

**PARKINSON'S DISEASE AND SEGMENTAL COORDINATION  
DURING MODIFIED FIGURE OF EIGHT WALKING AND  
TURNING TASK**

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## **ABSTRACT**

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Turning while walking is problematic for individuals with Parkinson's disease (PD). We hypothesized there would be instability and turning difficulty for the PD subjects while performing a complex motor skill task of the modified figure of eight (MFE) walking task. There were 26 subjects (10 males and 16 females) with clinical diagnosis of "idiopathic" PD and undergoing L-dopa treatment participating in this study. The PD subjects performed the clinical balance modified figure of eight (MFE) test. The 3-D positions of the head, trunk and pelvis were recorded and analyzed. The angular displacement and angular velocity of the head, trunk and pelvis were calculated. Counter-clockwise and clockwise direction was compared and the relationship between overstepping and time to complete the task were also calculated. For comparison two way analysis of variance (ANOVA). Pearson correlation test and Tukey's Studentized Range Test were performed. During the change of direction, the head rotates less than the trunk and pelvis; and has an earlier onset time than the trunk and pelvis. There was no significant difference in angular rotation in between the three relative to each other. There was no distinguishable difference in angular velocity between the three segments during turning of the whole 2 cycle of the MFE. There were also no significant differences between the segments when comparing counter-clockwise and clockwise directions. Also there is no relationship between the amount of overstep and time to complete the task. These results suggest PD subjects displayed signs of axial rigidity and en-bloc turning while walking two cycles of the MFE tasks. The slowness of movements reflects upon signs of bradykinesia. Therefore, rehabilitative approach may be needed to respond to the turning difficulty.

**KEYWORDS:** Parkinson's disease; modified figure of eight; walking; turning

# TABLE OF CONTENT

ABSTRACT

TABLE OF CONTENT

LIST OF ABBREVIATIONS

1 INTRODUCTION .....	7
2 LITERATURE REVIEW .....	8
2.1 Parkinson's disease overview .....	8
2.1.1 What is Parkinson's disease? .....	8
2.1.2 Incidence and cost of Parkinson's disease .....	9
2.1.3 Who is susceptible to Parkinson's disease? .....	9
2.1.4 Symptoms and clinical feature of Parkinson's disease .....	12
2.2 Neurobiology and pathophysiology of Parkinson's disease .....	14
2.2.1 Neuroanatomy .....	14
2.2.2 The Circuit Organization .....	15
2.2.3 Molecular Metabolism of Dopamine .....	18
2.3 Treatments for Parkinson's disease .....	19
2.3.1 Levodopa Medication .....	19
2.3.2 Deep Brain Stimulation .....	20
2.3.2 Physical Therapy .....	20
2.4 Motor Control Difficulties .....	21
2.4.1 Falls and fall prediction of Parkinson's disease .....	22
2.4.2 Risk factor of falling .....	23
2.4.3 Consequences of falling .....	24
2.4.4 Axial body rotation while walking on a curved path .....	25

2.4.4.1 Deficits of axial body rotation while on a curve path .....	25
2.4.4.2 Walking in a Figure of Eight Pattern .....	34
3 PURPOSE AND HYPOTHESIS OF THE STUDY .....	38
4 METHODS .....	39
4.1 Subjects .....	39
4.2 Protocol .....	41
4.2.1 Measurements .....	41
4.3 Data Processing .....	45
4.3.1 Calculations for Peak Angular Displacement and Angular Velocity .....	46
4.3.2 Statistical Analysis .....	49
5 RESULTS .....	51
5.1 Whole Modified Figure of Eight .....	51
5.1.1 Angular Displacement .....	51
5.1.2 Angular Velocity .....	52
5.2 Counter-Clockwise vs Clockwise Direction .....	54
5.2.1 Angular Displacement .....	54
5.2.2 Angular Velocity .....	54
5.3 Overstep vs Time to Complete .....	55
6 DISCUSSION .....	56
6.1 Observed Results vs Proposed Hypothesis .....	56
6.2 Segmental Relationship During Whole Modified Figure of Eight .....	56
6.3 Counter-Clockwise vs Clockwise Direction .....	58
6.4 Overstepping .....	59
6.5 Limitations of Study .....	59

6.6 Practical Application and Future Studies..... 60

7 CONCLUSION ..... 61

8 REFERENCES ..... 62

## LIST OF ABBREVIATIONS

<b>BG</b>	Basal Ganglia
<b>DT</b>	Difficulty turning
<b>Caud</b>	Striatum Caudate
<b>EMG</b>	Electromyography
<b>FO8</b>	Figure of eight
<b>GPI</b>	Pallidum globus pallidus pars interna
<b>GPe</b>	Globus pallidus pars externa
<b>HS</b>	Healthy Subject
<b>HSD</b>	Tukey's studentized range test
<b>L-Dopa</b>	L-3,4-dihydroxyphenylalanine
<b>MFE</b>	Modified figure of eight
<b>MPTP</b>	1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine
<b>P</b>	Significance value
<b>PD</b>	Parkinson's disease
<b>PT</b>	Physical Therapy
<b>Put</b>	Putamen
<b>ROM</b>	Range of motion
<b>SNe</b>	Substantia nigra pars compacta
<b>SNr</b>	Substantia nigra pars reticulata
<b>STN</b>	Subthalamic nucleus
<b>UPDRS</b>	Unified Parkinson Disease Rating Score

## 1. INTRODUCTION

Parkinson's disease (PD) is a common progressive neurodegenerative disorder that can be accurately diagnosed. Histological postmortem examination of the brains of the patients with PD characterized by the presence of severe pars-compact nigral-cell loss; decrease in the dopamine content of the striatum (more pronounced in the putamen) due to the degeneration of the nigrostriatal connection; and accumulation of aggregated  $\alpha$ -synuclein in specific brainstem, spinal cord and cortical regions (Latash 1998, pp 221-228; Lee et al. 2009). PD is characterized by four main cardinal signs: tremor, rigidity, bradykinesia, and postural reflex impairment (Muller et al. 1997; Kiernan 2005, pp 211).

Parkinson's disease has shown to be a neurodegenerative disease with a fast progression of motor disability, reaching Hoehn and Yahr stage 5, which is a bedridden state, usually after 10-14 years (Maetzler et al. 2009). One of the most troubling features of PD is postural instability leading to an increased susceptibility to falls (Wood et al. 2002). Therefore, understanding the biomechanical factors associated with postural instability in this population represents an important public health implication.

Even though the vast majority of PD gait research is on straight line walking, the ability to turn during walking is an integral part of functional locomotion (Morris et al. 2001). Falling while turning produces a high risk of hip fracture as the femur is exposed to a forceful impact. (Cumming & Klineberg 1994; Stack and Ashburn 1999).

The use of Modified Figure of Eight walking test in this study further represents the complex motor skill required to adapt to changes in the environment, such as circular walking while turning. The coordination of head, trunk, and pelvis movements during walking, changing directions, and turning full circles of modified figure of eight were studied. Such multitasking curved walking that requires gait adaptation maybe related to an increase in biomechanical challenges for the different segmental system, especially in the elderly and population with neurodegenerative diseases.

## **2. LITERATURE REVIEW**

### **2.1 Parkinson's disease overview**

PD is characterized by a slow degeneration of neurons, particularly in the mesencephalon of the brain. The causes are not clearly known but risk factors have been discovered. PD causes motor and non- motor (cognitive and limbic) deficits.

#### **2.1.1 What is Parkinson's disease?**

Parkinson's disease (PD) is the second most common neurodegenerative disease, after Alzheimer's disease, within the aging population (Nussbaum and Ellis 2003). The pioneer of PD, Dr. James Parkinson defined PD in his monograph, *An Essay on the Shaking Palsy* as "involuntary tremulous motion with lessened muscular power, in parts not in action even when supported with a propensity to bend the trunk forward and to pass from a walking to a running pace." (Parkinson 1817; Kempster et al. 2007). The understanding of the motor control and biology of PD has been advancing rapidly over the past 3 decades (Korczyn and Gurevich 2009). Biochemical and histochemical research in the 1960's has provided the basis for the modern therapy. The normally high concentrations of dopamine in the substantia nigra and striatum are greatly reduced in patients with PD (Kiernan 2005, pp 211), resulting in disabling motor manifestation. PD may also affect regions of the brain that regulate involuntary functions such as blood pressure and heart activity.

Genetic research has identified several genes that are responsible and associated to the development of PD. Currently there are 8 defined loci identified to be associated with high penetrant autosomal dominant or recessive PD, and there are 6 out of 8 mutations in the loci (Lee and Liu 2008). The 6 mutated genes are alpha-synuclein, parkin, UCH-L1, PINK1, DJ-1 and LRRK2/dardarin (Hofer and Gasser 2004; Shiba and Hattori 2004; Hardy et al. 2006; Tan and Skipper 2007; Lee and Liu 2008).



### **2.1.2 Incidence and cost of Parkinson's Disease**

In Europe, epidemiology studies have shown the prevalence and incidences rates for PD of approximately 108-257/100 000 and 11-19/100 000 per year, respectively (Von Campenhausen et al. 2005; Lindgren et al. 2005). The median age of onset is 60 years and the mean duration of the disease from diagnosis to death is 15 years, with a mortality ratio of 2 to 1 (Katzenschlager et al. 2008). Overall cost estimates vary from country to country, but the largest component of direct cost is typically inpatient care and nursing home costs, while prescription drugs are the smallest contributor (Findley 2007; Vossius et al. 2010). In Finland, the total cost of illness for PD outpatients was EUR 118 million, including the direct costs of EUR 49.2 million (Keränen et al. 2003). Such costly disease causes strains and effects both to the patients and on society as a whole. With the increasing proportion of the aging population in developed countries, motor function and disability of PD worsened significantly with time and neither definite curative or preventative treatment has been identified. As a result, PD patients have a decreased quality of life, face an increased risk of dementia, institutionalization and death (Elbaz 2007). Therefore, further research is required to understand the motor control pattern of PD patient, in order to provide for them a better treatment in the future.

### **2.1.3 Who are susceptible to Parkinson's disease?**

The risk factors for getting PD are age, gender, heredity, race (ethnicity), and exposure to environment/toxins. One study (Conley and Kirchner 1999) showed that the mean onset age of PD is between 55-60 years. In other studies (de Rijk et al. 1995; Bower et al. 1999) it was shown that the incidence of the disease rises steeply with age, from 17.4 in 100 000 person years between 50 -59 years of age to 93.1 in 100 000 person years between 70-79 years, with a lifetime risk of developing the disease of 1.5%. The incidence rapidly increased over the age of 60 years, with only 4% of the cases being under the age of 50

years (Stephen et al. 2003). Parkinson's disease occurs more in male than female, as shown in Figure 1.

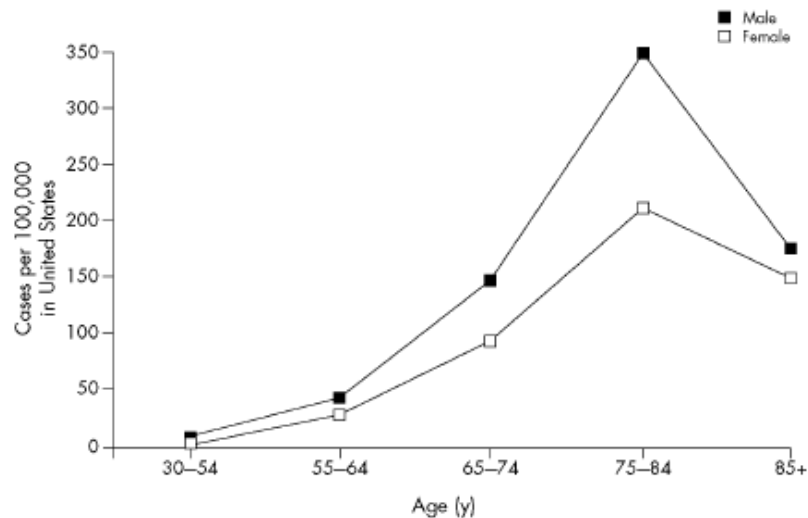


FIGURE 1. Incidence of Parkinson's disease at various age groups (Rajput et al. 1984)

In one epidemiological study, the rate of men (19.0 per 100,000) was 91% higher than that for women (9.9 per 100 000) (Stephen 2003). Some studies suggest that in women, the development of PD may be delayed due to higher physiological striatal dopamine levels. This could possibly be due to the activity and neuroprotection of oestrogens (Haaxma et al. 2007; Shulman 2007).

The inheritance pattern is still unknown, however epidemiological studies have revealed that family history has its contribution (Broussolle et al. 2002). Twin studies show a concordance rate of 10.5% in monozygotic and 10.8% in dizygotic twins, indicating against a major genetic basis for PD (Rajput et al. 1997). A study (Autere et al. 2000) on the familial aggregation of PD in a Finnish population was investigated. A family history was obtained on 268 patients with PD and 210 controls ascertained from the population of the province northern Finland. It was found that there was a crude segregation ratio of 0.27 for the siblings and 0.17 for the parents suggesting that recessive inheritance may be more common than dominant inheritance among Finnish patients with PD. However, it is also suggested that both genetic inheritance and sharing of common environment in the same

family can also explain the increased risk of PD, compared with familial aggregation studies (Logroscino 2005).

Data suggested that the incidence of PD varies by race/ethnicity of different parts of the world. With age-and gender adjusted rate per 100,000 was highest among Hispanics (16.6), followed by non-Hispanics Caucasians (13.6), Asians (11.3), and Africans (10.2) (Stephen et al. 2003). There is no significant difference in PD prevalence among four European countries (France, Italy, Spain and The Netherlands) (de Rijk et al. 1997; de Rijk et al. 2000). In one study (Schoenberg et al. 1988), it was suggested that the prevalence of PD is lower in Africans compared to African Americans, suggesting that environment could be a risk factor.

