Statistical Comparison of Results from the Timed Up and Go Test, Unified Parkinson's Disease Rating Scale, Falls Efficacy Scale, and Force Plate Balance Measures Concerning Risk of Falls among Patients with Parkinson's Disease

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A thesis submitted in partial fulfillment of the requirements of the Honours Program in the Department of Applied Human Sciences

This Thesis is Accepted

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Dean of Science
University of Prince Edward Island

May, 2018

ABSTRACT

Background

Parkinson's disease (PD) is the second most common neurodegenerative disorder in Canada. It is characterized by impaired gait and other motor symptoms that lead to falls.

Purpose

This study assessed changes in PD patient mobility and motor control over 1.5-years. These changes were used to determine the risk of falls in patients with PD.

Methods

Changes were tracked in timed up and go (TUG) tests, Unified Parkinson's Disease Rating Scale (UPDRS), and Falls Efficacy Scale (FES). Centre of pressure (COP) was recorded on a force plate to measure dynamic (DPC) and static (SPC) postural control tasks. Twelve individuals, five males and seven females aged 41-73, participated throughout five visits. Mixed model repeated measures ANOVAs, independent variables TIME and SEX, assessed differences in test measures. A Pearson correlation was conducted to determine relationships.

Results

RM ANOVAs revealed marginal significance of TIME in tremor ($p = 0.063$) and significance on gait ($p=0.013$), SD mediolateral ($p=0.012$) and SD anteroposterior ($p=0.046$). Similarly, SEX found a main effect for rigidity ($p=0.005$) and SD mediolateral ($p=0.043$), and marginal significance on FES ($p=0.067$). A significant interaction of TIME X SEX for tremor values ($p=0.021$) was found. Results of correlation analyses revealed several UPDRS items significantly correlated with DPC, but not SPC, tasks on the force plate.

Discussion

Overall, participants performed consistently over 1.5-years indicating motor ability did not decline substantially. Furthermore, correlations of motor symptoms with DPC tasks support that they may better predict falls in PD patients than SPC tasks.

ACKNOWLEDGEMENTS

I would like to thank my supervisor, Dr. Rebecca Reed-Jones, for her patience and cooperation through the development of this thesis. Without her knowledge, expertise, and guidance, this project would not have been possible.

I would also like to think my committee member, Dr. Travis Saunders, for his assistance in this project. Although potentially uneducated in the area of study, his input and feedback were highly beneficial and appreciated.

Lastly, I would like to thank the Department of Applied Human Sciences at the University of Prince Edward Island for this opportunity. With the availability of resources and the support of the faculty, I was successful in my pursuit of my Honours degree.

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LIST OF ABBREVIATIONS

A-P	Anteroposterior
COP	Centre of Pressure
DPC	Dynamic Postural Control
FES	Falls Efficacy Scale
FRT	Functional Reach Test
iTUG	Instrumented Timed Up and Go
M-L	Mediolateral
PD	Parkinson's Disease
RM ANOVA	Repeated Measure Analysis of Variables
SD	Standard Deviation
SNc	Substantia Nigra Pars Compacta
SPC	Static Postural Control
TUG	Timed Up and Go
TUGc	Timed Up and Go Cognitive
TUGm	Timed Up and Go Manual
UPDRS	Unified Parkinson's Disease Rating Scale

I. INTRODUCTION

On a regular basis, healthy individuals with no physical impairments can perform normal day-to-day activities without struggle. However, the presence of disease can make these activities of daily living more difficult. For a disease such as Parkinson's disease (PD), this is a frequently observed issue. PD is the second most common neurodegenerative disorder in Canada, next to Alzheimer's disease, effecting approximately 0.2% of the population of adults in Canada over the age of 18 living at home, and 4.9% of the population living in residential care facilities (Wong *et al.*, 2014). Some characteristics of the disease include joint rigidity, tremors, postural instability, bradykinesia (slow movement), and impaired gait (Hirsch *et al.*, 2013). Other cognitive and psychological symptoms have been said to be linked with PD, as well. The symptoms associated with PD progress at different rates and vary between cases (Fereshtehnejad *et al.*, 2017). Of the symptoms listed above, it has been determined that some individuals have very few of them with little change over long periods of time, while other experience a rather rapid onset of symptoms. Many tests are available to asses the severity of the disease in individuals, some of which are highly valid. Some of these tests were used in this study.

This study was based off the raw data collected over a one-and-a-half-year period. Five different test points throughout this time frame were analyzed through a mixed model repeated measures analysis of variables (RM ANOVA) to identify any changes in timed up and go (TUG) results, results from the Unified Parkinson's Disease Rating

Scale (UPDRS), the Falls Efficacy Scale (FES) results, as well as a static (SPC) and dynamic (DPC) postural control tasks measured on a force plate over time. The RM ANOVAs also looked for differences between genders within the sample. There was a Pearson correlation analysis done between clinical measures and the postural control tasks. These were compared to determine statistical significance.

II. LITERATURE REVIEW

The human brain is a miraculous system that regulates and controls all other systems in the body. It does so through nerve impulses, hormones, and neurotransmitters. A particular neurotransmitter, dopamine, is important in humans. Along with its association to pleasure and emotion, it is also responsible for the regulation of movement. People with PD tend to have a depletion of this neurotransmitter, which causes some movement dysfunction. A study by Fereshtehnejad *et al.* (2017) identified subgroups of PD based on some of the differences patients with the disease experience. The subgroups they categorized were those of "mild motor-predominant", "intermediate" and "diffuse malignant", diffuse malignant having a larger dopaminergic deficit. The reason for this variation is still yet to be determined.

Some knowledge of PD includes a link to a 140-amino acid protein called *α*-synuclein, a correlation to Lewy bodies, a presence of oxidative stress in the substantia nigra pars compacta (SNc) of the brain, as well as some other possible relationships (Schapira, 2009). The protein *α*-synuclein has been found to be a determinant of familial PD, caused by a particular gene mutation that leads to the 53rd amino acid to be changed from alanine with threonine, yet the mutation cause is still undiscovered (Polymeropoulos *et al.*, 1997). This mutation is also only shown in a small portion of patients with PD, but leads researchers to believe that similar mutations are probable reasons for the development of PD. Other mutations have been identified in other studies, as well.

Lewy bodies are found in multiple areas of the body in nervous tissues. These bodies are known as intracytoplasmic inclusion bodies, and they are abundant in patients suffering from PD (Polymeropoulos *et al.*, 1997). More simply put, Lewy bodies are abnormal clusters of protein within the nerve cells. These Lewy bodies are associated with lesions in nervous tissue, which can lead to PD symptoms. Braak *et al.*, (2003), found the Lewy bodies are made up of groups of Lewy neurites which increase in number as PD becomes more severe. They also found that in the first two stages of PD, Lewy bodies are confined to the medulla oblongata; in the third and fourth stages, the brain stem experiences lesions, and in stages five and six, the whole brain has evidence of damage from Lewy bodies (Braak *et al.*, 2003). Lastly, The SNc is located in the basal plate domain of the midbrain and holds dopaminergic neurons that are responsible for movement (Encyclopaedia Britannica, 2016). In the presence of PD, the SNc is much smaller than in healthy controls. Some studies show that this is related to oxidative stress, but the exact cause is still being investigated (Schapira, 2009). Regardless of the cause, knowledge of low dopamine levels exists, and treatments tend to focus on this issue.

