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Variability of EMG patterns: a potential neurophysiological marker of Parkinson's disease?

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Abstract

Objective—This study evaluated whether changes in the electromyographic (EMG) pattern during rapid point-to-point movements in individuals diagnosed with PD can: 1) distinguish PD subjects from healthy subjects and 2) determine if differences in the EMG pattern reflect disease severity in PD.

Methods—Three groups of 10 PD subjects and 10 age/sex matched healthy subjects performed rapid 72° point-to-point elbow flexion movements. PD subjects were divided, *a priori*, into three groups based upon off medication motor UPDRS score.

Results—Measures related to the EMG pattern distinguished all PD subjects and 9 out of 10 healthy subjects, resulting in 100% sensitivity. Further, significant correlations were shown between EMG measures and the motor UPDRS score. After 30 months, the one healthy subject whose EMG pattern was abnormal was reexamined. The EMG measures remained abnormal and the motor UPDRS score went from 0 to 10. Parkinson's disease was diagnosed.

Conclusion—Measures related to the variability of the EMG pattern during rapid point-to-point movements provide neurophysiological measures that objectively distinguish PD subjects from healthy subjects. These measures also correlate with disease severity.

Significance—EMG measures may provide a non-invasive measure that is sensitive and specific for identifying individuals with PD.

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Keywords

Isotonic movements; Parkinson's disease; electromyographic (EMG) activity; disease severity; disease progression

Introduction

When the diagnosis of Parkinson's disease (PD) is confirmed upon brain autopsy diagnostic accuracy can be as high as 90% (Hughes et al., 2001), but as low as 74% in community based samples (Hughes et al., 1992). This discrepancy has led to the development of tests which are designed to improve diagnostic accuracy. These tests range from simpler and less expensive tests such as tapping and olfactory tests to more expensive and complicated neuroimaging tests. When neuroimaging tests such as position emission tomography (PET) scans are used, the diagnostic accuracy can range from 85% (Morrish et al., 1995) to 100% (Hu et al., 2001) for distinguishing mild to severe PD subjects from healthy subjects. Similarly, when using single photon emission computed tomography (SPECT) scans an overall sensitivity and specificity of 96% was observed when distinguishing mild to severe PD subjects from healthy subjects (Benamer et al., 2000). The correlation of PET and SPECT scans with disease severity (motor UPDRS score) is much less impressive. The highest correlation for PET was $r = -0.60$ (Huang et al., 2007), while the highest correlation for SPECT was $r = -0.59$ (Ichise et al., 1999). However, several other studies have revealed no significant change between these neuroimaging tests and motor UPDRS score (Hu et al., 2001; Morrish et al., 1998; Antonini et al., 2001). PET and SPECT tests are also expensive and have the added risk of radiation exposure which may preclude repeated testing (Volkow et al., 1997).

The success of inexpensive and non-invasive objective tests to distinguish PD subjects from healthy subjects has varied (Camicioli et al., 2001; Montgomery et al., 2000a; Montgomery et al., 2000b). For example, a combination of wrist movements (reaction times and movement velocities), olfaction and mood assessment resulted in 69% sensitivity and 88% specificity (Montgomery et al., 2000a); however the sensitivity increased to 93% (specificity of 86%) with the combination of finger tapping and olfaction (Camicioli et al., 2001) when distinguishing PD subjects from healthy subjects. A modest, but significant correlation ($r = -0.43$) has been shown between olfactory discrimination and the motor UPDRS score in PD subjects (Tissingh et al., 2001).

Several studies have suggested that the EMG patterns for rapid point-to-point movements are different in PD subjects when compared to healthy subjects (Farley et al., 2004; Hallett and Khoshbin, 1980; Hallett et al., 1977; Robichaud et al., 2004; Vaillancourt et al., 2004). These differences may provide potential neurophysiological parameters that can both distinguish PD subjects from healthy subjects and relate to disease severity. Pfann and colleagues (2001) showed that PD subjects exhibit patterns of muscle activation that can vary from trial to trial, and vary with disease severity. For example, the duration of the first agonist burst can be short (Pfann et al., 2001) and have multiple cycles (Berardelli et al., 1986; Hallett and Khoshbin, 1980), or the duration of the first agonist burst can be longer than what is typically exhibited by a healthy subject (Pfann et al., 2001). While both short and long first agonist bursts are exhibited by mild to moderate PD subjects from trial to trial, most if not all of the movements performed by severe PD subjects exhibited a short first agonist burst (Pfann et al., 2001).