Previous epidemiological studies have linked environmental factors with increased risk of PD incidence, which includes rural living, farming, drinking well water, and exposure to agricultural chemicals (Tanner et al. 1989; Balklreschi et al. 2003; Elbaz et al. 2007). However, pesticide exposure has received the most attention due to the implications of widespread use of such agents on global public health risk. A number of pesticides have come under scrutiny regarding their potential neurotoxic actions resulting in the development of “environmental hypothesis of PD” (Drechsel et al. 2008). The discovery of the exposure of MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) has triggered studies on the relations between pesticides and PD development (Elbaz et al. 2007). In the early 1980’s, MPTP was identified as a chemical agent responsible for producing severe parkinsonian syndrome in a cohort of young adult drug users (Langston et al. 1983). Exposure to this synthetic environmental agent could produce an irreversible form of PD (Drechsel et al. 2008). MPTP is a neurotoxin that selectively transported into dopaminergic neurons and is metabolized to MPP+, a potent mitochondrial complex 1 inhibitor (Elbaz et al. 2007). MPTP has a close similarity to Paraquat, which is a widely used herbicide still available in many countries. (Elbaz et al. 2007). Studies have shown there is a neuroprotective effect of tobacco smoking, nicotine and caffeine (Lee et al. 2009). Some studies have shown there is an inverse relationship between the risk of developing PD and smoking (Gorrell et al. 1999; Elbaz et al. 2007; Elbaz et al. 2008). The brain monoamine

oxidase A is an enzyme that induces oxidative stress. It is inhibited in the brains of cigarette smokers (Fower et al. 1996), thus providing a neuroprotection, lowering the risk of developing PD (Lee et al. 2009).

### 2.1.4 Symptoms and Clinical Features of Parkinson's disease

PD is characterized by four main cardinal signs: tremor, rigidity, bradykinesia, and postural reflex impairment (Muller et al 1997; Latash 1998; Kiernan 2005). Table 1, describes that

TABLE 1. Description of the four cardinal signs of PD

Symptoms	Description	Physiological Reasoning
<b>Tremors</b>	Is characterized by 5-6 Hz alternating activity of antagonist muscles controlling a joint, leading to alternating joint movements that can be seen both at rest and during voluntary movements in the joint (Latash 1998). Tremor does not necessarily get worse with disease progression (Deuschl et al. 2000).	Caused by mechanical oscillations of a limb, enhanced reflexes, central oscillations or abnormally functioning feedback-loops within the central nervous system (Deuschl et al. 2000).
<b>Rigidity</b>	Is a sustained increase in the resistance to externally imposed joint movements (Latash 1998).	The pathophysiology of rigidity remains a matter of debate (Santens et al. 2003). The traditional view holds that a long loop reflexes originating in muscle spindles and running through cortical relays are at the basis of increased muscle tone. This is based on an increase in M2 response after voluntary movement. However this finding has not been accepted universally and do not fit the hypothesis of long loop reflex (Dewaide et al. 1990).
<b>Bradykinesia</b>	Usually refers to slowness of voluntary movements and difficulty in their initiation, although deficits in spontaneous and/or automated movements. It can affect any part of the body and be more or less generalized (Latash 1998).	PD patients have longer latency times before movements occur, they take longer before reaching appropriate forces to perform voluntary movements, and the movements are more frequently broken down in small steps, requiring multiple electromyography bursts to reach a target (Berardelli et al. 2001) (Fig 2). It is due to the changes in the basal ganglia (Santens et al. 2003)
<b>Postural Reflex Impairment</b>	It is a decrease in anticipatory postural adjustments and an increase in preprogrammed corrections in the activity of postural muscles associated with voluntary movements or in response to an external perturbation (Latash 1998).	Impairment leading to postural instability in PD, is slow force production necessary to counteract perturbations, which are characteristics of many movements (Hallett & Khosbin 1980; Stelmach et al. 1989).

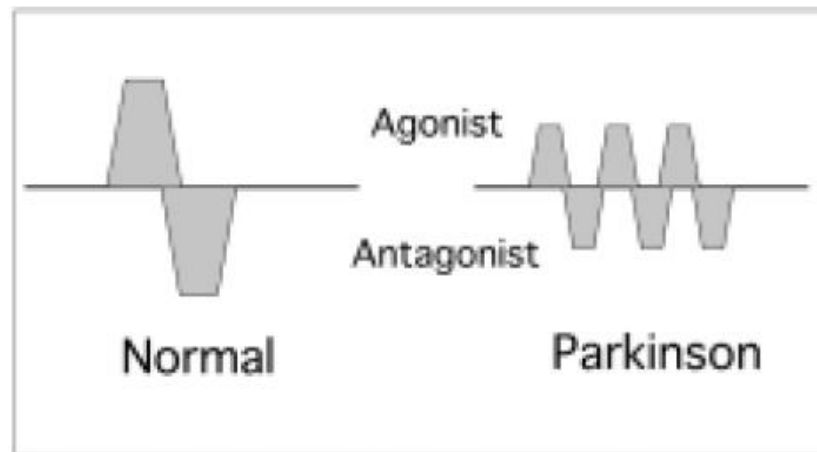


FIGURE 2. A schematic representation of EMG bursts in agonist and antagonist muscles during a reaching movement in normal controls and in PD. In normal controls the goal is reached by single agonist-antagonist mechanisms. In PD, agonist bursts are hypermetric, requiring multiple bursts to reach the target (scaling) (Berardelli et al. 2001).

PD commonly presents with impairment of dexterity or, less commonly, with a slight dragging of one foot. The onset is gradual and the earliest symptoms might be unnoticed or misinterpreted for a long time. Early motor symptoms can be subtle and easily missed. A change in a patient's writing can be present for several years prior to diagnosis (Lee et al. 2009). In the late stages of PD patients would demonstrate a poverty of movements addressed as akinesia (Latash 1998). As drawn in figure 3 by Lee et al. 2009, its typical symptoms manifest as a masklike and expressionless face, and difficulty in initiating movements such as arm swing when walking. All these features combined cause a shuffling of gait with a tendency to fall forward and difficulty in stopping (Kiernan 2005).



FIGURE 3. Drawing of a masklike face and flexed posture of a PD patient (Lee et al. 2009)

All dexterous movements are done slowly and awkwardly and assistance might be needed for dressing, feeding, bathing, getting out of bed/chairs, and turning in bed (Lee et al. 2009). Depressive disorder is the most common emotional symptom amongst the PD patients (Cummings 1992).

## **2.2. Neurobiology and Pathophysiology of Parkinson's Disease**

### **2.2.1 Neuroanatomy**

The basal ganglia (BG) is thought to play a role in the initiation of voluntary movements, facilitation of some motion (such as skeletomotor, oculomotor), suppressing some motion, and comparison of motor commands with feedback (Bartels 2009; Alexander and Crutcher 1990). It is also involved in various emotional and cognitive functions (Bartels 2009). The BG does not have direct output connections to the spinal cord, but their inputs arise

principally from diverse regions of the cerebral cortex. The output of the motor circuit is directed back to the prefrontal, premotor, and motor cortices through the thalamus (Kandel et al. 1996). The BG consists of interconnected nuclei that makes up the complex network of parallel loop as shown in figure 4: The striatum: caudate (Caud) and putamen (Put), the pallidum: globus pallidus pars interna (GPi) and globus pallidus pars externa (GPe), subthalamic nucleus (STN) and substantia nigra: substantia nigra pars compacta, (SNc) and substantia nigra pars reticulata, (SNr) (Kandel et al. 1996; Santens et al. 2003; Kiernan 2005; Bartels 2009).

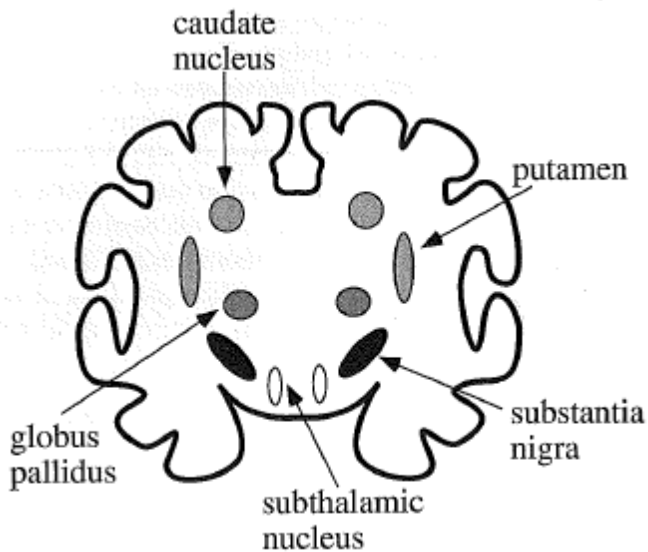


FIGURE 4. The Basal ganglia consist of five paired structures that include globus pallidus, putamen, caudate nucleus, subthalamic nucleus and substantia nigra (Latash. 1998).

### 2.2.2 The Circuit Organization

There are two basic pathways in the BG connectivity: direct and indirect. Both direct and indirect pathways originate in the matrix compartment of the striatum. Recently, it was suggested that a third pathway, originating in the strosomal compartment of the stiatum also exerts control over movements by means of its connections to the substantia nigra. This pathway therefore control dopamine release (Graybeil et al. 2000).

These two pathways have opposite effects on the output of the BG: The direct pathway has a net positive effect on the BG output, while the indirect pathway has a negative effect. Dopamine released from the striatal terminals has opposite effects on both pathways, resulting in a net release of thalamic output to cortical motor areas. In this way motor programs and inhibition of unwanted movements can be balanced to result in finely tuned motor behavior (Santens et al. 2003). Shown in figure 5 is a simplified diagram of the basal ganglia “motor circuit”, “direct” and “indirect” pathways (Alexander and Crutcher 1990; Delong 1990).

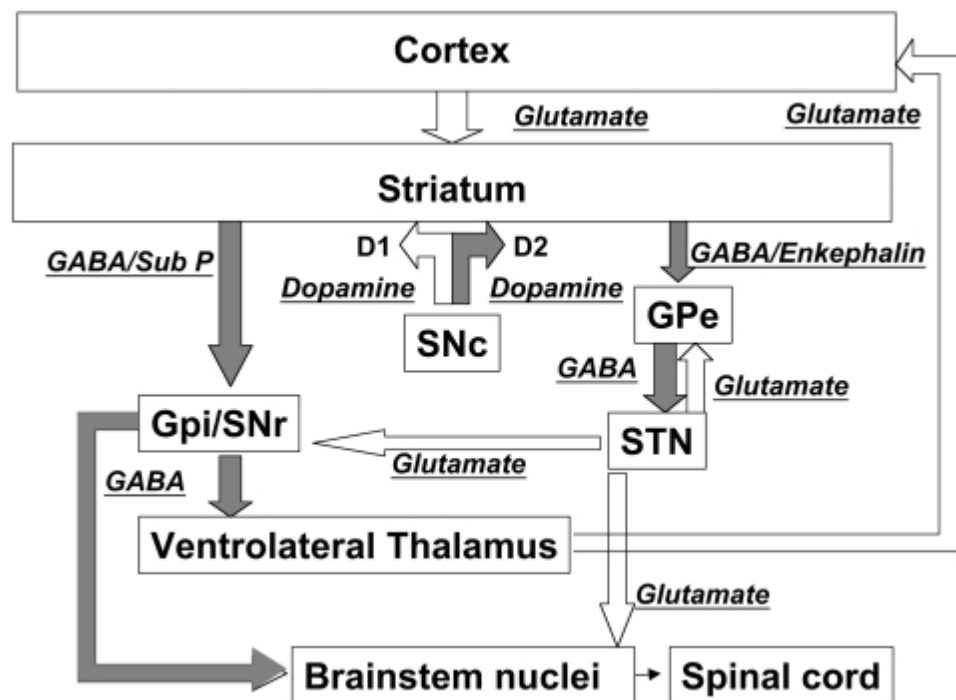


FIGURE 5. A schematic model of the circuitry and neurotransmitters of the basal ganglia as proposed by Alexander and Delong. White arrows indicate excitatory connection, dark arrows indicate inhibitory connection. Neurotransmitters involved in these connections are indicated in italics. The existence of two pathways, direct and indirect are indicated (Alexander and Crutcher 1990; Delong. 1990).

In the “direct pathway”, the neurons from the putamen project to the GPi and the SNr, the output nuclei of the BG. The neurons in this pathway would bear the Dopamine D1 receptors, and it co-expresses peptides substance P and Dynorphin. This pathway would



cause and direct inhibitory (GABA-ergic) effect on GPi/SNr neurons. Activation of this pathway reduces the inhibitory effect of the nuclei circuit on the thalamus (Alexander and Crutcher. 1990; Bartels 2009). As a result, it affects the facilitation of movements (Bartels 2009). The “indirect pathway”, connects the putamen with the output nuclei via the GPe and STN. The neurons contain D2 receptors. The circuit which passes to the GPe via striatal projection neurons that contains both GABA and Enkephalin. Connection from the GPe (a GABAergic pathway) projects to the STN, an output nuclei with excitatory glutamatergic projection. Stimulation of the GABA/Enkephalin from the striatal projection in the indirect pathway would lead to an inhibition of the GPe, disinhibition of the STN and the excitation of the GPi/SNr. The spontaneous discharge rate of most GPe neurons exerts a tonic inhibitory influence on the subthalamic nucleus. Activation of the inhibitory GABA/enkephalin, projection from the striatum tends to suppress the activity of the GPe neurons and would disinhibit the subthalamic nucleus, increasing the excitatory drive on the output nuclei and increasing the inhibition of their efferent targets within the thalamus. Thus resulting to an inhibitory effect on the thalamus and suppression of movements. (Alexander and Crutcher 1990; Bartels 2009).

In the direct and indirect pathway model, dopamine deficiency leads to reduced inhibition of the indirect pathway and reduced excitation of the direct pathway, with the net result of an excessive activation of the BG output nuclei (GPi and SNr) and inhibition of thalamocortical and brainstem motor systems, leading to parkinsonian motor features (Bartels 2009).

