Movement Disorders
Vol. 22, No. 3, 2007, pp. 328–333

Unilateral versus Bilateral Tasks in Early Asymmetric Parkinson's Disease: Differential Effects on Bradykinesia

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Abstract: Patients with Parkinson's disease (PD) have an impaired ability to perform two different simultaneous bimanual tasks. The differential effects of unilateral versus bilateral identical tasks on the bradykinesia scores of the more and less affected limbs in PD have not been examined. Twenty-seven patients with early and asymmetric PD underwent blinded, videotaped assessment, independently for each limb, using the bradykinesia items of the Unified Parkinson's Disease Rating Part III, Motor subscale (mUPDRS) and a Modified Bradykinesia Rating Scale (MBRS), which assessed amplitude, speed, and rhythm of movements. We found that the score for finger tapping in mUPDRS and MBRS, the score of amplitude of finger tapping in MBRS, and the lateralized scores of mUPDRS (sum of Items 23 to 25) of the most affected side significantly improved during the bimanual task. The improvement was associated with longer duration of illness, higher total scores in mUPDRS, and higher lateralized bradykinesia scores of the most affected side. There was a simultaneous deterioration of the lateralized bradykinesia scores in MBRS (sum of Items 23 to 25) and Item 25 of mUPDRS (rapid alternating movements) of the least affected side in bimanual tasks. In conclusion, identical bimanual tasks facilitate movement of the most affected side in early asymmetric PD at the cost of motor degradation in the least affected side. This observation also highlights the need to perform tasks of bradykinesia in one limb at a time for best accuracy. © 2007 Movement Disorder Society

Key words: Parkinson's disease; bimanual tasks; bihemispheric facilitation; bradykinesia

Bradykinesia or slowness of movement is a cardinal sign of Parkinson's disease (PD). The degree of nigrostriatal deficit measured with fluorodopa (FD) positron emission tomography (PET) correlates with clinical ratings of bradykinesia measured by a Modified Columbia Scale and Purdue Pegboard test.[1] The pathophysiological mechanisms that underlie bradykinesia have been the subject of much discussion. One of the current views suggests that bradykinesia results from a failure of basal ganglia output to reinforce the cortical mechanisms that prepare and execute the commands to move, a deficit that is most apparent in midline motor areas and particularly affects self-paced movements.[2] Functional magnetic resonance imaging (fMRI) and PET studies have shown under activation of the anterior supplementary motor area (SMA), anterior cingulate cortex, the dorsolateral premotor cortex, basal ganglia, and thalamus during such movements when compared to the resting state in patients with PD.[3–6] However, there appears to be increased recruitment of cortical circuits that may partially compensate for the deficit in basal ganglia function. This finding is evident from the overactivity in the lateral premotor and parietal cortices in comparison to normal controls during unilateral sequential finger movements.[7]

Either in addition to or as a component of bradykinesia, patients with PD have an impaired ability to perform both different and identical bimanual tasks simultaneously.[8–13] So far, no studies have evaluated the effects of unilateral vs. bilateral simultaneous performance of tests of bradykinesia on the most or least affected limbs in patients with asymmetric PD. This determination is of additional practical importance because there is inconsistency in the performance of clinical evaluation of bradykinesia of the limbs with some testing the limbs separately and others simultaneously.

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Received 13 January 2006; Revised 5 August 2006; Accepted 9 August 2006

Published online 10 January 2007 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/mds.21238

We hypothesized that, in early stages of PD with asymmetric bradykinesia, activation of motor cortical circuits of the less affected hemisphere may facilitate the performance of the more symptomatic side during identical bimanual tasks. In this study, we examined the effects of unilateral and identical simultaneous bilateral tasks of bradykinesia on the clinical scores of Items 23 to 26 of the mUPDRS and a modification of it, in patients with early and asymmetric PD.[14]