Currently there are some medications available for individuals with PD. These medications tend to be dopaminergic medications, due to this lack of dopamine. There are “on” and “off” phases of these medications; “on” is when the medication is working, and “off” is when it begins to wear off again. Throughout this study, the participants were always in the “on” stage of their medications. Several studies have looked at the use of these medications, one of which, by Fang *et al.*, (2015), looked at the severity of PD and the effects of the medications. They found that a combination of dopamine agonist and levodopa medications presented worse symptoms and cognitive function than dopamine

or levodopa alone (Fang *et al.*, 2015). They stated that this could be due to patients with more severe symptoms being on both medications, but they believe it is the combination of the medications that make symptoms more severe. More research needs to be done in order to better understand this. Another study focussed on speech dysfluency and the use of medication over a period of 3-6 years. These researchers found that there was an increase in dysfluency of speech compared to their healthy control (Tykalová *et al.*, 2015). These studies show that even though there are medications available, there is still a great need to further understand PD in order to find a proper cure and prevention. Hirsch *et al.* (2013) explain in their paper of the *Pathogenesis of Parkinson's Disease* that it is important to analyze all aspects of the disease both inside and outside of nerve cells to better understand PD and, consequently, find effective prevention tactics and a potential cure.

One area that makes it difficult to map out the patterns of PD is the fact that there are so many differences between individuals that suffer from the disease. One particular reason for these differences is thought to be sex. A paper by Picillo *et al.* (2017) shows that in women, PD tends to start benign, believed to be the cause of estrogens, which seem to have protective properties against dopaminergic damage. Women are less likely to get PD as a result of estrogen and estradiol, which is supported by the fact that PD typically only develops in women after menopause when estrogen levels are lower (Picillo *et al.*, 2017). Men, on the other hand, tend to have an earlier onset than women by about two years (Gillies *et al.*, 2014). It was also determined that estradiol therapy doesn't work the same in men, and in some cases may worsen the damage done by PD (Gillies *et al.*, 2014). Women are also thought to experience greater complications due to

medications than men (Picillo *et al.*, 2017). Since these complications occur, sex specific medications for patients suffering from PD should be created to avoid further difficulties (Gillies *et al.*, 2014). Gender differences appear to be quite interesting and were therefore an area of research of the current study. This study is more focussed on the motor aspects of PD and therefore the sex differences in motor symptoms. Szewczyk-Krolikowski *et al.* (2014) determined some motor differences between sexes, such as earlier onset of postural problems in women and significantly higher rigidity (p=0.002) in men. Very few studies, however, focus on motor symptom differences in PD as opposed to the non-motor symptoms. Similarly, these symptoms progress at different times and with different magnitudes.

There are not many differences noted in the symptoms of most patients with PD over a short period of time, and therefore longitudinal studies are important for determining any progression and development of these symptoms. Just as Tykalová *et al.* (2015) examined the effects of medication longitudinally, other aspects of symptoms should also be studied as such. A longitudinal study by Erro *et al.* (2016) looked into the non-motor side of PD while in the early stages and compared it to the patients' quality of life over a course of four years. They determined a great increase in symptoms over the four years; however, despite this increase, there was no relationship between non-motor symptoms and motor disability, meaning they are unrelated in development (Erro *et al.*, 2016). When focussing on the quality of life, their test showed a significant decrease in quality of life in relation to non-motor symptoms, but not in relation to motor features (Erro *et al.*, 2016). This information is important to keep in mind for this and other future studies as a person's quality of life is an important aspect in overall perception of

happiness. This study only looks at motor symptoms in patients with PD, but researchers were not ignorant to the presence of non-motor symptoms and their potential effects. Another longitudinal study by Paul *et al.* (2016) examined that fall risks can be mapped on a two-year trajectory to determine the chances of falls to occur. Knowing this risk trajectory is beneficial to the individual, their physician, and their family members as they can take preventative measures to protect the patient.

A paper by Rudzińska *et al.* (2013b) described the causes and consequences of falls in patients with PD. They determined that the most common falls were sudden. They also stated that intrinsic factors were a common cause of falling. Lastly, the determined that one-third of falls result in injuries, while five percent require hospitalization (Rudzińska *et al.*, 2013b). In another paper, also by Rudzińska *et al.* (2013a), stated that the incidence of falls in patients with PD is in the range of 38-68% and that history of falls is a risk factor for subsequent falls. They also stated that age and postural instability were predictors for falls, and that scores on the UPDRS tended to be higher in those with a higher risk of falling (Rudzińska *et al.*, 2013a). In a paper regarding balance as a predictor of falls, it was stated that the Functional Reach Test (FRT), the TUG and the FES all measure the effect of balance on falls, as well as can help to predict falls (Almeida *et al.*, 2016). The use of multiple tests together gives the best prediction of risk of falling.

Ideally, knowledge about PD can help to develop ways to prevent and cure the disease. With the little knowledge that is currently available, these are unfortunately still unknown. However, by being aware of current knowledge, it is possible to help those who are suffering from the disease to cope with it as best as possible. One important

application of a lot of these studies is to know the risk an individual with PD has of falling. By monitoring this risk level in these individuals, fall avoidance can occur, preventing injury and further disability. There are both subjective and objective tests that examine falling. These tests track the progression of PD so that those suffering from it, as well as their physicians, can track how their disease is developing. They also help to determine the risk of falling a patient has in order to take necessary precautions. The three tests used are the TUG, UPDRS and FES. The TUG test is known to be valid (Vance *et al.*, 2015) and is a simple mobility test that is often used to predict the risk of falling in older adults. The second test, the UPDRS, is also valid; it is made up of numerous different components, including Part III: Motor Examination, and Part V: Modified Hoehn and Yahr Staging. For this study, 6 subsections of the motor examination were used: arising from a chair, rigidity, gait, tremor, posture, and bradykinesia. The FES is also included in this study. It is a series of questions that analyze the patient's fear of falling. All these tests allow for a benchmark to refer to throughout the progression of the disease.

When considering the TUG, it is notable that some of the aspects are susceptible to human error. A study by Lummel *et al.* (2016), with no particular focus on PD, looked at the inter-rater, intra-rater and test-retest reliability of a variation of the TUG using an inertia sensing instrument, the iTUG. Although this variation is present, these reliabilities were also tested based on timing done by the raters, and directions they gave, which are the basic components of the normal TUG test. Therefore, this study pertains to the current study well. The results of the study by Lummel *et al.* (2016) showed that there was some variation in the stopwatch time and the time recorded by the inertial sensory

measurement system, but this could be due to human error. Similarly, the difference in the times could be because of the patient's reaction time to start the test when the rater says "go". Lastly, the test-retest reliability was lower than inter- and intra-rater reliability, which could be due to the patients being either in their "on" or "off" phase. Palmerini *et al.* (2013) used the iTUG to look at patients with PD, however they increased the walking distance from three to seven meters. Accelerometers were worn on the backs of patients. They determined that differentiation between groups in early stages of PD was not sensitive. They did find that as severity increased, however, it positively correlated with posture, rigidity and gait severity of the patient.