### 2.2.3 Molecular Metabolism of Dopamine

Dopamine is produced by neurons in the BG of the brain and has a key role in coordinating complex movements. Dopamine release is dependent on the prediction of reward of an action (Walters et al. 2000). The dopamine is produced from amino acid L-tyrosine converted into L-Dopa (Fahn 2008) by the enzyme tyrosine hydroxylase (Lawlor and During 2004). Unlike L-dopa, dopamine does not have the capability to cross the blood brain barrier. Therefore, the conversion of L-Dopa requires the enzyme aromatic amino acid decarboxylase to produce dopamine. In the brain, the enzymes involved in the catecholamine synthesis are transported from the cell body in the nigra into nerve terminals (Fahn 2008). Finally the dopamine, produced in the cytosol, would be sequestered into synaptic storage vesicles by the vesicular monoamine transporter 2 (Lawlor and During 2004). At the synaptic cleft, dopamine can act on both postsynaptic and presynaptic dopamine receptors. If there is an excessive amount of dopamine accumulated at the nerve terminal cytoplasm, the dopamine can be auto-oxidized into toxic products that could lead to neurodegeneration (Sulzer et al 2000; Fahn 2008). The dopamine can also be metabolized and inactivated by the enzymes, catechol-O-methyl transferase (COMT) and mono-amine- oxidase (MAO). COMT degrades the dopamine by incorporating a methyl group into catecholamine function. The MAO catalyzes the oxidative deamination of the monoamine group (Goole and Amighi 2009). Refer to figure 6 to show the synthesis and degradation of dopamine.

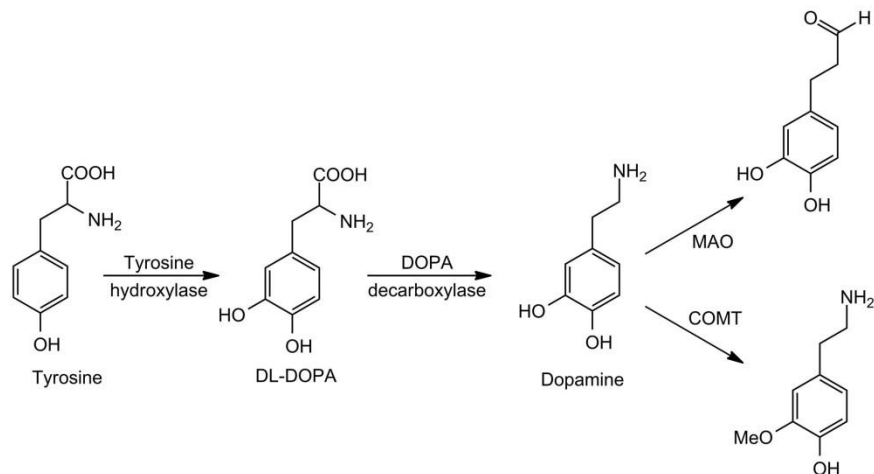


FIGURE 6. Synthesis and degradation of dopamine (Goole and Amighi 2009)

## **2.3 Treatments for Parkinson's Disease**

Since PD remains as an incurable progressive disease, treatment substantially improves the quality of life and functional capacity. The common treatments for PD would be medication, surgery, and physical therapy.

### **2.3.1 Levodopa Medication**

Since PD is a progressive loss of dopamine in the BG, the use of exogenous substitution with either dopamine agonist or dopamine's prodrug levodopa (L-dopa) would be used to correct the mechanical disorders during the early stage of the disease (Goole and Amigh 2009). L-dopa is an abbreviation for L-3,4-dihydroxyphenylalanine. It is a natural dopamine precursor that can cross the blood brain barrier. Trials on oral dopamine failed, leading to severe peripheral adverts, because dopamine cannot cross the blood brain barrier. Levodopa medication is considered to be the standard and most effective therapy in the treatment of PD (Fahn 2006). Therefore, is always the initial treatment. The clinical response to L-dopa can be seen over the first months to years of the treatment, and if there is a sustained improvement in the motor disability (Nutt et al. 1997). This medication has often improved symptoms like rigidity and bradykinesia (Lakke 1985).

Taking L-dopa improves Unified Parkinson Disease Rating Score (UPDRS) (Hauser et al. 2009). However, as the L-dopa treatment continued, most patients would develop motor fluctuations and motor disability that would vary during the day. The accepted explanation is that the response to each dose of L-dopa lasts brief duration from minutes to hours, becoming briefer during the long term L-dopa therapy. Therefore, parkinsonian signs re-emerge in between doses (Chase et al. 1989). Nevertheless, there is a de-sensitivity response to the long term drug therapy. The decrease in the duration of responsiveness to L-dopa is related to the progressive degeneration of nigral dopaminergic neurons and the loss of dopamine buffering, resulting in motor fluctuations known as dyskinesia and "on-off effect" (Antonini et al. 2010; Goole and Amighi 2009, Stocchi 2006; Direnfeld et al. 1978).

The “on off effect” is largely dependent on the dosage and the frequency of the administration of L-dopa. Therefore, modern research is focusing on strategies in slowing and targeting the release of L-dopa, in order to prolong the therapeutic effect and to reduce the amount of administrations (Goole and Amighi 2009).

### **2.3.2 Deep Brain Stimulation**

Deep brain stimulation is a surgical implantation of electrodes connected to an internalized neuro-pacemaker (usually programmable in amplitude, pulse width and frequency) into specific brain regions to provide symptomatic relief therapy (Benabid 2003). The goals of this technique are to be able to deliver continuous electrical stimulation to the neural brain structures. The electrodes are implanted in the pallidum, thalamus (ventralis intermedius thalamic nucleus) or subthalamic nucleus to produce a symptomatic relief (Panikar et al. 2003).

### **2.3.3 Physical Therapy**

Physical therapy (PT) treatment is often prescribed to PD. The role of PT for PD is to maximize functional ability and minimize secondary complications through movement rehabilitation (Deane et al. 2001). Exercise is useful adjunct to pharmacological therapy (Palmer et al. 1986). Pharmacological and neurological surgery may reduce the parkinsonian symptoms such as bradykinesia, rigidity and freezing, but it does not eliminate the symptoms (Kwakkel et al. 2007). Furthermore, taking medical therapy alone is less effective in improving coordination problems during axial body movements during locomotion. Studies have evaluated the effectiveness of physical exercise on the activities of daily living (De Goede et al. 2001; Crizzle et al. 2006; Yoursefi et al. 2009). The results concluded that the PD patient would gain benefits from physical exercise therapy in terms of positive impact on the activities of daily living. However, it does not mention about the neurological symptoms. Several other researchers have discovered individuals with PD

who have shown improvement in strength, aerobic capacity, muscle reaction time and functional characteristics of gait in response to rehabilitation (Bergen et al. 2002; Scandalis et al. 2001; Schenkman et al. 1998).

## 2.4 Motor Control Difficulties

PD has shown to be a neurodegenerative disease with a fast progression of motor disability, reaching Hoehn and Yahr (HY) stage 5, which is a bedridden state, usually after 10-14 years (Maetzler et al. 2009). During the progressive course of PD, most patients face mounting mobility deficits, which include difficulties with transfers, postures, balance, turning and gait control. This results in falls and fall related injuries. HY is a system used to describe the stages of symptoms in PD, as refer to table 2.

TABLE 2. The stages of Hoehn and Yahr scale (Goetz et al. 2004)

<b>Hoehn and Yahr Scale</b>	<b>Modified Hoehn and Yahr Scale</b>
1: Unilateral involvement only usually with minimal or no functional disability	1.0: Unilateral involvement only
2: Bilateral or midline involvement without impairment of balance	1.5: Unilateral and axial involvement
3: Bilateral disease: mild to moderate disability with impaired postural reflexes; physically independent	2.0: Bilateral involvement without impairment of balance
4: Severely disabling disease; still able to walk or stand unassisted	2.5: Mild bilateral disease with recovery on pull test
5: Confinement to bed or wheelchair unless aided	3.0: Mild to moderate bilateral disease; some postural instability; physically independent
	4.0: Severe disability; still able to walk or stand unassisted
	5.0: Wheelchair bound or bedridden unless aided

### **2.4.1 Falls and fall prediction in Parkinson's disease**

One of the most troubling features of PD is postural instability leading to an increased susceptibility to falls (Wood et al. 2002). Wood et al. (2002) attempted to accurately establish the incidence of falls in PD and to investigate predictive fallers. As a result, 68.3% of the subjects fell. Previous falls, disease duration, dementia, and the loss of arm swing were independent predictors of falling. There were also significant associations between disease severity, balance impairment, depression and falling.

Cole et al. (2010) compared the walking complexities between PD patients who reported falling during the 12 month follow-up and PD patients who did not fall. The results showed that PD patients had increased stride timing variability, reduced arm swing and walked with a more stooped posture than controls. Additionally, PD fallers took shorter strides, walked slower, spent more time in double support, had poorer gait stability ratios and did not project their center of mass as far forward of their base of support when compared with non-fallers. These stride changes were also accompanied by a reduced range of angular motion for the hip and knee joints. Relative to walking velocity, PD fallers had increased mediolateral head motion compared with PD non-fallers and controls.

Postural control problems, falls and fall related injuries are a common source of morbidity in elderly individuals, especially within the PD population (Dibble and Lange 2006). A review of several studies (Bloem et al. 2001; Grimbergen et al. 2004; Koller et al. 1989; Wood et al. 2002) estimated that up to 70% patients fall annually, 50% fall more than twice each year and 13% fall more than once weekly.

### **2.4.2 Risk factors of falling**

Identification of fall risk factors and modification of these risk factors allow the reduction of falls occurring to the elderly and PD patients. The risk of falling in the PD patients is approximately double compared to the community of elderly people (Canning 2009; Wood et al. 2002). During the early course of the disease, some degree of gait disturbances, including loss of arm swing, turning en-bloc, or shuffling, may be observed in the early stage of PD. However, recurrent falls are unusual in the initial stages (Wenning et al. 1999). Over a period of time, the patient develops to Hoehn and Yahr stage 2, where balance would be preserved. In contrast, Wood et al. (2002) had used a method to accurately establish the incidence of falls. It was concluded that certain PD subjects fall early in their disease. Bloem et al. (2001) used two different classifications of falls to describe the types of falls for the PD subjects: ‘intrinsic’ and ‘extrinsic’. From Bloem et al.’s (2001) analysis a fall usually occurs indoors for the PD subjects. Environmental hazards (extrinsic falls) cause only the minority of falls, as opposed to the high proportion of causes due to balance impairment disorder (intrinsic falls). Falling risk factors are summarized in Table 3. Falls are also most likely to occur when turns are made while performing a secondary task, such as talking or carrying an object (Ashburn et al. 2001)

TABLE 3. Falling risk factors for intrinsic and extrinsic (Ashburn et al. 2001; Gray et al. 2000; Robinson et al. 2005; Wood et al. 2002).

<b>Intrinsic falling risk factors in PD</b>	<b>Extrinsic falling risk factors in PD</b>
Osteoporosis	Loose rugs
mobility impairment (gait and balance)	Doorsteps
Sleep disturbances	Stairs
Rigidity	Unfamiliar environment
Bradykinesia	Poor lighting
Gait freezing	Improper footwear
Postural control disturbances	Low beds, toilets chairs
Impaired hand and foot motor function	Improper use of assistive device (e.g. canes and walkers)
Decreased arm swing during gait	
En bloc	
Transfer and rising	
Visual impairment	
Depression and anxiety	
Cognitive impairments	

### **2.4.3 Consequences of falling**

Falling can have catastrophic consequences. Falling resulting from postural instability has a huge impact on the health of the PD patient as a source of high morbidity and mortality. Patients affected by Parkinson's disease are at a high risk for fractures, mainly on the hip (Invernizzi et al. 2009). Johnell et al. (1992) had compared 138 PD patients with 138 age and sex matched non PD control group. The result was that the overall fracture rate at 10 years was 59% in the PD group and 44% in the control group. Moreover, 22.7% of the fractures in the PD group and 2.5% in the non PD control group were femoral neck fractures. Vertebral fractures in the PD group occurred more often, compared to the control group (Genever et al. 2005). As a final result, this would eventually lead to loss of independence, fear of falling, falling injuries, longer bed stay, and inactivity. Eventually,



this may result in social isolation, and an increase in further health risk, such as cardiovascular diseases and osteoporosis.

#### **2.4.4 Axial body rotation while walking on a curved path**

Walking is a common motor behavior in everyday life. Locomotion is a complex task that involves the coordinated activation of many muscles (Courtine and Schieppati, 2004). The process of walking is devoted to steering the body through space and sometimes through circuitous pathways (Courtine and Schieppati, 2003). During straight ahead walking, the symmetry of the body movements facilitates segment coordination. However, goal directed locomotion, such as that encountered in everyday life, often requires steering along curved paths. (Courtine and Schieppati 2004).

##### **2.4.4.1 Deficits of axial body rotation walking on a curve path with Parkinson's disease subjects**

Even though the vast majority of PD gait research is on straight line walking, the ability to turn during walking is an integral part of functional locomotion (Morris et al. 2001). Difficulty turning associated with freezing and falling (Bloem et al. 2001; Stack and Ashburn 1999; and Nieuwboer et al. 1998) is a characteristic of PD. At least two turns every 10 steps are used to perform daily activities such as going to the bathroom or making a cup of tea (Sedgman and Goldie 1994). Falling while turning produces a high risk of hip fracture as the femur is exposed to a forceful impact, particularly if protective reactions inadequately dissipate the landing force (Cumming and Klineberg 1994; Stack and Ashburn 1999). Research has been done to develop a clearer understanding about PD patients' turning strategies and characteristics.

The evaluation of turning while walking (Tinetti 1986; Thigpen et al. 2000) presents a methodological challenge in terms of defining beginning and end of the turn. Definitions are essential in order to count turning steps, time, and the maneuver reliably. Prescribing

where the turn should be made (marking a line or zone on the floor) restricts the subject's choice of how to complete the maneuver. In contrast to walking turns, "On the spot" turns (Tinetti 1986; Thigpen et al. 2000) have clearly defined start and end points, but there is another methodological weakness: The test is not especially balance demanding as the head stays over the base throughout the maneuver and is not representative of an everyday activity and focuses the subject's attention on turning alone. For people with PD who are temporarily better able to move when attending to a single task and/or under the facilitation of an external stimulus, the test is uninformative (Stack et al. 2004).

