Relation between ability to track force during dual tasking and function in individuals with Parkinson’s disease

Sujata D. Pradhan PT PhD, Bambi R. Brewer PhD, George E. Carvell PT PhD, Patrick J. Sparto PhD
PT, Anthony Delitto PT PhD FAPTA, Yoky Matsuoka PhD

Abstract—Force tracking using fine motor control with simultaneous cognitive dual tasking may provide a useful measure of disease progression in Parkinson’s disease (PD). Due to the challenging nature of the task, measures from this task may be useful in documenting changes in the progression of the disease especially since such changes are subtle in nature early on in the disease process. We have described a novel force tracking task and presented its relation to motor function based on the Unified Parkinson’s Disease Rating Scale as well as specific to hand function based on the Grooved Pegboard Test, in participants with PD. This work is the first step in a line of research with the overall goal of developing a clinical progression biomarker with the help of a haptic device for PD.

Index Terms—Parkinson’s disease, Force tracking, Fine motor function, disease progression

I. INTRODUCTION

Parkinson’s disease is a a progressive neurodegenerative disorder caused by the degeneration of the nigrostriatal dopaminergic pathways within the basal ganglia (BG). Clinically the disease is characterized by bradykinesia (slowness of movement), akinesia, resting tremor, and rigidity [1]. This disease affects 0.3 % of the entire population and 1% of the people over 60 years in industrialized countries. This is an age related disease which is rare before age of 50 yrs and the prevalence increases to up to 4 % in higher age groups [2]. Pathologic studies have shown that by the time the disease is diagnosed clinically, there is over 40% loss of dopaminergic neurons. The disease has a preclinical duration of about six years with the rate of progression being higher in the initial six years [3-4]. Neuroprotective effects of exercise have been well documented in animal models of PD [5]. Early intervention with exercise may help slow the progression of PD in humans [6-7]. Sensitive outcome measures are necessary to document such effects in human studies. Since motor deficits tend to be subtle in the earliest stage of the disease, sensitive tests that document outcome measures must be developed to reveal these subtle deficits. Both quantitative and self-report measures show reduced hand dexterity in Parkinson’s disease [8-11]. Among the various fine- and gross-motor activities of the upper extremity, precision haptic activities are inherently more challenging to perform. This can be inferred from the widespread activation of numerous areas of the cortex during precision tasks in comparison to gross motor activities despite of the fact that higher level of muscular forces that required during gross motor activities [12]. Another aspect of motor performance that could make it more difficult is the amount of cognitive involvement during the task. Activities that require attention to more than one thing at a time pose a greater challenge to the nervous system. It is well documented that the basal ganglia play an important role in attention [13-14] and that activities that require attention are difficult to perform in people with PD [15-16].

We created a task that that requires the subject to track the amount of force created between the index finger and the thumb using a precision grip. We used force tracking instead of distance tracking for our task, since the basal ganglia play a significant role in the control of force[17]. To make our task more challenging we included a cognitive distraction component during the task. This work is the first step in a line of research with the overall goal of developing a clinical progression biomarker for PD.

II. METHODS

A. Subjects

Thirty participants with mild to moderate PD participated. They were asked to stay off their medications for PD, 12 hours prior to testing to avoid potential effects of the medication on their motor performance. Demographic characteristics of participants are summarized in table 1.
B. Inclusion Criteria

1. Previously established diagnosis of Parkinson’s disease (noted by a physician) and a reported history of symptoms of slowed movement, tremor, difficulty initiating movement for a minimum of one year and/or Hoehn and Yahr scale rating documented by the participants neurologist.
2. Age ≥ 18 years of age
3. Subject does not experience abnormal movements including dyskinesia and other involuntary movements that would interfere with the test task except tremor.
4. Score of 27 or greater on the Mini Mental State Exam indicating that they are free of dementia [18].
5. No history of concurrent CNS disease.

C. Exclusion Criteria

1. Restriction of movement in the upper extremities.
2. Sensory loss in the hand, as determined by superficial sensory testing.
3. Loss of vibration sense in the hand.
4. Subjects unable to stay off medications 12 hours prior to the appointment.

D. Force Tracking task

We used two six-axial force sensors (nano-17, ATI automation Industries, USA) that are capable of sensing forces and torque each along three axes. For our study, we were interested in looking at the force data only. The sensors have a resolution for force of 0.003 N. These were mounted on two steel plates. The steel plates were mounted vertically on a plastic board at an angle of 45 degrees to the long axis of the forearm. The plastic board can be fixed to the edge of any table with the help of clamps. The experimental set up of the equipment is shown in Figure 1. The participants had to track two different waveforms shown on the screen by making adjustments to the amount of force between the thumb and the index finger.