Therefore, the present study tests the hypothesis that changes in the pattern of the duration of the first agonist burst during rapid elbow flexion movements can: 1) distinguish individual PD subjects from healthy individual subjects with high sensitivity and specificity and 2) determine

whether differences in the pattern of the first agonist burst correlates with disease severity in PD.

Methods and Materials

Subjects

Three groups of 10 PD subjects (mild, moderate and severe) and one group of 10 age and sex-matched healthy subjects were tested according to University of Illinois at Chicago and Rush University Medical Center Institutional Review Board approved protocols. PD subjects were accepted into the study if they: 1) had been diagnosed as having PD by a Movement Disorders Neurologist according to the United Kingdom Parkinson's disease Brain Bank criteria (Hughes et al., 1992), 2) had no other known neurological disorder as determined by history, and 3) had no known injury or other disease that might interfere with motor function. All individuals (healthy and PD) had a Mini-mental state examination (MMSE) score of 27 or greater (Folstein et al., 1975) and no subject was excluded because of their MMSE score. While the MMSE was used to screen subjects for cognitive ability, we did not screen for depression.

Experimental protocol

All subjects (healthy and PD) were examined using the motor subsection (part III) of the UPDRS (Fahn et al., 1987) and the MMSE. These tests were performed prior to beginning motor control testing. For PD subjects, testing was performed in the morning after a 12 hour overnight withdrawal of their antiparkinsonian medication. PD subjects were divided into three groups: 1) mild PD (motor UPDRS score 20 or below), 2) moderate PD (motor UPDRS score from 21 to 35), and 3) severe PD (motor UPDRS score greater than 35). PD subjects were tested on their most affected upper extremity. Within each of the three PD groups, the most affected limb was the dominant limb for half of the subjects. Therefore, the dominant limb was tested on half of the healthy subjects. Each group consisted of five males and five females, and there was no significant effect of group on age ($F_{3,36} = 0.97$, $p = 0.42$). Table 1 presents the demographic, disease and treatment information on each of the 40 subjects.

Experimental set-up

Individuals were seated with their arm abducted 90°. The forearm was placed on a rigid, lightweight manipulandum that freely rotated about a single axis (see Fig. 1). Surface EMG signals were recorded from the biceps and the triceps (lateral head). The EMG signals were bandpass filtered between 20–450 Hz using built-in Bagnoli filters and then amplified (gain 1,000) (Delsys Inc.). All signals were digitized at 1000 Hz with 12-bit resolution. For further detail see Vaillancourt and colleagues (2004).

Individuals viewed a computer monitor that displayed a vertical cursor (equivalent to 1° of elbow angular displacement), which corresponded to the angle of the elbow joint. A broad marker was located as the target at the desired angular distance. The width of the broad marker corresponded to 6° of angular elbow movement.

Task

Individuals performed thirty 72 elbow flexion movements “as fast as possible”. The subject aligned the cursor on a marker corresponding to the initial starting position. A tone signaled the subject to move. A second tone 3–5 seconds later signaled the end of the trial, at which time the subject returned to the initial start position.

EMG processing

Data were digitally processed offline. The onset and offset of the first agonist (biceps) burst was marked by a Matlab routine using the following procedures (Vaillancourt et al., 2004).

1. EMG data were full-wave rectified and filtered with a 2nd order low-pass filter with a 50 Hz cutoff.
2. Movement onset was identified from the acceleration signal by finding peak acceleration and then searching backwards to locate the first acceleration data sample that fell below 5% of peak acceleration.
3. Because of the electromechanical delay (~30 ms) between EMG and kinematic signals (Corcos et al, 1992), the algorithm searched for the biceps EMG onset before the onset of acceleration. Each data sample from the biceps EMG signal during this period was compared with the baseline biceps EMG activity (mean EMG activity for 50 ms before acceleration onset). If the biceps EMG data sample was greater than a threshold (5 times the standard deviation of the baseline biceps EMG activity) this was marked as the onset of the biceps EMG burst.
4. The algorithm then searched forward to find when the biceps EMG signal fell below a threshold value (6 times the standard deviation of the baseline biceps EMG activity) for 10 consecutive samples. This time point was set to the offset of the biceps EMG burst.

Subsequent to marking onset and offset of the first biceps burst by the computer algorithm, the data were visually inspected by one investigator (KP). Trials were rejected for the following reasons: 1) technical problems, 2) movement not completed in allotted time because movement initiation was dramatically delayed, 3) movement initiated in wrong direction, 4) movement not initiated from the given initial position, and 5) agonist offset or onset could not be marked. For the healthy subjects 2.6 out of the 30 trials were rejected. Similarly, for the PD subjects 2.7 out of the 30 trials were rejected.

