อนคลาย



13. การฝึกการเหยียดหลังในแนวเฉียง

ท่าเริ่ม: นั่งบนเก้าอี้หรือเตียง เท้าวางราบกับพื้น กัมหลังให้มากที่สุดเท่าที่จะทำได้ และเอามือทั้งสองเบี่ยงให้แตะหรือพันด้านนอกของข้อเท้าขวา

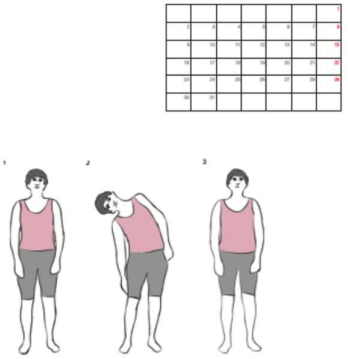
ท่าฝึก: **ทำท่าคล้ายๆ กับท่านเก็บของที่อยู่ข้างเท้าขวาด้วยสองมือ จากนั้นยกขึ้นมาเพื่อจะเอาของนั้นไปวางที่ชั้นเหนือหัวไหล่ข้างซ้าย** โดยคิดว่าชั้นนั้นอยู่สูงเท่าที่คุณจะทำได้ จากนั้นเปลี่ยนข้าง **ทำท่าคล้ายๆ กับท่านเก็บของที่อยู่ข้างเท้าซ้ายด้วยสองมือ จากนั้นยกขึ้นมาเพื่อจะเอาของนั้นไปวางที่ชั้นเหนือหัวไหล่ข้างขวา** ทำข้างละ 5 ครั้ง หรือทำจนรู้สึกผ่อนคลาย



14. การฝึกเอียงลำตัวในท่ายืน

ท่าเริ่ม: ท่านยืนตัวตรง หลังตรง หน้าตรง เท้าสองข้างห่างกัน 1 ช่วงไหล่ สามารถจับเก้าอี้เพื่อความปลอดภัย

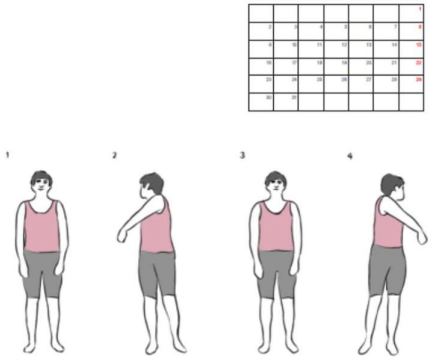
ท่าฝึก: ท่าน**ค่อยๆ** เอียงศีรษะไปทางด้านขวา โดยเอาหูชิดไหล่ และ**ค่อยๆ** เอียงลำตัวไปทางด้านขวา ปล่อยแขนตามสบาย จากนั้นเกลับสู่ท่ายืนตัวตรง และ**ค่อยๆ** เอียงศีรษะไปทางด้านซาย โดยเอาหูชิดไหล่ และ**ค่อยๆ** เอียงลำตัวไปทางด้านซ้าย ปล่อยแขนตามสบาย (ท่านสามารถเอียงตามจังหวะเมโตรโนมตามที่นักกายภาพบำบัดแนะนำได้) ทำจนรู้สึกผ่อนคลาย



15. การฝึกบิดหมุนลำตัว

ท่าเริ่ม: ท่านยืนตัวตรง หลังตรง หน้าตรง เท้าสองข้างห่างกัน 1 ช่วงไหล่ สามารถจับเก้าอี้เพื่อความปลอดภัย

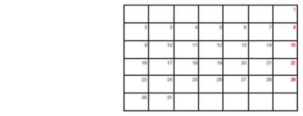
ท่าฝึก: หมุนลำตัวไปทางขวา โดยแกว่งแขนทั้งสองข้างไปด้วย ต้องรู้สึกว่าน้ำหนักถ่ายไปยังเท้าข้างซ้าย จากนั้นหมุนตัวกลับมาตรงกลาง และค่อยๆ เปลี่ยนเป็นหมุนลำตัวไปทางซ้าย โดยแกว่งแขนทั้งสองข้างไปด้วย ต้องรู้สึกว่าน้ำหนักถ่ายไปยังเท้าข้างขวาเช่นเดียวกัน (ท่านสามารถหมุนตามจังหวะเมโตรโนมตามที่นักกายภาพบำบัดแนะนำได้) ทำจนรู้สึกผ่อนคลาย

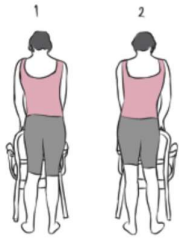


16. การฝึกบิดหมุนลำตัวส่วนล่าง

ท่าเริ่ม: ท่านยืนตัวตรง หลังตรง หน้าตรง เท้าสองข้างห่างกัน 1 ช่วงไหล่ สามารถจับเก้าอี้เพื่อความปลอดภัย