The first waveform consisted of a sine wave at a frequency of 0.2 Hz moving across the screen with a black line running through its centre, which posed an accuracy requirement. The sine wave pattern was chosen since it provided a continuous, dynamic, sequential activity (gradual and smooth transition between task components). The participants also had to switch between gradually increasing force production (in the up-going part of the wave) and gradually decreasing force production (in the down-going part of the wave). The amount of force required to track the target wave was set to 6 N at the highest peak of the wave and 2 N at the lowest trough of the wave. This range of force is comparable to normal amounts of forces required during performance of everyday activities involving precision grip [19].

The second waveform was generated by the integral of a pseudorandom ternary sequence. The wave displayed on the screen was pseudo-random in nature, meaning that it had both a low frequency (0.01 Hz) pattern and some high frequency (2.5 Hz) components. The subjects were shown only part of the wave on the screen and were asked to track it as it appeared on the screen. The subjects were thus unaware of the upcoming force requirements due to the asymmetric nature of the wave and presence of some high frequency components, introducing an unpredictable component to the task. Our aim in doing the second force tracking task was to see how well the subjects make rapid adjustments in their force with no visual prediction cues.

Both waveforms were tracked for a total duration of 200 seconds. The first 20 seconds of the display were a constant value of 4 N for the participants to adjust to the tracking. The next 1 minute was pure tracking without any mental distraction. At the end of minute 1 the participants saw a display on the screen that said “Count backwards from 100 by 1”. At this time, the participants were asked to count aloud backwards consecutively by one. At the end of minute 2 a statement was displayed saying “Count backwards from 100 by 3”. At this point, we asked them to count aloud backwards from 100 subtracting 3 every time. If the participants made a mistake greater than five numbers, we corrected it and they continued to count backwards from the corrected number. If the mistake was less than five numbers, they continued counting.

Participants were tested for both hands to reduce the effects of dominance and unilateral or asymmetrical involvement (see data analysis section).

E. Clinical measure of physical function in PD

1. Unified Parkinson’s Disease Rating Scale (UPDRS)
   We administered the Unified Parkinson’s disease rating scale (UPDRS) to all participants. The UPDRS is an instrument used for rating symptom severity in Parkinson’s disease based on history (2 sections) and physical examination (one section). Symptom severity is rated on 31 items in 3 sections; individual items are rated on a scale of 0 to 4, and total possible scores range from 0 to 176 with higher scores indicating greater severity of disease. The UPDRS has been widely used in clinical studies of Parkinson’s disease as a reliable composite scale of physical function in this population [20-21].

2. Grooved Pegboard Test (GPT)
   The grooved pegboard is a manipulative dexterity test that consists of 25 holes with a slot randomly positioned at one of the four primary compass directions (Figure 2). The participants placed the pegs into the board as quickly as possible. The task was performed once with the right hand and then once with the left hand. The subjects were allowed up to 5 minutes (300 seconds) to complete the task. The total time to place all 25 pegs were recorded in seconds. Higher scores reflect a lower level of performance. The grooved pegboard has been shown to correlate with nigrostriatal degeneration [22].

III. DATA ANALYSIS

To examine whether the data measured during our testing protocol could be used to predict an individual’s UPDRS score, we computed three summary variables for each trial and cognitive load condition. The first summary variable was
the tremor integral (TR); we quantified the tremor exhibited by an individual by computing the power spectral density and calculating the area under this curve between 2 and 8 Hz. This range includes the 4-5 Hz window that typically bounds Parkinsonian tremor [23]. After computing the tremor integral, data were filtered with a 2nd order dual-pass Butterworth filter with a cut-off frequency of 2 Hz. The filtered data were used to calculate the remaining summary variables. The second summary variable was the root-mean-square error (RMSE) between the target wave and the subject’s force response. The third summary variable was the lag between the target waveform and the subject’s force response during the pseudorandom trial, which was calculated as the time interval that maximized the cross-covariance between the two waves. The lag was bounded at 2 s for the sine target and 5 s for the pseudorandom target. If the maximum covariance was less than 0.35, the lag was automatically set to the maximum value. Although each variable was calculated separately for each of the three minutes, for the analyses presented here we will use variables from min 3 as these represent the motor performance with the additional effect of dual tasking (counting by 3). Many of our participants had asymmetrical motor symptoms of PD. For this reason, we divided the data collected for both hands based on the side of better/worse performance, rather than based on the right/left side. The side of better performance was defined as the side with the lower RMSE error averaged over the sine and pseudorandom trials.