When visual inspection did not agree with the algorithm markings, a second investigator (JR) reviewed the markings. Both investigators discussed the marking until agreement was reached. Across all 40 subjects, an average 30% of the marked trials were visually adjusted.

EMG dependent measures

In our analysis, we used two measures that were derived from the duration of the first agonist (biceps) burst. First, because many of the trials of the first agonist burst were quite long (positively skewed) within a block of trials for most of the PD mild and PD moderate subjects, we applied a base 10 logarithm transformation to the data. The second measure was the percentage of burst durations from the biceps that were short. Next, each of these two measures are described in detail.

1) Standard deviation of the $\log_{10}(x)$ transformed durations of the first agonist burst—This parameter characterizes biceps burst duration variability for the durations of the first biceps burst. It was calculated by obtaining the standard deviation of the $\log_{10}(x)$ transformed data for the durations of the first biceps burst. Figure 2 shows data for the duration of the first biceps burst from a representative subject from the healthy (Fig. 2A), mild PD (Fig. 2B) and severe PD (Fig. 2C) subject groups. Figures 2Ai–2Ci depict representative trials of the biceps EMG activity from a healthy subject (Fig. 2Ai; duration = 150 ms.), a mild PD subject with a long burst duration (top Fig. 2Bi; duration = 210 ms) and a short burst duration (bottom Fig. 2Bi; duration = 70 ms), and a severe PD subject (Fig. 2Ci; duration = 50ms). The durations of the first biceps burst for all trials are shown in Figure 2Aii for the healthy subject,

Figure 2Bii for the mild PD subject and Figure 2Cii for the severe PD subject. As can be seen in part Cii, all the trials for the severe PD subject reach baseline prior to 90 ms. In contrast, in part Bii, the trials for the mild PD subject form two data clusters. The trials in the first cluster reach baseline prior to 90 ms, while the second cluster of data points exhibits biceps burst durations that are all longer than 125 ms. Figures 2Aii and 2Cii show individual trial data which are tightly clustered (as is commonly seen in healthy individuals and in PD individuals with short, fixed durations of the first agonist burst at all distances). The last column of Figure 2(iii) shows the $\log_{10}(x)$ transformed data for the durations of the first biceps burst. Figures 2Aiii and 2Ciii show the $\log_{10}(x)$ transformed data where the standard deviations between these two data sets are similar. As shown in Figure 2Bii, individual trial data (open circles) are spread out and the standard deviation of the $\log_{10}(x)$ transformed data is large (Figure 2Biii).

2) Percentage of trials exhibiting short first agonist (biceps) burst durations—

This parameter, which characterizes an inability to produce a biceps burst of normal duration, was calculated by determining the percentage of trials exhibiting a short first biceps burst duration (less than 90 ms) compared to the total number of trials completed. Previous data has shown that, in trials where there is evidence of multiple agonist bursts, the duration of the first agonist burst is usually less than 90 ms (Robichaud et al., 2002; Farley et al., 2004).

Statistics

Separate one-way ANOVA's were performed to determine whether biceps burst duration variability and the percentage of short first biceps burst durations differed among the four subject groups. Bonferroni/Dunn *post hoc* tests were used for follow-up analyses.

Receiver Operating Characteristic (ROC) curves were used to summarize the sensitivity (proportion of PD subjects who had a positive test result) and specificity (proportion of subjects without PD who had a negative test result) (Pepe, 2003) for biceps burst duration variability, the percentage of trials with a short biceps duration burst, and a measure which combined the above two parameters (see combined score in results). Finally, for the PD subjects, linear regression was used to determine whether measures derived from the duration of the first biceps burst correlated with disease severity as measured by the motor UPDRS score.

Results

Biceps burst duration variability and the percentage of short first agonist burst durations

A one-way ANOVA demonstrated significant group effects for biceps burst duration variability. Follow-up analyses revealed that both the healthy (mean = 0.298) and severe PD (mean = 0.369) groups exhibited less variable data when compared to both the mild (mean = 0.624) and moderate (mean = 0.599) PD groups (see Table 2).

A one-way ANOVA also revealed significant group differences for the percentage of short first agonist burst durations. Follow-up analyses demonstrated that the healthy group (mean = 13%) exhibited a lower percentage of short biceps burst durations when compared to all three PD groups. Further, the PD severe group (mean = 85%) exhibited a greater percentage of short biceps burst durations when compared to both the mild (mean = 53%) and moderate (mean = 55%) PD groups (see Table 3).