Another study looked at the ability of the TUG to predict the likelihood of a patient to fall. In this test they looked at older adults in general, rather than patients with PD. Shumway-Cook *et al.* (2000) considered how sensitive and specific the TUG test is when it comes to predicting falls in older adults. Their study concluded that the TUG is a simple test that can reliably determine and predict the risk of falling in older adults. In the current study, falls are a major concern for the population, so using this test highly benefits the researchers. This study also incorporates dual task TUG tests, including a TUG cognitive (TUGc) and a TUG manual (TUGm) to increase the sensitivity of the test. A study by Vance *et al.*, (2015) examined the effects of dual tasking during the TUG. It was determined that adding in a second task while conducting in the TUG enhanced the ability to predict fall risk in patients with PD. They noted that cognitive tasks while performing the TUG had the highest sensitivity (76.5%) and specificity (73.7%). Therefore, it can be said with confidence that the TUG test is a valid tool to use when studying patients battling PD.

Regarding the UPDRS, the six chosen parameters were decided to be the most relatable to fall risk. The UPDRS is subjective, meaning that there is likely to be some variability between raters. To account for this, one rater was used to analyze patients throughout most of the duration of this study. A study by Jenkins *et al.*, (2010) examined the ability of the UPDRS to determine falls in individuals with PD. The group analyzed the UPDRS against the FRT. They assumed that since many falls involve some extent of reaching, this test would be a great determinant of falling. Their results concluded that UPDRS is more functional in determining differential diagnosis while the FRT is much better at predicting the chance of falls. However, a study assessing the posture of patients with PD, irrelevant to the postural stability test, showed that rating posture can help with the prediction of fall risk (Nair *et al.*, 2017). This is likely due to the centre of pressure (COP) being off-centre from the base of support, making it easier to move out from it, resulting in a fall. When considering the Hoehn and Yahr portion of the UPDRS, a study by Tsanas *et al.* (2012) focussed on the statistical analysis and mapping of the UPDRS to this staging system. They determined that the postural stability, gait, arising from a chair and bradykinesia were the most correlated between the two. This supports that the use of these specific parameters in the current study may be better used isolated from the entire UPDRS test for determining fall risk.

The third test, the FES, was developed by Tinetti *et al.* (1990). It is strictly subjective and determines the patient's confidence in doing everyday tasks. Therefore, there is a chance for variability to be present. However, determining the confidence someone has in performing everyday activities gives a good baseline to compare to. It also allows for a general idea of one's risk of falling as they would likely be less

confident if they tend to fall more frequently or have close calls of falling. Although there is a correlation between scores on the FES and falling, Thomas *et al.* (2010) found that those who fell less often sometimes had higher scores than those who felt very frequently. However, they acknowledged that this could be due to frequent fallers being familiar with falling, and the lack of severe consequences may make them less nervous to fall. On the contrary, Nilsson *et al.* (2010) determined that the Swedish version of the FES was highly correlated with many other determining factors of falls with regards to walking, as walking accounts for many falls in patients with PD. Nonetheless, this is a useful tool to determine the general ability of individuals to complete daily activities with confidence. Relationships between the other tests and this one may give a well-rounded idea of one's risk of falling.

Along with these tests, which are typical used as clinical measures for PD, this study also looked at SPC and DPC tasks. A force plate was used to gather variables related to COP. Many studies have used SPC tasks to examine PD, but very few have used DPC tasks. Mezzarobba *et al.* (2018) looked at highly applicable DPC tasks such as walking, initiating gait, and sit-to-walk. They found that sit-to-walk determined the greatest difference between patients with and without freezing of gait, as well as between patients and healthy controls. It found that sit-to-walk allowed for greater discriminability of postural behaviors compared to walking or initiating gait. Another study by Kim *et al.* (2012) showed that when initiating gait around an obstacle, patients with PD had smaller displacements than those of age-matched controls, which has been shown to put individuals at increased risk of falls. This supports the use of DPC task for analysis of patient disease progression and fall risk.

Although the literature on PD is extensive, there are still many holes and areas that need further investigation. One area where research could be furthered would be that in sex differences in motor symptoms. Most sex differences are viewed in the non-motor side of symptoms rather than the motor. Secondly, very few longitudinal studies have been conducted. Some with follow up studies have been done, but very few track the progression and fall risk in patients with PD. Third, no studies have considered the relationships between the TUG, UPDRS, FES and postural control tasks. Similar to this, UPDRS is often used as a whole test, rather than some specific portions of it, which makes it difficult to compare to other tests due to the wide variety of symptoms studied. Lastly, most research involves the use of SPC tasks rather than DPC, so some research should be done in the area of the DPC tasks as falls typically occur when the COP is off-centre. Accordingly, each of these areas are examined to some extent in the study at hand.

III. METHODS

i. Participants

Twelve participants volunteered for the study, five are male and seven are female with an age range from 41 to 73 years. All participants were diagnosed with PD by a neurologist, with a mean of 4.2 years since diagnosis at the commencement of the study. Each patient was on dopaminergic medication for their symptoms. Participants gave informed consent prior to inclusion in the study.

ii. Procedures

Participants completed 5 laboratory visits. These visits were conducted over the duration of a year and a half. The first collection was in the spring of 2016 and was repeated an additional three consecutive times with a four-month duration between each. The fifth test bracket occurred six months following the fourth visit in the late fall/early winter of 2017.

In each visit, the participants were asked to do four different tests. These tests include the TUG, UPDRS, FES, and standing and figure eight tests on a force plate. The TUG test was conducted by a minimum of two researchers, or raters. One of the raters used a stopwatch to time the test while the other gave instructions and spotted the participant as they went through. The participant started in a seated position; when the rater said “go”, they arose, walked three meters, turned around a pylon, walked back to the chair, and returned to the seated position in which they started. The researcher with the stopwatch started the time when they said “go” and stopped the timer once the patient

was seated again. The time it took the patient to finish the test was their score for the test. Essentially, a shorter time is more desirable. The participant completed this twice and the best of the two trials was used. Following the two trials, two different dual task TUG tests were then conducted. Each of these included the same procedure, however a secondary task was added to simulate multitasking, which distracted them from the focussing on the walking itself. The first of the two dual task TUG tests was a cognitive TUG in which the participant performed the TUG test while attempting to count backwards from 100 in increments of sevens. The second dual task TUG was a manual TUG in which the individual performed the TUG test while carrying a small cup of water. The goal for this test was to not spill the water while completing the TUG. Participants were given two trials for both of the dual task TUG tests, as well. Issues tend to arise if an individual has a greater than four second variant between the single task TUG and the dual task TUG. This suggests that their risk of falling is increased.

