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Shoulder muscle activity in Parkinson's disease during multijoint arm movements across a range of speeds

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Abstract Bradykinesia is one of the primary symptoms of Parkinson disease and leads to significant functional limitations for patients. Single joint movement studies, that have investigated the mechanism of bradykinesia, suggest that several features of muscle activity are disrupted, including modulation of burst amplitude and duration, and the number of bursts. It has been proposed that it is the blending of these different burst deficits that collectively defines bradykinesia. This study adds two new approaches to the study of bradykinesia. First, we examined the features of shoulder muscle activities during multijoint arm movement in bradykinetic and control subjects, such that previously reported single joint hypotheses could be tested for generalized arm movement. Second, we directly manipulated speed while keeping distance constant for a large range of speeds. In this manner, we could compare individual trials of muscle activity between controls and subjects with Parkinson's disease (PD) for movements matched for both speed and movement duration. Our results showed that while a multiple burst pattern of shoulder muscles was a common strategy for all subjects (young, elderly controls and PD), subjects with PD showed several burst abnormalities, including deficits in initial agonist burst amplitude and duration at both fast and slow speeds. Subjects with PD also (1) failed to produce a one-burst pattern at fast speeds and, instead, produced a predominance of multiple burst patterns and (2) showed a relationship between the number

of burst deficits and the severity of disease. These results extend the findings of single joint studies to multi-joint and similarly indicate that a combination of burst modulation abnormalities correlate with bradykinesia and disease severity.

Keywords Bradykinesia · Reaching · EMG · Parkinson's disease · Shoulder

Introduction

Bradykinesia, or slowness of movement, is a characteristic feature of Parkinson's disease affecting many types of movement, including discrete (Baroni et al. 1984; Berardelli et al. 1986a), sequential (Benecke et al. 1987), simultaneous (Benecke et al. 1987; Bond and Morris 2000; Brown and Marsden 1991; Talland and Schwab 1964), and rhythmical movements (Morris et al. 1994; Phillips et al. 1994; Van den Berg et al. 2000). The mechanism of bradykinesia is still debated but numerous studies have investigated muscle activities during arm movements to determine the motor deficit leading to bradykinesia (Baroni et al. 1984; Berardelli et al. 1986a, 1986b; Hallett et al. 1977; Hallett and Khoshbin 1980; Pfann et al. 1998). Hallett and Khoshbin were the first to propose that subjects with PD are unable to properly modulate the amplitude of muscle activity. Recent results from a comprehensive investigation (Pfann et al. 2001) suggest that several features of burst modulation are disrupted, including burst amplitude, duration, and number of bursts.

In the above-mentioned studies, single joint movements were used, and distances were manipulated to affect speed, based on the known relationship that velocity increases for movements of greater distance. Velocities of the subjects with PD were always slower than the velocities of normal subjects for any given distance. This means that trials of similar speed between PD and controls occurred with different movement durations because they occurred at different distances. While Pfann et al. reported data for a

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large range of speeds; trials of similar speed were not directly compared between controls and subjects with PD. In contrast, Teasdale et al. 1990 directly manipulated movement duration in controls and subjects with PD but only compared data for two speed conditions, the fastest and slowest trials. To extend these findings, we have directly manipulated speed (a speed-sensitive strategy) and characterized the normal progression of muscle burst patterns across a large range of the matched speeds (ten different speeds) in both control and PD subjects. We have chosen to use a multijoint reaching task to extend the results of single joint studies to more functional movements. Most studies of multijoint arm movements in subjects with PD have reported kinematics and even kinetics (Alberts et al. 2000; Majsak et al. 1998; Ketcham et al. 2000; Phillips et al. 1994; Poizner et al. 2000; Rand et al. 2002), but have not reported muscle activities. In a few studies, muscle activities have been characterized during multijoint tasks, such as sequential or simultaneous arm movements (Benecke et al. 1986, 1987; Schwab et al. 1954) and multijoint reaching (Godaux et al. 1992). Most recently, Seidler et al. (2001) examined muscle activities and intersegmental torques during shoulder-elbow movements. These studies did not, however, vary speed and only studied movements performed as fast as possible.

Features of muscle activity for bradykinetic multijoint movements might be similar to those observed for bradykinetic single joint movements, because similar rules for muscle activity patterns are apparent in single and multijoint arm tasks of normal subjects. For instance, agonist-antagonist muscle patterns are reciprocal during both single and multijoint movements, despite the influence of intersegmental dynamics associated with multijoint movements (Gribble and Ostry 1999; Koshland et al. 2000; Almeida et al. 1995). In addition, muscle amplitude and joint velocity scale with speed for both single joint (Brown and Cooke 1981; Gottlieb et al. 1989) and multijoint movements (Flanders and Herrmann 1992; Wadman et al. 1980) in a predictive and systematic manner. Given these similarities, we predicted that during multijoint reaching, the shoulder joint, which has dynamics most similar to single-joint dynamics (Galloway and Koshland 2001; Gribble and Ostry 1999), would demonstrate inadequate agonist activation and multiple bursts in patients with PD. Indeed, the results supported this prediction as bradykinetic multijoint movements showed similar features of abnormal agonist amplitude and burst number as those observed for bradykinetic single joint movements.

Materials and methods

Subjects

Three groups of subjects participated in this study: eight young control (YC) subjects (30 ± 7 years) and eight elderly control (EC) subjects (76 ± 7 years) with no known history of neurological disorders (Table 1), and eight subjects with idiopathic Parkinson's disease (PD) (66 ± 7 years) (Table 2). In order to study a range of

movement speeds and to reduce the effect of rigidity and tremor, subjects with PD chosen for this study were mildly or moderately affected (Stages 1–3 (on medication), Hoehn and Yahr 1967) and were all tested when their medication was most effective (e.g., the same relative period of their drug cycle). Despite testing on peak medications, 7/8 subjects with PD presented with bilateral upper extremity symptoms as evaluated with selected items (#31, 22, 32, 20) representative of bradykinesia, rigidity, dyskinesia, and tremor from the Unified Parkinson's Disease Rating Scale (UPDRS, Fahn and Elton 1987) (Table 2). To be consistent, we studied the dominant arm in all subjects, which was the right arm for all subjects and was the most impaired arm in 7/8 PD subjects. For the one subject with unilateral involvement (Hoehn and Yahr I), the studied arm was the unimpaired arm with almost no clinical impairment while on medication, but nonetheless showed deficits in the EMG measures of this study. Subjects gave informed consent and all procedures were approved by the Human Subject Committee, in accordance with the ethical standards in the Declaration of Helsinki.

Tasks and procedures

Subjects sat facing a table with the right arm supported in a low-friction rolling apparatus (Koshland et al. 1999) that allowed shoulder and elbow motion in the horizontal plane. Initial position was similar for all subjects with the shoulder abducted and horizontally flexed (both $\sim 60^\circ$), the elbow flexed ($\sim 90^\circ$, 0° = full extension), and the forearm semi-pronated with the hand in line with the forearm (wrist neutral) (Fig. 1A). Subjects were instructed to make a single point-to-point reaching movement from the initial position to one target located on the table medially and in front of the arm, 30° counterclockwise from a line extending through the forearm and hand. The target was a Plexiglas plate (2×2 cm) held above the table at a target distance of eight inches. An LED inside the target was turned on to indicate when to go and all recorded data were synchronized with this event.

To obtain a measure of their maximal capacity, subjects were first asked to complete the single point-to-point arm movement as fast as

Table 1 Profile of control subjects. Antagonist muscle (PDL) recorded from all subjects: *PEC* clavicular head of pectoralis muscle, *ADL* anterior deltoid muscle

Subject#	Age (years)	Height	Weight (lbs)	Sex	Muscle ^a
YC					
1	29	56"	138	M	PEC
2	23	53"	144	F	PEC
3	50	56"	128	F	ADL/PEC
4	42	54"	125	F	ADL/PEC
5	24	56"	130	F	ADL/PEC
6	25	53"	120	F	ADL/PEC
7	37	55"	110	F	ADL/PEC
8	30	57"	139	M	ADL/PEC
EC					
1	74	56"	134	F	ADL/PEC
2	83	57"	140	M	ADL/PEC
3	84	53"	175	F	ADL/PEC
4	84	53"	115	F	PEC
5	80	56"	150	F	ADL/PEC
6	65	53"	116	F	ADL
7	73	58"	188	M	ADL
8	71	52"	136	F	ADL

^aLocation of agonist muscle recordings

Table 2 Profile and clinical features of subjects with Parkinson disease

Subject #	Age (years)	Height	Weight (lbs)	Sex	Scores on selected UPDRS ^a items					Peak velocities >1.05 m/s ^c	Muscle ^d
					Bradykinesia #31	Rigidity #22	Dyskinesia #32	Tremor #20	Hoehn & Yahr stage ^b		
1	57	5'1"	115	M	1	0	1	0	2	Y	PEC
2	57	5'6"	120	F	1	1	0	1	1	Y	ADL/PEC
3	65	5'10"	173	M	1	1	0	1	2	Y	ADL/PEC
4	75	5'1"	96	F	2	1	1	0	3	N	ADL
5	69	5'5"	133	F	2	1	2	0	2.5	N	PEC
6	77	6'2"	200	M	3	2	0	0	2.5	N	ADL
7	64	6'	185	M	1	1	2	0	2	Y	ADL
8	64	5'10"	180	M	3	2	0	1	3	N	PEC

^a0 = no impairment, 4 = marked impairment

^b0 = no signs of disease, 5 = w/c bound or bedridden

^c"Y" indicates PD-fast subjects

^dSee Table 1

possible. All subjects were allowed to practice until they felt confident that they could perform their best. To obtain a range of speeds, subjects were then asked to match each point-to-point arm movement to one cycle of a metronome. Metronome trials were started using an initial tempo setting near 100 beats per minute (bpm), as pilot studies showed that mid-range metronome tempos were easier to match. The settings were first increased above, and then decreased below the initial tempo in 15 bpm increments until a full range of settings (50–200 bpm) were completed. This tempo range corresponds to movement speeds of very slow to very fast. To help subjects entrain their movement duration of the point-to-point movement with the specified tempo, verbal counting (1–2–3–go) in time with the metronome and visual pacing of the metronome arm was used for feedback. All subjects were exposed to the same number of tempo settings (10), unless they became frustrated or were obviously unable to keep pace with the metronome (n=4). These four subjects were our slowest group of PD subjects (PD-slow).

