Young-Onset Versus Late-Onset Parkinson's Disease: Clinical Features and Disease Progression

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Abstract

Objective: To determine whether age at onset is a predictor of the future disease progression and response to levodopa.

Background: Several studies have suggested that patients with young-onset Parkinson's disease (YPD) have a more favorable course but are at higher risk for levodopa-induced motor complications than those with late-onset Parkinson's disease (LPD), but no consensus has been reached.

Methods: We studied 100 patients with YPD (onset between 20 and 40 years) and compared them to 110 patients with LPD (onset at 60 years or older). The Unified Parkinson's Disease Rating Scale (UPDRS) was used to determine disease severity, and medical records were reviewed to determine the initial symptoms and levodopa complications.

Results: Patients with LPD reported more postural instability ($p < 0.006$) and gait difficulty ($p < 0.04$) at onset, while YPD presented more often with rigidity ($p < 0.002$). Final UPDRS scores on measures of tremor, bradykinesia, and postural-instability-gait-difficulty (PIGD) scores were higher in the LPD group. Regression analysis showed that LPD patients had worse tremor and PIGD score irrespective of disease duration. Patients with YPD experienced significantly more levodopa-induced dyskinesias ($p < 0.0006$), wearing off dystonia ($p < 0.0007$), and wearing off complications ($p < 0.00001$).

Conclusions: While YPD and LPD have overlapping clinical features, YPD patients are more likely to have rigidity as an initial symptom and worse levodopa related motor complications, whereas LPD patients have more severe PIGD scores and more severe disease progression.

Introduction

The clinical heterogeneity of Parkinson's disease (PD) is well recognized and various subtypes, including young-onset PD (YPD) and late-onset PD (LPD) have been identified [Jankovic and Kapadia, 2001]. Although the preponderance of evidence favors the view that YPD patients have a better response to levodopa, but are more likely to develop dyskinesias and motor fluctuations earlier than LPD patients [Kostic et al, 1991], this has not yet been universally accepted [Blanchet et al, 1996]. In an attempt to resolve some of these controversies we compared YPD and LPD patients with respect to clinical characteristics and response to treatment to better define which features differentiate the two groups and to address the question whether age at onset is a predictor of the future disease course.

Methods

Patients evaluated in the Parkinson's Disease Center and Movement Disorders Clinic at Baylor College of Medicine, Houston, Texas who met the diagnostic criteria for PD [19] were included in this study. The two study groups were defined as: 1) patients whose age at onset of PD symptoms ranged between 20 and 40 years (YPD) and 2) patients whose age at onset of PD symptoms was at 60 years or later (LPD). In order to study two distinct populations, YPD and LPD, and to minimize a distribution overlap we excluded patients with onset of symptoms between 41 and 59 years.

Results

Data was initially collected from 225 patients, but 15 were subsequently eliminated because they did not meet the inclusion-exclusion criteria. Demographic information on the remaining 210 patients, 100 YPD (49 males) and 110 LPD (67 males), is presented in Table 1 with statistical group differences within duration of symptoms, and ages at initial visit, tremor onset, and onset of PD symptoms ($p < 0.0001$). Initial presentation was different among the groups as patients with LPD reported more postural instability ($p < 0.006$) and gait difficulty ($p < 0.04$), while YPD presented initially more often with rigidity ($p < 0.002$). No difference was seen in the proportion of patients reporting initial symptoms of tremor and bradykinesia. UPDRS scores from the last office visit showed group differences in tremor, bradykinesia, and PIGD scores (UPDRS -part III) with significantly higher scores in patients with LPD [Table 2]. Patients with YPD experienced significantly more levodopa-induced dyskinesias ($p < 0.0006$), wearing off dystonia ($p < 0.0007$) and wearing off complications ($p < 0.00001$).

*Table 1. Demographic Information Among Late-Onset vs Young-Onset PD **

	Young onset (N = 100)			Late onset (N = 110)		
Demographics	Mean	SD	Range	Mean	SD	Range
Age at initial visit	41.8	± 8.0	29 – 77	72.9	± 6.3	61 – 87
Age at onset of PD Sx	34.9	± 6.1	22 – 68	67.4	± 5.5	60 – 85
Duration of Sx, yrs	8.0	± 8.9	0.5 – 55	4.9	± 4.0	0.5 – 18

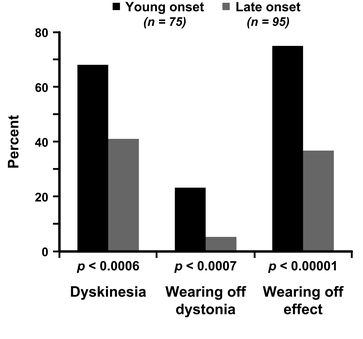
* All comparisons except sex, $p < 0.0001$; Sx = Symptoms

Table 2. Clinical Assessment in Late-Onset vs Young-Onset PD

	Young onset (N = 93)			Late onset (N = 110)		
Clinical Assessment	Mean	SD	Range	Mean	SD	Range
UPDRS						
Part I	2.2	± 2.0	0 – 8	2.4	± 2.1	0 – 11
Part II	13.7	± 9.3	0 – 47	12.8	± 7.6	0 – 34
Tremor score ^	2.2	± 3.3	0 – 16	3.7	± 3.6	0 – 15
Bradykinesia score #	1.3	± 0.9	0 – 4	1.6	± 0.8	0 – 4
PIGD score ^	2.0	± 1.6	0 – 8	2.7	± 1.7	0 – 8
H/Y Stage	2.0	± 0.8	1 – 4	2.1	± 0.8	1 – 5
S/E ADL	83.1	±13.1	40 – 100	83.9	±13.1	30 – 100

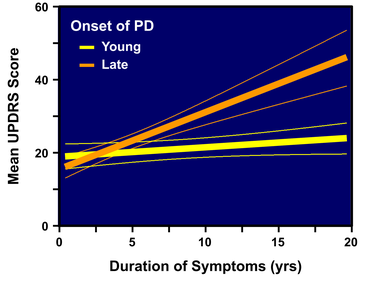
# $p < 0.05$, ^ $p < 0.0001$

Figure 1. Levodopa Complications in Late-Onset vs Young-Onset PD



Patients with young-onset PD have significantly more frequent levodopa-related dyskinesia, wearing off effect, and wearing off dystonia.

Figure 2. Severity in Late-Onset vs Young-Onset PD as a Function of Disease Duration



For each group, the linear regression line is represented as the middle line with the 95% confidence lines depicted above and below the regression line. Based on disease progression after Year 5, the rate of disease severity as assessed by the UPDRS for the late-onset PD group (1.55) increases faster than that of the young-onset PD group (0.25), $p < 0.05$.

Discussion

Our finding of significantly more frequent occurrence of rigidity in the YPD, relatively slow progression in young patients and with tremor-dominant presentation, and more rapid progression in patients, particularly if they have co-existent dementia, is consistent with findings from other studies [Jankovic et al, 2000, Jellinger et al, 2002]. The most robust difference between YPD and LPD is the response to levodopa and the frequency of motor fluctuations [Table 2]. Our study, involving larger population of patients confirmed the results from the smaller studies in that dyskinesia (68% vs. 41%, $p < 0.001$), "wearing off" effect (75% vs 37%, $p < 0.001$), and wearing off dystonia (23% vs. 5%, $p < 0.001$) were significantly more frequent in our patients with YPD as compared to LPD. Although it is not clear what mechanisms are responsible for the differences between YPD and LPD in the clinical features and the rate of progression, it is possible that neuronal plasticity in YPD patients plays a role in their response to the neurodegenerative process.

Selected References

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