Individual Subject Analysis

Figure 3A shows a scatterplot which compares biceps burst duration variability and percentage of short duration first biceps bursts for each subject. This plot reveals that, when standard deviation values greater than 0.47 for biceps burst duration variability and values greater than 36% for the percentage of short duration biceps burst were used, all PD subjects could be

distinguished from 9 out of 10 healthy subjects (solid black squares). Based upon this observation, a combined score was computed from these two parameters which was based upon the maximum value of the cut-off score of both scaled values. Since these parameters are measured in different units ($\log_{10}(x)$ and percentages, respectively), the combined score was computed by the following equation.

$$\text{combined_score} = \left(\frac{\frac{\text{the standard deviation of the log } 10(x) \text{ transformed data}}{\text{cutoff value for the standard deviation of the log } 10(x) \text{ transformed data } \{0.47\}} + \frac{\text{percentage of short first agonist burst durations}}{\text{cutoff value for the percentage of short first agonist burst durations } \{36\% \}} \right)$$

The ROC curves for each parameter alone, along with the combined score are illustrated in Figure 3B. This figure shows the PD subjects are well separated from the healthy subjects when the percentage of short first biceps burst durations (dashed and dotted line) or the combined score (dotted line) are used (areas under the ROC curve of 0.953, 0.967, respectively), however, this separation is considerably less when using biceps burst duration variability (solid line) (area under the ROC curve of 0.833). Figure 3B also shows the combined score resulted in 100% sensitivity and 90% specificity when distinguishing PD subjects from healthy subjects (denoted by the black X).

Follow-up testing on the one atypical healthy subject

The EMG data from one healthy female subject differed from the other healthy subjects. Figure 3A shows that the data point for this subject falls within the distribution pattern exhibited by the PD subjects. At the first visit, this subject had no clinical signs of parkinsonism, with a score of 0 on the motor subsection of the UPDRS. Further, there were no signs of bradykinesia on motor testing [peak velocity averaged 364°/s for the 72° rapid elbow flexion movement; a value within the range noted for older females (Buchman et al., 2000)]. This subject was re-examined 30 months after her initial testing. At the second examination, the subject had rest and postural tremor of the right arm, and both clinical and motor control signs of bradykinesia [peak velocity averaged 279°/s for the 72° rapid elbow flexion movement; a value within the range noted for females subjects with PD (Pfann et al., 2001)]. The percentage of short duration biceps bursts increased from 53% to 57% while biceps burst duration variability went from 0.57 to 0.60. At this re-examination, the subject's motor UPDRS score was 10 and she was diagnosed with PD by a movement disorder specialist.

Individual trial spread of the duration of the first agonist burst and disease severity

A significant positive linear relationship was demonstrated between biceps burst duration variability and the motor UPDRS score ($r = 0.41$; $F_{1,29} = 5.9$, $p < 0.02$). A significant positive linear relationship was shown between the percentage of short first biceps burst durations and the motor UPDRS score ($r = 0.66$; $F_{1,29} = 22.0$, $p < 0.001$). Additionally, when both of these parameters were entered into a multiple regression model the percentage of variance explained only increased by 4% over the variance explained by the percentage of short first biceps burst durations ($r = 0.70$; $F_{2,29} = 12.9$, $p < 0.001$).

Discussion

This study showed that measures related to the duration of the first agonist EMG burst during rapid point-to-point elbow flexion movements can distinguish PD subjects from healthy subjects. It also demonstrated that these measures correlate with disease severity.

Variability of EMG Patterns in Parkinson's disease

Consistent with the findings from Pfann and colleagues (2001), we showed that in mild to moderate PD subjects there is trial to trial variability in the duration of the first agonist burst. With increased disease severity the variability of the duration of the first biceps burst decreases until most if not all of the movements performed by subjects with severe PD exhibit burst durations that are 90ms or less. The biological basis for the increased variability that occurs in most mild or moderate PD subjects is not understood. It is important to point out that when healthy subjects perform movements in joints which have a low moment of inertia (i.e. wrist), the duration of the first agonist burst tends to be very short (90 ms) (Pfann et al., 1998). As such, the measure of EMG variability may well only apply to long movements made by large muscle groups such as the biceps.