Data collection

Reflective markers were placed on both shoulders, and on the elbow, wrist, and tip of the index finger on the right (dominant) side of the body. Movements were videotaped at 120 Hz and digitized (Peak Performance Technologies). Coordinate data (x , y) were smoothed using a fourth-order Butterworth digital filter with a 4 Hz cut-off and used to calculate linear displacement of the fingertip, angular shoulder velocity, and angular shoulder acceleration. Movement onset and movement termination was determined by 10% peak fingertip velocity.

Bipolar surface electrodes were used to record electromyographic (EMG) activity of three muscles: anterior deltoid, clavicular head of pectoralis, and posterior deltoid. In most subjects, only one shoulder agonist was recorded, either pectoralis (PEC) or anterior deltoid (ADL) (see Table 1). In some subjects, however, both agonist muscles were recorded simultaneously (YC = 6; EC = 4; PD = 2). The EMG signals were pre-amplified, digitized at 500 Hz, and stored on a computer. Three features of the EMG were compared among groups and across speeds: (1) amplitude of initial agonist and antagonist muscle activity, (2) shape of agonist muscle activity throughout trials, and (3) agonist burst features (number and duration).

Data analysis

The focus of this study was to measure shoulder EMG across a full range of movement speed, including speeds typical of everyday movements. Due to the complicated changes in EMG burst duration and shape across trials with significant speed differences, the traditional methods for calculating amplitude beginning from burst onset were not adequate. We chose, therefore, to use a consistent marker, movement onset, to define a window in time. From this location we used two windows to capture the spatial-temporal changes in EMG across speed. The first window starting from movement onset up to 100 ms was used to characterize initial amplitude (SUM100), and the second window starting 100 ms before movement onset to the end of movement was used to characterize the EMG shape throughout the trial (CUSUM). These two techniques are further described below.

Amplitude of initial muscle activity

For amplitude analysis, EMG signals were full-wave rectified and baselines were subtracted before smoothing (70 ms moving average). For each subject, EMG was then normalized to the maximum amplitude (peak value, raw data) from individual trials that occurred across all trials. The amount of initial muscle activity (SUM100) was then determined by summing the amplitude of individual, normalized data points from the processed EMG records during the first 100 ms, starting from movement onset (see solid vertical line and horizontal arrow in Fig. 1B for location of 100 ms window). The summed points were then divided by 100, resulting in arbitrary values between 0 and .4.

This fixed window (movement onset plus 100 ms), related to the same mechanical event (i.e., movement onset), and was selected as the best amplitude measure that could consistently address the complicated changes in EMG burst duration and shape that occur across trials with significant speed differences (see EMG records in Fig. 5). Thus, the SUM100 always captured the initial EMG activity but the nature of the EMG differed across speeds and will be described in detail in the results. Nonetheless, in one-burst trials, the SUM100 generally captured the initial rise and most of the initial agonist EMG (solid vertical line in Fig. 5A). In multiple burst trials, the SUM100 captured an initial short burst and a portion of a second burst, or a portion each of two consecutive bursts (see location of 100 ms window in Fig. 1 and Fig. 5B, C). In slower trials with no bursts and only tonic activity, the SUM100 captured the plateau (Fig. 5D, E). To determine how subjects modified their agonist SUM100 across the range of speeds, a regression analysis was

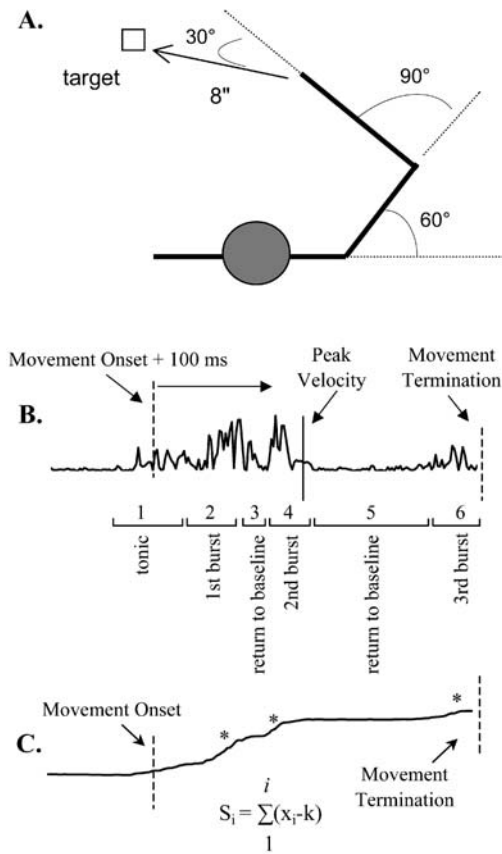


Fig. 1A–C Methods for subject set-up and calculation of SUM100 and CUSUM. **A** Schematic showing initial position of subject's arm, direction of reach, and target location. **B** An individual multiple burst EMG trial for a shoulder agonist (PEC) during a movement at a fast speed (1.54 m/s). Movement onset, termination, and peak fingertip velocity are indicated by *dashed and solid vertical lines*. *Horizontal arrow* indicates time period used for calculation of SUM100. In **C** the resulting CUSUM trace is shown after subtracting resting levels (k) from each data point in **B** and then adding each point consecutively beginning 100 ms before movement onset (start of EMG record) (see formula below CUSUM trace). Six different regions that bracketed below **B** to illustrate changes in EMG amplitude that correspond to changes in slope of the CUSUM trace. For instance, in **B**, during the first initial period (labeled 1), a tonic level of EMG led to a slowly increasing CUSUM with a positive slope. In the next period (labeled 2), an EMG burst occurred which resulted in a sudden increase in positive slope in the CUSUM trace (noted by *). Following the EMG burst, EMG levels returned to baseline during period 3, and the CUSUM trace returned to a zero slope. This baseline period was followed by another EMG burst (labeled 4), a return to baseline for a long duration (labeled 5), and another burst prior to movement termination (labeled 6). This is reflected in the CUSUM by the second and third increases in positive slope (noted by *), which are divided by a long duration with zero slope. This third burst would not be counted as it occurred after peak velocity. This trial is representative of the multiple burst category with two bursts

performed with data from individual trials for each subject. The slopes and y -intercepts were tested for differences among groups (YC, EC, PD), using a one factor ANOVA. In addition, to compare how subjects modified their agonist SUM100 at the slower speeds (<1.0 m/s), a two factor ANOVA was used in which one between-subject factor was group (YC, EC, PD) and the other within-subject factor was a repeated measure of speed (data were collapsed into three speed levels).

Shape of muscle activity throughout a trial

The SUM100 provided insight into the modulation of initial agonist/antagonist amplitude at movement onset across a range of speeds. It did not, however, quantify changes in shape and pattern of EMG that occurred across a trial, such as the presence of multiple bursts. Qualitative analysis of our EMG records showed that muscle burst patterns throughout a trial showed significant changes across speeds. We chose, therefore, to use a method that would allow us to visualize the nature of EMG pattern for the entire movement. This method involved the calculation of a cumulative sum (CUSUM) from the raw rectified EMG for each trial (Ellaway 1978).

The CUSUM method has been used to study the features of both intracellular and surface EMG and to quantify differences between waveforms (Awiszus et al. 1991; Glas et al. 1995). The technique as used in this study is illustrated in Fig. 1B, C. For each individual trial, the CUSUM was calculated beginning 100 ms *before* movement onset to movement termination. After subtracting resting levels (k) from each data point, a new series of points was created by adding each point consecutively (see formula in Fig. 1C). In this manner, changes in the slope of the CUSUM trace indicate changes in EMG amplitude (explained in Fig. 1 legend). As shown in Fig. 1B, C, the CUSUM trace depicts the moment-to-moment modulation of EMG amplitude that is not captured by the SUM100 or other typical reports of integrated EMG.

Burst features (number and duration)

Onsets and terminations of initial agonist bursts with thresholds above background activity were determined by visual identification of individual EMG records on computer display similar to previous reports (Baroni et al. 1984; Benecke et al. 1987; Berardelli et al. 1986; Pfann et al. 2001; Teasdale et al. 1990; Wierzbicka et al. 1991). Criterion for burst identification was when amplitude reached two times baseline amplitude and remained above this threshold more than 20 ms. In addition, the burst was counted only if it was identified within the time window, starting at 100 ms prior to movement onset and ending at peak fingertip velocity (see Figs. 1, 5). Sometimes, however, an initial agonist burst occurred that was longer than this defined time window. These long duration bursts, whose onsets occurred prior to the beginning of our time window or whose termination occurred after peak velocity, were still included if their burst activity was clearly visible and predominantly within the time window (see Fig. 5C, D). Burst duration was only measured for those trials with an identifiable initial burst, and thus did not include trials of gradually increasing tonic activity. These methods are consistent with earlier single joint studies of PD subjects (Pfann et al. 2001; Teasdale et al. 1990). To compare how subjects modified their burst number or burst duration, a two factor ANOVA was used in which one between-subject factor was group (YC, EC, PD) and the other between-subject factor was speed level.