SUBJECTS AND METHODS

Subjects

We recruited 27 consecutive patients with PD fulfilling the UK Parkinson's Disease Society's Brain Bank Clinical Diagnostic Criteria,[15] in Hoehn & Yahr Stages 1 to 3, with asymmetric bradykinesia, from the Movement Disorders Centre, Toronto Western Hospital, Canada. Patients recruited had a minimum difference of at least 1 point between the scores of the two sides for each task of limb bradykinesia (Items 23 to 26 in mUPDRS) and a minimum score of 1 of 4, for each test of bradykinesia, on the more affected side. Patients were excluded if they had tremor significant enough to interfere with assessment of bradykinesia, evidence of lower motor neuron involvement or pyramidal dysfunction from any etiology, local pain or deformity interfering with movement of the limbs, cognitive impairment that in the opinion of the treating neurologist impaired the understanding or performance of the tasks required, or had undergone a previous neurosurgical procedure. Patients with mirror movements were not excluded if mirror movements were seen during unimanual tasks.[16] In patients receiving antiparkinsonian drugs, the tasks were performed when the patients believed that they had reached their usual *off* state or after a minimum of 6 hours after their last dose of levodopa in those who were not experiencing motor fluctuations. Dopamine agonists were discontinued 24 hours before the test. All patients gave their informed consent for the study and the Research Ethics Board of the University Health Network approved the study.

Methods

Limb bradykinesia was measured using Items 23 to 26 of mUPDRS (23 = finger tapping, 24 = hand movements, 25 = rapid alternating movements, and 26 = foot tapping). Patients were asked to perform the tasks with as large amplitude and as fast as possible during one practice session with the examiner. These four tasks were performed for 10 seconds by each limb alone (unimanual task) or simultaneously with the opposite side (bimanual task). There was a 30-second gap between the unimanual and bimanual task. After each item, the patient was given 1 minute to rest. The tasks were performed in randomized order for side (right or left extremity) and condition (unimanual or bimanual) for all patients. Videotape recordings were made during each task, focusing on one limb at a time. The same examiner documented all tests. Patients were blinded to the purpose of the tasks performed by them and were not aware of whether one or both extremities were recorded during a bimanual task. No instruction was given regarding attention to any side in bilateral tasks. At the end of the study, the video of each patient was independently evaluated by 2 raters unaware of the subjects' clinical state and individual task condition (the raters could not identify whether the video segment of the limb represented unilateral or bilateral performance). The raters were asked to use the mUPDRS rating scale first and then apply the modified bradykinesia rating scale (A–C) for the study for each task. The modified bradykinesia rating scale scored speed, amplitude, and rhythm separately as follows. (A) Speed: 0 = normal; 1 = mild slowing; 2 = moderate slowing; 3 = severe slowing; 4 = can barely perform the task. (B) Amplitude: 0 = normal; 1= mild reduction in amplitude in later performance, most movements close to normal; 2 = moderate, reduction in amplitude visible early in performance but continues to maintain 50% amplitude through most of the tasks; 3 = severe, less than 50% amplitude through most of the task; 4 = can barely perform the task. (C) Rhythm: 0 = regular, no arrests or pauses in ongoing movement; 1 = mild impairment, up to two brief arrests in the 10 seconds, none lasting $>$ 1 second; 2 = moderate, 3 to 4 arrests in 10 seconds; 1or 2 lasting $>$ 1second; 3 = severe, 5 or more arrests/10 seconds; more than 2 lasting $>$ 1 second; 4 = can barely perform.

A total score was generated from the sum of A, B, and C for each task. Lateralized bradykinesia scores were calculated by summing scores of Items 23 to 25 for the upper extremity and Items 23 to 26 for the hemibody, in the modified bradykinesia rating scale MBRS and mUPDRS. UPDRS Part 1 scores were also recorded to exclude patients with abnormalities in mood and behavior.

Statistical Analyses

The scores of mUPDRS and modified bradykinesia rating scale for each task between unimanual and bimanual scores were compared using paired *t* tests with correction for multiple analyses. The scores for individual intrascale items of speed, amplitude, and rhythm between unimanual and bimanual scores were compared using the Wilcoxon signed rank test. The degree of agreement across the raters on each of the individual

TABLE 1. *Clinical characteristics of patients*

Male: Female	21:6
Mean age at study, yr	59.3 ± 13.9
Mean duration of illness, yr	4.5 ± 3.4
Mean Hoehn & Yahr	1.9 ± 0.6
Mean lateralized bradykinesia of the most affected side (sum of Items 23 to 26 in mUPDRS)	5.7 ± 2.6
Mean lateralized bradykinesia of the least affected side (sum of Items 23 to 26 in mUPDRS)	2.2 ± 2
Mean UPDRS Part I score in *off*	1.1 ± 1
Mean UPDRS Part II score in *off*	9 ± 5.6

UPDRS, Unified Parkinson's Disease Rating; mUPDRS, UPDRS Part III, Motor subscale.

item scores was evaluated using a series of kappas and intraclass correlations following proposed guidelines.[17] A kappa of >0.8 = almost perfect, 0.61 to 0.80 = substantial, 0.41 to 0.60 = moderate, 0.21 to 0.40 = fair, 0.00 to 0.20 = slight, <0.00 = poor.