The second test conducted was the UPDRS. The UPDRS is a subjective test that analyzes the patients' ability to carry out day-to-day activities without any difficulties, as well as determining a possible risk of falling. There are multiple different questions associated with the UPDRS, and they all pertain to different aspects of the disease. For this study, only the motor portion of the UPDRS was used. From this section, six specific items were isolated and looked at separately, as they were the items that were deemed most relative to risk of falling in PD patients. However, this could be up for debate. The six items analyzed were tremor at rest, rigidity, arising from a chair, posture, gait, and body bradykinesia and hypokinesia. The idea behind this was that those who suffered more in these areas were potentially more likely to have higher scores on other tests

conducted. Similarly, if the values for these selections were to increase, then other test values would be likely to increase as well. The entire score of the motor portion of the UPDRS was not used as different symptoms may score differently for different patients, potentially resulting in similar total scores at the end. These scores may not reflect the individual's potential risk of falling. Consequently, total values of the UPDRS would likely not relate to the other tests as far as fall risk prediction.

The third test conducted during the visits was the FES. The FES questioned the patient's fear of falling, or their confidence in their ability to do day-to-day tasks. There are ten different examples of daily activities that the individual is to rate their confidence in completing. The ratings range from one to ten, one being very confident, and ten being not at all confident. The scores were then totalled, and these numbers were used to asses fall risk, as well as to compare to the other tests. Scores of 70 or higher are considered to put the patient at an increased risk of falling, and these individuals should have certain parameters in place to help them in case of a fall at home.

Lastly, the participants were asked to stand on a force plate for two additional tests, a SPC and DPC task. The SPC task entailed having the participant stand silently for 60 seconds. The DPC task was only 30 seconds long, and consisted of the individual, while keeping their feet planted, shifting their weight about their ankles in a figure eight motion. The force plate measured the COP in the mediolateral (M-L), anteroposterior (A-P) and inferosuperior directions during each of the tests. The COP M-L and COP A-P were used to calculate the path length at each millisecond, which was calculated by the use of Pythagorean Theorem. The resulting values were then added together to determine the added path lengths, which determines the total distance the COP moved over the

duration of the test. The average velocity of the COP in each direction was also calculated to determine how fast the COP moved during the test. These values were then used to compare amongst the other tests.

iii. Data Analysis

All the data from the five different visits was collected and incorporated into Microsoft Excel spreadsheets. Select data were then graphed for each of the visits to show any increase or decrease in results. These data were then analyzed in the SPSS statistical analysis system by the use of RM ANOVAs and a Pearson correlation. These values were then observed and interpreted by the researchers.

IV. RESULTS

i. Demographics

Five males and seven females participated in the study. *Table 1* illustrates various demographics of the participants based on sex. Some of this data is missing so numbers are not exact. On average, when starting the program, men and women were both around the age of 61, with a range in age from 39 to 71 years at the commencement of the study. The greatest number of years since diagnosis ranged from one to as high as fourteen from 2016 when the study began.

Table 1. Sample demographics

Demographic	**Males (SD)**	**Females (SD)**
Date of Birth	1955.75 (4.82)	1955.7143 (11.67)
Years Since Diagnosis	3 (4)	2.5 (2.3)

ii. Clinical and Postural Control Measures

Over the 5 test brackets, a lot of data were collected. During the initial visit, however, the process was not properly laid out and many values were missing. Therefore, for the statistical analysis, the data from the first timepoint were excluded. The remaining data were analyzed, and the results were categorized into two groups: clinical measures, and postural control. The clinical measures included the results from the TUG, UPDRS, and FES. The postural control section reflects on the results from the force plate data during the figure eight and silent stance tests. Two statistical analyses were performed,

and the results were gathered. The first type, a mixed model RM ANOVA that focused on independent variables TIME and SEX, was used to assess the differences in clinical test measures. A second mixed model RM ANOVA was used to analyze the effects of TIME and SEX on the SPC test, and a third analyzed the effects of TIME and SEX on the DPC test. These were both done for the second, third, and fourth timepoints to maintain the analysis of the largest sample size. The second type of statistical analysis test performed was a Pearson Correlation. This was done between the clinical measures and the postural control measures of the second timepoint. Once again, timepoints were chosen based on the maximal number of participants to create the largest sample size.

iii. Mixed Model RM ANOVAs

For the clinical data collected, a mixed model RM ANOVA, with independent variables TIME and SEX, was used to assess the differences in test measures from time two to time five. Results of the RM ANOVA revealed significant main effects of TIME in tremor ($F(2.5, 17.3) = 3.08$; $p = 0.063$; $n2¬ = 0.306$) and in gait ($F(2.3, 16.2)=5.44$; $p=0.013$; $n2=0.437$) for the UPDRS values, as shown in *Figure 1*. Interestingly, there appears to be a pattern in this graph that seems to relate to the time of year or the changing of the seasons. Secondly, SEX found a significant main effect for rigidity ($F(1,7)=16.534$; $p=0.005$; $n2=0.703$) on the UPDRS and a marginally significant effect on FES ($F(1, 7)=4.708$; $p=0.067$; $n2=0.402$) scores, as shown in *Figure 2*. Lastly, a significant interaction of TIME X SEX was observed for tremor values ($F(2.5, 17.3)=4.52$; $p=0.021$; $n2=0.392$) of the UPDRS, as well, as illustrated in *Figure 3*. No discrete pattern was determined in this figure, but this could be investigated.

For the additional RM ANOVAs, the focus was on the SD in both the M-L and A-P directions as well as the velocity of movement in the COP in the M-L and A-P directions of both the SPC and DPC tests. The second RM ANOVA was conducted to look at the effects of TIME and SEX on the SPC test. No significant results were found in this test.

A final RM ANOVA was conducted on the DPC task for timepoints two, three and four. This analysis determined that there was a significant effect of TIME on the SD of movement in the M-L ($F(2,12)=6.497$; $p=0.012$; $n=0.520$) and A-P ($F(1.9,11.3)=4.169$; $p=0.046$; $n=0.410$) directions (*Figure 4*). There was also a significant effect of SEX on the SD of movement in the M-L direction ($F(1,6)=6.544$; $p=0.043$; $n=0.522$), which is illustrated in *Figure 5*.

iv. Pearson Correlation

For our final statistical analysis, we compared all the postural control measures and the clinical measures from the second timepoint using a Pearson correlation. This time point had the most values available of all the timepoints and therefore could give us more reliable data. Interestingly, the DPC test had high correlations with many of the clinical measures, but the SPC test had none.

Specifically, SD in the M-L direction correlated with arising from a chair ($r= - 0.643$; $p=0.024$), gait ($r= - 0.600$; $p=0.039$), and bradykinesia ($r= - 0.0726$; $p=0.08$). SD in the A-P direction correlated with posture ($r= - 0.692$; $p=0.013$), gait ($r= - 0.662$; $p=0.019$), and bradykinesia ($r= - 0.630$; $p=0.028$). Velocity of the COP in the M-L direction correlated with TUG ($r= - 0.680$; $p=0.021$), TUGm ($r= - 0.693$; $p=0.018$), TUGc ($r= - 0.647$; $p=0.031$), rigidity ($r= - 0.655$; $p=0.021$), and gait ($r= - 0.587$; $p=0.045$).