Crenna et al. (2007) conducted a study to analyze the corner turning while walking in a group of idiopathic PD patients specifically selected on the basis of motor clinical impairment and normal locomotive performance on linear walking. It is unclear, whether the turning difficulties were due to basic walking difficulties or axial rigidity. Crenna et al. (2007) tested (as shown in figure 7) the ability to turn in the early stages of PD, when the symptoms of the disease are mild and the locomotors and balance problems are negligible or absent. "Straight walking" and "walking and turning" were tested in patients and controls.

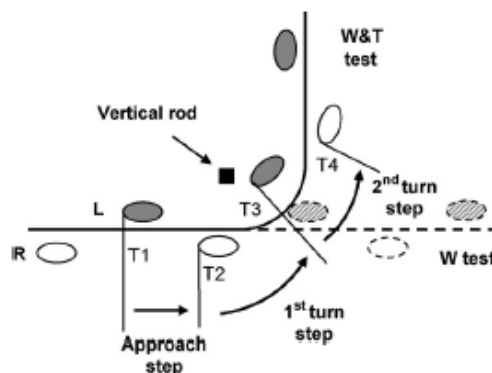


FIGURE 7. Schematic representation of steps during the walking and turning (W&T) test. T1-T2: approach step; T2-T3: first turn step; T3-T4: Second turn step. R: Right foot, L: Left foot- The straight walking (W) test is represented with dotted line (Crenna et al. 2007)

As a result of the study by Crenna et al. for straight walking there was no significant differences between the PD and control group in stride length and durations of stance. PD displayed normal range of motion (ROM) of the hip, knee and ankle joints in the sagittal

plane, normal trunk and pelvis excursions in all three planes, and no significant changes in the head trunk rotation in the horizontal plane compared to the healthy control. Compared to the age matched controls, PD patients turn with slower steps and took greater number of steps when completing a turn. PD displayed significantly reduced maximum head trunk relative rotation, as well as reduced head rotation after two turn step. Crenna et al. (2007) suggested that turning disturbances in mild PD are not necessarily related to basic locomotive deficits, axial rigidity or postural instability. However, they could be task specific pathophysiological mechanism effects. Neural mechanisms controlling turning are more susceptible to functional impairments associated with PD, compared with the structures supporting basal locomotor patterns and dynamic postural/balance control during linear walking (Crenna et al. 2007). However, in this study they did not specify whether the PD patients were “on” or “off” phase of the medication. The experiment had a precise protocol where the external foot is the right foot. If the dominant side of the PD patients were to be known, perhaps there may have been an effect on the turning. The gait cycle was defined based on the left and right heel strike, in order to calculate the head and upper trunk rotation. However, the rotation of the pelvis was not included in the calculation for the “walking and turning” but was included in the ROM “straight walking” calculations.

Stack et al. (2006) conducted a study with a home based experiment using an everyday task, such as making a cup of tea to investigate turning strategies for PD patients who reported turning difficulties. Video recording was used to tape the PD patients “on the spot” 180 degree turn (standard turn test) and an everyday task necessitating spontaneous turn (functional turn test). The group reported having difficulty in turning (DT group), appeared to be more unstable, lacked heel strike, used support, and took more steps, than the no DT group. PD patients took more steps to change direction than other groups. This finding was also supported by other literature (Tinetti 1986; Lipsitz et al. 1991; Simpsons et al. 2002; Hong et al. 2009). However, the methodology of using a single camera for recording provides only a single perspective, where essentially it ignores other perspectives that can be relevant to the study. The advantages of a home based study are the opportunity to capture more spontaneous turning movements; it enhances participation, and promotes an

informative performance. However, it would require a constant proper positioning of the camera, the wires may lead to trip hazards, and only a limited amount of data can be analyzed.

Guglielmetti et al. (2009) conducted an experiment that required the subject to walk along a linear and circular trajectory in a clockwise (CW) and counter-clockwise direction (CCW) for 1 minute. As shown in figure 8, step cadence was affected by walking condition, but not affected by group (PD vs. healthy subjects (HS)). The cadence was significantly lower during curved than straight walking; but no difference was found in CW and CCW. Figure 9 shows that there was a difference between the groups in travel distance. The overall distances travelled during straight walking by the PD patients were shorter than HS. The rotation of CW and CCW did not affect the difference in walking distance in either HS or PD. The distance during curved trajectory was shorter in the patients with PD than in HS (regardless of direction).

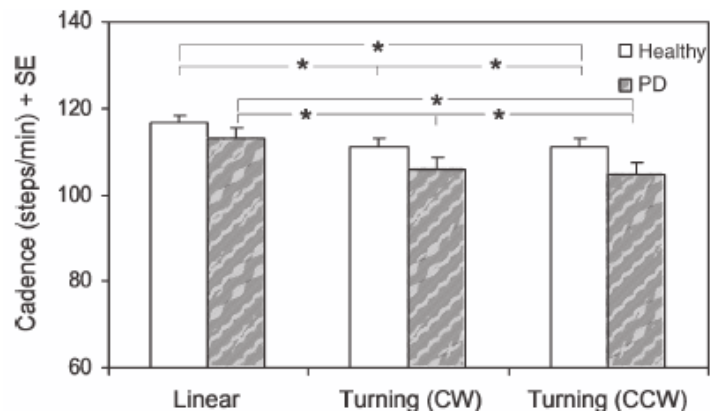


FIGURE 8. Average cadence during linear and curved walking in normal subjects and patients with PD (Guglielmetti et al. 2009).

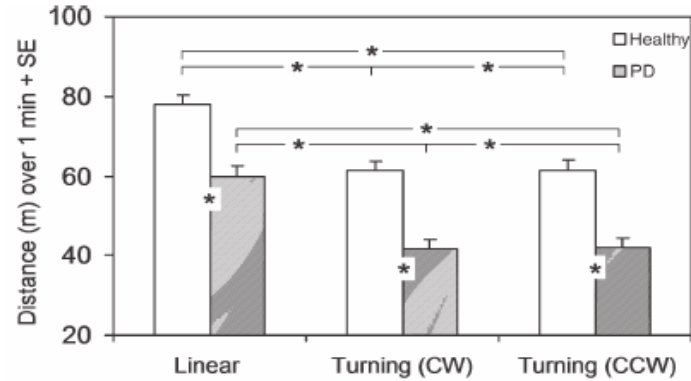


FIGURE 9. Average distance traveled during 1 minute linear and curved walking in normal subjects and patients with PD (Guglielmetti et al. 2009).

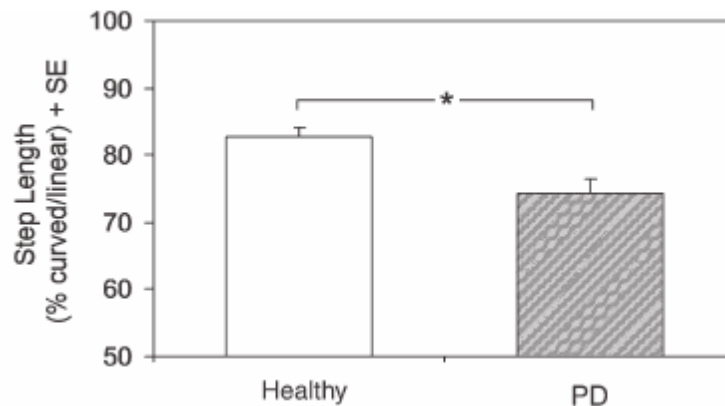


FIGURE 10. Average step length during curved walking (mean of CW and CCW direction) as percent of the length during linear walking (Guglielmetti et al. 2009).

Figure 10 shows that step length decreased significantly more in patients with PD than in HS during curved compared to linear walking. The study of Guglielmetti et al. (2009) is one of the few studies that has compared different types of walking direction (e.g. linear walking, CW, CCW) in order to further understand the characteristics of continuous circular walking. This is a good initiative to start understanding more about continuous circular walking characteristics for patients with PD. However, further research is needed, such as looking from a kinematics point of view to provide a wider understanding of continuous circular walking characteristics for people with PD.

There are several studies that have had healthy young and older people engage in a craniocaudal sequence of movements to turn while walking, with head rotation leading the

trunk, then pelvis rotation in the yaw plane to orient the body toward the new direction (Patla et al. 1999; Fuller et al. 2007; Hong et al. 2009; Hong et al. 2010). To compare in-place turning between PD (after medication stopped="off" phase") and unimpaired people, Hong et al. (2009) used yaw rotation onset times for the head, trunk, and pelvis, as well as the amplitudes of relative yaw rotation angles between different segments, and the EMG (electromyography) onset time of the muscle in the lower extremities. As a result, Figure 11 shows that in the unimpaired person the craniocaudal sequence of movement is evident, whereas in the person with PD, it is difficult to distinguish the order in which the different segments started turning. It also shows that PD patients took more steps and took longer time to complete the turn. The amplitude of yaw rotation at the head, trunk, pelvis and foot were significantly different between the two groups, as shown in Figure 12. The lower extremity muscle activation patterns appeared similar between groups.

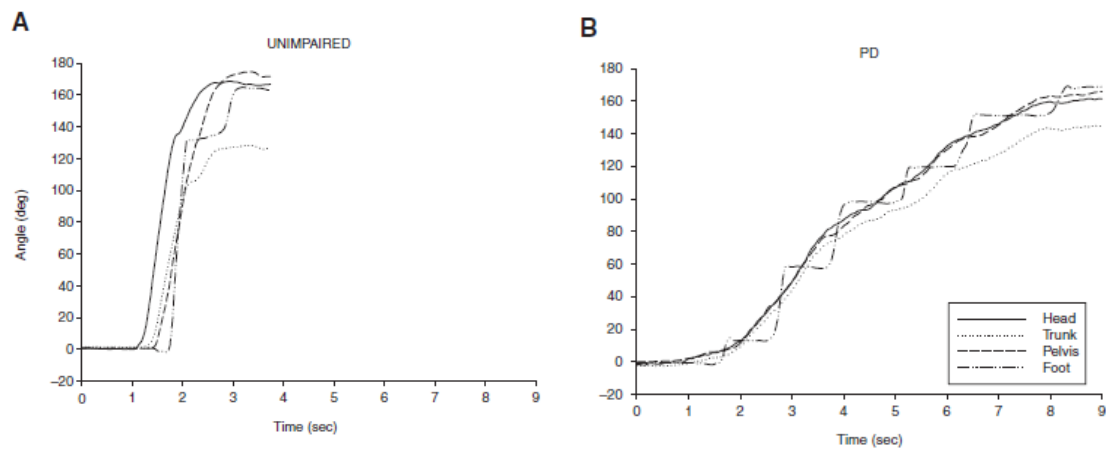


FIGURE 11. Kinematic plots of transverse plane angles for different segments for unimpaired person and PD patients as they turn 180 degrees (Hong et al. 2009).

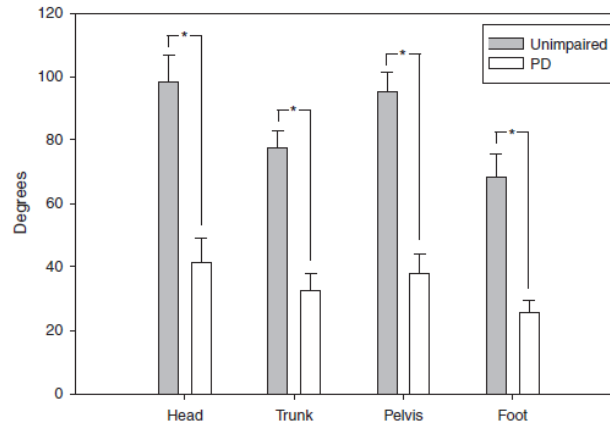


FIGURE 12. Comparison of amplitude of absolute yaw rotation angles for the head, trunk, pelvis, and starting foot for unimpaired and PD groups (Hong et al. 2009). Note: \*indicates statistically significant differences between 2 groups (all  $P < 0.001$ ). Error bars indicates the standard error.

The method of controlling the effect of medication is crucial because medication can mask disease symptoms. Medicated patients introduce unwanted variability because each individual takes different medications in different combinations and different dosages (Hong et al. 2009). However, in the study only the muscle activation of the lower extremities was taken. There would be more data available if the upper extremities were included as well. For this study, examining both kinematics and EMG together, may provide too many variables of measure and may appear to have lack of focus for the main purpose of the study, unless EMG was used to provide a supportive finding for the kinematic. However, for this study it was not.

Akram et al. (2013) examined the effect of PD on segment coordination (head, shoulder, pelvis, and foot movements) when turning during the “off” and “on” medication state.  $45^\circ$  and  $90^\circ$  angle turns were examined to determine whether disruptions to coordination are exacerbated with increased turn magnitude. The angular displacement and angular velocity of each segment were compared. The result was that both healthy control and PD patients “off” displayed a top-down sequence of segment reorientation, but differed with respect to the delay time between the segments. PD “off” medication has a shorter delay between the onset of the head and shoulder reorientation and had displayed a longer time delays for pelvis and foot reorientation (as shown in figure 13). Also, the peak angular velocities of all the segments were lower for the PD patients than for the healthy control group, with greater

differences between the two groups as the turn gets larger, as shown in figure 14. The velocity and magnitude, as shown in figure 15 of all the segments were greater during larger turns ( $90^\circ$ ), but the relative timing of reorientation of segments remained the same in both turns ( $45^\circ$  and  $90^\circ$ ). The Functional Axial Rotation scores reveal that medications had no significant effect on the timing and sequence of the segments reorientation (Akram et al. 2013).