The effect of covariates such as age, duration of illness, handedness, side of worse symptoms (dominant vs. nondominant), Hoehn & Yahr stage, total mUPDRS score, lateralized scores of bradykinesia for the most affected side and least affected side on the mUPDRS, asymmetry score of bradykinesia on the mUPDRS, and treatment status as predictive factors of change in performance between unimanual and bimanual tasks, were assessed using a series of logistic regression analyses pooling scores from the 2 raters.

An odds ratio (OR) of >1 indicates an increased likelihood of improved task performance, whereas OR < 1 indicates that the presence of the factor decreases the likelihood of improvement under the bimanual condition compared to the unimanual condition. A P value of less than 0.05 was considered statistically significant.

RESULTS

Twenty-seven patients with asymmetrical PD participated in the study (Table 1). Of these patients, 26 were right handed. In 16 cases, the dominant side was the more affected side. Six patients had hemiparkinsonism with clinical signs restricted to one side. There were motor fluctuations in 2 patients and L-dopa induced dyskinesias in 4 patients in the *on* state. Six patients were not receiving any antiparkinsonian treatment. There were 11 who were taking only L-dopa (mean dose = 452 ± 290 mg) and 10 patients who were on ropinirole or pramipexole therapy (mean L-dopa equivalent dose of 110.6 ± 63 mg).One case each was additionally on amantadine and selegiline.

Comparisons of the performance of the tasks in the more affected side revealed significant improvement of the amplitude of finger tapping ($P = 0.01$) and total finger tapping scores in the MBRS corresponding to Item 23 ($P = 0.04$) and also in mUPDRS Item 23 ($P = 0.03$) and lateralized scores of mUPDRS (sum of Items 23 to 25 and 23 to 26) during bimanual versus unimanual tasks (Table 2). There was no significant improvement or deterioration in the performance of the more affected side in the remaining tasks as measured by the MBRS or mUPDRS. Comparisons of the performance of the less affected side did not reveal any significant differences in the unimanual vs. bimanual tasks. However, Item 25 of mUPDRS of the less affected side and the lateralized bradykinesia scores in MBRS (sum scores of Items 23 to 25 and 23 to 26) deteriorated during bilateral tasks when compared to unilateral performance ($P = 0.03$, 0.02, and 0.01, respectively). The inter-rater reliability was substantial between the raters for all items, with a $P < 0.001$ for all tests (unweighted kappa = 0.7). Logistic regression showed that the improvement in finger-tapping performance on the most affected side during bimanual task was more likely to occur with a longer duration of illness (OR, 1.8; $P = 0.009$), in those with higher total mUPDRS scores (OR, 1.6; $P = 0.003$), worse lateralized bradykinesia score for the more affected side (sum of Items 23 to 26 in mUPDRS at baseline; OR, 1.6; $P = 0.002$), and higher asymmetry scores for limb bradykinesia (OR, 3.3; $P = 0.01$). There were no factors that significantly predicted the deterioration of the total scores of the least affected side in bilateral task performance. There was no statistically significant difference between the unilateral finger-tapping scores and the corresponding unilateral hand movement, rapid alternating movement, and foot-tapping scores. There was a significant correlation between the total scores of mUPDRS and MBRS, for each of the tasks, unilateral and bilateral and for worst and least affected sides ($P < 0.01$ and $r > 0.7$ for all comparisons).

DISCUSSION

We found an improvement of the finger-tapping score on the most affected side and a deterioration of the lateralized bradykinesia scores on the least affected side during simultaneous identical bimanual task compared with unimanual performance. The improvement of the more affected side was associated with higher lateralized bradykinesia scores in mUPDRS for the limbs on the most affected side, higher total mUPDRS scores, and longer duration of illness. These observations suggest that bihemispheric activation of motor circuits during bimanual tasks in early asymmetric PD may facilitate movement of the most affected side at the cost of motor degradation of the least affected side.