Changes in the EMG pattern can distinguish individuals diagnosed with PD from healthy individuals

As we outlined in the introduction, PET and SPECT scans are sensitive at distinguishing PD subjects from healthy subjects. However, obvious limitations of cost, non-portability, safety concerns with repeated scanning and limited access of scanners in most clinical settings may preclude the use of these scans. While simple and non-invasive measures, such as tapping and/or olfaction can distinguish PD subjects from healthy subjects, the sensitivity of these measures do not approach the levels demonstrated by PET and SPECT scans (Camicioli et al., 2001; Montgomery et al., 2000a; Montgomery et al., 2000b). They also do not demonstrate the sensitivity of our measures.

Recently, changes in surface EMG morphology have been used to distinguish PD subjects from healthy subjects. For instance, Rissanen and colleagues (2007) showed that the distribution of the zero crossings of the EMG signal resulted in 72% sensitivity and 86% specificity when distinguishing PD subjects from healthy subjects. However, the analysis did not take into account that the EMG signal in PD changes with disease severity, which may have affected the use of their measure. We showed that a combined score, which does take into account how disease severity affects the EMG pattern, correctly identified 100% of PD subjects from healthy subjects. At this sensitivity level, specificity only dropped to 90%. Since the sensitivity and specificity levels exhibited by parameters related to the duration of the first agonist burst were as high as those reported in studies using PET and SPECT scans, it appears that these parameters may provide a non-invasive method whereby PD subjects can be distinguished from healthy subjects.

The fact that specificity dropped to 90% was due to the parameters related to the duration of the first agonist burst for one initially "healthy" subject being similar to those parameters exhibited by the individuals with PD (see Fig. 3A-solid black square located outside the black rectangular box). While this healthy subject initially had no clinical signs of PD, her EMG pattern was similar to that seen in the PD subjects. This raises the question as to whether she might have had pre-clinical PD. Upon re-evaluation of this subject 30 months later, this subject was now diagnosed with PD. When the ROC analysis was re-calculated and the initially "healthy" subject was now included in the PD group, the specificity increased to 100% while the sensitivity remained at 100%. Although no definitive conclusions can be drawn from a single subject, this suggests that the EMG pattern abnormalities may precede the onset of clinical signs of PD (Michell et al., 2004).

It may be suggested that the changes observed in the parameters related to the duration of the first agonist EMG burst in PD subjects may simply be related to the slower movement speeds which are classically exhibited by these subjects. When healthy subjects move at slower speeds, the duration of the first agonist burst either remains constant or increases while the magnitude

of the agonist signal decreases (Corcos et al., 1989; Pfann et al., 1998). This pattern of change is not consistent with the short agonist burst duration exhibited by most PD subjects. In addition the “healthy” individual with the abnormal EMG pattern at initial testing moved at normal speeds. As such, we suggest that the changes in the EMG signal which are observed in PD subjects are changes which begin in the early stages of PD and are caused by PD.

Relationship between neurophysiological parameters and severity of motor symptoms

The most impressive correlation between the uptake of various tracers and disease severity using either PET or SPECT scans can be considered only a moderate correlation ($r=-.60$) (Huang et al., 2007). Similarly, the correlation between the simple and non-invasive olfactory discrimination test and disease severity, while significant ($r=-0.43$), is much less impressive (Tissingh et al., 2001). Therefore, the correlation ($r=0.66$) shown by the present study between the percentage of trials exhibiting a short first agonist burst duration and disease severity is as good as correlations exhibited between PET, SPECT or simple non invasive measures and disease severity. We have previously shown that relaxation time ($r=0.71$ in flexion and $r=0.76$ in extension), which is the time it takes to passively relax a contracted muscle, increases with disease severity in PD subjects off medication (Robichaud et al., 2005; cf. Corcos et al., 1996). We also showed that the percentage of trials exhibiting a short first agonist burst increased with disease severity in PD subjects. The reason this parameter did not relate better to the motor UPDRS score was because for the mild PD group there was a large variation in this parameter, while there was little variation for the motor UPDRS scores. We expect that adding the measure of relaxation time would improve our ability to more accurately assess disease severity because relaxation time continues to increase as disease severity increases.

Conclusion

This study showed that two changes in the EMG pattern are sensitive and specific measures of PD at distinguishing PD from health. It is quite possible that other movement disorders may also show specific EMG changes. As such, further studies are needed to determine the extent to which the EMG changes observed in this study are specific to PD. The future of early detection of PD depends on the development of measures that accurately reflect the pathology (Michell et al., 2004). It is apparent that multiple diagnostic measures might be needed due to the heterogeneity of PD (DeKosky and Marek, 2003; Michell et al., 2004).

