Published in final edited form as:
J Neurol Neurosurg Psychiatry. 2011 October ; 82(10): 1122–1124. doi:10.1136/jnnp.2010.209783.

Handedness and motor symptom asymmetry in Parkinson's disease

Matthew J Barrett[1], **Scott A Wylie**[2], **Madaline B Harrison**[2], and **G Frederick Wooten**[2]
[1]Department of Neurology, Beth Israel Medical Center, New York, USA

[2]Department of Neurology, University of Virginia, Charlottesville, Virginia, USA

Abstract

Background—The objective of this study was to confirm whether an association between handedness and the side of symptom onset exists and to evaluate the impact of this association on specific clinical characteristics of Parkinson's disease (PD).

Methods—1173 PD patients were identified from a clinical database. Patients with asymmetrical onset (n=1015) were divided into those with dominant-side onset and those with non-dominant-side onset, and the clinical characteristics of the two subgroups were compared.

Results—In our PD sample, 86.5% of patients presented asymmetrically. There was a significant association between handedness and the side of the initial symptom; that is, the dominant side was affected first in the majority of both left- and right-handed patients. Compared with patients with non-dominant side onset, more patients with dominant-side onset presented with bradykinesia, while fewer patients presented with gait difficulty. Patients with dominant-side onset were diagnosed and began dopaminergic medication after a longer symptom duration than patients with non-dominant-side onset. The only difference in Unified Parkinson Disease Rating Scale scores between the two groups was in a subscore addressing dominant-hand tasks.

Conclusions—An association exists between the dominant hand and the side of the initial motor symptom in PD. Whether the initial symptom occurs on the dominant or non-dominant side has implications for the reported first symptom, the time to diagnosis and the time to dopaminergic treatment initiation. The side of disease onset does not affect the severity of disease, as measured by the Unified Parkinson Disease Rating Scale.

INTRODUCTION

Why the signs and symptoms of Parkinson's disease (PD) frequently present asymmetrically remains unclear.[1] The largest study to characterise the asymmetry of PD found that the side of the initial symptom and the dominant hand were independently associated with the more affected side in asymmetrical disease.[2] Smaller studies reported either no association or a non-significant trend suggesting initial PD symptoms present more often in the dominant hand.[3–5] We undertook this study (1) to determine whether an association exists between the dominant hand and the side of symptom onset in PD and (2) to characterise the clinical features of PD for patients with symptoms beginning on their dominant or non-dominant side. We hypothesised that patients with initial symptoms on their dominant side would seek

Correspondence to: Dr Matthew J Barrett, Beth Israel Medical Center, Department of Neurology, 10 Union Square East, Suite 5K, New York, NY 10003, USA; mabarrett@chpnet.org.

Competing interests None.

Ethics approval Ethics approval was provided by the University of Virginia IRB.

Provenance and peer review Not commissioned; externally peer reviewed.

diagnosis and treatment sooner than patients with initial symptoms on their non-dominant side.

METHODS

Patients evaluated in our tertiary care clinic (1995–2008) and diagnosed as having idiopathic PD by a movement disorders specialist were enrolled in a clinical database during their initial visit (n=1267). After institutional review board approval, we retrospectively identified 1173 PD patients with complete data for sex, age at symptom onset, age at diagnosis, age at clinical evaluation, handedness, initial motor symptom and site of initial motor symptom. Patients specified their dominant hand as left or right. The examiner elicited the initial motor symptom and recorded it as rest tremor, action tremor, bradykinesia, rigidity, balance problem, dragging leg/shuffling, decreased arm swing, diminished facial expression, speech, swallowing, dystonia, stooped posture, micro-graphia or other. In the same manner, the site of initial motor symptom was recorded as head or neck, right arm, left arm, trunk or gait, right leg, left leg or other. If the reported initial motor symptom or initial symptom site applied to more than one category, the examiner selected the most fitting answer. Initial motor symptoms were later reclassified as (1) tremor, encompassing both rest tremor and action tremor; (2) bradykinesia, including micrographia; (3) rigidity, including decreased arm swing; (4) gait difficulty, encompassing balance problems, dragging leg or shuffling, and stopped posture; or (5) other, including diminished facial expression, speech problems, swallowing difficulty and dystonia. The site of initial motor symptom was also later reclassified as head/neck, right arm, left arm, trunk/gait, right leg, left leg or other.