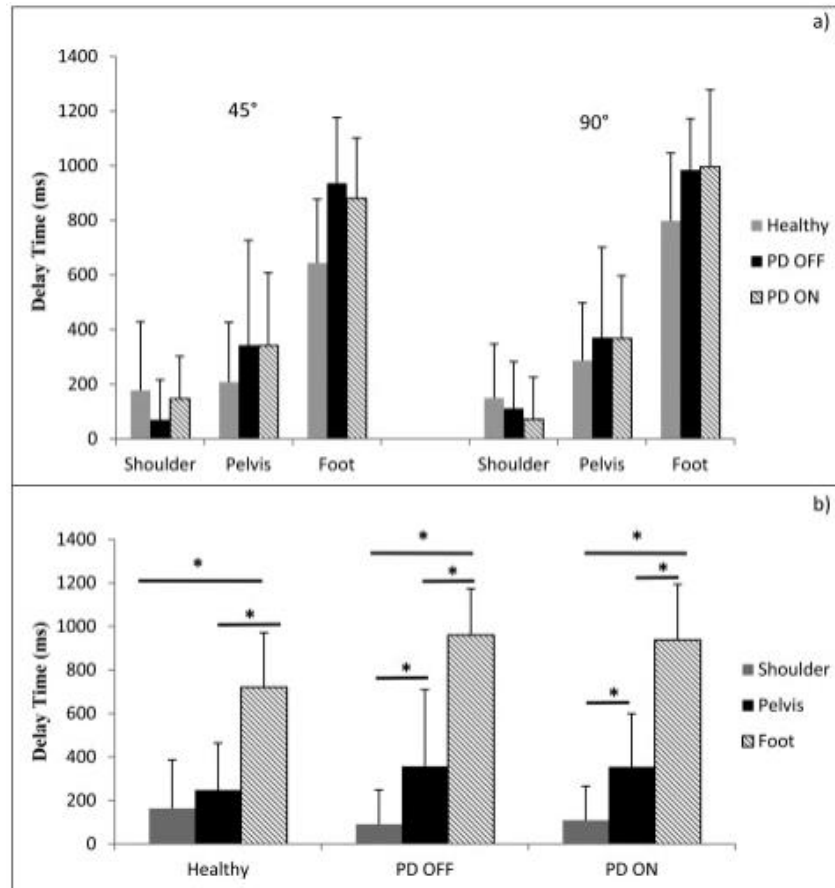


FIGURE 13. Mean and standard deviation (error bars) of the delays in initiation of reorientation of shoulder, pelvis and foot during  $45^\circ$  and  $90^\circ$  turns for healthy control and PD patients “off” and “on” medication (a). (b) shows each segments averaged across the two magnitudes for healthy control and PD patients “off” and “on” medication. Stars represents significant differences (Akram et al. 2013).



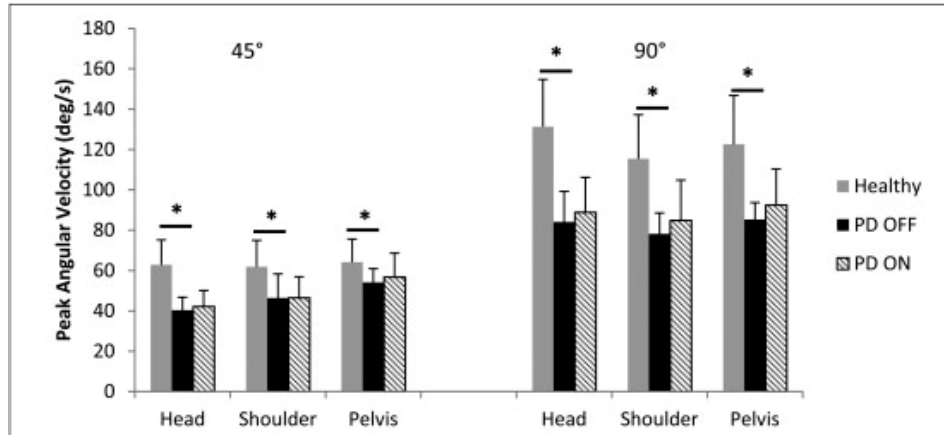


FIGURE 14. Mean and standard deviation (error bars) of the peak velocity of the segments (head, shoulder, and pelvis) during 45° and 90° turns for healthy controls and PD patients “off” and “on” medication. Stars represents significant differences (Akram et al. 2013).

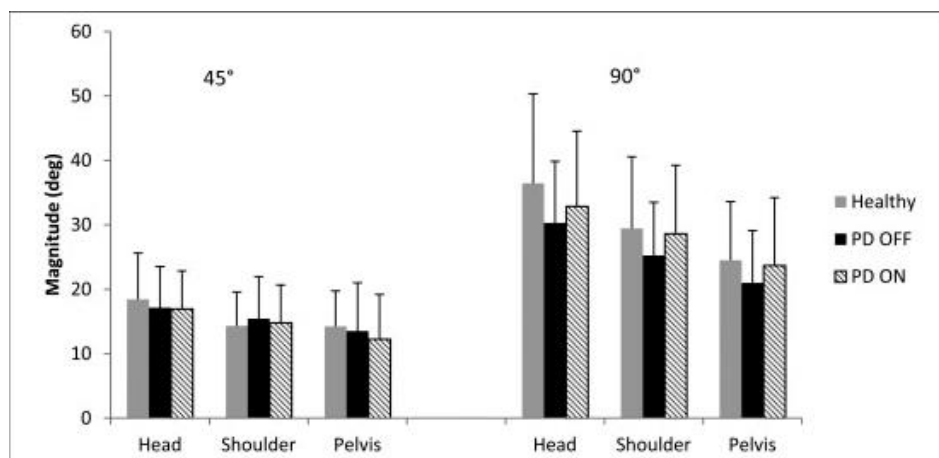


FIGURE 15. Mean and standard deviation (error bars) of the amplitude of the segments (head, shoulder, and pelvis) turn at the time of the onset of the foot reorientation during 45° and 90° turns for healthy control and PD patient “off” and “on” medications (Akram et al. 2013).

Due to the limited amount of space, the data collected in this study was limited to only right turn trials. If both side turns had been collected, it would have provided a greater picture whether the dominant side had an effect.

#### 2.4.4.2 Walking in a Figure of Eight Pattern

Previous studies have shown that curve walking is a difficult motor skill for older adults. The figure-of-eight (FO8) is a new experiment setting. It requires the ability to walk slightly in a lateral direction to both sides in an eight in combination with a narrow step width (Johansson and Jarnlo 1991). To assess balance control during turning before and after training program for the elderly subjects, Johansson and Jarnlo (1991) first constructed a FO8 test task. The FO8 tests walking capacity in different directions, to avoid abrupt turns and to correct gait in combination with a small step width. The 10-m FO8 comprised of two circular paths, each 150 mm wide with an inner diameter of 1.5 m and an outer diameter of 1.65 m, as shown in Figure 16.

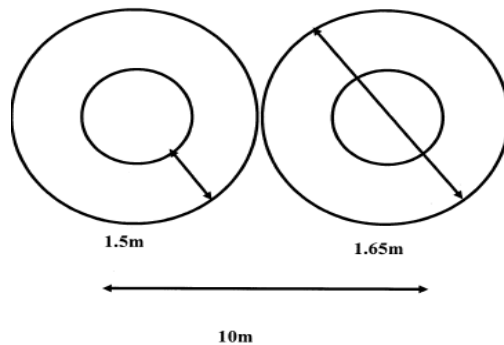


FIGURE 16. Walkway of figure of 8 walking task (Shkuratova et al., 2004)

Johansson and Jarnlo (1991), asked the subject to walk the FO8 twice at a given speed of 52 steps per minute. The number of steps made outside the FO8 was recorded. As a result, the subjects had improved significantly in the FO8 test post training. The specified speed was changed to a comfortable walking speed by Frandin et al. (1995).

To test for the effect of age on balance control during walking, Shkuratova et al. (2004) had used the same design as described by Johansson and Jarnlo (1991). However, two different tasks were used for the FO8 walk; 1) Uni-task: figure- of- eight walking at preferred speed and 2) Dual-task: figure-of-eight walking while performing a secondary motor task. For the first task, the subjects were instructed to walk within the FO8 in a CW direction at a comfortable speed when instructed “go” and not to step on or over the blue lines. For the second task, the subjects were instructed to walk within the FO8 in a CW direction, same as

the first task, except this time they were required to concentrate on a coins task while walking. Subjects would try to transfer as many coins as possible from the right to the left pocket using right/left hand. Straight walking task was done as well in this study to compare with the FO8 turning uni-task. As a result, all subjects (young and older) decreased their walking speed, stride length and cadence when changing from straight line walking to walking and turning FO8 uni-task walk.

When changing from uni-task to dual task FO8 walking all subjects walked with shorter steps, and the older group walked with a higher cadence. However double limb support and the duration of the walking speed was unchanged. The use of FO8 walking test in this study further represents the complex motor skill required to adapt to changes in the environment, such as circular walking while turning. Such gait adaptation for curved paths may be difficult for older adults with mobility problems (Hess et al. 2010). However, Shkuratova et al. (2004) only asked the subject to walk in a CW direction. If the study had included the subject to walk from counterclockwise (CCW) to clockwise (CW) direction it would provide more difficult maneuvering. And it would provide more characteristics of continuous circular walking as each direction has its different characteristics. For circular walking in a CCW direction, medial balance (center of mass distributed over the medial aspect of the foot) is the predominant pattern for the outer foot. Walking in a CW direction results in balance over the lateral aspect of the inner foot, whereas for straight path walking balance is more equitably shared by the medial and lateral aspect of both feet (Kiriya et al. 2005). Therefore, such gait adaptation for circular path walking can be difficult for elderly adults with mobility difficulties.

Also in the study of Shkuratova et al. (2004) the number of oversteps outside the FO8 was not taken. Counting the number of oversteps is essential because it may indicate some learning effect (Lindmark et al. 1999), lower ability to perform the test due to moderate disability (Noren et al. 2001), cognitive decline (Pettersson et al. 2002) or other impairment. Also, majority of oversteps to the same side may be provoked by a sub-clinical vestibular asymmetry, which was found in about one third of a healthy population 62-92 years (Kristinsdottir et al. 1997). In order to make it easier to observe oversteps and still allow the

subjects to walk with a small step width, Jarnlo and Nordell (2003) developed a modified figure of eight (MFE), which has a 4 cm single broad line instead of two; and each loop has an internal diameter of 163 cm.

Jarnlo and Nordell (2003), investigated the test-retest reliability of the MFE and the validity between the MFE and four other balance performance tests (one legged stance, tandem stance, standing on foam, walking 30 meters at a comfortable and then maximal speed) within the healthy elderly women subjects. The result showed very high inter rater and very high test retest reliability. Thus, MFE can be regarded as a reliable measure of balance performance test for elderly people. Franzen et al. (2009) used the MFE test to conduct a study whether axial tone of the PD subjects was related to the functional performances such as MFE. It was found that there was a strong relationship between the neck tone and the MFE with PD subjects on levodopa treatment. However, improvement in the MFE with levodopa, and without improvement in the axial tone, suggests that the MFE is also constrained by bradykinesia and limb rigidity, which can be improved by levodopa (Franzen et al. 2009).

Hess et al. (2010) designed a FO8 walk test to validate it in older adults with walking difficulties. Speed (time for completion), amplitude (number of steps taken), and accuracy (a tight versus an overly wide curved path) were measured. Bivariate correlations for the FO8 with each variable (gait, physical function, and movement control and planning) were constructed to test for the validity of the FO8 walk test. Figure 17 is a schematic diagram of the walking path for the subject. The path requires walking on a curved path with alternating CCW and CW; and walking on a straight path between the curved paths. The alteration between straight and curved paths would require switching motor strategies, including biomechanical and movement control adjustments.

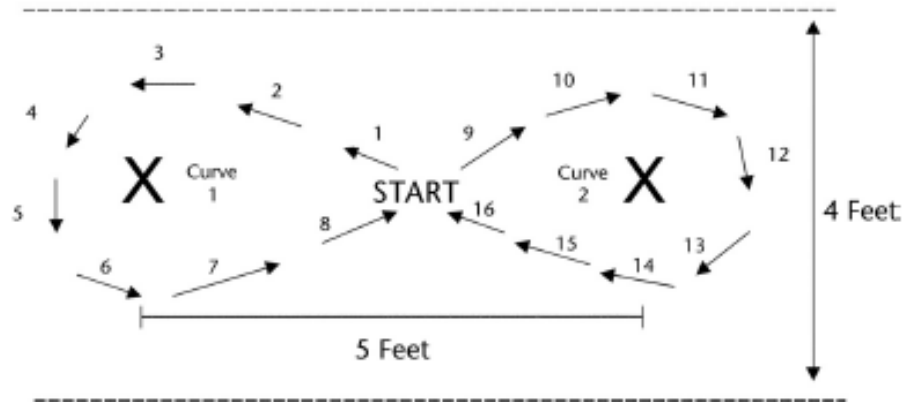


FIGURE 17. Figure-of-eight walk test design. Cons are represented by Xs. Arrows illustrate steps taken and the direction of the walking path. Numbers correspond to steps taken. (straight steps: 1,2,7,8,9,15,16); curve steps: 3,4,5,6,10,11,12,13,14 (Hess et. 2010)

There was a correlation between the FO8 walk test and each variable measured. All correlations were significant. Therefore, the result supports the validity of the FO8 as a measure of walking skill amongst the older adults with mobility disability.

### **3. PURPOSE AND HYPOTHESIS OF THE STUDY**

From the problems identified from previous literature, turning is problematic for people with PD. Knowledge of kinematics of the segmental system during walking and turning is helpful for the design of future clinical dynamic balance and gait testing, fall prevention devices and planning programs for the prevention for falls and fall related injuries in individuals with PD. Axial rotation is little investigated to this group and up to date no research has examined the coordination of head, trunk, and pelvis movements during walking, changing directions, and while turning full circles of modified figure of eight (MFE).

The purpose of this study was to examine the effect of Parkinson's disease on segment coordination when "ON" medication state; while performing a complex motor skill task of the MFE curvature walking task.

In normal walking, the head orientation gazes toward the direction of travel, followed by rotation of the trunk and pelvis. In healthy subjects, the magnitude of the head rotation during the first step is greater than the upper trunk and pelvis. Instability and turning difficulty in turning occurs, when the segments rotate almost simultaneously; and the amounts of rotation are not significantly different from each other. The first research question: Does the angular displacement differ between all three segments while performing the MFE walking task? We hypothesize there would be no significant differences in the angular rotation across the three segments. The second research question: Does the angular velocity differ between all three segments while performing the MFE walking task? We hypothesize there would be no significant differences in the angular velocity across the three segments. The third research question: Is there a relationship between the number of oversteps taken outside the MFE and the time to complete the task? We hypothesize that there would be no relationship. As the research hypotheses reflect, the PD subjects would be displaying turning difficulty and instability while performing the MFE task.