TABLE 2. *Scores of unilateral vs. bilateral task performance*

Task	Side	Unilateral score (mean ± SD)	Bilateral score (mean ± SD)	Statistical significance ($P=$)
Item 23, MBRS				
Finger tap – Speed	Most	0.9 ± 0.8	0.9 ± 0.8	1.0
	Least	0.6 ± 0.6	0.6 ± 0.7	1.0
Finger tap – Amplitude	Most	1.2 ± 0.8	0.9 ± 0.6	0.01*
	Least	0.6 ± 0.6	0.6 ± 0.6	0.79
Finger tap – Rhythm	Most	0.6 ± 0.6	0.4 ± 0.5	0.22
	Least	0.2 ± 0.4	0.3 ± 0.4	1.00
Finger tap – Total score	Most	2.7 ± 1.5	2.3 ± 1.2	0.04*
	Least	1.3 ± 1.0	1.5 ± 1.1	0.46
Finger tap – mUPDRS, Item 23	Most	1.6 ± 0.9	1.3 ± 0.9	0.03*
	Least	0.8 ± 0.6	0.8 ± 0.6	1.0
Item 24, MBRS				
Hand movements – Speed	Most	0.8 ± 0.5	0.9 ± 0.5	1.0
	Least	0.6 ± 0.6	0.7 ± 0.5	0.62
Hand movements – Amplitude	Most	0.9 ± 0.6	0.9 ± 0.7	1.00
	Least	0.5 ± 0.6	0.5 ± 0.6	1.00
Hand movements – Rhythm	Most	0.3 ± 0.4	0.3 ± 0.5	1.00
	Least	0.2 ± 0.4	0.2 ± 0.4	1.00
Hand movements – Total score	Most	2.0 ± 0.9	2.0 ± 1.1	0.86
	Least	1.3 ± 1.1	1.4 ± 1.1	0.86
Hand movements – m UPDRS, Item 24	Most	1.1 ± 0.5	1.0 ± 0.5	0.61
	Least	0.7 ± 0.5	0.8 ± 0.6	0.77
Item 25, MBRS				
Rapid alternating movements – Speed	Most	1.1 ± 0.7	0.9 ± 0.7	0.22
	Least	0.4 ± 0.5	0.6 ± 0.5	0.17
Rapid alternating movements – Amplitude	Most	1.2 ± 0.8	1.0 ± 0.8	0.12
	Least	0.4 ± 0.6	0.6 ± 0.8	0.34
Rapid alternating movements – Rhythm	Most	0.5 ± 0.5	0.6 ± 0.7	1.00
	Least	0.2 ± 0.5	0.3 ± 0.5	0.75
Rapid alternating movements – Total score	Most	2.7 ± 1.3	2.4 ± 1.5	0.28
	Least	1.0 ± 1.2	1.4 ± 1.4	0.10
Rapid alternating movements – mUPDRS, Item 25	Most	1.4 ± 0.7	1.2 ± 0.8	0.34
	Least	0.5 ± 0.7	0.9 ± 0.7	0.03*
Item 26, MBRS				
Foot tap – Speed	Most	0.7 ± 0.5	0.8 ± 0.5	0.68
	Least	0.4 ± 0.5	0.5 ± 0.5	1.00
Foot tap – Amplitude	Most	0.7 ± 0.7	0.7 ± 0.6	1.00
	Least	0.5 ± 0.6	0.5 ± 0.6	1.00
Foot tap – Rhythm	Most	0.6 ± 0.5	0.5 ± 0.5	0.77
	Least	0.3 ± 0.4	0.3 ± 0.5	1.00
Foot tap – Total score	Most	2.0 ± 1.3	2.0 ± 1.2	0.89
	Least	1.2 ± 1.2	1.3 ± 1.2	0.75
Foot tap – mUPDRS Item 26	Most	1.0 ± 0.6	1.0 ± 0.5	1.00
	Least	0.6 ± 0.7	0.6 ± 0.6	1.00
Sum of Items 23-25, MBRS	Most	7.3 ± 2.3	6.7 ± 2.6	0.20
	Least	3.7 ± 2.4	4.4 ± 2.6	0.02*
Sum of Items 23-26, MBRS	Most	9.0 ± 3.0	9.5 ± 3.1	0.27
	Least	5.0 ± 2.9	5.9 ± 3.4	0.01*
Sum of Items 23-25, mUPDRS	Most	3.9 ± 1.3	3.4 ± 1.4	0.02*
	Least	2.2 ± 1.5	2.4 ± 1.6	0.13
Sum of Items 23 to 26, mUPDRS	Most	4.9 ± 1.8	4.5 ± 1.6	0.05*
	Least	2.8 ± 1.8	3.1 ± 2.0	0.19

Asterisks indicate statistical significance..
MBRS, Modified bradykinesia rating scale; UPDRS, Unified Parkinson's Disease Rating Scale; mUPDRS, UPDRS Part III, Motor subscale.