Results

Maximal speed and range of speeds

All young and elderly control subjects were able to perform reaching movements in time with the metronome and produced a variety of speeds as indicated by fingertip velocities ranging from 0.30–2.24 m/s (YC) and 0.30–1.88 m/s (EC) (Table 3). This range of fingertip velocities in the controls was associated with movement durations of 250–1359 ms and to shoulder angular velocities of 24–225°/s. Four out of eight subjects with PD attempted to match the fastest metronome tempos performed by our control subjects and produced a similar range of fingertip

velocities (0.33–1.81 m/s) and movement durations (242–1000 ms). Only one of them, however, could routinely match the highest tempos, and thus perform speeds that matched the highest control speeds (PD3–1.81 m/s). Maximum fingertip velocity for the other three subjects with PD was lower at 1.29, 1.23, and 1.18 m/s, but within range of our slower elderly controls (1.37, 1.26, 1.23 m/s). In addition, all four of these faster PD subjects were graded at the same level of bradykinesia (1.0) using Item #31 from the UPDRS (Table 2) and were classified with Hoehn and Yahr stage 1.0 or 2.0 Parkinson's disease. Other motor symptoms of rigidity, dyskinesia, and tremor were variable across PD-fast subjects (Items #22, #32, #20). These subjects are hereafter referred to as PD-fast.

The overlap in maximum velocity of individual trials between our control and PD-fast group occurred despite the finding of bradykinesia during clinical testing. This may have been due to a gender imbalance among groups (i.e., more female control subjects and more male PD subjects). Thus, as shown in previous studies (Pfann et al. 2001), males tend to move faster than females and thereby our data may underrepresent the maximal speed differences that exist between our controls and PD-fast subjects. However, when we calculated an average maximum fingertip velocity for all fast trials (>1.06 m/s), speed differences were distinctly different among all three groups. That is, the *average maximum* fingertip velocity was highest for YC (mean = 1.75 ± 0.28 m/s), moderate for EC (mean = 1.53 ± 0.24 m/s) and lowest for PD-fast (mean 1.38 ± 0.29 m/s. This corresponded with reduced shoulder angular velocities in our PD-fast group (see Table 3).

In contrast, four other subjects with PD were unable to fully match the faster metronome tempos of the controls, despite practice attempts, and displayed a truncated range of fingertip maximal velocities from 0.31–1.03 m/s. Average maximum fingertip velocity for this group of subjects with PD was, therefore, lowest (mean = 0.98 ± 0.05 m/s). In addition, the shortest movement durations were 425 ms, and the largest shoulder angular velocities were $111^\circ/\text{s}$. These subjects are hereafter referred to as PD-slow. These slower subjects with PD showed greater clinical involvement using the UPDRS. Scores for bradykinesia were ≥ 2.0 and Hoehn and Yahr stages were 2.5 or 3.0. Other motor symptoms were variable across subjects (Items #22, #32, #20). As expected, the best clinical predictor of the ability to achieve peak velocities ≥ 1.0 m/s, therefore, was a score of ≤ 1.0 on UPDRS item #31 (bradykinesia) and Hoehn and Yahr stage ≤ 2.0 . The presence of rigidity, dyskinesia, or tremor did not show a

systematic relationship with ability to achieve faster velocities.

Scaling of initial agonist burst activity

In producing the point-to-point movement of this study, all subjects initiated the movement with shoulder flexor activity. Shoulder extensor activity occurred later in the movement, producing the typical reciprocal pattern. The SUM100 EMG data for the shoulder agonist (PEC) are shown for three individual subjects, one from each group (YC, EC, PD) in Fig. 2A. Values of the PEC SUM100 from each trial were plotted against movement speed (peak fingertip velocity) and are shown with a line of best fit. PEC SUM100 values increased with speed in a non-linear manner, best fit with an exponential curve. The change in slope can be best described by considering two epochs: a mild slope at slower speeds (first epoch), and a steep slope at faster speeds (second epoch). For most subjects, the transition point of the steeper slope occurred near 1.0 m/s.

The exponential rise in SUM100 for the individual subjects exemplified in Fig. 2A occurred for all subjects. Data from individual trials for all control subjects are shown in Fig. 2B; the YC are shown on the left and the EC are shown on the right. Both control groups showed a non-linear increase of PEC SUM100 across speeds. In the YC, one outlier subject (YC-8), that achieved faster maximal speeds than other subjects in the group, was plotted separately and is indicated by the unfilled squares and the lighter line of best fit. This faster subject showed that the first epoch of an exponential line of best fit was shifted lower on the Y-axis (Fig. 2B), indicating that PEC SUM100 at slow speeds began at lower values than in other control subjects.

Data from individual trials for all subjects with PD with PEC recordings ($n=5$) are shown in Fig. 2C. Three of the four PD-fast subjects (PD1–3) are shown on the left, and two of the four PD-slow subjects (PD5 and 8) are shown on the right. Both the PD-fast and PD-slow subjects showed a non-linear increase of agonist SUM100 across speed as controls. In the PD-fast group, one outlier subject (PD-3, mentioned earlier) achieved faster maximal speeds than other subjects and was plotted separately and is indicated by the unfilled squares and the lighter line of best fit. This faster subject with PD (PD-3) also showed an exponential line of best fit, but in this case, SUM100 values began at lower values than other PD-fast (Left graph in Fig. 2C). This is similar to the faster YC subject (YC-8) in the figure above (left graph in Fig. 2B). In

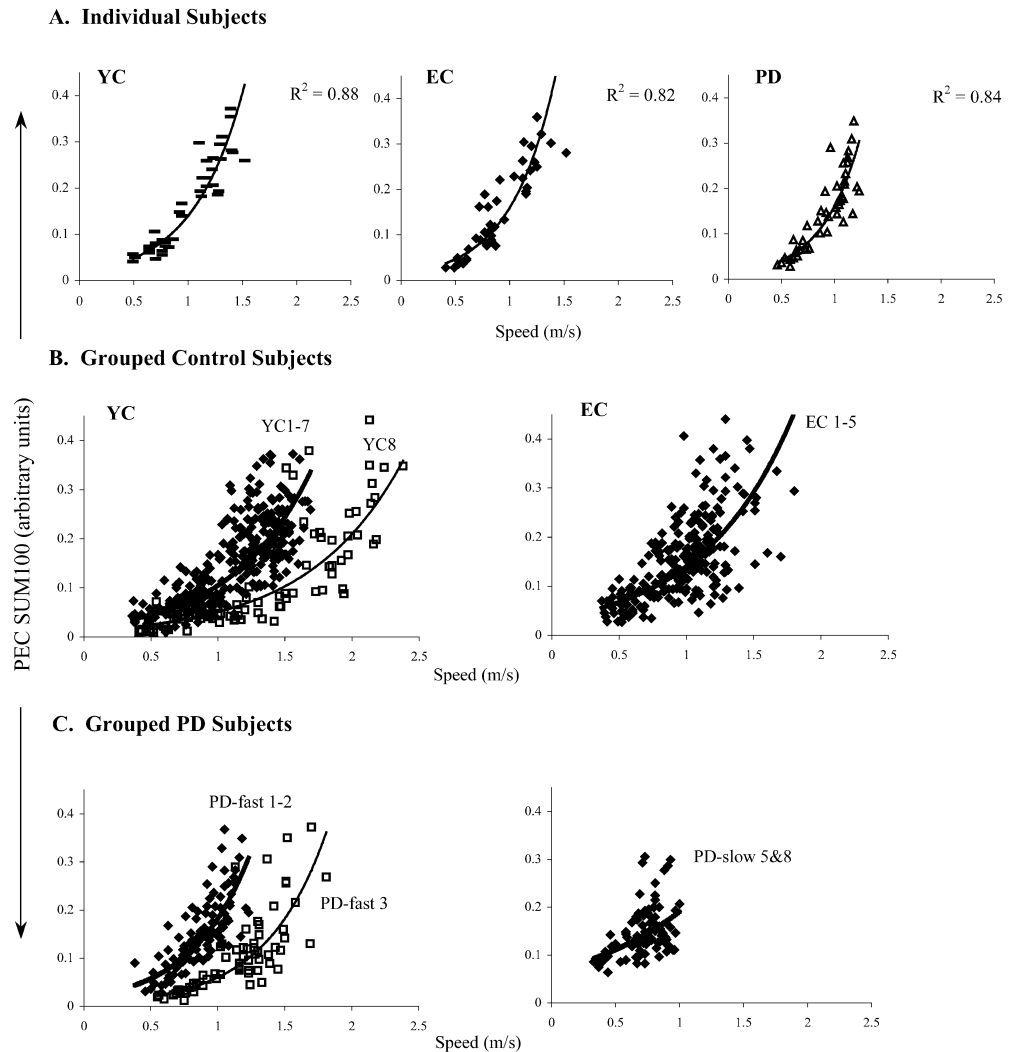
Table 3 Comparison of speeds across groups

Group	N	Fingertip velocity (m/s)		Movement duration (ms) (range)	Shoulder velocity ($^\circ/\text{s}$) (range)
		Maximum ^a	Range ^b		
YC	8	1.74 ± 0.28	$.30 \pm 2.24$	250–1341	24–218
EC	8	1.53 ± 0.24	$.30 \pm 1.88$	280–1359	17–225
PD-fast	4	1.38 ± 0.29	$.33 \pm 1.81$	242–1000	11–102
PD-slow	4	0.98 ± 0.05	$.31 \pm 1.03$	425–1175	19–111

^aAverage of the fastest trials for all subjects

^bMatched to metronome

Fig. 2A–C Values of PEC SUM100 are plotted across speed (fingertip velocity) and shown with lines of best fit. **A** Data for three subjects, one from each group, are plotted in which each point represents an individual trial. **B** Data from all control subjects are plotted: to the left young controls and to the right elderly controls. The number of subjects in each graph corresponds to Tables 1 and 2. One outlier subject (YC-8) who achieved faster speeds than other YC subjects was plotted separately (indicated by the *unfilled squares* and the *lighter line of best fit*). **C** Data from all PD subjects are plotted with faster subjects in the left graph and slower subjects in the right graph. One outlier subject (PD-3) who achieved faster speeds than other PD subjects was plotted separately. Data for PD-slow subjects is truncated and values are shifted higher up the y-axis



contrast, the slowest PD subjects (PD-slow) showed PEC SUM100 values at slow speeds that began at higher values than other PD-fast or control subjects (right graph in Fig. 2C). Thus, values were offset higher on the Y-axis and, yet, never reached the maximal values observed in the controls and PD-fast subjects. These data qualitatively indicate a deficit in agonist burst modulation at slow speeds in PD subjects and suggest that the initial agonist amplitude at *slow* speeds (first epoch) may be related to a subjects' or groups' maximal speed. For example, initial agonist values at slow speeds may be offset higher in subjects with the slowest maximal speed (PD-slow subjects) and offset lower in subjects with the highest maximal speed (YC8 and PD3). A larger number of slow and fast subjects with PD would be necessary to be able to determine if this trend is statistically significant and correlated with disease severity. In this study, as illustrated in Table 2, the degree of bradykinesia, and therefore location on the y-axis (higher), does not appear to be directly related to rigidity as measured on the UPDRS (on medications).