The force tracking variables included the RMSE from the sine wave trial (RMSE_S) since this was the trial with the symmetrical target waveform where the primary outcome of interest was whether they could track the target closely with the least amount of error, the tremor (TR_S) from the sine wave trial and the lag (LAG_PR) from the pseudorandom trial since the pseudorandom trial was the one where the participants did not know the upcoming force requirements and were expected to react as the wave appeared on the screen, thus the lag measure in this trial reflected the time required for them to react.

A hierarchical multiple regression analysis was performed using the combined score of the UPDRS subsections for activities of daily living and motor subscale (UPDRS-AM) score as the dependent variable and clinical performance measures (GPT score and force tracking variables) as the predictor variables. For the first block of predictor variables, we entered the GPT scores and for the second block, we entered the force tracking variables to examine the additional potential of these variables in predicting function based on the UPDRS-AM, over and above what could be explained by the traditional test of fine motor control used in this population represented by the GPT.

IV. RESULTS

Demographic characteristics of our participants along with their clinical test scores are summarized in Table 1. Descriptive statistics about the force tracking variables are summarized in Table 2. Bivariate correlations were computed between the combined scores of the motor and activities of daily living subsections of the UPDRS (UPDRS-AM) and the force tracking variables. Variables that correlated significantly with the UPDRS-AM (Table 3) were entered as independent variables in the multiple regression model. Auto correlation among predictor variables was examined using the Durbin-Watson statistic which was found to be 1.78. A value of 2 indicates there appears to be no autocorrelation. If the Durbin–Watson statistic is substantially less than 2, there is evidence of positive serial correlation. As a rough rule of thumb, if Durbin–Watson is less than 1.0, there may be cause for alarm. We looked at the contribution of the established GPT score in prediction of the combined ADL and motor score of the UPDRS. In addition we also looked at what additional contribution the force tracking variables could have on the ability to predict the UPDRS score. Due to our limited sample size of 30 participants, we chose to enter force tracking variables for the better performance side only. However, a similar analysis with force tracking variables from the side of worse performance produced similar results. We found that the GPT score alone could explain about 64% of the variance in the UPDRS (F=24.3, df=2,27, p=0.000) and an additional 12% could be explained by the force tracking variables (F=3.8, df=3,24, p=0.022) (See Table 4).

V. DISCUSSION

A. Unique contributions from our study

Numerous studies have used manual tracking paradigms to quantify motor function. But most of these studies utilized tracking as a means to evaluate the effects of medication, adjusting medication dosage, evaluating effects of deep brain stimulation or other surgeries [24-25] for PD, evaluating cognitive or emotional profiles of people with PD [26] and investigating tremor [27]. Other investigators have used larger movements of the arm [28] or the wrist [29] which may not be effective in documenting subtle changes in motor control that appear early on that may require using tracking tasks involving precision control. Other proposed assessment tools utilize target tracking, an established paradigm for measuring differences between individuals with and without PD [30-32]. For example, Allen et al. [33] used a joystick and steering wheel designed for video games to measure the ability of individuals to track pseudorandom or sinusoidal waveforms; they measured a significant between-group difference for individuals with and without PD. We have created a force tracking task with simultaneous cognitive distraction and investigated its relation to function based on the GPT as well as the UPDRS. Our aim is to use this pilot data to develop a clinical progression biomarker for PD.

B. Interpretation of our results and future direction

Although significant, the improvement in prediction due to the force tracking variables is modest but it adds an important objective measure of the quality of movement that the GPT fails to capture. This is illustrated in Figure 3 where both participants had a ceiling score on the GPT (300 sec) but performed significantly differently from each other on the
force tracking task. The force tracking task can objectively measure such qualitative differences that may be predictive of motor dysfunction at the earliest stages of the disease. The GPT involves a dynamic movement component which is lacking in our test and hence the next step in our research is to have a combined measure of force as well as movement modulation that will be more representative of functional activities performed everyday. Direct comparisons between the resolutions of the UPDRS and the measures from the force sensor data are inapt, since they measure different concepts – the UPDRS measures function while our test measures impairment. Also, since motor symptoms in PD progress non linearly [34], such comparisons cannot be made on the basis of cross sectional data. An alternative would be for future work to compare resolutions of the two tests independently to the gold standard (imaging) in measuring disease progression using a prospective cohort of individuals with PD.