Velocity of the COP in the A-P direction correlated the TUG (r= - 0.780; p=0.005), TUGm (r= - 0.773; p=0.005), TUGc (r= - 0.659; p=0.027), gait (r= - 0.644;p=0.024), and bradykinesia (r= - 0.619; p=0.032). All these correlations were negative so much as when the postural control measures decreased, clinical measures increased. In other words, as patients' symptoms worsened, they moved slower and less variably on the force plate. Significant correlations were also found between clinical measures.

Specifically, all TUG scores were highly correlated [TUG & TUGc (r=0.951; p=0.000); TUG & TUGm (r=0.980; p=0.000); TUGc & TUGm (r=0.961; p=0.000)], which was to be expected. Tremor had no significant correlations. Rigidity significantly correlated with posture (r=0.643; p=0.024), gait (r=0.692; p=0.013), bradykinesia (r=0.598; p=0.040) and FES (r=0.730; p=0.007) scores. Arising from a chair significantly correlated with gait (r=0.746; p=0.005), bradykinesia (r=0.748; p=0.005), and FES (r=0.842; p=0.001). Posture correlated with gait (r=0.818; p=0.001), bradykinesia (r=0.675; p=0.016) and FES (r=0.622; p=0.031). Gait significantly correlated with TUG (r=0.618; p=0.043), TUGm (r=0.610; p=0.046), bradykinesia (r=0.902; p=0.000), and FES (r=0.889; p-0.000). Bradykinesia correlated with FES (r=0.869; p=0.000). Lastly, FES correlated with TUG (r=0.660; p=0.027) and TUGm (r=0.660; p=0.027).

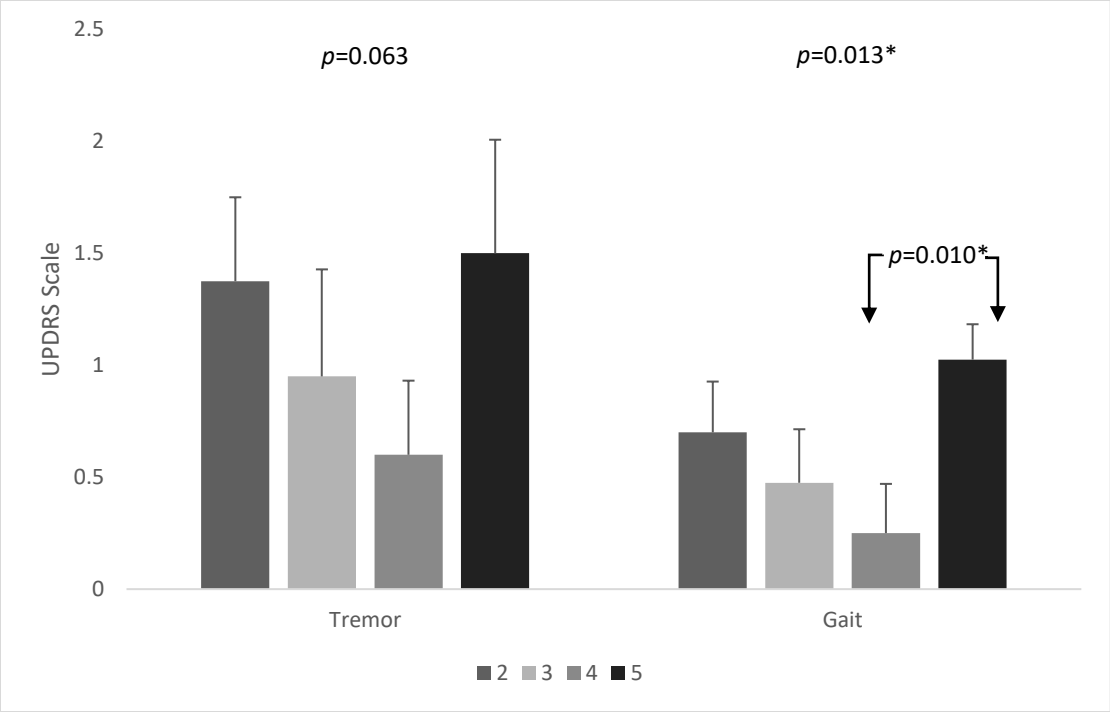

Figure 1. Effect of TIME on tremor and gait scores of UPDRS.

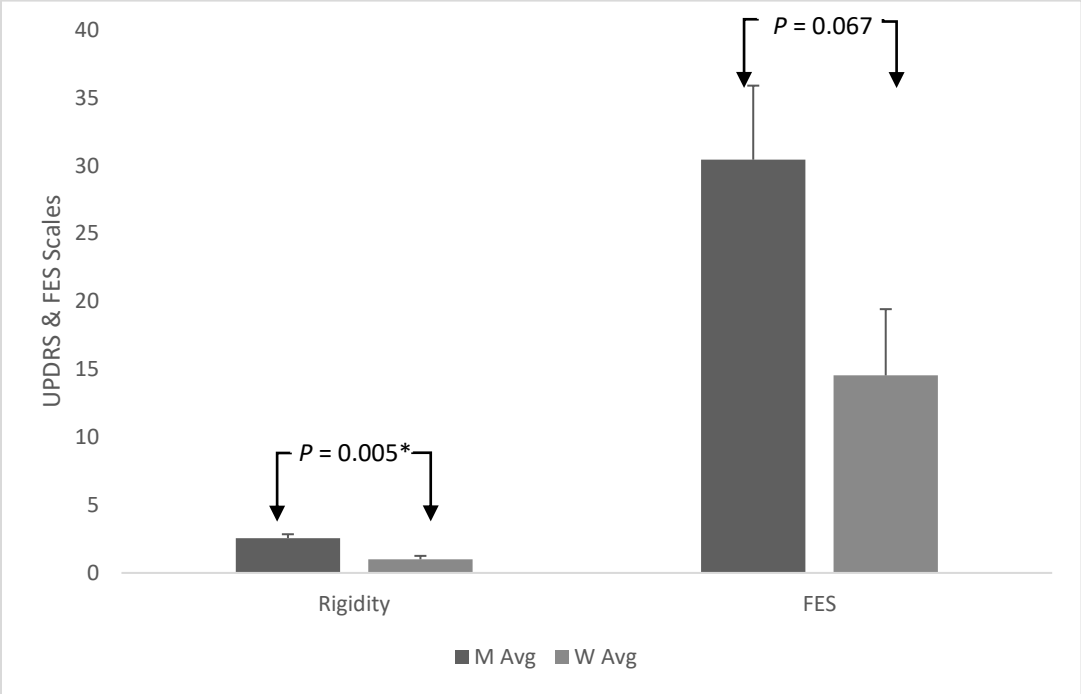

Figure 2. Effect of SEX on rigidity scores on UPDRS and FES scores.

