# The Accuracy of Diagnosis of Parkinson's Disease

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Parkinson's disease is the most common movement disorder among adults, with onset in middle life. However, *parkinsonian* – or the popular designation "extrapyramidal" – features are much more frequent than classical or idiopathic PD. Indeed, about 50% of people older than 85 years will show such features. Given that elderly patients with "parkinsonism" are usually first seen by general practitioners, family physicians and internists, it is imperative that the diagnosis of PD be accurate since the beneficial effect of levodopa and other dopa-mimetic medications is dramatic in PD only. Unfortunately, the accurate diagnosis is at present based on clinical judgment only. In the present report, the currently known data on the accuracy of diagnosis of PD using the different "classical" clinical signs of PD are reviewed.

In a large-scale epidemiologic study conducted among the residents of Olmsted county, Minnesota in the USA, it was found that for the period 1976–1990, the incidence of parkinsonism was estimated as 114.7/100,000 in the age group 50–99 years. The incidence was significantly highest in the age group 80–99 (304.8/100,000). Of the 364 patients with parkinsonism, 42% had PD, 20% suffered from drug-induced parkinsonism, 14% had parkinsonism with dementia, 7% had other movement disorders, and 17% were unspecified [1]. The known and remarkable increase in the occurrence of parkinsonism with age is reflected in the fact that 52% of people over the age of 85 years show parkinsonian features [2].

Being a progressive disorder of middle-age onset with an impressive temporary amelioration of signs and symptoms following levodopa replacement, its treatment is frequently in the hands of the general practitioner or the family physician. Neurologists and non-neurologists alike have no laboratory test to confirm the diagnosis, which is absolutely based on clinical grounds. This results in over-diagnosis and subsequently over-treatment.

Despite the notable progress in the understanding of this common movement disorder, there is still a need for a single laboratory test to confirm the diagnosis. Furthermore, even the criteria for justifying the diagnosis of "typical" or "classical" PD are not agreed upon. Like our colleagues around the world, we teach our students and residents that the clinical diagnosis of PD requires the presence of two of the four primary motor signs, namely tremor, bradykinesia, rigidity, and postural instability [3]. However, if we use those criteria are we correctly diagnosing *all* patients?

Parkinson's disease may have an insidious onset and thus can be easily missed during the early stages. In a recently published paper, Jankovic et al. [4] followed 800 patients who originally received a diagnosis of PD 0.9–3.5 years (mean 2.2) prior to their enrollment in the DATATOP study (**D**eprenyl **A**nd **T**ocopherol **A**ntioxidative **T**herapy **O**f **P**arkinsonism). All patients were mildly affected at the onset of the study (Hoehn & Yahr stage 1-2). After a mean 6 years of follow-up (0.2–7.6), only 8.1% did not have PD according to "multifactorial clinical diagnostic criteria," but without neuropathologic confirmation. Indeed, the investigators had available data on 13 of only 18 autopsied cases. Even without autopsy-proven cases, one might be impressed by the high accuracy of diagnosis of PD in this study. This accuracy could be attributed to the fact that those patients were diagnosed by physicians who had a major interest in movement disorders, which qualified them to participate in the DATATOP study. Even if autopsies were performed only in atypical cases, it is important to note that only 4 of the 13 patients (31%) were found to have uncomplicated PD [5].

Can we rely on clinical motor signs only? Resting tremor is undoubtedly a cardinal sign for idiopathic PD. However, patients may also demonstrate action tremor, positional tremor or both. Even the characteristic 3–6 Hz distal resting tremor may change during the course of the disease. Not all patients with PD have tremor and not every patient with parkinsonian features and tremor has PD. In three different studies where the diagnosis of PD was made on clinical grounds only, 79–90% of the patients had tremor [6–8]. However, resting tremor is present in a significant number of patients with other "extrapyramidal disorders." In pathologically confirmed studies, resting tremor was present in 13–34% of patients with multiple system atrophy, in 17% with progressive supranuclear palsy, in 29% with cortico-basal ganglionic degeneration, and in 27% with dementia with Lewy bodies [9–11]. Rigidity was reported in 89–99% of patients with PD and bradykinesia in 77–98%. Postural instability was present in only 37% of patients with disease duration of less than 5 years. Evidently, using rigidity, postural

PD = Parkinson's disease

instability or bradykinesia as the only clinical sign for the diagnosis of PD is incorrect since these signs are non-specific and might be seen also in normal aging [12].

Can we count absolutely on a neuropathologically confirmed diagnosis? The classical neuropathologic features of idiopathic PD seem to be straightforward. There is neuronal loss in the substantia nigra together with the presence of Lewy bodies, which are usually also present in the locus ceruleus, nucleus basalis of Meynert, dorsal motor nucleus of the vagus, and hypothalamus. Curiously, there are no data on the specificity and sensitivity of those individual neuropathologic findings. Some patients exhibit typical clinical features and neuronal loss in the substantia nigra *without* Lewy bodies. Others have Lewy bodies without neuronal loss and even without clinical abnormalities [12]. The presence of Lewy bodies in the aging brain raises the question of whether their presence implicates presymptomatic PD or normal aging [13,14]. Furthermore, it was shown that about 10–40% of brains from patients with Alzheimer's disease, motor neuron disease, sub-acute sclerosing panencephalitis, ataxia telangiectasia, cortico-basal ganglionic degeneration and Hallervorden-Spatz syndrome contain Lewy bodies [14,15]. This suggests that their presence is rather non-specific for PD. To complicate the issue, it is not unusual to find neuritic plaques and neurofibrillary tangles similar to Alzheimer's disease.

It has frequently been emphasized that the distribution of Lewy bodies has important diagnostic implications. However, the data available are unclear. Several reports have described Lewy bodies in the neocortex of nearly all patients with PD [16,17]. This may suggest that the formation of Lewy bodies may not be disease-specific, but a continuum from pure brain stem presence as in PD, to neocortical distribution as in diffuse Lewy body disease. Although a number of investigators claim that there is a correlation between the number of neocortical Lewy bodies and the severity of dementia in PD [18], others have described similar patients with only a few cortical Lewy body plaques and tangles [19,20].

Considering the above mentioned pitfalls in the diagnosis of PD, we should adopt the approach of utilizing the terms "probable" and "possible" PD, and the designation "definite" PD for cases with characteristic clinical features and neuropathologic confirmation. Indeed, a proposed diagnostic approach according to these guidelines was proposed by Gelb and coworkers [12].

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*The most expensive habit in the world is celluloid, not heroin, and I need a fix every few years*

*Steven Spielberg (1947– ), American film-maker*