The time to diagnosis was calculated as the difference between age at motor symptom onset and age at diagnosis. Disease duration was calculated as the difference between age at symptom onset and age at evaluation in our clinic. For a subset of patients with known dates of L-dopa or dopamine agonist initiation, time to dopaminergic medication initiation was calculated as the difference between age at symptom onset and age at dopaminergic medication initiation.

A subset of patients completed parts I–III of the Unified Parkinson Disease Rating Scale (UPDRS) at their initial visit. To adjust for disease duration, scores for each part of the UPDRS were divided by the individual's disease duration. This technique approximates the disease deterioration rate.[6–8] Using UPDRS items 20–26, we calculated a right-minus-left difference score by subtracting left-handed values from right-handed values.[2]

Analytical approach

The first set of analyses focused on the effect of handedness (right vs left) on clinical features of PD. The second set of analyses focused on differences in clinical features of PD based on whether the onset of PD symptoms occurred in the dominant versus the non-dominant side of the body. Continuous and frequency data were analysed with t tests and two factor χ^2 tests of association, respectively, with appropriate adjustments for multiple comparisons. Proportional differences of interest were analysed with standardised z-ratios with appropriate adjustments to the α value for multiple comparisons.

RESULTS

Characteristics of the overall sample

The majority (91.3%) of patients reported right-hand dominance. Males and females comprised 61.1% and 38.9% of our sample, respectively. The mean age of onset was 58.1 years, with mean time to diagnosis occurring within 2 years of symptom onset (mean=20.7 months, SEM=0.7). The mean duration of disease at the time of evaluation was 7.1 years

(±SD=5.6 years). The initial symptom was tremor in 59.2%, bradykinesia in 14.6%, rigidity in 10.3% and gait difficulty in 11.0% of patients. The majority of patients (86.5%) presented with unilateral symptoms. Of those, 85.3% experienced their initial symptom in an upper extremity.

Age at symptom onset, age at diagnosis, time to diagnosis, gender ratios, asymmetry of symptom onset and the pattern of initial symptoms did not vary as a function of handedness ($p>0.10$). However, of patients with asymmetrical onset (n=1015), there was a significant association between handedness and side of disease onset ($\chi^2(1)=6.82$, $p<0.001$). For right-handed patients with asymmetrical onset, 56.5% experienced their first symptom on the right side and 43.5% on their left side (proportional difference; $z=5.62$, $p<0.001$). For left-handed patients with asymmetrical onset, 58% experienced their first symptom on the left side and 42.0% on the right side (proportional difference; $z=-2.11$, $p<0.05$). Of the 1015 patients who experienced asymmetrical onset of PD motor symptoms, 575 (56.7%) had initial symptoms on their dominant side, and 440 (43.3%) experienced initial symptoms on their non-dominant side (proportional difference; $z=5.99$, $p<0.001$).

To determine the potential impact of this association, we created two subgroups, patients with initial PD symptoms on their dominant side and patients with initial PD symptoms on their non-dominant side. These groups were indistinguishable in their age at disease onset, sex distribution, and mean disease duration ($p>0.10$). However, these subgroups showed different patterns in reported initial symptom (table 1, $\chi^2(4)=25.51$, $p<0.0001$).

Contrary to our predictions, patients with initial symptoms on their dominant side tended to be diagnosed after a longer duration of symptoms than patients with initial symptoms on their non-dominant side (table 1). In a subset of 752 patients, 56.8% presenting with dominant-side symptoms and 43.2% presenting with non-dominant-side symptoms, the average time to dopaminergic medication initiation was 33.5 months for patients with symptom onset in their dominant side compared with 27.3 months for patients with symptom onset in their non-dominant side ($t(750)=2.59$, $p=0.01$).