ท่าฝึก: หมุนสะโพกขวาไปทางซ้าย โดยลำตัวตรง ท่านต้องรู้สึกว่ามีการถ่ายน้ำหนักจากข้างขวาไปทางซ้าย จากนั้นเปลี่ยนหมุนสะโพกซ้ายไปทางขวาโดยลำตัวตรง ท่านต้องรู้สึกว่ามีการถ่ายน้ำหนักจากข้างซ้ายไปทางขวา (ท่านสามารถหมุนตามจังหวะเมโตรโนมตามที่นักกายภาพบำบัดแนะนำได้) ทำจนรู้สึกผ่อนคลาย

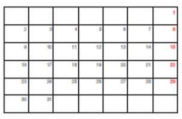


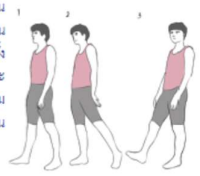


17. การฝึกยืนและโยก

ท่าเริ่ม: ท่านยืนตัวตรง หลังตรง หน้าตรง เท้าขวาอยู่หน้าต่อเท้าซ้าย 1 ช่วงก้าว

ท่าฝึก: ท่านถ่ายน้ำหนักไปทางด้านหน้า โดยเคลื่อนสะโพกไปยังเท้าขวา ค่อยๆ เคลื่อนจนกว่าเท้าซ้ายจะเปิด จากนั้นค่อยๆ ถ่ายน้ำหนักกลับมาทางด้านหลังโดยเคลื่อนสะโพกไปยังเท้าซ้าย เคลื่อนมาด้านหลังจนเท้าขวายกจากพื้นเล็กน้อย ทำหลาย ๆ ครั้ง จากนั้นเปลี่ยนเป็นเท้าซ้ายอยู่ข้างหน้า และทำซ้ำ (ท่านสามารถทำตามจังหวะเมโตรโนมตามที่นักกายภาพบำบัดแนะนำได้) ทำจนรู้สึกผ่อนคลาย

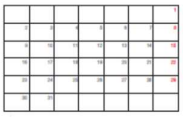


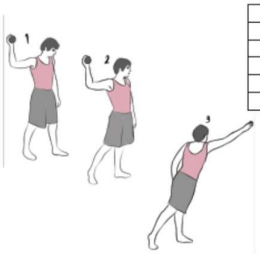


18. การสร้างสรรค์การเคลื่อนไหว

ท่าเริ่ม: ท่านยืนตัวตรง หลังตรง หน้าตรง เท้าขวาอยู่หน้าต่อเท้าซ้าย 1 ช่วงก้าว

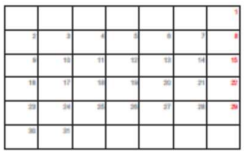
ท่าฝึก: ท่านสามารถฝึกท่าทางคล้าย ๆ กับท่านกำลังกว้างลูกบอลไปข้างหน้า โดยฝึกถ่ายน้ำหนักจากเท้าหนึ่งไปยังอีกเท้าหนึ่ง และมีการบิดหมุนร่างกาย

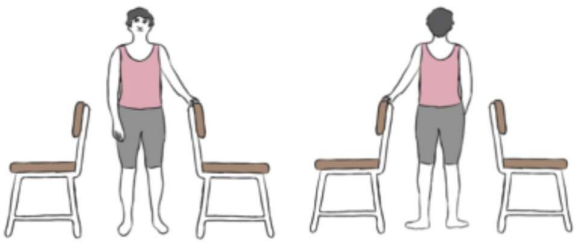




19. การฝึกหมุนตัว

ท่านจะฝึกหมุนตัวตามสัญลักษณ์ที่ติดบนพื้น โดยท่านจะยืนระหว่างเก้าอี้ 2 ตัว ทำการฝึกหมุนไปทางขวาก่อน 5 ครั้ง แล้วเปลี่ยนมาฝึกหมุนไปทางซ้ายอีก 5 ครั้ง ทำทั้งสิ้น 2 รอบ พักระหว่างรอบ 5 นาที การฝึกนี้ท่านสามารถจับพนักเก้าอี้ได้เพื่อความปลอดภัย





********** เครื่องสิ้นโปรแกรม **********

จากผู้เขียน ท่าออกกำลังกายทั้งหมดได้ประยุกต์มาจาก Professor Margaret Schenkman, PhD, Physical Medicine & Rehabilitation, University of Colorado ต้องขอกราบขอบพระคุณมา ณ ที่นี้ด้วย

List of Conference Proceedings

1. The 2017 International Society of Posture & Research World Congress. Fort Lauderdale, Florida, US, 25-29 June 2017. “Why are Parkinson’s disease patients prone to falls during turning? Can we model dysfunction in healthy young participants?” (Poster presentation)

2. World Confederation for Physical Therapy Congress 2019 Geneva, Switzerland, 10-13 May 2019. “Effectiveness of exercise-based rehabilitation for the treatment of axial rigidity in people with Parkinson’s disease: *A Scoping Review*”. (Poster presentation)

3. The 2019 International Society of Posture & Research World Congress, Edinburgh, Scotland, UK, 1-4 July 2019. “Effects of modified exercise programme for improving axial rigidity and turning dysfunction in individuals with Parkinson’s disease”. (Poster presentation)