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References

- Antonini A, Moresco RM, Gobbo C, De Notaris R, Panzacchi A, Barone P, et al. The status of dopamine nerve terminals in Parkinson's disease and essential tremor: a PET study with the tracer [11-C]FE-CIT. *Neurol Sci* 2001;22:47–48. [PubMed: 11487195]
- Benamer TS, Patterson J, Grosset DG, Booij J, de Bruin K, van Royen E, et al. Accurate differentiation of parkinsonism and essential tremor using visual assessment of [123I]-FP-CIT SPECT imaging: the [123I]-FP-CIT study group. *Mov Disord* 2000;15:503–510. [PubMed: 10830416]
- Berardelli A, Dick JP, Rothwell JC, Day BL, Marsden CD. Scaling of the size of the first agonist EMG burst during rapid wrist movements in patients with Parkinson's disease. *J Neurol Neurosurg Psychiatry* 1986;49:1273–1279. [PubMed: 3794733]
- Buchman AS, Leurgans S, Gottlieb GL, Chen CH, Almeida GL, Corcos DM. Effect of age and gender in the control of elbow flexion movements. *J Mot Behav* 2000;32:391–399. [PubMed: 11114231]

- Camicioli R, Grossmann SJ, Spencer PS, Hudnell K, Anger WK. Discriminating mild parkinsonism: methods for epidemiological research. *Mov Disord* 2001;16:33–40. [PubMed: 11215590]
- Corcos DM, Chen CM, Quinn NP, McAuley J, Rothwell JC. Strength in Parkinson's disease: relationship to rate of force generation and clinical status. *Ann Neurol* 1996;39:79–88. [PubMed: 8572671]
- Corcos DM, Gottlieb GL, Agarwal GC. Organizing principles for single-joint movements. II. A speed-sensitive strategy. *J Neurophysiol* 1989;62:358–368. [PubMed: 2769335]
- Corcos DM, Gottlieb GL, Latash ML, Almeida GL, Agarwal GC. Electromechanical Delay: an experimental artifact. *J Electromyography Kinesiol* 1992;2:59–68.
- DeKosky ST, Marek K. Looking backward to move forward: early detection of neurodegenerative disorders. *Science* 2003;302:830–834. [PubMed: 14593169]
- Fahn, S.; Elton, RL. members of the UPDRS Development Committee. Unified Parkinson's disease rating scale. In: Fahn, S.; Marsden, CD.; Calne, DB.; Goldstein, M., editors. *Recent developments in Parkinson's disease*. Vol. II. New Jersey: MacMillan Health Care Information; 1987. p. 153–163.
- Farley BG, Sherman S, Koshland GF. Shoulder muscle activity in Parkinson's disease during multijoint arm movements across a range of speeds. *Exp Brain Res* 2004;154:160–175. [PubMed: 14564435]
- Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189–198. [PubMed: 1202204]
- Hallett M, Khoshbin S. A physiological mechanism of bradykinesia. *Brain* 1980;103:301–314. [PubMed: 7397480]
- Hallett M, Shahani BT, Young RR. Analysis of stereotyped voluntary movements at the elbow in patients with Parkinson's disease. *J Neurol Neurosurg Psychiatry* 1977;40:1129–1135. [PubMed: 591980]
- Hu MT, White SJ, Herlihy AH, Chaudhuri KR, Hajnal JV, Brooks DJ. A comparison of (18)F-dopa PET and inversion recovery MRI in the diagnosis of Parkinson's disease. *Neurology* 2001;56:1195–1200. [PubMed: 11342685]
- Huang C, Tang C, Feigin A, Lesser M, Ma Y, Pourfar M, et al. Changes in network activity with the progression of Parkinson's disease. *Brain* 2007;30:1834–1846. [PubMed: 17470495]
- Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases [see comments]. *J Neurol Neurosurg Psychiatry* 1992;55:181–184. [PubMed: 1564476]
- Hughes AJ, Daniel SE, Lees AJ. Improved accuracy of clinical diagnosis of Lewy body Parkinson's disease. *Neurology* 2001;57:1497–1499. [PubMed: 11673599]
- Ichise M, Kim YJ, Ballinger JR, Vines D, Erami SS, Tanaka F, et al. SPECT imaging of pre- and postsynaptic dopaminergic alterations in L-dopa-untreated PD. *Neurology* 1999;52:1206–1214. [PubMed: 10214745]
- Michell AW, Lewis SJ, Foltynie T, Barker RA. Biomarkers and Parkinson's disease. *Brain* 2004;127:1693–1705. [PubMed: 15215212]
- Montgomery EB Jr, Koller WC, LaMantia TJ, Newman MC, Swanson-Hyland E, Kaszniak AW, et al. Early detection of probable idiopathic Parkinson's disease. I. Development of a diagnostic test battery. *Mov Disord* 2000a;15:467–473. [PubMed: 10830410]
- Montgomery EB Jr, Lyons K, Koller WC. Early detection of probable idiopathic Parkinson's disease. II. A prospective application of a diagnostic test battery. *Mov Disord* 2000b;15:474–478. [PubMed: 10830411]
- Morrish PK, Rakshi JS, Bailey DL, Sawle GV, Brooks DJ. Measuring the rate of progression and estimating the preclinical period of Parkinson's disease with [18F]dopa PET. *J Neurol Neurosurg Psychiatry* 1998;64:314–319. [PubMed: 9527140]
- Morrish PK, Sawle GV, Brooks DJ. Clinical and [18F] dopa PET findings in early Parkinson's disease. *J Neurol Neurosurg Psychiatry* 1995;59:597–600. [PubMed: 7500096]
- Ottaviani S, Tinazzi M, Pasquin I, Nothdurfter W, Tomelleri G, Fincati E, et al. Comparative analysis of visual and semi-quantitative assessment of striatal [123I]FP-CIT-SPET binding in Parkinson's disease. *Neurol Sci* 2006;27:397–401. [PubMed: 17205224]
- Pepe, MS. *The Statistical Evaluation of Medical Tests for Classification and Prediction*. Oxford: Oxford University Press; 2003.