A subset of PD patients with asymmetrical onset (n=909), 56.6% presenting with dominant-side symptoms and 44.1% presenting with non-dominant-side symptoms, completed UPDRS Parts I–III. This subset of patients displayed a similar gender ratio, age at onset and disease duration compared with the larger sample. For this group, we verified that the reported side of symptom onset was consistent with the right-minus-left difference score. Patients who reported right-side symptom onset exhibited a greater right side motor impairment (difference score=4.12 (±SD=4.36)), while patients reporting left-side symptom onset exhibited a greater left-side motor impairment (difference score=−5.54 (±SD=4.88)) ($t(907)=31.52$, $p<0.001$). Subgroups based on dominant versus non-dominant side of PD onset did not differ in mean UPDRS scores after adjusting for disease duration on an individual basis (table 1). We examined a combined score of select UPDRS Part III items generally performed with the dominant hand (eg, handwriting, cutting food/utensils, dressing and hygiene), and as expected, patients whose first symptom appeared on their dominant side reported a greater disability on activities that typically require engagement of the dominant hand ($t(907)=2.86$, $p=0.004$).

DISCUSSION

Consistent with previous studies,[2, 5] we found an association between handedness and the side of symptom onset in PD. For the vast majority of patients, the reported side of symptom onset corresponded with the more affected side as measured by the UPDRS Part III. Why unilateral onset of PD symptoms is more likely to occur in the dominant hand currently

lacks an explanation. One hypothesis is that the motor symptom asymmetry of PD may be an epiphenomenon of underlying anatomical asymmetry. This idea is supported by evidence from pathological studies [9, 10] and the asymmetry of drug-induced parkinsonism.[11, 12]

Importantly, the UPDRS scores (Parts I–III) of patients with dominant versus non-dominant-side onset were indistinguishable after adjusting for disease duration. However, when we analysed a subscore of Part II items primarily involving use of the dominant hand, we found a significant difference between the dominant-side onset and non-dominant-side onset groups. Contrary to our prediction, patients with dominant-side onset were diagnosed and prescribed dopaminergic therapy later than patients with non-dominant-side onset. This counterintuitive pattern might occur because patients with dominant-side onset identify symptoms at an earlier, milder stage, before they are significant enough to prompt an evaluation, allow definitive diagnosis and require pharmacological treatment. Comparison of the two subgroups also revealed different patterns of initial symptoms. Specifically, patients with dominant-side onset more often reported initial symptoms consistent with bradykinesia. Conversely, patients with non-dominant-side onset more often reported gait difficulty. The difference in initial symptom frequencies may reflect how symptoms are experienced in the two groups. Patients with dominant-side onset may be more likely to report functional impairment in an activity (eg, micrographia), whereas patients with non-dominant-side onset may be relatively less sensitive to upper-extremity disability and first notice gait dysfunction (eg, dragging leg). Since the majority of our patients were right-handed, mirroring the population frequency, our findings for the dominant and non-dominant-side onset groups may apply more to right-handed patients.

As in all studies that rely on patient report, this study was subject to recall bias, especially for patients evaluated years after symptom onset. We also recognise that patients, in reporting their first symptoms, may have overlooked earlier, milder motor symptoms in favour of more apparent symptoms, such as rest tremor. Another limitation relates to the method of obtaining handedness. We relied on self-report and did not assess degree of handedness or mixed handedness. There were also limitations in our method of obtaining certain disease features. In assessing the site of symptom onset, available choices did not include bilateral limbs. This may in part explain the higher number of patients with asymmetrical onset in our sample. Lastly, our classification of the initial motor symptom differentiated bradykinesia or rigidity in a lower extremity from gait difficulty, arguably overlapping categories. Notably, only a small number of patients (n=14) were categorised as having bradykinesia/rigidity in a lower extremity.

In conclusion, the association between handedness and the side of PD symptom onset does not appear to influence the severity or functional effect of the disease apart from obvious effects on tasks associated with dominant-hand use. Unexpectedly, patients with non-dominant-side onset were diagnosed and prescribed dopaminergic medication after a shorter symptom duration than patients with dominant-side onset. To determine if the presentation of PD is truly different depending on the side of onset will require future research in a group of patients followed longitudinally shortly after symptom onset.

