SHORT REPORT

Effects of levodopa on upper limb mobility and gait in Parkinson's disease

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Background: Most clinicians rely on clinical scales such as the unified Parkinson's disease rating scale (UDPRS) for evaluating parkinsonian patients and assessing their response to levodopa. Gait analysis is not commonly used, probably because of the equipment required and the time needed. Few data have been published on the relations between gait variables and measures of arm and hand mobility.
Objectives: To evaluate the correlation between dopa induced gait improvement and upper limb motor improvement using a rapid and simple method; and to evaluate the correlation between gait improvement and UPDRS III improvement.
Methods: A finger tapping test and a simple walking test were used to measure the OFF-ON variations of upper limb motor function and gait in 23 patients with Parkinson's disease. The UPDRS motor score and the Hoehn and Yahr stage were measured in the OFF and the ON state.
Results: There was no correlation between OFF-ON variation of the number of hits with the finger tapping test and OFF-ON variation in the gait variables. OFF-ON variation in the UPDRS motor score was not correlated with OFF-ON variation in the gait variables.
Conclusions: There was a dissociation between the effect of levodopa on upper limb and gait. The findings suggest that simple measures like the finger tapping test and a walking test should be included in the usual evaluation of patients with Parkinson's disease.

Patients with Parkinson's disease have abnormal voluntary movements and gait.[1 2] Most clinicians rely on clinical scales such as the unified Parkinson's disease rating scale[3] (UPDRS) for their evaluation of parkinsonian patients and to assess their response to levodopa. The UPDRS is widely used, especially section III (UPDRS III), which provides a semiquantitative evaluation of motor impairment. UPDRS III is easy to learn and reasonably short; however, it does not assess gait to any great extent and concentrates more on the upper limbs. Others have already underlined the need to include more quantitative measures of gait in the evaluation of patients with Parkinson's disease.[2 4–10] However, gait analysis is not commonly used, probably because of the equipment required and the time needed. In addition, there are few data on the relations between gait variables and measures of upper limb motor function and the clinical rating scales.

The first aim of our study was to evaluate the correlation between dopa induced gait improvement and upper limb motor improvement using a fast and simple method that can easily be applied in an office setting. Our hypothesis was that there is a dissociation between the effect of levodopa on the upper limbs and on gait. Our second objective was to evaluate the correlation between gait and improvements UPDRS III score.

METHODS

Patients

From May 2000 to December 2001, consecutive patients fulfilling the UK Parkinson's Disease Society brain bank criteria[11] for the diagnosis of Parkinson's disease, with no other known pathology affecting gait or arm mobility, were included after giving written informed consent. Patients older than 80 years were excluded from the study. Patients had to be able to walk 14 metres in OFF state to be included. All patients scored at least 24/30 in the mini-mental state examination.[12] All had a dopa response better than 50% when assessed by the UPDRS III OFF/ON ratio.

Procedure

The first evaluation started between 8:00 and 8:30 in the OFF state and included successive clinical, upper limb, and gait evaluations. Dopaminergic agonists and slow release levodopa were stopped at 13:00 while levodopa was stopped at 20:00 the day before evaluation. After this, a second evaluation was undertaken in the ON state, 50 minutes after taking an appropriate oral dose of dispersible levodopa. The appropriate dose of levodopa was calculated to be equal to 150% of the usual morning dose of levodopa plus the morning dopaminergic agonist equivalent levodopa dose (10 mg bromocriptine = 100 mg levodopa; 1 mg pergolide = 100 mg levodopa).

Clinical evaluation

UPDRS III and Hoehn and Yahr stage were once measured in the OFF and the ON state. The sum of upper limb UPDRS III items 20 to 25 (tremor at rest + action or postural tremor of hands + rigidity + finger taps + hand movements + rapid alternating movements of hands) was used to determine the most affected upper limb in the OFF state.

Upper limb motor function: the finger tapping test

Subjects had to hit two buttons separated by 30 cm alternately during a 30 second period. When a patient missed a button, the instruction was to continue the test going directly to the other button. The size of the buttons was 1 × 1 cm. The sum of hits on both buttons was the result of the test. Four consecutive finger tapping test trials (successively two with the right hand and two with the left) were done in the OFF and the ON state.