In normal subjects, bimanual coordination is controlled by a distributed network including SMA, primary and secondary motor area, cingulate motor area, premotor cortex, cerebellum and posterior parietal cortex, depending on the task. The SMA proper is considered to be also involved in suppressing default symmetric mirror movements and is active in both unimanual and bimanual tasks, indicating that restrictive function is relevant in both unimanual and bimanual tasks.[18] Koenke and colleagues, using appropriately controlled unimanual tasks, did not find any significant additional activation in bimanual tasks in this network in normal subjects.[18]

The impaired ability of patients with PD to perform two different tasks simultaneously is well known. This finding was initially interpreted as impairment in executing simultaneous bimanual tasks when the two different tasks used two different time elements.[11] Subsequently, Horstink and colleagues demonstrated that the disturbance in two separate bimanual tasks was not due to disturbance in time sharing, but due to a decreased ability to shift attention from a visually cued to a nonvisually cued task.[12] In identical simultaneous bimanual tasks such as bimanual peg placement in holes, PD patients had worse overall scores in bimanual performance compared to unimanual performance.[13] Such studies have included patients in all stages of PD and have only examined the mean scores of bimanual task versus mean of unimanual scores of the hands without determining the effect of bimanual task performance on individual hand function.

An unusual enhancement of motor performance during bimanual movements in PD was reported by Brown and Jahanshahi[19] In their cohort, when performed at the same time as repetitive tapping tasks, the ability to rapidly place pegs in holes improved in comparison to the unimanual performance of the peg task. The investigators invoked withdrawal of attention from the task permitting a more automatic execution mode such as tapping to placing pegs in holes or facilitation provided by sensory feedback from the simultaneous tapping task. The tapping task in PD is less automatic than in normal subjects and a shift of attention to the task performed by the more affected side could explain the deterioration in performance of the less affected side and the improvement on the worse side during a bimanual task that we observed. However, there may be alternative mechanisms that could explain changes that we found in our study.

We postulate that activation of the motor cortical circuits of the less affected hemisphere may facilitate the performance of the more affected hemisphere during bimanual tasks in PD and thereby enhance the performance of the more affected limb in bimanual tasks. Lack of such a similar facilitation from the more affected hemisphere on the less affected hemisphere may lead to the relative deterioration of performance of the least affected limb in bimanual tasks. The hemispheric mechanism that might explain our findings during bimanual tasks in PD could be that the less affected hemisphere facilitates bimanual tasks as a result of less impairment in transcallosal facilitation of the SMA and primary motor areas of the more affected hemisphere. These areas are underactive during sequential finger movements in PD, a deficit which is known to improve with dopaminergic treatment.[3] Alternatively or additionally there could be ipsilateral facilitation and direct recruitment of uncrossed motor pathways of the less affected hemisphere during bimanual tasks, which improves the performance of the most affected limb.

The total scores for each of the tasks rated using the two scales showed a significant positive correlation. Comparing the results using the two rating scales, we found that the changes in the mUPDRS and MBRS during bimanual tasks were concordant for the most affected hemibody and the most affected upper limb. MBRS was useful in detecting a significant improvement in the amplitude component of the finger-tapping test, in addition to the changes in the total scores for the upper limb. This finding suggests that MBRS may be more sensitive in identifying different aspects of bradykinesia that are rated together in mUPDRS. In addition, it was only the MBRS that detected a significant worsening in the least affected hemibody in bimanual tasks, although significant changes were not detected in individual test items. This finding highlights the need to validate MBRS in future studies.

The finger-tapping scores of the most affected side in unilateral performance were not significantly different from the scores of other unilateral tasks. It, therefore, seems that finger-tapping test may be more suitable to measure changes in bradykinesia scores for the upper limbs.

In conclusion, we found a novel pattern of change in bradykinesia scores of the worse and less affected sides in patients with early asymmetric PD during bimanual tasks. This finding may result from a shift of attention to the performance of the more affected side or alterations in intrahemispheric and interhemispheric patterns of motor activations, during bimanual tasks in asymmetric disease. Functional MRI and neurophysiological studies may provide further insight into the alterations of motor activation or motor excitability in the two hemispheres during bimanual identical tasks in PD. Our study also highlights the need to perform tests of bradykinesia in mUPDRS independently on both sides and not simultaneously, to accurately measure the motor deficits of PD in clinical research.

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