It was possible that the exponential rise in PEC SUM100 muscle activity may have been the result of a

trade-off with other synergists, such that the line of best fit for the ADL SUM100 would show an inverse relation to PEC SUM100 (i.e., when PEC SUM100 is large, ADL SUM100 would be small and when PEC SUM100 is small, ADL SUM100 would be large). Thus, the pattern of recruitment across speeds for PEC and ADL was compared for all subjects with simultaneous recording of both agonists (YC=6, EC=5, PD=2). For each of these subjects, the pattern of PEC-ADL recruitment was categorized into one of the two patterns shown in Fig. 3. No other patterns emerged from the data. In Pattern 1, both PEC and ADL increased with increased speed (Fig. 3A), albeit, ADL never rose as steeply as PEC. In Pattern 2, PEC increased with increased speed whereas ADL remained relatively constant (at a low level) regardless of speed (Fig. 3B). As shown in the summary table in Fig. 3, more than half of the YC and EC subjects and both of the PD subjects showed Pattern 1: that is, a similar increase in PEC and ADL activity with increased speed. Two YC and three EC showed Pattern 2; thus, PEC increased with increased speed, while ADL was unchanged. For five additional subjects (2 EC, 3 PD), ADL was recorded but not PEC. Four of these subjects showed

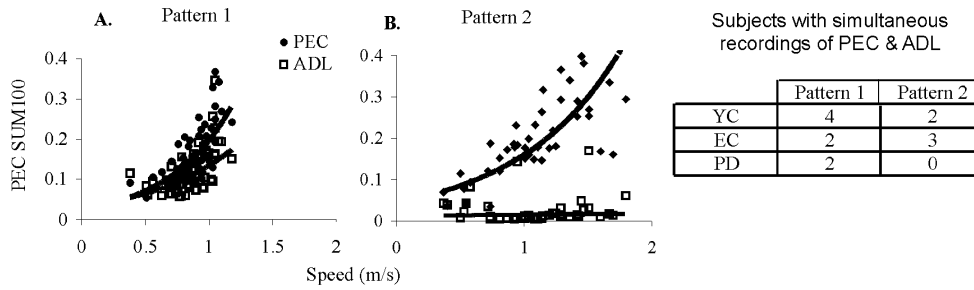


Fig. 3A, B Patterns of PEC and ADL SUM100 across speeds. **A** Data from one subject representative of Pattern 1 is illustrated in which both PEC and ADL increased similarly with increased speed. **B** Data from another individual subject representative of Pattern 2 is illustrated in which PEC increased with increased speed while ADL was unchanged (flat) across speed. The *table to the right*

summarizes available data from all subjects with simultaneous recordings of both agonist muscles (PEC/ADL). More than half of the control subjects (YC and EC) and all the PD subjects showed Pattern 1: that is, a similar increase in PEC and ADL activity with increased speed

increasing ADL with increases in speed, suggesting that Pattern 1 was the most frequent pattern. Together, these findings do not support predictions based on a trade-off strategy between PEC and ADL. That is, no trials showed a pattern of increased ADL to compensate for decreased PEC activity (or vice versa, increased PEC to compensate for decreased ADL).

Initial antagonist burst activity

Some PD subjects exhibited SUM100 levels similar to controls but still exhibited reduced fingertip speeds (Fig. 2C, left graph). One possible explanation could be that the agonist activity was needed to overcome abnormal antagonist activity. Rigidity is a common clinical symptom of PD and it is hypothesized that it is expressed due to inappropriate coactivation of agonists-antagonists. To date, the mechanism for rigidity is still unknown, and

consistent coactivation of agonists-antagonists has yet to be confirmed for PD. We further addressed this issue by determining the SUM100 for the shoulder antagonist, PDL. Typically, the PDL should not be active at the beginning of the arm movement of this study (SUM100) but would become active at the end of the agonist burst or shortly before it is terminated. Abnormally increased levels of the antagonist, PDL, should then be readily detected. Moreover, if PEC levels were augmented due to an abnormal level of PDL, then PEC would increase with increased PDL. Data for the antagonist SUM100 (PDL) were plotted against the agonist SUM100 (PEC) for each trial, and data from the controls was compared to the subjects with PD. Strong coactivation between agonist (PEC) and antagonist (PDL) would be indicated if points lined up along a line of 1 (unity) (Fig. 1A). As shown in Fig. 4A and B for a typical young and elderly control subject, agonist PEC SUM100 activity did not covary with antagonist PDL SUM100 activity, as no trials fell along

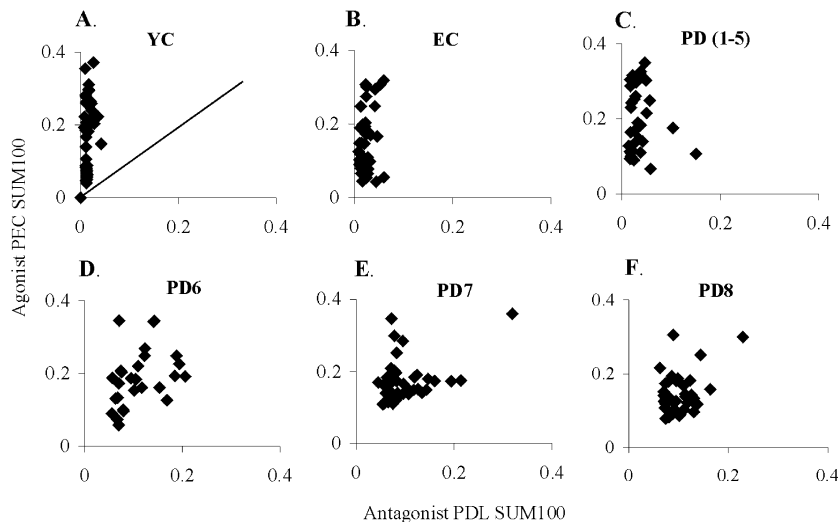


Fig. 4A–F Antagonist SUM100 (PDL) plotted vs. agonist SUM100 (PEC). Data from individual trials are plotted for a representative YC in **A** and a representative EC in **B**, and a PD representative of five other PD subjects in **C**. In these graphs, PDL SUM100 did not covary with PEC SUM100. In **D**, **E**, and **F**, three other subjects with PD (6–8), however, were notably different and showed increased

antagonist levels with a shift of data points towards the right because of increased antagonist levels. Nonetheless, even in these trials with high antagonist SUM100, there was no systematic relationship of agonist-antagonist SUM100, such as a one-to-one correlation (line of unity plotted in **A**)

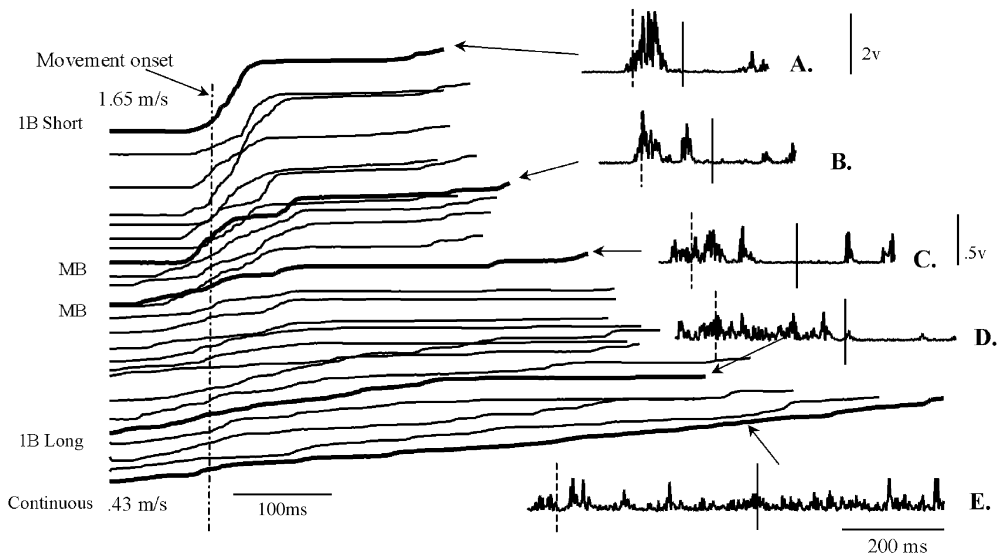


Fig. 5A–E CUSUM analysis for a YC subject. Each CUSUM trace on the left represents an individual trial from 100 ms before movement onset (beginning of trace) to movement offset (end of trace). Movement onset depicted by *dashed vertical line*. Traces are arranged in order by increasing peak velocity, from the slowest trials at the bottom to the fastest trials at the top. Selected EMG records are illustrated on the right for the CUSUM traces highlighted in *bold*. As speeds decreased, there was a tendency for CUSUM traces

and the corresponding EMG patterns to progress from single bursts (*1B*) to multiple bursts (*MB*) to continuous activity. However, there was overlap and, for example, **D** shows a single burst trial that occurred at a slower speed. CUSUM traces represent about 50% of total number of trials for this subject. The window for determining the number and duration of bursts is also illustrated in the EMG records from 100 ms before movement onset (the start of each EMG record) to peak fingertip velocity (*solid vertical line*)

the line of unity or along any linear relationship. Indeed, PDL SUM100 levels remained at very low levels regardless of the PEC SUM100 levels. This was the same for the ADL SUM100 (data not shown). Similarly, a lack of covariation between PEC and PDL SUM100 occurred for five out of eight subjects with PD (PD 1–5), as illustrated in the representative subject with PD in Fig. 4C (PD4). In these five PD subjects PDL SUM100 was again very low regardless of PEC SUM100 levels.