Acknowledgments

Funding This study was funded by Morris K Udall Center at the University of Virginia, Grant Number: NIH-NINDS-P50-NS39788; American Parkinson Disease Association Advanced Center; and Parkinson Disease Research at UVA.

References

1. Djaldetti R, Ziv I, Melamed E. The mystery of motor asymmetry in Parkinson's disease. Lancet Neurol. 2006; 5:796–802. [PubMed: 16914408]
2. Uitti RJ, Baba Y, Whaley NR, et al. Parkinson's disease: handedness predicts asymmetry. Neurology. 2005; 64:1925–30. [PubMed: 15955945]
3. Reynolds LM, Locke S. Relation between handedness and side of onset of Parkinsonism. Lancet. 1971; 2:714. [PubMed: 4105754]
4. Van Rooden SM, Visser M, Verbaan D, et al. Letter to the editor. handedness associated to side of onset of Parkinson's disease? Parkinsonism Relat Disord. 2009; 15:546–7. [PubMed: 19073372]
5. Yust-Katz S, Tesler D, Treves TA, et al. Handedness as a predictor of side of onset of Parkinson's disease. Parkinsonism Relat Disord. 2008; 14:633–5. [PubMed: 18346926]
6. Pillon B, Dubois B, Cusimano G, et al. Does cognitive impairment in Parkinson's disease result from non-dopaminergic lesions? J Neurol Neurosurg Psychiatry. 1989; 52:201–6. [PubMed: 2703838]
7. Green J, McDonald WM, Vitek JL, et al. Cognitive impairments in advanced PD without dementia. Neurology. 2002; 59:1320–4. [PubMed: 12427877]
8. Linazasoro G. Rate of progression determines the clinical outcome after neural transplantation in Parkinson's disease. Brain. 2006; 129:E48. [PubMed: 16803834]
9. Glick SD, Ross DA, Hough LB. Lateral asymmetry of neurotransmitters in human brain. Brain Res. 1982; 234:53–63. [PubMed: 6120746]
10. McRitchie DA, Halliday GM, Cartwright H. Quantitative analysis of the variability of substantia nigra pigmented cell clusters in the human. Neuroscience. 1995; 68:539–51. [PubMed: 7477964]
11. Arblaster LA, Lakie M, Mutch WJ, et al. A study of the early signs of drug induced parkinsonism. J Neurol Neurosurg Psychiatry. 1993; 56:301–3. [PubMed: 8096240]
12. Sethi KD, Zamrini EY. Asymmetry in clinical features of drug-induced parkinsonism. J Neuropsychiatry Clin Neurosci. 1990; 2:64–6. [PubMed: 1983774]

Table 1

Characteristics of dominant and non-dominant-side onset groups

Patients with asymmetrical onset (n=1015)	Side of onset		p Values
	Dominant (n=575)	Non-dominant (n=440)	
Age (years) at symptom onset, mean (SD)	57.3 (11.1)	57.1 (11.2)	0.86
Disease duration (mo), mean (SD)	87.2(68.2)	82.5 (66.8)	0.27
Time (mo) to diagnosis, mean (SD)	21.5 (25.4)	18.4 (21.4)	0.038
Initial motor symptom, n (%)			
Tremor	380 (66.1)	292 (66.4)	0.0001
Bradykinesia	101 (17.6)	40 (9.1) *	
Rigidity	53 (9.2)	54 (12.3)	
Gait difficulty	23 (4.0)	40 (9.1) *	
Other	18 (3.1)	14 (3.2)	

Patients with asymmetrical onset and complete UPDRS (Part I–III) scores (n=909)	Side of onset		p Values
	Dominant (n=508)	Non-dominant (n=401)	
Corrected UPDRS Part I, mean	0.035	0.037	0.68
Corrected UPDRS Part II, mean	0.223	0.209	0.39
Dominant hand subscore, mean	0.095	0.075	0.004
Corrected UPDRS Part III, mean	0.591	0.664	0.21

* In individual comparisons, the percentages of patients initially presenting with bradykinesia and gait difficulty were significantly different in the dominant and non-dominant-side onset groups ($p<0.001$).

Mo, months; UPDRS, Unified Parkinson Disease Rating Scale.