- Pfann KD, Buchman AS, Comella CL, Corcos DM. Control of movement distance in Parkinson's disease. *Mov Disord* 2001;16:1048–1065. [PubMed: 11748736]
- Pfann KD, Hoffman DS, Gottlieb GL, Strick PL, Corcos DM. Common principles underlying the control of rapid, single degree-of-freedom movements at different joints. *Exp Brain Res* 1998;118:35–51. [PubMed: 9547076]
- Rissanen S, Kankaanpää M, Tarvainen MP, Nuutinen J, Tarkka IM, Airaksinen O, et al. Analysis of surface EMG signal morphology in Parkinson's disease. *Physiol Meas* 2007;28:1507–1521. [PubMed: 18057515]
- Robichaud JA, Pfann KD, Comella CL, Brandabur M, Corcos DM. Greater impairment of extension movements as compared to flexion movements in Parkinson's disease. *Exp Brain Res* 2004;156:240–254. [PubMed: 14747885]
- Robichaud JA, Pfann KD, Comella CL, Corcos DM. Effect of medication on EMG patterns in individuals with Parkinson's disease. *Mov Disord* 2002;17:950–960. [PubMed: 12360544]
- Robichaud JA, Pfann KD, Vaillancourt DE, Comella CL, Corcos DM. Force control and disease severity in Parkinson's disease. *Mov Disord* 2005;20:441–450. [PubMed: 15593316]
- Tissingh G, Berendse HW, Bergmans P, DeWaard R, Drukarch B, Stoof JC, et al. Loss of olfaction in de novo and treated Parkinson's disease: possible implications for early diagnosis. *Mov Disord* 2001;16:41–46. [PubMed: 11215591]
- Vaillancourt DE, Prodoehl J, Metman LV, Bakay RA, Corcos DM. Effects of deep brain stimulation and medication on bradykinesia and muscle activation in Parkinson's disease. *Brain* 2004;127:1–14.
- Volkow ND, Rosen B, Farde L. Imaging the living human brain: magnetic resonance imaging and positron emission tomography. *Proc Natl Acad Sci U S A* 1997;94:2787–2788. [PubMed: 9096295]

Figure 1.
Shows an individual in the arm movement apparatus.

Figure 2.

Agonist EMG activity, individual trial duration for the first biceps burst and the $\log_{10}(x)$ transformed data for the duration of the first biceps burst. The left panel (i) in A, B, and C shows the biceps EMG activity for a representative trial, center panel (ii) in A, B, and C shows all the duration values for the first biceps burst and right panel (iii) in A, B, and C shows the $\log_{10}(x)$ transformed data. A, is from a healthy subject. B, shows an individual with mild PD. C, shows an individual with severe PD.

Figure 3.