Gait analysis

Two consecutive walking trials were done in the OFF and the ON state. We asked the patients to walk 14 metres as fast as possible (without running) between two lines drawn on the floor. No other visual clues were drawn except two marks at metre 2 and metre 12. In order to assess the steady state gait, we asked patients to walk the 14 metre distance but we recorded the number of steps and walking time only between

Table 1 Descriptive statistics

	n	Mean	Median	Minimum	Maximum
Hoehn and Yahr stage, OFF	23		3	1	4
Hoehn and Yahr stage, ON	23		2	0	3
UPDRS III, OFF	23		39	12	91.5
UPDRS III, ON	23		9.5	2	41.5
Number of hits, OFF*	23	40.48	41	4	71
Number of hits, ON	23	57.26	50	28	89
Gait velocity, OFF†	23	83.87	75	42.86	150
Gait velocity, ON	23	114.81	100	42.86	200
Gait cadence, OFF‡	23	137.50	137.14	103.64	180
Gait cadence, ON	23	142.83	140	60	240
Stride length, OFF¶	23	0.61	0.56	0.26	1.0
Stride length, ON	23	0.79	0.71	0.56	1.25
ΔUPDRS III	23	69.02			
ΔNumber of hits	23	67.31			
ΔGait velocity	23	39.88			
ΔGait cadence	23	3.66			
ΔStride length	23	38.03			

*Number of hits at the best finger tapping test trial of the most affected upper limb in the OFF state.
†Gait velocity (m/min) at the best walking trial.
‡Gait cadence (steps/min) at the best walking trial.
¶Stride length (m) at the best walking trial;
OFF, OFF state; ON, ON state; UPDRS III, unified Parkinson's disease rating scale motor score (/108); Δ, OFF-ON variation: [("OFF" minus "ON")/"OFF" × 100] (%).

Table 2 Differences between trials: Wilcoxon's signed rank test

	State			
	OFF		ON	
	NH 1R – NH 2R	**NH 1L – NH 2L**	**NH 1R – NH 2R**	**NH 1L – NH 2L**
T	106.5	149.5	60.0	158.0
p Value	0.9854	0.2572	0.0973	0.3209
	NH 1R – NH 1L	**NH 2R – NH 2L**	**NH 1R – NH 1L**	**NH 2R – NH 2L**
T	147.5	161.5	137.5	193.5
p Value	0.7998	0.5009	0.7502	0.098
	NS 1 – NS 2	**WT 1 – WT 2**	**NS 1 – NS 2**	**WT 1 – WT 2**
T	23	24	36	55
p Value	0.1563	0.4609	0.1289	0.0537

1, trial 1; 2, trial 2; L, left; NH, number of hits in the finger tapping test; NS, number of steps; OFF, OFF state; ON, ON state; R, right; WT, walking time.

metre 2 and metre 12. If freezing occurred once, the number of steps during the freezing period was not recorded. The trial was not valid if freezing occurred more than once. The walking time was clocked by hand by one investigator while the number of steps was counted by another. The steps made on the marks were counted. Gait velocity (m/min), gait cadence (steps/min), and stride length (m) were calculated from the number of steps and the walking time.

RESULTS

Twenty three of 28 screened patients were included. The five excluded patients had a response to levodopa worse than 50%. No patient had a freezing episode during the walking test. Sixteen men and seven women took part, mean (SD) age, 60 (9) years. One patient was left handed and the rest were right handed. The mean levodopa dose was 237 (48) mg. Descriptive statistics are shown in table 1.

There was no significant difference between the first and the second trial in the number of hits in the finger tapping test, neither was there a significant difference between the number of hits between the two hands (table 2). On the walking test, there was no difference between the first and the second trial in the number of steps and the walking time (table 2). The best result in the finger tapping test done with the most affected upper limb in the OFF state (as defined in Methods) was chosen for statistical analysis. The best walking trial was defined as the lowest result when calculating the product, [number of steps] × [walking time]; this was used for statistical analysis. Gait velocity, gait cadence, and stride length were then calculated from the number of steps and walking time from this best walking trial.

Correlations between UPDRS III score, the number of hits in the finger tapping test, and the gait variables are shown in table 3. The main result of our study was that there was no correlation between the OFF-ON variation in the number of hits on the finger tapping test and the OFF-ON variation in the gait variables. Although the UPDRS III score was moderately correlated with the number of hits on the finger tapping test, it is worth noting that it was not correlated with any of the gait variables, either in the OFF state or in the ON state. Moreover, the OFF-ON variation in the UPDRS III score was not correlated with the OFF-ON variation in the number of hits in the finger tapping test or with the variation in the gait variables. Correlations between UPDRS III items 26 (leg agility), 29 (gait), and 31 (body bradykinesia and hypokinesia) and the gait variables were weak ($r^2 < 0.26$). The best correlations were obtained between gait velocity and item 31 (r^2 OFF: 0.2553, $p < 0.05$; r^2 ON: 0.2076, $p < 0.05$). Similarly, correlations between UPDRS III items 23 (finger taps), 24 (hand movements), and 25 (rapid alternating movements of hands) for the most affected upper limb and the number of hits on the