Three other subjects with PD showed substantial antagonist SUM100 levels across trials and were notably different from both controls and the other five subjects with PD. Data from each of these subjects with PD (PD6, PD7, and PD8) are shown in Fig. 4D, E, and F, respectively. In contrast to the subjects in Fig. 4A, B, and C, the data points for these three subjects with PD were shifted towards the right because of the increased antagonist levels. The agonist activity, however, did not consistently covary with the antagonist activity. That is, even on trials with high antagonist activity, agonist activity was unpredictable and could be increased or decreased. This suggests that a tight one to one correlation between increased antagonist activity and increased agonist activity did not exist. Thus, although some subjects with PD showed increased antagonist levels (increased PDL SUM100) across all speeds, this did not necessarily result in a compensatory increase in agonist levels (increased PEC SUM100) on every trial or for all speeds. This is consistent with an earlier onset of antagonist activity without a concomitant increase in agonist activity, similar to the temporal coactivation shown by Pfann et al.'s Fig. 10 (2001) for single joint movements. Interestingly, of

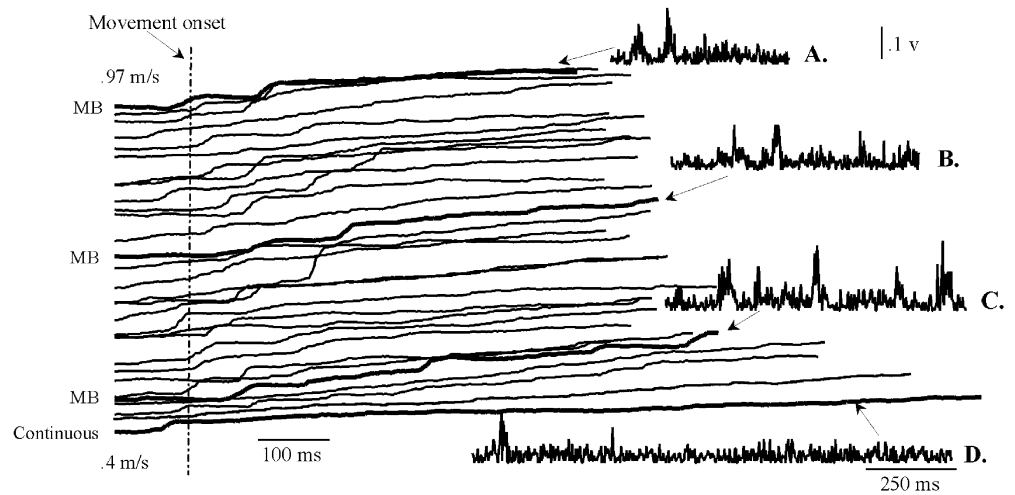
the three subjects with increased and variable antagonist activity, only one was in the PD-slow group and thus this antagonist burst deficit cannot, on its own, account for bradykinesia.

EMG patterns across speeds

Control subjects

The SUM100 data demonstrated that initial agonist activity increased in an exponential fashion across speed. Although the initial muscle activity is important for starting the acceleration of the arm, the EMG throughout the movement is also important for accelerating and decelerating the arm. As a result, the pattern of EMG that occurred through the duration of individual trials was examined. The pattern of EMG throughout a trial showed a progression across speed, and is illustrated for a YC subject (Fig. 5). Each CUSUM trace represents an individual trial (left side of Fig. 5), with traces arranged in order by increasing peak velocity. Only about 50% of the total trials for one subject are illustrated in Fig. 5 to allow visualization of slope changes. The top EMG record (Fig. 5A) represents one of the fastest trials and shows the typical one large burst rising from a quiet baseline level, followed by a late small burst near movement termination (a “one-burst” trial). The corresponding CUSUM showed a characteristic steep slope followed by a return to a zero slope and a late increased slope near movement termination. As speeds decreased, EMG patterns showed more bursts. The EMG record in Fig. 5B showed two early large

Fig. 6A–D CUSUM analysis for a subject with PD unable to exceed speeds of 1.0 m/s. Format similar to Fig. 5. All CUSUM traces for this subject fell into the multiple burst or continuous categories. No one-burst traces/EMG trials occurred and, in fact, the trial with the fastest speed (**A**) showed multiple bursts in the CUSUM trace/EMG record. In addition, there was considerable overlap between the multiple burst and continuous trials as speed decreased



bursts, followed by two late small bursts near movement termination (a “multiple burst” trial). The corresponding CUSUM showed a characteristic step pattern with two large and two small increases in positive slope in the CUSUM. The EMG record in Fig. 5C is another example of a step CUSUM pattern, but in this trial, the first EMG burst (positive slope change on the CUSUM trace) began before movement onset. The last two EMG records in Fig. 5D, E were typical of the slowest movements. In the EMG record in Fig. 5D, muscle activity began very early (earlier than 100 ms before movement onset) and continued tonically until more than halfway through the movement before returning to resting levels (a “one-burst” trial). The corresponding CUSUM showed a long and gradual positive slope with a return to zero slope before movement termination. The EMG record in Fig. 5E illustrates another slow trial, but in this case the tonic activity occurs throughout the trial (a “continuous” trial), resulting in a CUSUM with a long and gradual positive slope for the duration of movement.

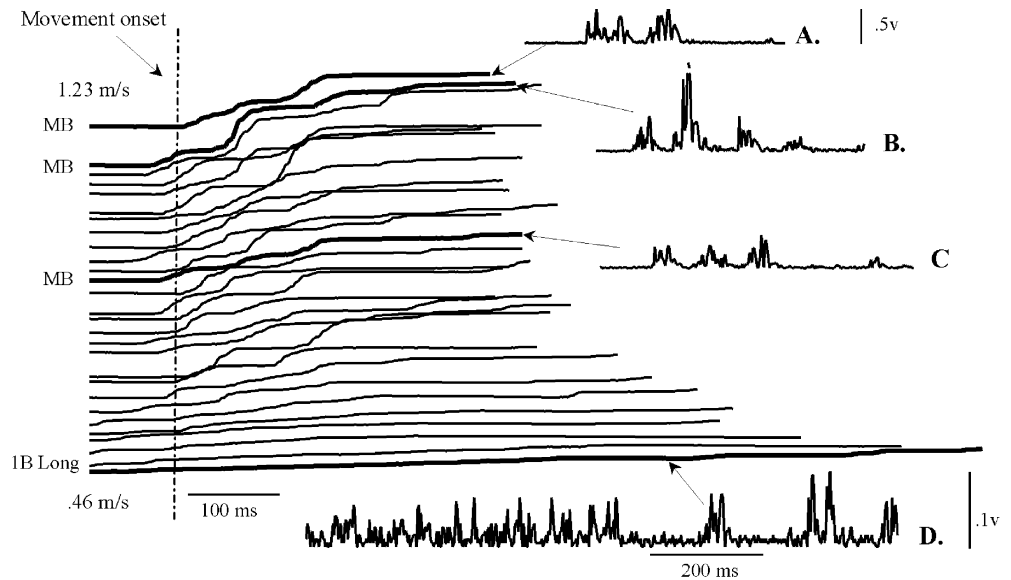
In summary, for this representative YC, EMG patterns for individual trials progressed from continuous to multiple bursts to one-burst as speed increased. As can be seen in the CUSUM traces and on the left axis, these categories overlapped, and the absolute speeds for the transitions between categories were unique to individual subjects. One-burst patterns often occurred at all speeds, but those at slower speeds were characterized by long durations. At very fast speeds, EMG patterns showed one-burst and multiple burst CUSUM patterns. For the subject shown in Fig. 5, the other agonist (ADL) was coactivated with PEC and showed a similar progression in CUSUM categories across speed (not shown). In addition, reciprocity occurred between agonist and antagonist muscles (not shown) although an antagonist burst did not always follow every agonist burst (see Fig. 11).

Subjects with PD

In Fig. 6, typical EMG patterns and CUSUM traces across speeds are shown for a subject with PD with similar format as Fig. 5. This subject was one of the PD-slow subjects who could *not* move faster than 10 m/s. For many trials, EMG patterns were characterized by multiple bursts occurring on top of a tonic background as shown in Fig. 6A–C. The corresponding CUSUMs on the left showed a characteristic step pattern. In addition, as compared to Fig. 5, the CUSUM traces were wavier and slopes rarely returned to horizontal, reflecting the tonic background activity that persisted throughout the movement. For slower trials illustrated in Fig. 6D, muscle activity began very early with one burst and continued tonically for the duration of the movement. This was reflected in the CUSUM by an early step followed by a gradual positive slope that continued throughout the movement. As shown on the left axis, no trials representative of steep CUSUM category occurred for this subject. In addition, no clear progression occurred between multiple burst and continuous categories.