Positron Emission Tomography (PET) and Single Photon Emission Computerized Tomography (SPECT) imaging is the current gold standard in the area of biomarkers for PD [35], but nigrostriatal damage accounts for less than half the variability observed in motor impairment in individuals with PD [36]. At the same time, clinical scales such as the UPDRS cannot precisely quantify motor symptoms early in the disease process [37]. By combining precise technology and a simultaneous task paradigm, we hope to create a quantitative functional assessment for PD that can be used for measurement of disease progression.

One of the limitations of our study was its cross sectional design. This was appropriate given the preliminary nature of our work and in the next phase we will follow participants longitudinally over a period of 24 months to document progression of the disease over time. Due to the isometric nature of the task our associations with a measure of function are moderate since most activities of daily living involve simultaneous control of force as well as movement along with dual tasking. We plan to make our test more challenging and functional by incorporating a dynamic kinematic component to the test. We have accomplished this by incorporating the force sensors with haptic devices capable of tracking position accurately to improve the applicability of our test. The haptic devices that have been used for this purpose are the commercially available PHANTOM robots (Sensable Technologies, MA) that are capable of sensing position along three axes and providing force feedback if needed (Figure 4). Monitoring kinetics as well as kinematics of fine motor control along with simultaneous dual tasking will allow us to challenge performance for early detection of PD, and to monitor subtle changes in motor control as the disease progresses.

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REFERENCES


Figure 1: Figure on the left shows position of the upper extremity during the experiments. Figure on the right shows the force sensors mounted on the steel plates for ease of grasp.

Figure 2: Grooved Pegboard Test

Figure 3: Performance of 2 participants with PD on the force tracking task (Dotted line represents target force, solid line represents subject’s performance on the sine trial during the third minute when participants were counting backwards by 3 during simultaneously tracking force. Both participants scored the same on the timed GPT (300 sec) but have quite different precision force control on this force-tracking task. Participant on the left shows the sinusoidal pattern of produced force in an attempt to track the target, whereas participant on the right shows extremely poor performance on the tracking task.
Figure 4: PHANTOM robots (Sensible technologies, MA) capable of monitoring position along three axes as well as providing force feedback.

<table>
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<th>Table 1: Descriptive Statistics Clinical Measures</th>
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<td>Age</td>
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<td>UPDRS-AM</td>
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<td>GW</td>
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UPDRS: Unified Parkinson’s Disease Rating Scale, UPDRS-AM: UPDRS- Activities of daily living and motor score combined, GB: Grooved pegboard score – better performance side, GW: Grooved pegboard score – worse performance side

<table>
<thead>
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<th>Table 2: Descriptive Statistics: Force Tracking variables</th>
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Lag( LAG_PR), Tremor from sine trial(TR_S), Root mean square error from the sine trial(RMSE_S), The prefix BP denotes side of better performance, WP denotes side of worse performance (based on average combined RMSE scores from the sine and pseudorandom trial)
Table 3: Independent Correlations between predictors and the dependant variable

<table>
<thead>
<tr>
<th></th>
<th>UPDRS-AM</th>
<th>RMSE_S</th>
<th>TR_S</th>
<th>LAG_PR</th>
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<td>UPDRS_AM</td>
<td>0.58**</td>
<td>0.41*</td>
<td>0.44*</td>
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<tr>
<td>RMSE_S</td>
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<td>0.71**</td>
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<td>LAG_PR</td>
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* Sig at 0.05 level
**Sig at 0.01 level

Lag (LAG_PR), Tremor from sine trial (TR_S), Root mean square error from the sine trial (RMSE_S), Unified Parkinson’s Disease Rating Scale- Activities of daily living and motor score (UPDRS-AM).

Table 4: Regression Analysis

<table>
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<td>Sig F Change</td>
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| | a | .80 | .64 | .62 | 7.65 | .64 | 24.28 | 2 | 27 | 0.00 |
| b | .87 | .76 | .71 | 6.66 | .12 | 3.86 | 3 | 24 | 0.02 |

a. Predictors: (Constant), Grooved Pegboard test for worse performed side (GPT_W), Grooved Pegboard test for better performed side (GPT_B)
b. Predictors: (Constant), GPT_W, GPT_B, Lag (LAG_PR), Tremor from sine trial (TR_S), Root mean square error from the sine trial (RMSE_S)

Dependent Variable: Unified Parkinson’s Disease Rating Scale- Activities of daily living and motor score (UPDRS-AM).