Table 3 Correlations between the unified Parkinson's disease rating scale motor score (UPDRS III), finger tapping test, and gait variables: r^2 values

		NH*	GV†	CAD‡	SL¶
UPDRS III	OFF	0.5804**	0.2103*	0.0679	0.1996*
	ON	0.3708**	0.1173	0.0611	0.0848
	Δ	0.0383	0.0143	0.0033	0.0242
NH*	OFF		0.3860**	0.2731*	0.1916*
	ON		0.3811**	0.2387*	0.2506*
	Δ		0.0568	0.0185	0.0098
GV†	OFF			0.3836**	0.7351**
	ON			0.7574**	0.4326**
	Δ			0.0514	0.5641**
CAD‡	OFF				0.0220
	ON				0.0450
	Δ				0.2119*

*Number of hits in the best finger tapping test of the most affeated upper limb in the OFF state.
†Gait velocity (m/min) in the best walking trial.
‡Gait cadence (steps/min) in the best walking trial.
¶Stride length (m) in the best walking trial.
*p < 0.05; **p < 0.01.
OFF, OFF state; ON, ON state; Δ, OFF-ON variation.

finger tapping test were also weak ($r^2 < 0.32$). The best correlations were obtained between the number of hits on the finger tapping test and item 25 (r^2 OFF: 0.3175, $p < 0.05$; r^2 ON: 0.2553, $p < 0.05$). In the OFF state, gait velocity was best correlated with stride length, while in the ON state it was best correlated with gait cadence. When comparing upper and lower limb variables, we showed that the number of hits on the finger tapping test was moderately correlated with gait velocity and not correlated with gait cadence or stride length.

DISCUSSION

We chose the finger tapping test as a simple measure of upper limb motor function and simple gait variables to reflect lower limb motor function. The walking test was simple, fast, and robust; however, our study included only selected patients. All the patients had to be able to walk 14 metres in the OFF state, and thus patients with severe Parkinson's disease were not included. We analysed gait in the steady state and did not accept walking trials with repeated freezing. This did not seem to be a problem as none of our 28 patients had a freezing episode during the walking tests. Finally, we included only patients with marked improvement induced by levodopa, increasing our chances of selecting patients with idiopathic Parkinson's disease.

Our data showed that the number of hits on the finger tapping test was moderately correlated with the UPDRS III score. However, there was no correlation between the OFF-ON variation of the UPDRS III score and the OFF-ON variation of the number of hits on the finger tapping test. Gait variables did not correlate with the UPDRS III score in the OFF or the ON state. Furthermore the OFF-ON variation in the UPDRS III score did not correlate with the OFF-ON variation in gait velocity, stride length, or gait cadence. These findings suggest that one could miss some important clinical changes when using only the UPDRS III without gait evaluation. Finally the improvement in upper limb motor function was not correlated with the improvement in gait. This observation suggests that these two motor tasks have some degree of independence from each other. Our data confirmed that the UPDRS III score is only a partial assessment of dopa induced motor improvement.[4 5] This was confirmed by the low correlations between gait variables and UPDRS III subitems 26, 29, and 31.

As expected,[5 6 13] gait cadence was the least dopa responsive gait variable, with a median OFF-ON increase of only 2.9%, whereas gait velocity and stride length showed a median increase of 33.3% and 28.6%, respectively. Others have suggested that stride length is predominantly modulated by the basal ganglia, whereas gait cadence is not.[2]

Our study showed no significant difference between the number of hits at the first and second finger tapping test trial or between the number of hits when finger tapping test was done with the right or left hand. In view of the asymmetrical characteristics of Parkinson's disease, we considered the best result of the finger tapping test performed with the most affected hand to be the most accurate assessment of upper limb motor function.

Conclusions

Our study shows that there is dissociation between the effect of levodopa on the upper limb and on gait. Variations in motor performance induced by levodopa in patients with Parkinson's disease are complex and cannot be assessed by a single rating scale. The OFF-ON variation in upper limb motor performance did not correlate with the variation in gait performance or with the variation in the UPDRS III score. Our findings suggests that simple measures like the finger tapping test and a walking test should be included in the usual evaluation of patients with Parkinson's disease.

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