In Fig. 7, typical EMG patterns and CUSUM traces across speeds are shown for another subject with PD who was able to perform at speeds faster than 1.0 m/s (PD-fast). For the trial with the fastest speed, the EMG pattern showed two early bursts rising from quiet baseline levels resulting in a step CUSUM trace. As speeds decreased, EMG patterns continued to show multiple bursts, and the corresponding CUSUM traces showed multiple steps. For the slower trial (Fig. 7D), tonic activity began early before movement onset and continued until more than halfway through the movement. Activity then returned to baseline and several bursts occurred until the end of movement. The corresponding CUSUM showed a gradual positive slope with small steps occurring near movement termination. Despite the ability to achieve peak velocities ≥ 1.0 m/s, no trials representative of steep CUSUM (one short burst) occurred for this subject. The ADL from this subject showed a similar progression across speed. Thus, ADL activity, when present, was coactive with PEC and, in

Fig. 7 CUSUM analysis for a subject with PD able to perform speeds >1.0 m/s. Format similar to Fig. 5. Despite the ability to achieve speeds >1.0 m/s, no trials with one short burst occurred for this subject. Multiple burst trials occurred for most trials, with a few trials with continuous bursts



general, reciprocity, not coactivity, occurred between agonist and antagonist muscles (not shown).

Comparison of all subjects

To summarize the CUSUM data for each group, each trial was categorized as either one-burst (one change in slope that leveled off before peak velocity), multiple bursts (two or more slope changes separated by a return to baseline before peak velocity, or continuous (one gradual slope change that continued for the duration of the trial with no obvious return to baseline. The total number of trials for each category was then sorted into four speed levels. The three slower levels represented equal divisions at intervals of .2 m/s. The fastest level represented all the trials greater than 1.06 m/s, due to an unequal distribution of trials at the very fastest speeds. For each speed level, the percentage of trials within each category was calculated as shown in Fig. 8. A progressive change in the proportion of trials belonging to each category across speeds and across groups was apparent ($p = .01$). More continuous trials occurred at the slowest speeds (white columns in Fig. 8, $p < .0001$), whereas multiple burst trials occurred across all speeds but were more predominant at the intermediate speeds (hatched columns in Fig. 8, $p < .0001$). Although one-burst trials occurred at all speeds, the number of one-burst trials (black columns in Fig. 8) was greatest at the faster speeds ($p = .0008$). The one-burst trials included short bursts found mostly at fast speeds and increasingly longer bursts at slower speeds. The proportion of one-burst trials at each speed differed among the three groups of subjects ($p = .01$). While EC and YC subjects showed a significant increase in one-burst trials with speed, subjects with PD showed a significant decrease in the percentage of one-burst trials with speed (PD = 26% of 65 trials at the fastest speed, EC = 61% of 91 trials, YC = 62% of 228 trials). This finding is even more striking since all but 2/17 of the one-burst PD trials at fastest speeds came from only

one PD subject. In contrast, no differences occurred among the three groups for the multiple and continuous burst categories ($p > .01$).

Burst features

Number of bursts

From the findings in Figs. 5, 6, 7, and 8, it was clear that individual trials with multiple bursts frequently occurred for all subjects. We further investigated characteristics of these trials, and representative trials with multiple bursts are shown for a PD and a YC subject in Fig. 9A, B, respectively. Each trial demonstrates multiple bursts in the PEC for trials of various speeds within intermediate speed levels (0.65–1.1 m/s). From these records there are four and five bursts for both PD and YC at the slowest speeds (0.71 and 0.76 m/s, respectively), in contrast to three and two bursts at the fastest speeds (1.1 and 1.2 m/s, respectively). Two more trials at very fast speeds (1.5 and 1.4 m/s) from other PD and YC subjects also showed multiple (two) bursts (Fig. 9C, D). These records raise the possibility that the number of multiple bursts per trial could differ among the groups and/or across speed. Hence, we counted the number of bursts using qualitative visual inspection, similar to previous reports (Pfann et al. 2001; Teasdale et al. 1990) and described in “Materials and methods.” The number of bursts/trial up to the time of peak velocity was not significantly different among groups at any of the speeds (Fig. 10). Thus, even at peak velocities ≥ 1.05 m/s, YC, EC, and PD averaged 2.5, 2.3, and 2.3 bursts/trial, respectively. For all three groups, the average number of bursts/trial seemed to decrease with increased speed, but this was not statistically significant.

Interestingly, the presence of multiple bursts did not seem to affect shoulder joint kinematics as velocity curves were bell shaped (not shown) and the accelerations were typically biphasic as shown for slow four- and five-burst

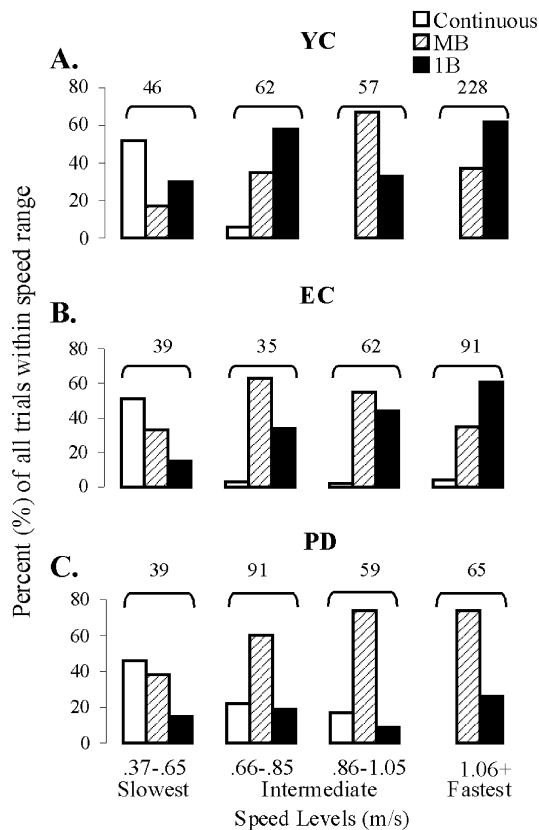


Fig. 8A–C Categorization for all subjects. The distribution of categories across speed is illustrated for the YC group in **A**, for the EC group in **B**, and for the PD group in **C**. For each speed level, the total number of trials is identified above the *horizontal bracket*. The percentages of this total number that were categorized into continuous (*white*), multiple burst (*hatched*), or one-burst (*black*) are indicated by the height of each of the *three bars*. The graphs show that the percentage of trials within the three categories differed across speed. For all groups, continuous trials occurred more at the slowest speeds. For YC and EC groups, one-burst trials occurred across speeds but increased in number with faster speed. In addition, multiple burst trials occurred across all speeds but were more predominant at the middle speeds. The distribution was different for PD in that the PD group demonstrated a lower percentage of one-burst trials at faster speeds with a greater percentage of multiple burst trials. In fact, most of the one-burst trials in Fig. 8C are attributed to the one fastest PD subject

patterns in Fig. 9A.3 and B.3 and for fast two-burst patterns in Fig. 9C, D. Moreover, antagonist activity did not seem to affect the presence of multiple bursts in the agonist muscle. For both groups (PD and YC), reciprocity occurred between agonist and antagonist muscles, with antagonist onset usually occurring around the time of peak velocity. Occasionally, antagonist activity occurred between multiple bursts before the time of peak velocity, but this was not different between groups (Fig. 9).

Burst duration

The EMG/CUSUM data from Figs. 5, 6, 7, and 8 suggest that one-burst trials occur for all speeds and that there may be a progression of increasing burst duration with

decreasing speed (also increasing movement duration). As a result, initial burst duration was measured (see “Materials and methods”), and findings from all one-burst trials for all subjects for each group are illustrated in Fig. 11A. Significant differences were found across speed and among the groups ($p < 0.0001$). The controls demonstrated a gradual increase in burst duration from the fastest to slowest speeds (156 to 567 ms). Although EC increased durations, burst durations at the slowest speeds (.37–.65 m/s) were still much shorter than YC (342 ms). In contrast, PD subjects showed the same burst duration across all speeds (154 to 162 ms), except for a slight increase at the slowest speeds, but this duration was still much less than YC (282 ms). When data were collapsed for speed, variability of burst duration (SE) was lowest for PD subjects (± 17), moderate for YC (± 25) and highest for EC (± 34). Interestingly, 15/17 of the one-burst trials for the PD subjects were produced by the outlier PD-fast subject (PD-3). Thus, deficits in burst duration are noted early at slower speeds, may precede the loss of the one-burst pattern in PD subjects, and thus may not interfere with the ability to produce one-burst patterns or directly contribute to bradykinesia.

Similar changes in the duration of the first burst were also observed for individual trials of the multiple burst category. Average initial burst duration was calculated for all multiple burst trials (burst numbers 2–5 were collapsed) across four speed levels for all subjects for each group and findings are illustrated in Fig. 11B. Significant differences occurred among the groups ($p < 0.02$) but not across speed. In this case, both YC and EC showed larger burst durations than PD at all speeds. When averaged across speed, EC burst duration was less than YC, 100 and 138 ms, respectively. PD subjects showed the smallest averaged burst duration across all speeds (74 ms) and were different from controls ($p < 0.005$). Similar to one-burst trials, when data were collapsed for speed, burst durations for multiple burst trials were the least variable for PD subjects (± 6) as compared to the most variable YC (± 15). However, while EC were the most variable in one-burst trials they were much more like the PD subjects during multiple burst trials with minimal variability (± 5). Thus, PD subjects showed the least variability (SE) in burst duration during both one-burst and multiple burst trials.