## **4. METHODS**

### **4.1 Subjects**

A total of 26 subjects, 10 males and 16 females ( $68 \pm 6$  years old) with a clinical diagnosis of “idiopathic” PD and undergoing treatments with L-Dopa, participated in this study. The PD subjects were recruited voluntarily through the Neurology Clinic at Karolinska Institutet and by advertisements on the Swedish Parkinson Association web homepage and newsletter. All subjects had no other existing neuromuscular disorders, including severely flexed posture. Disease severity and cognition were broadly quantified by the HY scale (Hoehn and Yahr, 1967) at the beginning of the study. The HY scale rates the PD patients from scale of 0 to 5, indicating the higher the score, the more severe the disease. Based on the HY scale, the subjects participated in this study were from stage I to stage II, indicating mild impairment. All the characteristics of the PD subjects are presented in Table 4. All subjects were provided with an informed consent and could withdraw from the study at will. The ethics of this study were approved by the regional ethics committee in Stockholm (2008/276-32), and conformed to Declaration of Helsinki (1964) requirements.

TABLE 4. Parkinson's disease subject characteristics

<b>PD subjects</b>	<b>Sex</b>	<b>Age (yrs)</b>	<b>Height (cm)</b>	<b>Body mass (kg)</b>
1	M	74	178	83
2	M	76	173	67
3	F	68	160	57
4	F	67	173	66
5	M	74	180	84
6	F	71	161	53
7	F	73	170	75
8	M	68	180	81
9	F	71	164	55
10	F	73	164	61
11	M	80	170	70
12	F	70	155	65
13	F	69	166	55
14	M	64	172	64
15	F	64	161	59
16	F	62	159	89
17	F	71	170	76
18	M	60	174	75
19	M	64	170	70
20	F	52	161	49
21	F	64	160	52
22	M	69	185	72
23	M	59	179	77
24	F	76	161	60
25	F	6	160	69
26	F	62	171	64



## 4.2 Protocol

### 4.2.1 Measurements

The PD subjects performed the clinical balance walk test “figure of eight”, which includes walking on a broad line of figure of 8 trajectory, which was marked on the floor (Jarnlo and Nordell 2003). Each loop was marked with a 4 cm wide tape, with an internal diameter of 163 cm, as refer to Figure 18.

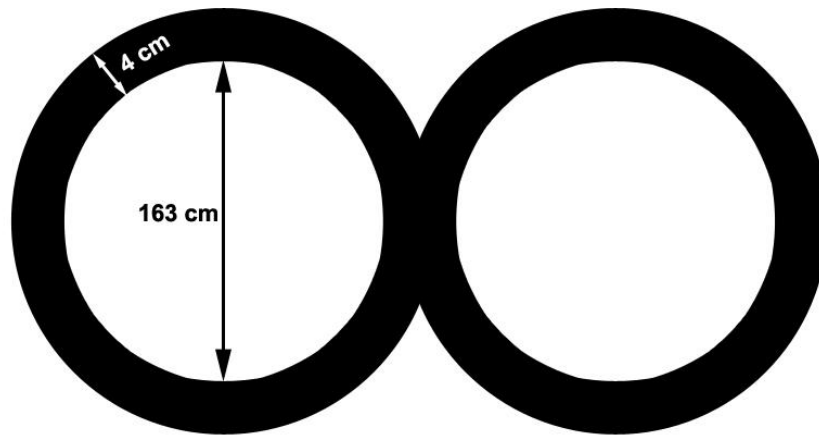


FIGURE 18. Figure-of-8 walk floor design

The kinematic data were recorded by an eight-camera (3-D) Elite motion analysis system (BTS, Milan, Italy) at a sampling frequency of 100 Hz. The margin of error for the 3-D motion capture system is within 0.8 mm. A total of 22 passive and retro reflective markers (diameter of 15 mm) were positioned on bony anatomical landmarks of each participant: 3 on the head (right head, left head, and top head), 4 on the trunk (right acromion, left acromion, right scapula, and C7), 5 for the pelvis (sacrum, right anterior superior iliac spine, left anterior superior iliac spine, right greater trochanter, left greater trochanter), 10 on the leg (right femoral condyle, left femoral condyle, right fibular head, left fibular head, right calcaneus, left calcaneus, right malleoli, left malleoli, right fifth metatarsal head, and

left fifth metatarsal head), refer to Figure 19. The extra marker on the right scapula was used for distinguishing the right and the left side during the labelling of the markers. The head markers were attached to a headband and the center marker was attached to the vertical stick of the head band for easier detection during the tracking process. The markers on the right and left anterior superior iliac spine were in some subjects hard to be detected by cameras due to the arm occluding the markers and also that the subjects were slightly bending forward during the task. In such cases the markers were moved to the right and left posterior superior iliac spine.

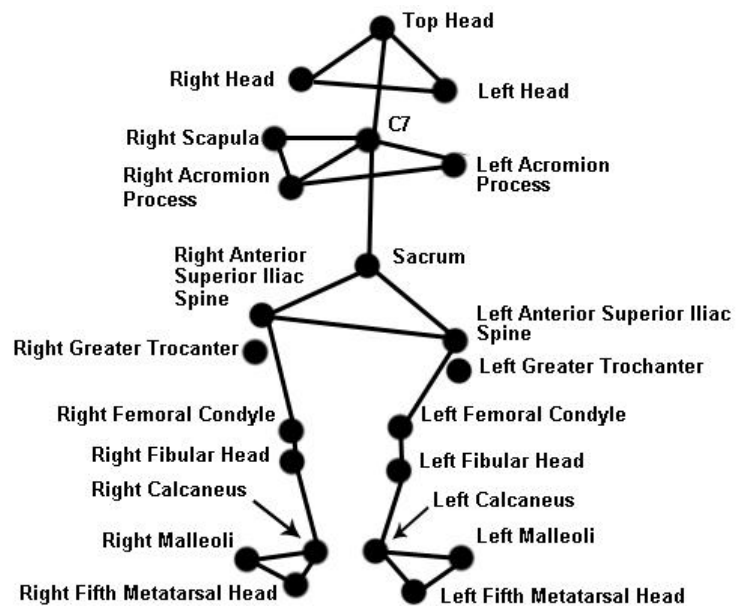


FIGURE 19. Model of the reflective markers positioned on 22 bony anatomical landmarks, as seen on the tracking system.



FIGURE 20. Photo of the reflective markers positioned on the PD subjects with pelvis reflector on the posterior superior iliac spine

The experimental measurements were conducted in the Motor Control Laboratory at Karolinska Institutet. During the experiments the PD subjects were “ON” medication. The PD subjects were asked to start from the center, between the two circles of the eight as the test describes. The subjects started walking in their own comfortable speed when the experimenter provided them the command “you can start to go”. From the middle of the eight, the subject would first walk in a counter-clockwise (CCW) direction around the first circle, cross the center, walk around the second circle in a clockwise (CW) direction, and end back in the center, see figure 21. The subjects were asked to walk around in two complete cycles in the figure of eight. The time to complete two full cycles were measured by a hand held stopwatch. If the subject stepped outside or inside the line i.e. the foot was not touching the 4 cm wide tape, it was measured as a clinical overstep as described by Jarnlo and Nordell (2003). Overstep is registered when no part of the feet touches the line. This task was repeated four times. The first trial was considered to be a practice training trial and was not used for the analysis.

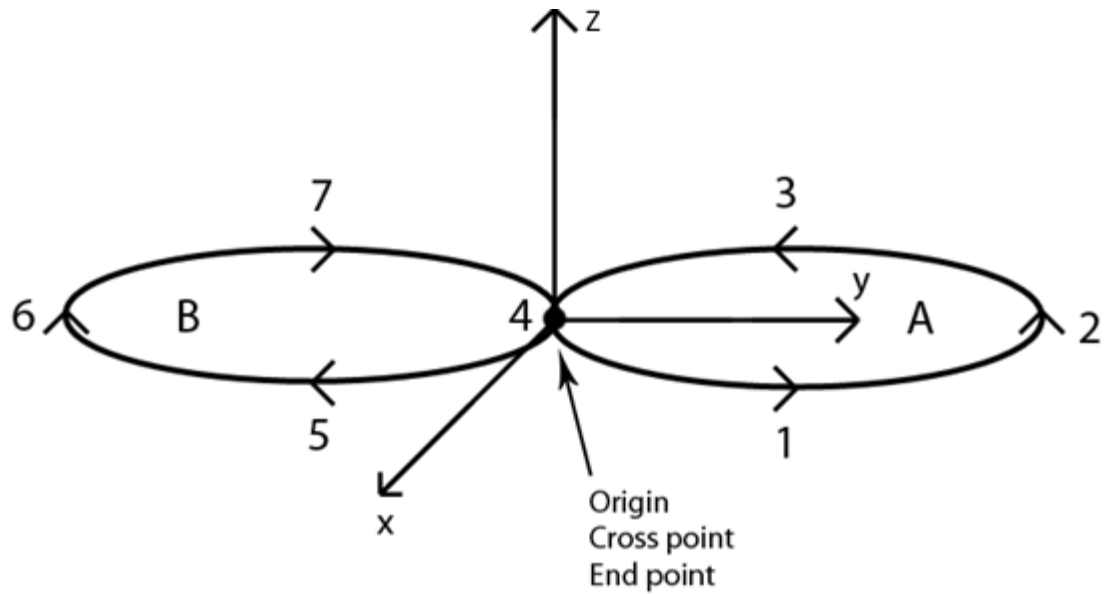


FIGURE 21. The direction of the Figure of Eight the PD subject had walked. The task starts from the center, around the first circle (A) in counter-clockwise (CCW) direction, cross the center, around the second circle (B) in a clockwise (CW) direction, back to the start position in the center. This completed in two cycles. The coordinate x is frontal or (mediolateral) axis, y is sagittal or (antero-posterior) axis and z is longitudinal or (superior-inferior) axis.

### 4.3 Data Processing

The key independent variables of interest are the angular rotation of each segment: head, trunk and pelvis. The motions of the three segments are determined from the angular displacement and the angular velocity. The head, shoulder, pelvis and foot movements were recorded to provide a more complete picture of segment coordination.

The Biomech Tracklab software was used to label each marker seen by the cameras. By using the model editor, we were able to make a reference model and label the reflective markers according to the names of the specific bony anatomical landmark. After tracking, we were able to obtain ASCII file of each trial of all the subjects. The data was returned as text file containing the x, y, and z coordinates of each marker in each time frame. The x and y are distances measured along two horizontal axes and z is the distance of the vertical direction. The coordinate x is frontal (or mediolateral) axis, y is (sagittal or antero-posterior) axis and z is (longitudinal or superior-inferior) axis. The text files were then imported into Matrix Laboratory (MATLAB) software (MathWorks, Natick, United States of America) and were then converted into mat files. All signal data were low pass filtered at 7 Hz using a second order Butterworth filter. Head, trunk, and pelvis angle were calculated by running through a programmed Matlab script. In the Matlab script, segmental angles were calculated from a number of each segments have been displaced.

If a marker was missing during the trial because the cameras were not able to see all of them, another reference marker on the segment was used for angle calculation (for example, if right acromion marker was missed by two cameras at the same time, the right scapula marker was used to calculate the trunk angle instead). Now, another script would be run to calculate the linear displacement of each segment. Top head marker provides the linear displacement of the head. The C7 marker would be used to provide the linear displacement of the trunk. The sacrum marker will be used to provide the linear displacement of the hip. A plot would be produced, marking 2 points on the graph to obtain the linear displacement. Another script was run to calculate the angular velocity during the gait cycle. By using feet markers, the coordinate data was cropped to the gait cycles, which

were defined from heelstrike to heelstrike. The toe replacement profiles were used to determine the onset of change in the mediolateral foot replacement for the right and left feet (Jog et al., 2003). Finally, the last script was run to obtain the linear and angular output components of each segment. Four outputs were: linear displacement, linear velocity, angular displacement and angular velocity. The linear displacement and angular displacement were calculated through the plot of the coordinates and the minimum and the maximum value of the displacement plot were cropped. Applying the minimum and maximum value to the script that was run for the segmental angle, the angular displacement was obtained. The minimum and maximum value of the velocity plot was cropped. The average velocity and variability were calculated from the cropped minimum and maximum value to calculate the angular velocity.

#### **4.3.1 Calculations for Peak Angular Displacement and Velocity**

In order to show how each segment rotates in relation to each other during the whole MFE, the peak angle displacement would be calculated. To see a more detailed description of how each segment moves during each change of direction, the counter clockwise and clockwise direction of each segment were compared. Figure 22 shows a graph of the angular displacement output containing two cycles. The average and the peak-to-peak values of the three segmental motions were computed for the entire duration of the two cycles.

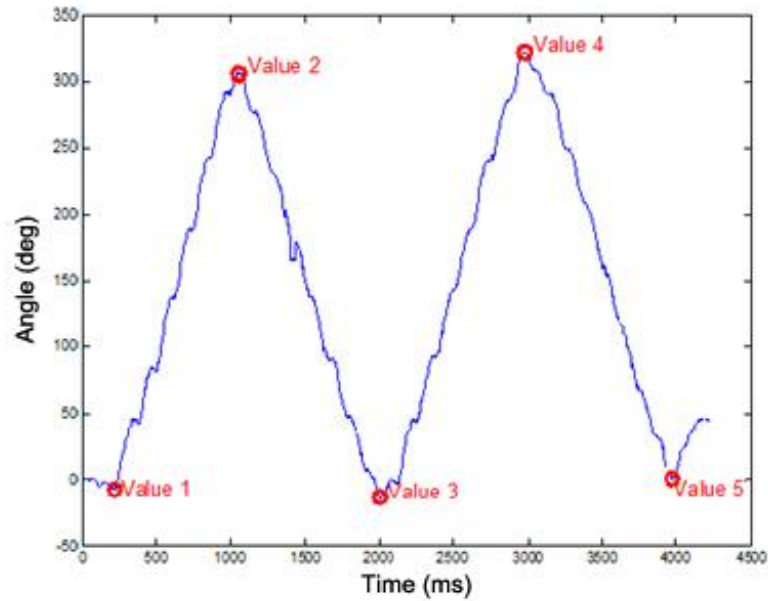


FIGURE 22. Graph of angular displacement output, containing two cycles. Values 1, 3 and 5 represent peak to peak angular displacement output in the counter-clockwise direction. Values 2 and 4 represent peak to peak angular displacement output in the clockwise direction.