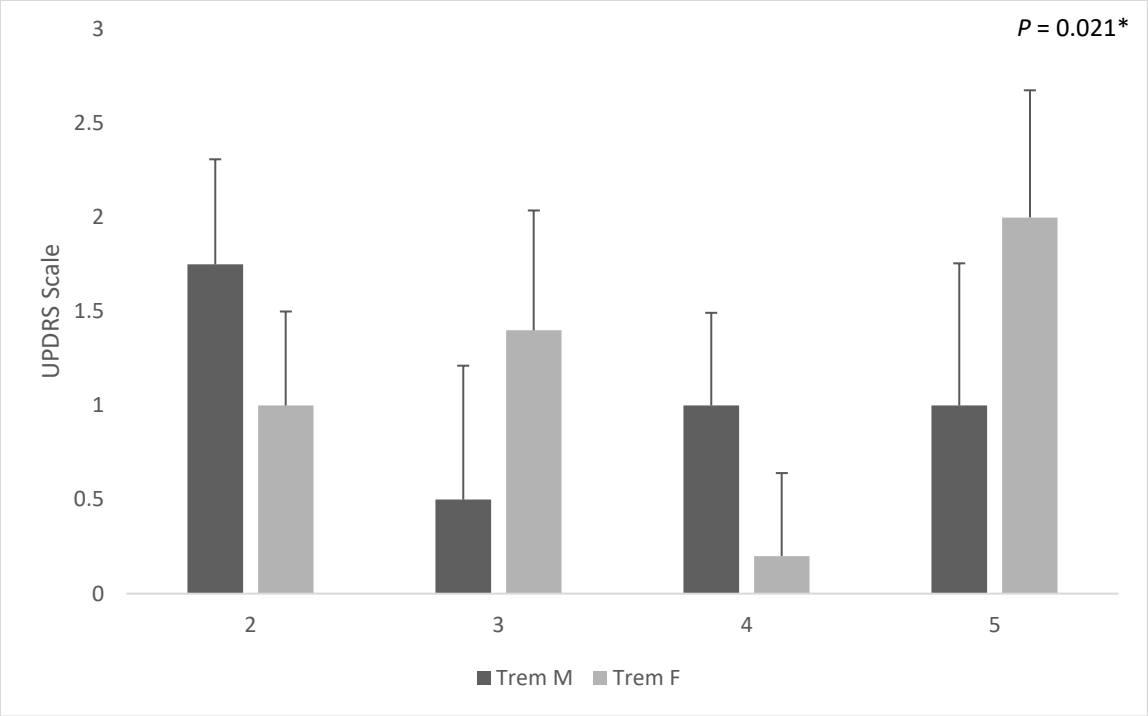

Figure 3. Effect of TIME X SEX on tremor scores on the UPDRS.

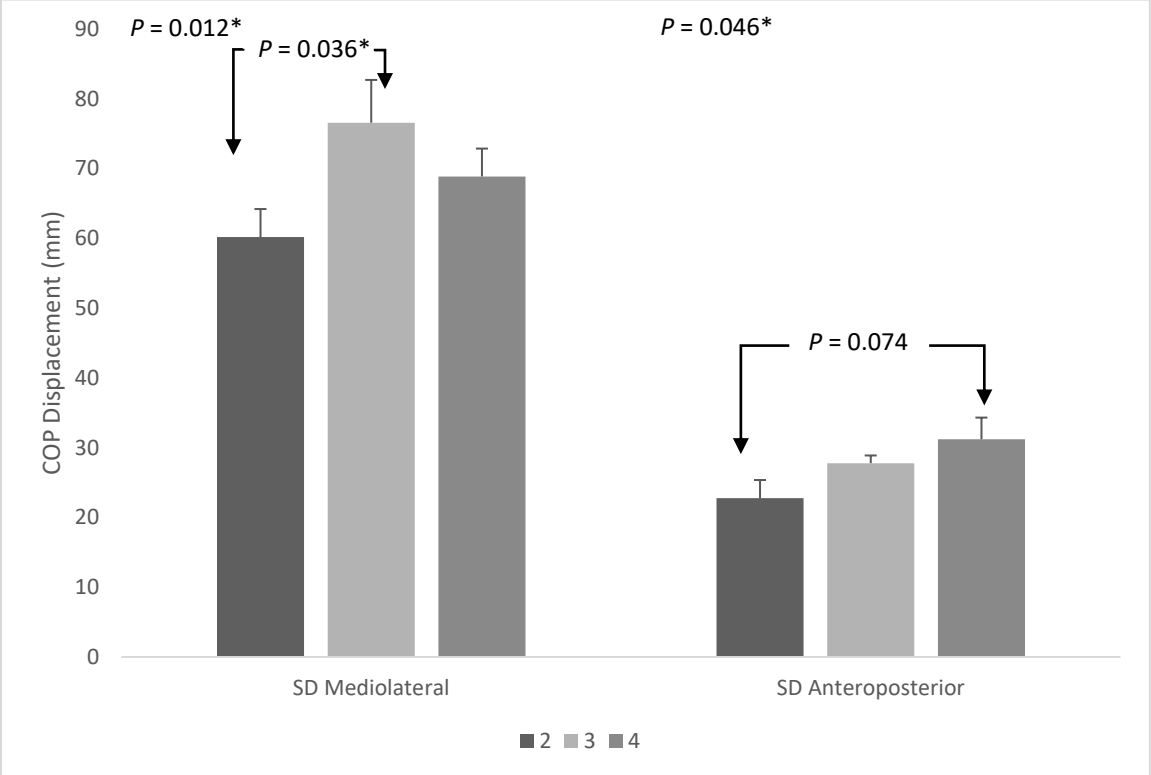

Figure 4. Effect of TIME on the SD of movement of COP in the mediolateral and anteroposterior directions.

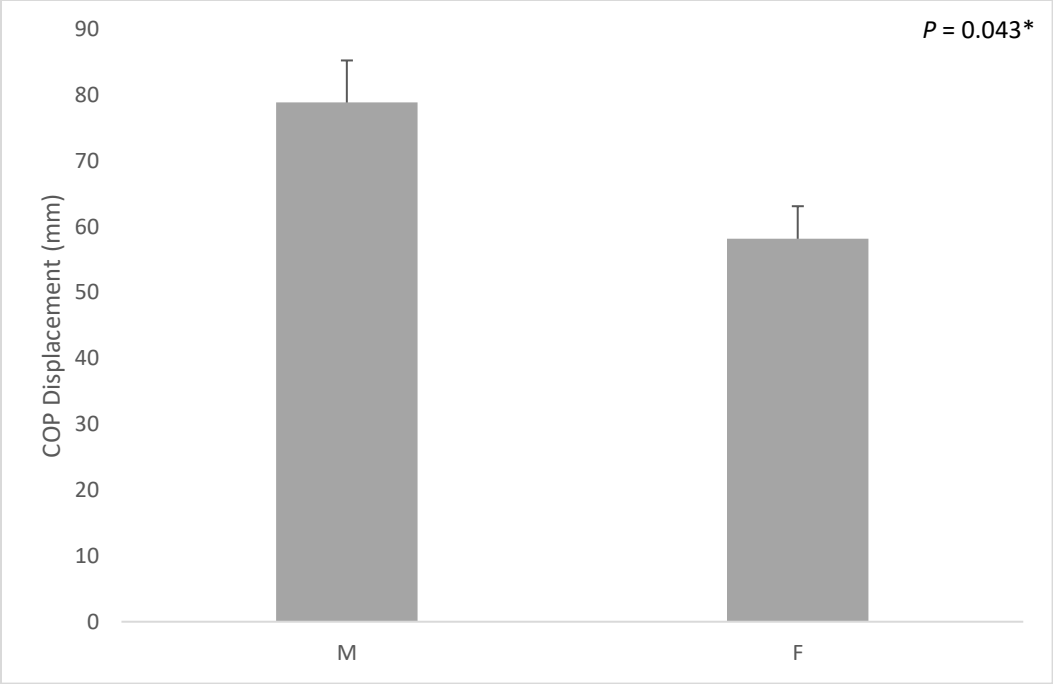

Figure 5. Effect of SEX on the SD of movement of COP in the mediolateral direction.