Discussion

Subjects with PD in this study could not be placed in one homogeneous group and seemed to fall into three categories. The first category included one fastest PD subject because this was the only subject able to achieve maximal speeds (peak fingertip velocities) similar to young controls. This fastest PD subject showed only abnormal modulation of burst duration, whereas all other features were normal, such as the typical progression of EMG across speed, including the one-burst pattern, and normal scaling of the initial agonist amplitude (SUM100). The next category included other fast PD subjects ($n = 3$)

Fig. 9A–D Individual records of agonist and antagonist EMG (PEC, PDL) are shown that demonstrate multiple bursts. All trials depict the EMG from 100 ms before movement onset until movement offset. *Solid vertical lines* in the EMG records indicate location of peak fingertip velocities, and values of peak fingertip velocities are indicated by *numbers in the upper right corner of each record*. Records are arranged in order of speed from the slowest trials at the bottom (**A.3/B.3**) to fastest trials at the top (**A.1/B.1**), for a PD subject in **A** and a YC subject in **B**. **A** and **B** demonstrate the presence of multiple bursts for all these trials at intermediate speeds with an increased number of bursts in the slower trials and greater variability of initial burst duration in the YC trials. In **C** and **D**, two trials from different PD and YC subjects demonstrate the presence of multiple bursts even in these trials at very fast speeds (>1.1 m/s). Shoulder joint accelerations were typically bi-phasic despite the four and five burst patterns in **A.3** and **B.3**, respectively, or the two burst patterns in **C** and **D**. *Vertical calibration lines* in the acceleration graphs indicate 200%/s. EMG scaled to max for each record. *Solid horizontal lines* below EMG graphs indicate 100 ms window for calculating SUM100

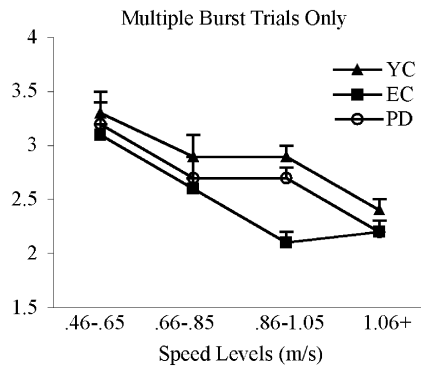
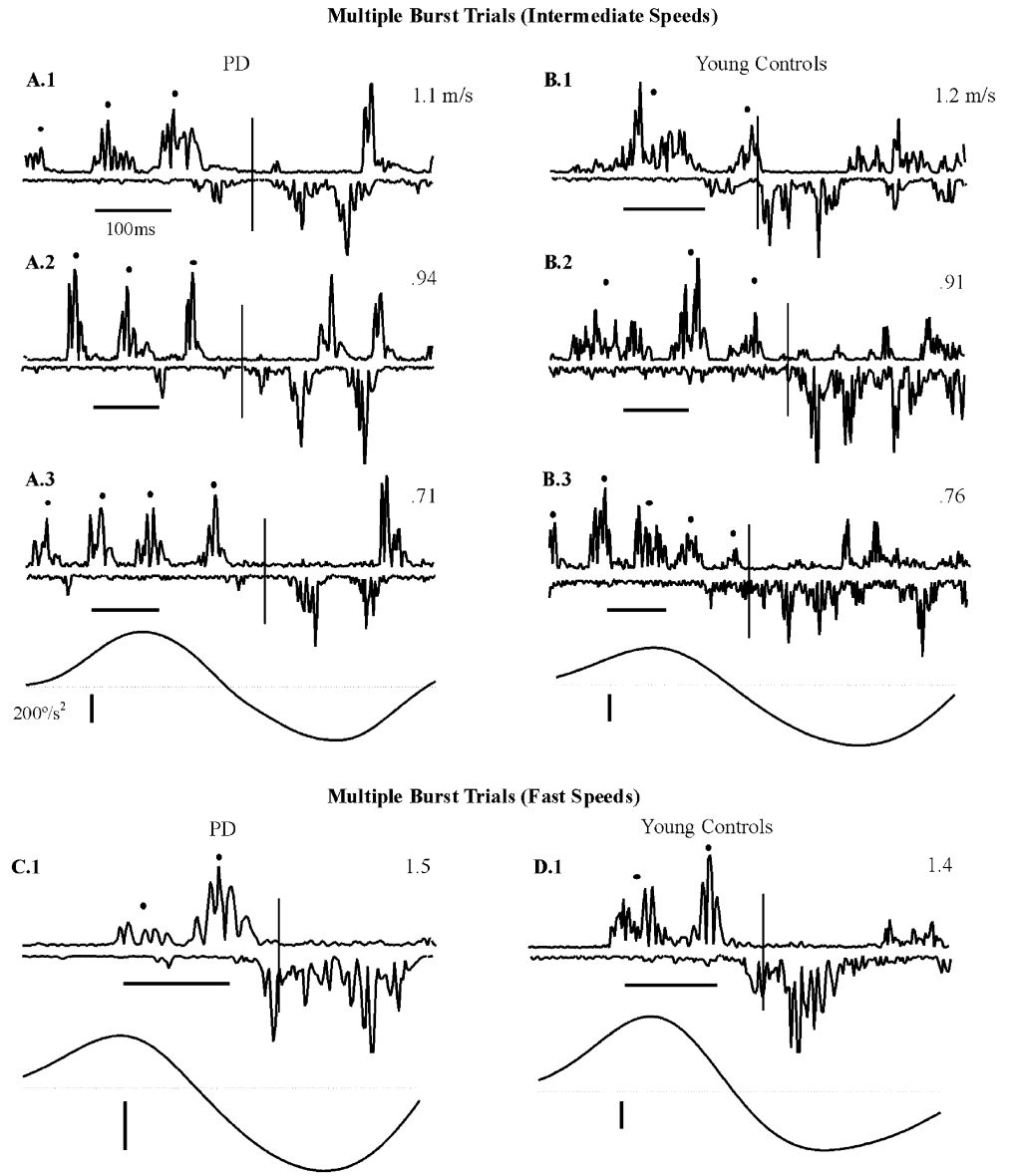
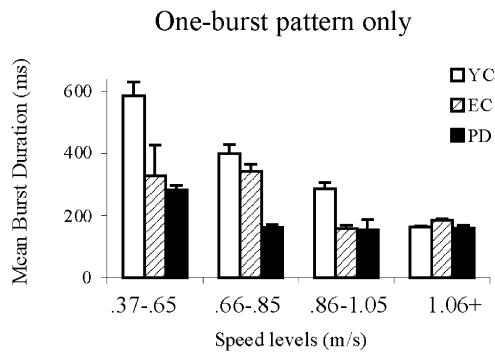


Fig. 10 Average number of bursts across speed for multiple burst (MB) trials for each group, YC (*triangles*), EC (*squares*), and PD (*circles*). No difference occurred among groups at any of the speed levels. The number of bursts tended to increase with slower trials (increased movement duration)

who, although fast and similar to EC, could not achieve the maximal velocities of YC. This group of subjects showed a deficit of the one-burst pattern at the fast speeds and, thus, relied on the multiple burst pattern. This group also showed abnormal modulation of burst duration but had normal agonist amplitude (SUM100) scaling. Finally, the third category included the slow PD subjects ($n = 4$) who showed even greater EMG deficits. These slow subjects showed significantly reduced maximal speeds of movement (peak fingertip velocities). They used short, constant duration, multiple burst patterns for almost all trials. They also showed abnormal scaling of agonist amplitude (SUM100) at all speeds, reflected in a ceiling at fast speeds and a higher y-axis offset at slow speeds. Other studies of PD patients have similarly described different categories of patients (Pfann et al. 2001; Wierzbicka et al. 1991). Although our categories and others' seem to generally follow a continuum, the categories include a mixture of symptoms, suggesting that the burst deficits

A.



B.

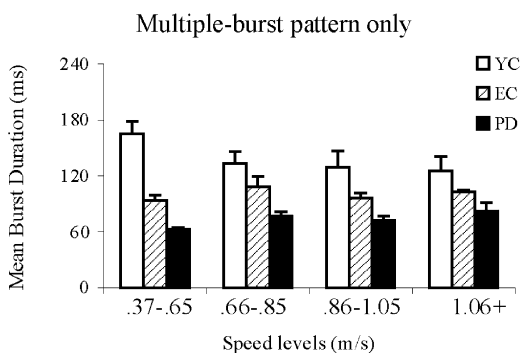


Fig. 11 Distribution of average burst duration across speed for all one-burst trials for each group in **A** and for all multiple burst trials for each group in **B**. In **A**, the YC (*striped bars*) demonstrated a gradual decrease in burst duration from the slowest to fastest speeds, 567–156 ms, respectively. At the fastest speeds (≥ 1.06 m/s), all three groups showed similar burst durations. In **B**, YC and EC showed large burst durations at all speeds; EC were always less than YC. PD subjects showed the smallest burst durations across all speeds. Shown with standard error bars. Multiple burst trials (burst #2–5) were collapsed for the comparison in **B**

that contribute to bradykinesia are progressive and multifactorial and correlated to the severity of the disease.

Comparison of multijoint and single joint studies in Parkinson's disease

One purpose of this study was to determine deficits in the muscle activities exhibited by patients with Parkinson's disease while performing a multijoint arm movement, and thereby generalize the results of prior studies employing single joint movement. The most similar comparison between the experimental design of our multijoint and previous single joint studies is the comparison of trials performed at maximum speeds. Looking at these trials, control subjects showed the typical one burst of reciprocal agonist-antagonist shoulder muscle pattern at the fast speeds (Figs. 5, 8), while all but one PD subject showed multiple bursts (Figs. 6, 8), as has also been shown for PD subjects performing single joint movements. This same group of PD subjects also reached a ceiling in their initial EMG amplitude (SUM100) (Fig. 2C, right graph), which

parallels the findings of Hallett and Khoshbin (1980) for inadequate agonist activation in single joint movement. Thus, the major changes in EMG observed in PD subjects performing single joint movements as fast as possible were also observed in PD subjects performing a multijoint movement as fast as possible.

Multijoint control of speed in PD subjects

Another purpose of this study was to examine the general control of speed and, hence, we tested a full range of speeds at constant distance. In this manner, we are able to discuss the deficits of performing at desired speeds, not just maximal performance (i.e., as fast as possible) for PD subjects, compared to control subjects.