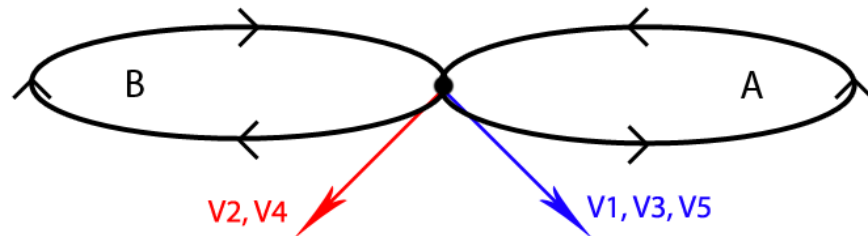


FIGURE 23. Graph of data points value 1 to 5: V1, V3, and V 5 represent the PD subject is at the origin facing to the direction of the blue arrow in the beginning of the figure of eight. Data points V2 and V4 represent the PD subject has walked half of the figure of eight and is now at the origin facing the direction of the red arrow.

The peak to peak value shown represents subject crossing the same point to change direction, this provides the maximum number of data points. The values of V1 to V5 represent the angle the PD subject faces when facing the origin as shown in figure 23. Values of V1, V3, and V5 represent the counter-clockwise direction (CCW) direction the subjects are walking. The V1 represents the origin. V2 and V4 represent the clockwise direction (CW) direction the subjects are walking. Data points at the end of the turn, before

the change of direction, were gathered and calculated using 3 different measurements (V 1,3,5) and 2 different measurements (V 2,4) of the same position. The reason to get the mean value of V1, V3, V5 and value of V2, V4 is to have the average data of the 2 laps. In order to calculate the peak absolute angular displacement of each segment during the whole two cycles MFE, the differences of the mean values of V2, V4 and values V1, V3 were taken. In order to observe how each segment moves, in relation to each other during the two cycle of the MFE, each segment were integrated into one graph. The graph shows the angular displacement of each segment in relations to time.

To get a detailed description of how each segment moves after each turn, CW and CCW turn of each segment was compared. In order to calculate the absolute angle of each segment when the PD subject is in origin, after turning CW or CCW, the absolute angle value difference of V2 and V1, V4 and V3 was taken to represent the CCW turn. The difference of V3 and V2, V5 and V4 was taken to represent the CW turn. From the differences, the mean of each segment during the CCW and CW turn was calculated. The statistics p-value for each segment was used, to compare the CCW and CW turn.

The angular velocity of each segment provides a more complete picture of segment coordination. Figure 24 represents the peak angular velocity graph taken from a head segment. The values were calculated with the peak mean and standard deviation of the values during each turn. Mean 1 and 3 represents the counter-clockwise turn. Mean 2 and 4 represents clockwise turn. In order to calculate the peak angular velocity of each segment for the duration of the whole 2 cycles of the MFE, the difference of mean (mean 1, 3 and mean 2, 4) was taken. The peak angular velocity of each segment during the CCW and CW turn was calculated and compared with the p-value. The differences of mean 2 and 1 represent the subject turning CW. The mean of the differences of mean 3 and 2, and mean 4 and 3 represent the subject turning CCW. In order to observe the angular velocity of each segment, in relation to each other during the two cycle of the MFE, each segment was integrated into one graph. The graph shows the angular velocity of each segment in relation to time.



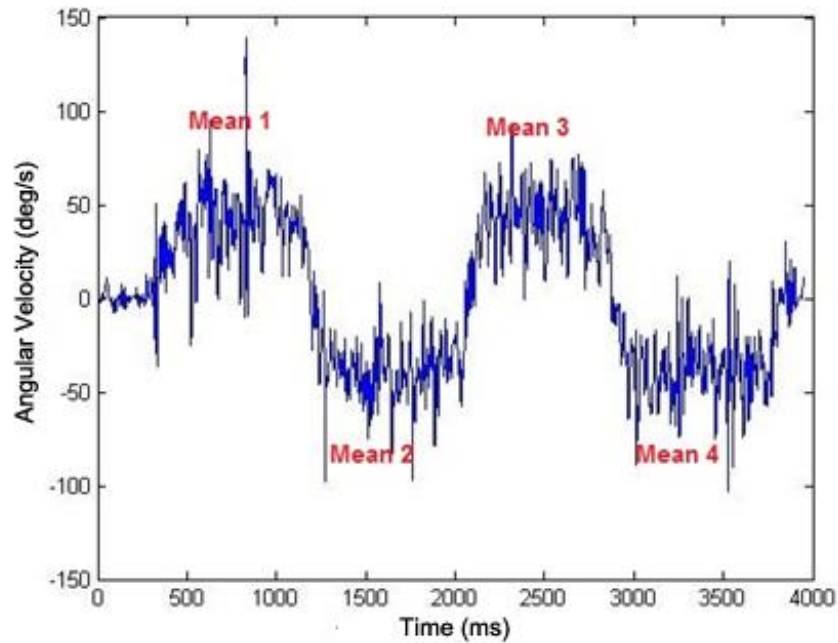


FIGURE 24. The peak angular velocity graph taken from a head segment. This graph represents how the values are calculated with the peak mean and standard deviation of the values during each turn. Mean 1 and 3 represents the counter-clockwise turn. Mean 2 and 4 represents clockwise turn.

### 4.3.2 Statistical Analysis

Statistica (StatSoft Inc, Tulsa, Oklahoma) was used to perform all the statistical tests. The data was checked to ensure that it was normally distributed in order to use the parametric statistical test. Due to the lack of main effect for gender and affected side, this factor was removed in further analysis.

#### WHOLE MODIFIED FIGURE OF 8

Data collected from the PD subjects were used to compare the angular rotation of the three segments during the whole two cycle of the MFE. One-way analyses of variance (ANOVA) were used.

## COUNTER-CLOCKWISE VS. CLOCKWISE DIRECTION.

CCW and CW of each segment was compared. This was done by using two-way analysis of variance ANOVA. A t-test was performed to compare each segment with CCW and CW in order to get a detailed description of how each segment moves after each turn.

## OVERSTEPPING

Pearson correlation between the time to complete the whole two cycles of MFE and overstepping the tape were completed to determine if there was a relationship between time and accuracy.

For conditions showing a main or interaction effect of a factor, Tukey's Studentized Range Test (HSD) was performed to determine which means were different from the others. A significance value (P) of less than 0.05 was used to test statistical significance.

## 5. RESULTS

### 5.1 Whole Modified Figure of Eight

#### 5.1.1 Angular Displacement

Figure 25 reveals angular displacement of the top-down sequence of head, shoulder and pelvis orientation during the whole 2 cycle of MFE. The plot shows during the first cycle, the top-down sequence between the segments have indistinguishable differences. During the change of direction, the head has a lower rotation than the trunk and pelvis; and has an earlier onset time during the change of direction. The three segments top-down sequence returned to difficult to distinguish the top-down sequence of the segments, during the second cycle of the MFE. ANOVA revealed significant differences between the angular displacement amplitude of the head, trunk and pelvis ( $F(2,18) = 12,18, P < 0.001$ ). Post hoc analysis of the segments revealed that head rotation relative to the trunk ( $P < 0.001$ ) and to the pelvis ( $P < 0.001$ ) is statistically different. The rotation of the trunk relative to the pelvis was statistically insignificant ( $P > 0.05$ ), as shown in figure 26.

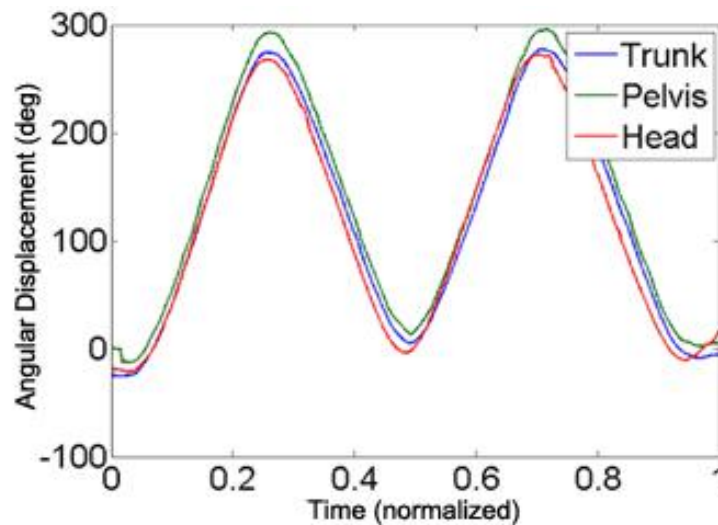


FIGURE 25. Angular displacement graph of each segment during the whole modified figure of eight.

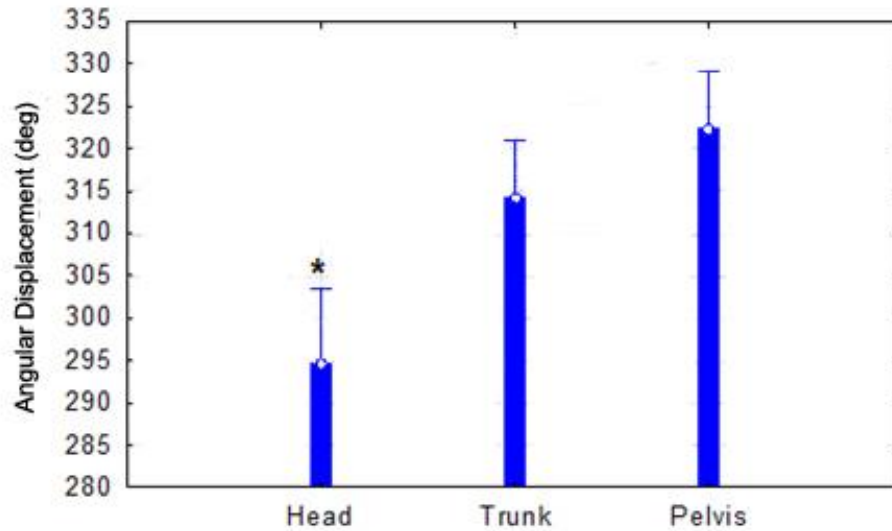


FIGURE 26. Mean and standard deviation (error bars) of the peak angular displacement of the head, trunk and pelvis during the whole 2 cycle of the modified figure of eight. \*Indicates statistically significant difference between head relative to the trunk and pelvis.

### 5.1.2 Angular velocity

Figure 27 shows there are no distinguishable differences in angular velocity between the three segments during the turning of the whole 2 cycle of the MFE. Figure 28 reveals angular velocity of the top-down sequence of head, shoulder and pelvis orientation during the whole 2 cycle of MFE. ANOVA revealed no significant differences in angular velocity between the head, trunk and pelvis ( $F(2,124)=0,3018$ ,  $P>0.05$ ).

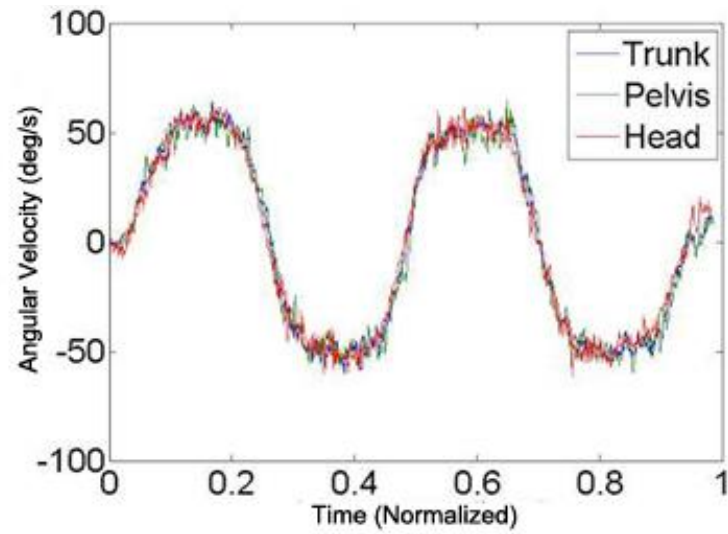


FIGURE 27. Angular velocity graph of each segment during the whole modified figure of eight.

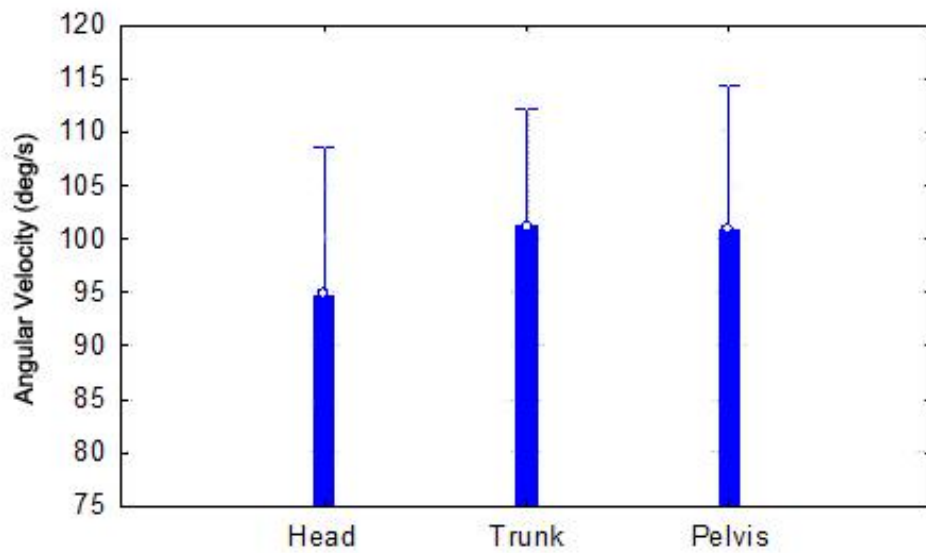


FIGURE 28. Mean and standard deviation (error bars) of the peak angular velocity of head, trunk and pelvis during the whole 2 cycle of the modified figure of eight.