V. DISCUSSION

Through the one-and-a-half years of data in this study, we have found TIME to have a significant effect on tremor and gait from visits two to five, as well as on SD M-L and A-P from visits two to four. SEX was found to have a significant effect on rigidity and FES for visits two to five, and on SD M-L for visits two to four. This result agrees with a study by Szewczyk-Krolikowski *et al.* (2014) where a similar significant effect on rigidity (p=0.002) was found between sexes in PD. Lastly, TIME X SEX was found to have a significant effect on tremor. However, despite these changes, there has been very little difference in patients over the course of the five years. This is believed to be due to therapeutic reasons, such as the medication dosage these patients are taking. In one example, a patient has increased their dosage seven-fold over only a few years, but regarding motor symptoms during their on-phase has demonstrated very few changes. Meanwhile, their off-phase condition has decreased dramatically.

Interestingly, there appears to be a pattern in motor symptoms, as shown in *Figure 1*, in regard to season. In this figure, time 2 and time 5 show the highest scores on the UPDRS. These timepoints occur in fall (time 2) and late fall/early winter (time 5). Timepoints 3 and 4 occur at late winter/early spring, and early summer, respectively. Therefore, there seems to be an effect of the time of year on the motor symptoms as well. It is speculated that this could be due to individuals being more docile due to inclement weather. Although Postuma *et al.* (2005) found there to be no significant difference among seasons for motor symptoms in PD, further research should be done to confirm

this. If seasonal variation does occur, especially in more variable climates, then this could be an implication for better, more adaptable treatments for patients.

Regarding the significant effect of TIME X SEX on tremor, no clear pattern is evident. When examining *Figure 3*, the values appear to be sporadic and unrelated. Curiously, the men and women flip-flop each visit for their tremor values on the UPDRS. A potential cause could be due to a lack of test-retest reliability or the extent to which medications have worn off by the time of visit. Lastly, this may be related to the seasonal changes. This appears to be more accurate for the women then the men. It would be interesting to see if there are any sex differences between subjects regarding their susceptibility to the changing of seasons. This could be a potential area for further investigation, as well.

One of the most fascinating findings of this study was that the DPC task was much more relevant to fall risk prediction than the SPC task as it was highly correlated with many of the clinical measures used. In this regard, DPC tasks should be further investigated to determine their validity and reliability for predicting a patient's risk of falling as well as for the potential tracking of their disease. Simple clinical measures, such as the TUG, are valid for clinical use, as they are also cheap and easy to conduct. Therefore, a DPC task is not being suggested as a replacement of these tasks, but instead it is being suggested that DPC tasks be used in place of SPC tasks. These tasks are often used for other research and, as shown in this study, have little relevance to clinical determination of fall risk. DPC tasks may be better for these studies and should be further validated to ensure they do predict fall risk. Adkin *et al.* (2003) found a relationship between their SPC tasks and UPDRS posture and gait measures, as well as their

confidence questionnaire. Although these results disagree with ours, they used many variations of SPC, including eyes closed, one-legged stance, standing on foam, and narrow stance, and found that the more variation in the stance, the greater the relationship to the other tests. Therefore, this agrees with our DPC task as it shows that adding variables to relate postural control to movement and other activities of daily living allows for a better prediction of risk for instability. Mezzarobba *et al.* (2018) also support the notion of using DPC tasks as they discovered that the greater the complexity of the DPC activity, the great the ability to recognize postural behaviors. This could lead to better prediction of falls risk and disease progression. Other studies should consider using DPC tasks for patients with PD in order to increase the sensitivity of their tests.

i. Limitations

Although there were some benefits of this study, there were also some limitations. Despite some significant findings, the sample size of 12 individuals was rather small, especially as some were excluded from the results due to missing data. Similarly, some significant effects could have been skewed by one or two individuals who displayed much worse motor symptoms than others. In the future, a larger sample size will give much more accurate and generalizable results. Secondly, there was no age-matched, healthy control group to compare with. Although symptoms would be unrelated, looking into the DPC task between patients with PD and the control may further support the use of the DPC task. Third, there was no regulation of the doses of medication taken throughout the duration of the study. Similarly, patients were not tested at the same time of their "on" phase throughout each visit, either. In the future, it would be helpful to track the progression of the doses of medication over time to see how they compare to the "on"

phase motor symptoms. It would also be important to test at the same time during the "on" phase for all patients during every visit.Similar to the lack of monitoring of the medications, fall frequency was not determined, either. In future research, analysing the frequency of falls, as well as the mechanisms of the falls, in comparison to the data collected may be of interest to help determine what precautions could be taken to prevent future or potentially consequential falls.

ii. Future Directions

Although this study was able to find some significant effects despite the small sample size, there are other things that were overlooked that could potentially help explain some symptomatic changes. It would be interesting to examine the differences in symptoms at different times throughout the year to determine if the changing seasons affect the prevalence and magnitude of the symptoms. It would also be interesting to see if the seasonal changes effect one sex more than the other. This would allow for more personalized and adaptable medical therapies for patients. Another future direction of this study could be to moderate the medication timing. Similarly, studying patients in their "off" phase, if possible, could help to determine how their motor symptoms of their disease are progressing without the medication use. Lastly, looking at the trajectories for the patients could potentially be another area of interest. Paul *et al.* (2016) look at the trajectory of fall risk, which determined to be rather effective, but not at the trajectories of disease progression. More so, it would be interesting to compare these trajectories to the future data collected to see whether trajectories could be beneficial to disease management for patients.

VI. CONCLUSION

This study looked at data from the results of tests done by patients with PD over five different time points. The length of time throughout each of the time points was about one-and-a-half years. Three different clinical measure tests were completed during each visit, including the TUG, UPDRS, and the FES. Two tasks were completed on a force plate, including a SPC and a DPC task. Mixed model RM ANOVAs and a Pearson correlation were conducted to determine if there was any significance within the study. Tremor and gait scores, as well as M-L and A-P SD of COP, were found to be significantly affected by time. Tremor was also significantly affected by time and sex, together. Similarly, rigidity and FES scores, as well as M-L SD of COP, were found to be significantly affected by sex. Lastly, many significant correlations were determined to exist between clinical measure scores, as well as between these scores and DPC measures. No significance was found between clinical measures and SPC measures. In the future, examining the use of DPC tasks could be a potential area to further this study, as well as monitoring medication dosage and stage in “on” and “off” phases.