Burst duration across speed

Controls generally showed changes in burst duration with changes in speed. For instance, they showed more variable burst durations across all speeds but also a systematic increase in burst duration with decreased speed. In contrast, PD subjects showed a constant, short burst duration across all speeds (Fig. 11). These multijoint findings are consistent with single joint findings of fixed burst durations in PD subjects and more variable and scaled burst durations in controls during single joint elbow movements to varying distances (Hallett and Khoshbin 1980; Pfann et al. 2001). On the other hand, we had one outlier PD subject still capable of achieving normal control velocities, yet showed shorter, less variable burst durations during both one-burst and multiple burst trials. This suggests that change in burst duration is an early deficit and by itself insufficient to result in detectable bradykinesia, a hypothesis put forth by Pfann et al. (2001).

Scaling of initial agonist amplitude (SUM100) across speed

In our study, control subjects scaled initial agonist activity in a nonlinear (exponential) relation to speed. While it is generally accepted that muscle activities scale with speed and/or distance (Gottlieb et al. 1989, 1996; Hoffman and Strick 1990; Mustard and Lee 1987; Wadman et al. 1980), recent studies by Flanders and Herrmann (1992) and Buneo et al. (1994) explored the nature of this scaling for multijoint movements and also reported a non-linear relationship between muscle intensities and speed. Similar to controls, our PD-fast subjects showed normal agonist scaling and were able to reach similar high levels of SUM100 across speed (Fig. 2B, C). Interestingly, most of these PD-fast subjects showed only multiple bursts trials at fast speeds, unlike controls, yet initial agonist amplitude levels scaled and were similar to controls in amplitude. This suggests that one-burst trials were not necessary to achieve generally fast multijoint speeds and that the initial

EMG amplitude (SUM100) is modulated similarly for one-burst or multiple burst patterns.

PD-slow subjects, however, appeared to have a deficit in initial agonist amplitude (SUM100) as agonist amplitude levels showed a ceiling effect as subjects reached their maximum velocities (Fig. 2C). This is in agreement with the hypothesis of Hallett and Khoshbin that agonist amplitude saturates in PD subjects. This truncated agonist amplitude in the slower PD subjects of this study cannot be attributed to a change to a multiple burst pattern, as three out of four of the faster PD subjects also used multiple burst patterns and yet showed normal agonist amplitude levels. Nor could the changes in initial agonist activity in the slower PD subjects be attributed to trade-off with other synergists or co-activation with antagonist (Figs. 3, 4). Instead, it appears initial agonist amplitude deficits occur for some PD subjects in both single joint and multijoint movements, although it is not the first or only burst feature to deteriorate.

In addition to a ceiling effect at maximum speeds, the PD-slow subjects also showed a trend towards higher levels of initial agonist activity at slower speeds, in the form of a higher PEC SUM100 offset on the y -axis (Fig. 2C). Deficits at slow speeds have not been previously identified in single joint studies and it remains to be studied how higher levels of initial agonist amplitude at slow speeds contribute to, or compensate for, bradykinesia in PD subjects. One hypothesis is that increased initial agonist amplitude at slow speeds occurs in compensation for the deficit of shorter, less variable burst duration.

Number of bursts/trial

The control subjects demonstrated a clear progression of three types of muscle patterns during individual trials across speed (Figs. 5, 8). Continuous patterns were most prevalent at slow speeds, multiple burst patterns were more predominant at intermediate speeds, and one-burst patterns were more predominant at fast speeds. These results are important for our general understanding of control of speed in several ways: (1) normal subjects not only scale amount of muscle activity with changes in speed, but also modulate burst number, and (2) while a multiple burst pattern can be observed in some individual trials, other trials (at the same speed) show a single burst that is part of the classic tri-burst (or biphasic) agonist-antagonist EMG pattern.

Our results show that not only do the PD subjects (fast and slow) lose the ability to produce the single burst for the fastest trials, the PD subjects also lose the ability to produce single burst trials for any speed. This means that, at fast and moderate speeds, they do not intermix single burst trials and multiple burst trials, similar to the controls. Rather they rely solely on the multiple burst pattern. While our findings of increased multiple burst trials at fast speeds are consistent with other studies, our findings of multiple bursts across speeds for PD, taken together with multiple bursts in normal subjects, suggest a different interpretation

for the occurrence of multiple bursts in individual trials. We would propose that as PD subjects lose their one-burst pattern, they are forced to use the *pre-existing* multiple burst pattern, rather than using a *novel* multiple burst pattern. The use of a possibly pre-existing MB pattern in PD subjects does not suggest that it is a normal pattern; in fact, it is altered in burst duration (Fig. 11B).

Previous single-joint studies that have counted bursts with similar methodology (Baroni et al. 1984; Benecke et al. 1987; Berardelli et al. 1986; Pfann et al. 2001; Teasdale et al. 1990; Wierzbicka et al. 1991) have not typically reported multiple bursts during individual trials in controls. One reason may be that multiple bursts may be unique to shoulder muscles as most single joint studies have investigated elbow muscles (also wrist and finger muscles) and have not previously recorded from shoulder muscles. In addition, multiple bursts may be a feature of slower joint velocities, since angular joint velocities in multijoint movements tend to be slower than single joint movements. For example, in this study, the movements demonstrated a range of angular velocities from 20–200°/s (Table 3). Published figures in other multijoint studies in which subjects were instructed to move quickly or as fast as possible (Gottlieb et al. 1997; Gribble and Ostry 1999; Hollerbach and Flash 1982) still show slow joint velocities that range from 30–120°/s. Hence, it appears that joint velocities during this study and other multijoint studies are relatively slow. In contrast, for most single joint studies, the joint angular velocities are in the range of 100–500°/s for movement durations of approximately 200–400 ms (e.g., Gottlieb et al. 1989; Almeida et al. 1995; Pfann et al. 2001). Even the recent study by Pfann et al. (2001), which examined an extended range of speeds in single joint movements, showed joint velocities that barely slowed to 100°/s for their shortest distance movements (5° and 8° targets) performed by their control subjects. The difference in velocities may arise due to the different mechanics of single vs. multijoint movements. That is, in single joint movements, endpoint velocity is entirely determined by the one joint velocity. In contrast, for multijoint movements to achieve a given endpoint velocity and its movement duration, the joint excursions and joint velocities are dispersed among the multiple joints (most often, shoulder and elbow). Moreover, the shoulder tends to move through a smaller excursion and with slower angular velocity than at the elbow joint (Gottlieb et al. 1997; Gribble and Ostry 1999; Hollerbach and Flash 1982).

Despite the difference in joint velocities between single and multijoint arm movement, multiple bursts have been briefly mentioned for the slowest single joint movements in a few studies. For instance, an earlier study by Teasdale et al. (1990) reported multiple bursts in individual trials that occurred in elderly control subjects when their speed overlapped with their PD subjects. Moreover, Pfann et al. (2001) showed that the average number of bursts was greater than 1.0/trial for female control subjects at the shorter distances (see their Fig. 5). Considering these findings from single joint studies, along with the present

results from multijoint movement, we hypothesize that multiple bursts may only be observed when angular velocities drop below a threshold ($\sim 100^\circ/\text{s}$). A future study needs to examine individual trials of both multi- and single joint movements with matched angular velocities below $100^\circ/\text{s}$ to determine if multiple bursts occur with slow angular velocities.

While multiple bursts have occasionally been mentioned in single joint studies, the one multijoint study of muscle activities that has studied a similar range of speeds to this study has not reported multiple bursts (Buneo et al. 1994). This suggests that other differences between our paradigm and earlier studies must also be operative. For example, they examined movements in the vertical plane, so even though it is unlikely, it cannot be ruled out that multiple bursts might be present for movements in the horizontal plane, but not for the vertical plane. More importantly, their EMG records were averaged (4–8 trials) and smoothed to address questions regarding the underlying change in shape across speed using a principal component analysis. It is well understood that averaged trials result in fused EMG bursts and would be very unlikely to show multiple bursts. The difference between the Buneo et al. study and ours is therefore to be expected. At this time, the functional importance of multiple bursts in individual trials is not known, and the contribution of different firing rates of motor units within a motor neuron pool to multiple bursts on a surface EMG record is unclear. Nonetheless, the findings of this study demonstrate that a progression occurred in which the number and type of bursts during individual trials changed with decreasing speed (one burst, multiple burst, continuous), and, most importantly, most PD subjects lost a part of this progression due to a loss of one-burst trials and an increase of multiple burst trials.

Severity of symptoms and interaction of burst deficits

Subjects with PD in this study showed a range of symptoms as depicted by the UPDRS and Hoehn and Yahr scores (Table 2), and they showed a range of deficits in burst features, including burst pattern, burst duration, and initial burst amplitude. It was interesting that the cumulative effect of multiple impairments in the burst features in this study tended to correlate with the severity of bradykinesia as measured by the UPDRS. That is, the fast PD subjects (including the fastest) with fewer burst deficits scored 1 on the bradykinetic measure of UPDRS and were at stage 1–2 of Hoehn & Yahr. The slow PD subjects with more burst deficits scored 2–3 on the bradykinetic measures and were at stage 2.5–3 Hoehn & Yahr. Other specific UPDRS measures of rigidity, dyskinesia and tremor did not correspond with the degree of deficits in burst characteristics or speed capacity of the subjects. In this manner, the clinical measures of bradykinesia corresponded with the physiologic measures of arm speed and the combination of burst deficits, while other clinical symptoms of PD did not.

One EMG feature occurred in PD subjects but was not consistently correlated with clinical levels of bradykinesia. Several subjects with PD showed increased antagonist activity that was not always accompanied by increased agonist activity (coactivation). This suggests a deficit in antagonist amplitude and/or timing is not a primary but may be a secondary mechanism contributing to bradykinesia. Therefore, there appears to be an interaction among different types of burst deficits that may act in concert to produce bradykinesia. This relationship is similarly described by Pfann et al. (2001), who showed an interaction of disease severity and EMG burst features for single joint movements of greater distance. Thus, whether PD subjects are intending to move big or small distances, or intending to move slow or fast speeds, there are several different deficits that may interfere with their success. The greater the number of deficit features interacting, the greater difficulty they may have in achieving their distance or speed goals.

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