A, shows how the Combined score was calculated using data from the healthy (solid black squares), mild PD (crosses), moderate PD (open black circles), and severe PD (closed black circles) subjects. B, illustrates the ROC analysis curves used to classify the healthy subjects from the PD subjects using biceps burst duration variability (solid line), percentage of short first biceps burst durations (dashed and dotted line) and the combined score (dotted line).

Table 1

Description of Subjects

Age	Dominant limb	Limb Tested	UPDRS "off"	Disease group	Gender	Disease duration	Hochm and Yahr	PD medications
75	R	R	48	severe	M	7	3	LD, Sel
76	R	L	42	severe	F	11	2.5	LD, Pra, Tri
52	L	L	42	severe	M	12	3	LD, Pra
51	R	L	39	severe	M	5	3	LD, Sel
51	R	L	44	severe	M	12	3	LD, Pra,
48	R	R	38	severe	M	4	2	LD
74	R	R	54	severe	F	20	4	LD, Per, Que
65	R	L	38	severe	F	11	2	LD, Sel, Ama
70	R	R	50	severe	F	17	3	LD, Ama, Rop
74	R	L	48	severe	F	13	3	LD, Ama
71	R	R	35	moderate	M	4	3	LD, Ama, Ter
58	R	L	27	moderate	M	1	2	Rop
65	R	R	25	moderate	M	16	2	LD, Pra, Ama
73	R	L	22	moderate	F	3	2	LD
50	R	L	21	moderate	F	2	2	none
51	R	R	25	moderate	F	4	2	Pra
46	R	R	30	moderate	M	14	3	LD, Pra, Ama
61	R	L	35	moderate	M	6	2.5	LD, Rop, Ter
56	R	L	22	moderate	F	4	2	LD, Pra
47	L	L	35	moderate	F	5	3	LD, Rop, Ama
75	R	L	19	mild	M	5	2	LD, Per
76	R	R	19	mild	F	5	2	Pra
69	R	R	20	mild	M	3	2	LD
59	R	R	17	mild	F	4	1.5	Pra
71	R	L	19	mild	F	10	2	LD, Ama
62	R	R	18	mild	M	3	2	Rop
48	L	R	18	mild	M	3	2	none
49	R	R	13	mild	F	5	1.5	Pra, CoQ10
66	R	L	15	mild	M	1	1.5	none

Age	Dominant limb	Limb Tested	UPDRS "off"	Disease group	Gender	Disease duration	Hoehn and Yahr	PD medications
64	R	L	20	mild	F	13	2	LD, Pra
76	R	L	0	control	F	n/a	n/a	n/a
49	R	L	0	control	M	n/a	n/a	n/a
48	R	R	0	control	F	n/a	n/a	n/a
61	R	L	0	control	M	n/a	n/a	n/a
74	R	R	0	control	M	n/a	n/a	n/a
50	R	L	0	control	F	n/a	n/a	n/a
58	R	R	0	control	F	n/a	n/a	n/a
65	R	R	0	control	M	n/a	n/a	n/a
54	R	R	0	control	M	n/a	n/a	n/a
51 *	R	L	0	control	F	n/a	n/a	n/a

LD=levodopa/carbidopa, Pra=Prampexole, Sel=Selegiline, Tri=Trihexyphenidyl; Per= Pergolide, Que=Quetiapine, Sel= selegilin, Rop=Ropinirole, Ama= amantadine, Ter=terazosin, CoQ10= CoenzymeQ10

Table 2

Biceps burst duration variability

ANOVA - Main Effects	F-value	P-value
Group _{3,36}	9.3	0.0001
<i>Post-hoc</i> Analysis (Bonferroni/Dunn)	Mean Difference	P-value
Healthy vs PD mild	−0.326	0.0001
Healthy vs PD moderate	−0.302	0.0003
Healthy vs PD severe	−0.071	0.3507
PD mild vs PD moderate	0.025	0.7455
PD mild vs PD severe	0.255	0.0018
PD moderate vs PD severe	0.230	0.0044

Table 3

Percentage of short first agonist burst durations

ANOVA - Main Effects	F-value	P-value
Group _{3,36}	20.2	<0.0001
<i>Post-hoc</i> Analysis (Bonferroni/Dunn)	Mean Difference	P-value
Healthy vs PD mild	-39.7	0.0001
Healthy vs PD moderate	-41.8	<0.0001
Healthy vs PD severe	-71.6	<0.0001
PD mild vs PD moderate	- 2.1	0.8197
PD mild vs PD severe	-31.9	0.0014
PD moderate vs PD severe	-29.8	0.0027