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Appendix A – UPDRS

I. MOTOR EXAMINATION

5. Speech
0 = Normal.
1 = Slight loss of expression, diction and/or volume.
2 = Monotone, slurred but understandable; moderately impaired.
3 = Marked impairment, difficult to understand.
4 = Unintelligible.

6. Facial Expression
0 = Normal.
1 = Minimal hypomimia, could be normal "Poker Face".
2 = Slight but definitely abnormal diminution of facial expression
3 = Moderate hypomimia; lips parted some of the time.
4 = Masked or fixed facies with severe or complete loss of facial expression; lips parted 1/4 inch or more.

5. Tremor at rest (head, upper and lower extremities)
0 = Absent.
1 = Slight and infrequently present.
2 = Mild in amplitude and persistent. Or moderate in amplitude, but only intermittently present.
3 = Moderate in amplitude and present most of the time.
4 = Marked in amplitude and present most of the time.

6. Action or Postural Tremor of hands
0 = Absent.
1 = Slight; present with action.
2 = Moderate in amplitude, present with action.
3 = Moderate in amplitude with posture holding as well as action.
4 = Marked in amplitude; interferes with feeding.

7. Rigidity (Judged on passive movement of major joints with patient relaxed in sitting position. Cogwheeling to be ignored.)
0 = Absent.
1 = Slight or detectable only when activated by mirror or other movements.
2 = Mild to moderate.
3 = Marked, but full range of motion easily achieved.
4 = Severe, range of motion achieved with difficulty.

8. Finger Taps (Patient taps thumb with index finger in rapid succession.) 0
= Normal.
1 = Mild slowing and/or reduction in amplitude.
2 = Moderately impaired. Definite and early fatiguing. May have occasional arrests in movement.
3 = Severely impaired. Frequent hesitation in initiating movements or arrests in ongoing movement.
4 = Can barely perform the task.

9. Hand Movements (Patient opens and closes hands in rapid succesion.) 0
= Normal.
1 = Mild slowing and/or reduction in amplitude.
2 = Moderately impaired. Definite and early fatiguing. May have occasional arrests in movement.
3 = Severely impaired. Frequent hesitation in initiating movements or arrests in ongoing movement.
4 = Can barely perform the task.

10. Rapid Alternating Movements of Hands (Pronation-supination movements of hands, vertically and horizontally, with as large an amplitude as possible, both hands simultaneously.)
0 = Normal.
1 = Mild slowing and/or reduction in amplitude.
2 = Moderately impaired. Definite and early fatiguing. May have occasional arrests in movement.
3 = Severely impaired. Frequent hesitation in initiating movements or arrests in ongoing movement.
4 = Can barely perform the task.

11. Leg Agility (Patient taps heel on the ground in rapid succession picking up entire leg. Amplitude should be at least 3 inches.)
0 = Normal.
1 = Mild slowing and/or reduction in amplitude.
2 = Moderately impaired. Definite and early fatiguing. May have occasional arrests in movement.
3 = Severely impaired. Frequent hesitation in initiating movements or arrests in ongoing movement.
4 = Can barely perform the task.

12. Arising from Chair (Patient attempts to rise from a straightbacked chair, with arms folded across chest.) 0 = Normal.
1 = Slow; or may need more than one attempt.
2 = Pushes self up from arms of seat.
3 = Tends to fall back and may have to try more than one time, but can get up without help.
4 = Unable to arise without help.

13. Posture
0 = Normal erect.
1 = Not quite erect, slightly stooped posture; could be normal for older person.
2 = Moderately stooped posture, definitely abnormal; can be slightly leaning to one side.
3 = Severely stooped posture with kyphosis; can be moderately leaning to one side.
4 = Marked flexion with extreme abnormality of posture.

14. Gait
0 = Normal.
1 = Walks slowly, may shuffle with short steps, but no festination (hastening steps) or propulsion.
2 = Walks with difficulty, but requires little or no assistance; may have some festination, short steps, or propulsion. 3 = Severe disturbance of gait, requiring assistance.
4 = Cannot walk at all, even with assistance.

5. Postural Stability (Response to sudden, strong posterior displacement produced by pull on shoulders while patient erect with eyes open and feet slightly apart. Patient is prepared.)
0 = Normal.
1 = Retropulsion, but recovers unaided.
2 = Absence of postural response; would fall if not caught by examiner.
3 = Very unstable, tends to lose balance spontaneously.
4 = Unable to stand without assistance.

6. Body Bradykinesia and Hypokinesia (Combining slowness, hesitancy, decreased armswing, small amplitude, and poverty of movement in general.)
0 = None.
1 = Minimal slowness, giving movement a deliberate character; could be normal for some persons. Possibly reduced amplitude.
2 = Mild degree of slowness and poverty of movement which is definitely abnormal. Alternatively, some reduced amplitude.
3 = Moderate slowness, poverty or small amplitude of movement.
4 = Marked slowness, poverty or small amplitude of movement.

I. MODIFIED HOEHN AND YAHR STAGING

STAGE 0 = No signs of disease.
STAGE 1 = Unilateral disease.
STAGE 1.5 = Unilateral plus axial involvement.
STAGE 2 = Bilateral disease, without impairment of balance.
STAGE 2.5 = Mild bilateral disease, with recovery on pull test.
STAGE 3 = Mild to moderate bilateral disease; some postural instability; physically independent. STAGE 4 = Severe disability; still able to walk or stand unassisted.
STAGE 5 = Wheelchair bound or bedridden unless aided.

Appendix B – Tinetti Falls Efficacy Scale

Falls Efficacy Scale

Take a bath or shower

1:Very Confident 2 3 4 5 6 7 8 9 10:Not At All Confident

Reach into cabinets or closets

1:Very Confident 2 3 4 5 6 7 8 9 10:Not At All Confident

Walk around the house

1:Very Confident 2 3 4 5 6 7 8 9 10:Not At All Confident

Prepare meals not requiring carrying heavy or hot objects

1:Very Confident 2 3 4 5 6 7 8 9 10:Not At All Confident

Get in and out of bed

1:Very Confident 2 3 4 5 6 7 8 9 10:Not At All Confident

Answer the door or telephone

1:Very Confident 2 3 4 5 6 7 8 9 10:Not At All Confident

Get in and out of a chair

1:Very Confident 2 3 4 5 6 7 8 9 10:Not At All Confident

Getting dressed and undressed

1:Very Confident 2 3 4 5 6 7 8 9 10:Not At All Confident

Personal grooming (i.e. washing your face)

1:Very Confident 2 3 4 5 6 7 8 9 10:Not At All Confident

Getting on and off of the toilet

1:Very Confident 2 3 4 5 6 7 8 9 10:Not At All Confident