## 5.2 Counter-clockwise vs Clockwise Direction

### 5.2.1 Angular Displacement

The angular displacement of each segment was compared between counter-clockwise and clockwise direction, as shown in figure 29. ANOVA revealed there were no significant differences between the segments when comparing counter-clockwise and clockwise direction ( $F(2,508)= 0,58582, p>0.05$ ).

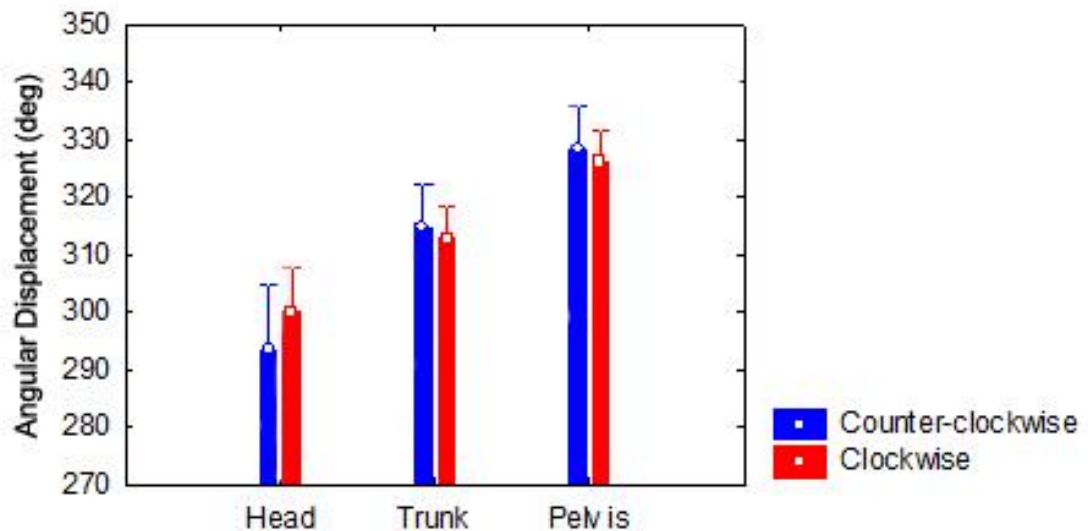


FIGURE 29. Mean and standard deviation (error bars) of the peak angular displacement of head, trunk, and pelvis, during counter-clockwise and clockwise direction.

### 5.2.2 Angular Velocity

The angular velocity of segments was compared between counter-clockwise and clockwise direction, as shown in figure 30. ANOVA revealed there were no significant differences between the segments when comparing counter-clockwise and clockwise ( $F(1,418)= 0,68579, P>0.05$ ).

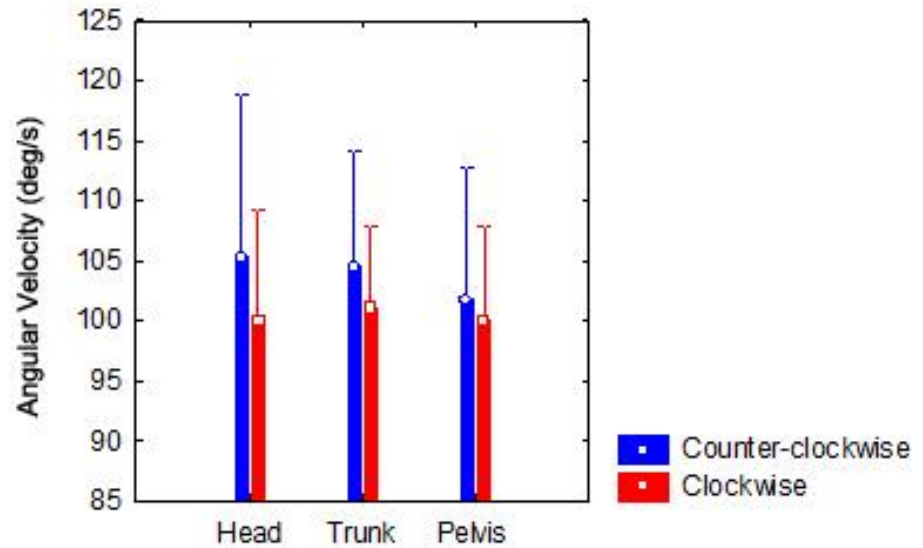


FIGURE 30. Mean and standard deviation (error bars) of the peak angular velocity of the head, trunk and pelvis during counter-clockwise and clockwise direction.

### 5.3 Overstep vs Time to Complete

Overstep is not linearly dependable on the time to complete the walking of the full two cycle of the MFE ( $P > 0.05$ ), as shown in figure 31.

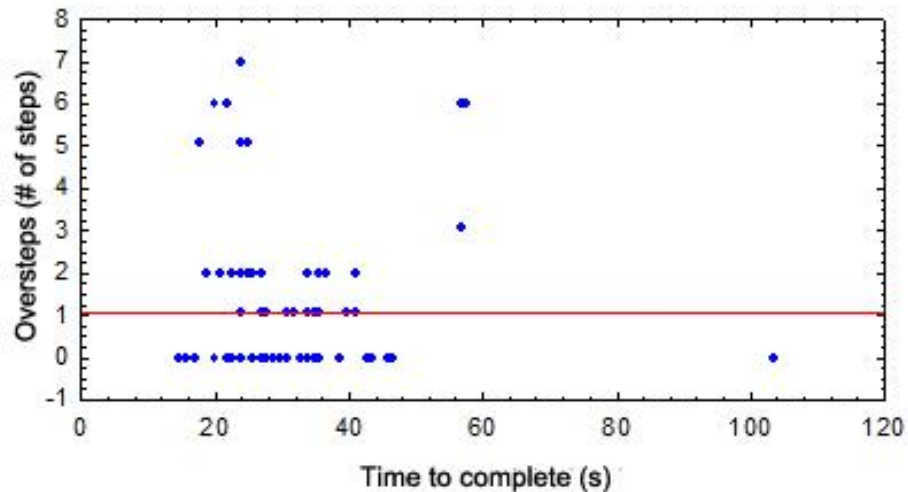


FIGURE 31. There is no relationship between the number of overstep and time to complete the task ( $r^2=0.00$ ).

## **6. DISCUSSION**

### **6.1 Observed Results vs Proposed Hypothesis**

The effects of Parkinson's disease on the segment coordination of the head, trunk, and pelvis while turning the MFE in the "ON" medication state. The proposed hypothesis was that the angular displacement and the angular velocity of all three segments (head, trunk, and pelvis) would not differ significantly; and there would be no relationship between overstepping and time to complete the task. Therefore, our data has revealed that there were turning difficulties and instability. During the whole two cycles of the MFE, the angular rotation of the head towards the intended direction of the travel followed by the rotation of the trunk and pelvis. The peak angular velocity across all segments did not differ. A comparison of the angular rotation and the angular velocity between walking in a CCW and CW direction revealed that the walking direction did not affect the differences between the segments. There is no relationship between the time it takes to complete the task and the mistake of the overstepping during the MFE task

### **6.2 Segmental Relationship During the Whole Modified Figure of Eight**

This study is the first to examine the influence of PD, during "ON" medication state on segmental coordination during constant turning 2 full cycle of the MFE. Previous studies limited their examination of PD effects turning behavior when walking on a curvilinear direction. The use of MFE walking test in this study further represents the complex motor skills required to adapt to changes in the direction, such as circular walking while turning.

The PD subjects displayed turning difficulty while steering in the first circle of MFE, as our data shows no significant differences in angular displacement between the body segments. However, when steering toward the point of origin to change direction, the head rotates toward the intended direction follow by the reorientation of the trunk and pelvis. After the change of direction, there were no differences in angular displacement again, between the



segments. During the whole MFE, the angular displacement of the head rotates less than the trunk and pelvis. Other studies of curvilinear studies have shown that when approaching the turn, the head and upper trunk turn in unison, followed by the reorientation of the pelvis (Carpinella et al. 2007. Crenna et al. 2007; Ferrarin et al. 2006). The magnitude of the head rotation during the turning step was significantly greater than that of the upper trunk for healthy elderly, but similar magnitude for the PD subjects (Ferrarin et al. 2006). The findings of Akram et al (2013), differed from our results. During 45° turns, the head rotates greater than shoulder and pelvis and the amount that the shoulder and pelvis rotated were similar (Akram et al. 2013). During the 90° turn, the head rotated greater than the shoulders and the shoulders rotated greater than the pelvis. The findings of Hong et al. (2010) also differ from our results. During the 180° turn, it was difficult to distinguish the order in which the different segments would start turning. Our findings were similar to Huxham et al. (2008) who reported an initial turning of the head, followed by blocked turning of the trunk and pelvis, when approaching a turn. The block rotation between the trunk and pelvis reported by Huxham et al. (2008) may be result from axial rigidity (Van Emmerik et al. 1999; Steiger et al. 1996).

The angular rotation of the head is less than the trunk and pelvis during the second half of the MFE because the head steers first, toward the starting point, as the PD subject changes direction. Progression along the curve was accompanied by head rotation in space and head yaw with respect to heading direction (Grasso et al. 1996; Grasso et al. 1998a; Grasso et al. 1998b.; Hollands et al. 2001; Glasauer et al. 2002). The adaptive behavior of the head is probably part of global orientation mechanisms allowing humans to steer their body in the desired direction (Hicheur et al. 2005). The head contains gravitoinertial sensors (vestibular system) and visual system. They must be stabilized in space to provide a steady internal reference. Vestibular as well as visual and proprioceptive inputs have been found to play a major role allowing humans, for instance, to steer their whole body along a given trajectory while maintaining dynamic stability (Heicheur et al. 2005). Axial rigidity and En bloc turning has been shown in the PD, as the top-down sequence of rotation during the turning has been difficult to distinguish (as shown in figure 25). Hong et al. (2009) had similar

findings to 180° turn and Akram et al. (2013) also had similar findings for 45° and 90° turns.

During the change of direction towards and away from the origin, the angular velocity pattern of the three segments did not rotate differently relative to each other. Akram et al. (2013) had similar result for peak angular velocity as us for 45° and 90° turns.

The peak angular velocity pattern does not differ too much across all three segments. The slowness and the lack of differences in speed rotation between the segments would reflect upon bradykinesia or to limit the amount of destabilizing influence of the angular momentum.

### **6.3 Counter-clockwise vs Clockwise Direction**

Walking along the MFE requires substantial complexity of changes in visual condition under dynamic balancing condition and adaptation to the prolonged continuous direction changes. Therefore, the relationships between the segments sequence pattern before the turn and during the turn were compared. Guglielmetti et al. (2009) reported that cadence was unaffected by continuous turning between CCW and CW directions for the PD subjects. Our results reported that walking direction did not have effect on the angular rotation and angular velocity across all three segments. This shows consistent deficits in the processes of preparation toward and control during the curved turning. Walking on a continuous circular path for an extended period of time may pose problems as a result of subject's mediolateral instability (Horak et al. 2005; Vaugoyeau et al. 2007), difficulty in shifting the center of foot pressure from one foot to the other (Mille et al. 2007) and difficulty in producing anticipatory postural adjustments (Rocchi et al. 2006). Little is known of continuous segmental turning in comparing CCW vs CW turning direction. Therefore, more research should be done in the future to gain further knowledge.

## 6.4 Overstepping

Measuring overstep and observing the relationship with the time to complete the two full cycles of MFE provides more information of whether the PD oversteps less if they perform the task longer. Oversteps may indicate a lower ability to perform the test, due to moderate disability (Noren et al. 2001), cognitive decline (Pettersson et al. 2002) or other impairment. The overstep counted for the MFE test was significantly larger in the PD “OFF” than the control group but not between the PD “OFF” and “ON” groups (Franzen et al. 2009). In the study conducted by Jarnlo and Nordell (2003), MFE time was significantly correlated to walking speed while oversteps significantly correlated to walking speed and one-legged stance. Our results suggest that overstepping has no relationship with the time required to complete the task. Therefore, the PD subjects show signs of moderate disability regardless the amount of time it takes to complete the task.

## 6.5 Limitation of Study

A limitation in our study was starting from the systematic error during the measurement done by the Elite motion analysis system. Even though each body segment was defined by the tracking device, there were problems with the data. For example, a part of data concerning the head segment had to be discarded because the data would either be missing or corrupted. This may be due to the leveling of the calibration wand where the areas of the data should be collected. There were also problems during the tracking. Due to the limitation of the tracking software itself, it had problems tracking the segments during large turns, therefore precise tracking was required frame to frame. The markers were occluded by the arms, while the subjects were walking. This may have been eliminated, if we were to ask the subjects to walk cross armed. In addition, some subjects were walking in a slight bent posture. Our findings may have been limited because the patients turn towards a predictable target location and at a self-selected pace, posing little risk to fall in such conditions. Also since the trial was done three times, there would have been a learned behavior effect, as opposed to performing toward an unanticipated target.

## **6.6 Practical Application and Futures Studies**

Most of other previous studies on segmental turning have compared the PD subjects during “OFF” phase and to normal elder age matched subjects. Hence, these subjects can be used in the future study, to observe the impact of “OFF” phase medication for the PD subjects and to normal age matched population. Since the MFE requires multitasking balance curve walking, the MFE should be used as mobility and balance performance test before and post physical therapy treatment. In order to understand the broader implications of fall prevention risk and physical therapy, further research on segmental coordination during MFE or other balancing performance test, under the influence of PD would be required. The MFE test has been shown to be a reliable functional performance test and to date not many studies have been conducted using the PD subjects. More future studies should be done using the MFE test on PD subjects to get a more of a broader understanding of how multi segmental reorientation is affected by turning difficulties. Future studies, employing both kinematic and EMG measures alongside with MFE may be needed to.

## **7. CONCLUSION**

The results of this study suggest the PD subjects displayed signs of axial rigidity and en-bloc turning while walking the whole two cycles of the MFE task. The slowness of movements during the MFE task reflects upon signs of bradykinesia. The direction of turning has no effect. Furthermore, overstepping has no relationship with the time it takes to complete the MFE tasks. Hence, the PD subjects displayed turning difficulty and some disability during the complex MFE walking while turning task.

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