The Progression Towards Motor Symmetry in Parkinson's Disease

Richard Buesa1, Nicole McLaughlin PhD 1,2, Richard Jones ScD2, Joseph Friedman MD3

1 Warren Alpert Medical School of Brown University, 2Department of Psychiatry and Human Behavior, Alpert Medical School, 3Butler Hospital Movement Disorders Program

Introduction

Parkinson's Disease is a complex neurodegenerative disorder, the classical motor symptoms of which most often present asymmetrically. It was long thought (1) that even as the disease progresses to bilateral involvement, the initially affected side remains more affected: a retained asymmetry (2). However, recent publications have called this into dispute, suggesting instead that there is a tendency toward symmetry.

Background

One study (3) found that 61% of patients who were asymmetric at baseline became symmetric within a 5-year follow up while 79% of the patients symmetric at baseline remained symmetric. Asymmetric disease is regularly associated with younger age, younger age of onset, and shorter disease duration, while symmetric disease is associated with worse functional ability (4) (ADLs, cognitive function, dementia) and physical symptoms. The notion of symmetric disease may represent a more advanced stage of disease seem to be corroborated by neuropathological findings. A recent 8-year longitudinal cohort study (5) following three different PET tracers (DAT, DTBZ, Fluoro-L-Dopa) found that there was a clear exponential decline in dopamine function, and then a progressive symmetry between the initially asymmetric—though bilaterally affected (6)—right and left putamen. However, it still remains to be seen whether or not most patients symptomatically tend towards symmetry.

Purpose

The aim of this study is to expand our understanding of the evolution of (as)ymmetry of the motor symptoms across the course of Parkinson's disease, by examining whether or not a trend towards symmetry exists in our patient cohort and , the nature of the progression in the initially more and less affected side, and if either of these is associated with age, disease duration, or medication.

Methods

We performed a retrospective chart review of 108 patients seen during the period 5/2015 to 6/2015 with diagnosed idiopathic Parkinson's disease based on the U.K. Brain Bank criteria, seen by one movement disorders specialist (JF) as outpatients. We tracked the seventy of patient's motor symptoms from up to five years prior. Symptoms had been measured using the standardized UPDRS scoring system, and were combined into three master categories: Bradykinesia, Tremor, and Rigidity. For each of the 5 annual time points, the absolute value of the difference between summed scores of the right and left side symptoms scores were calculated. Age, disease duration, and usage of dopaminergic agonists were also noted since other papers have reported a link between age, disease duration, and an increased likelihood of having a symmetric form of the disease, and since some have claimed that dopamine-agonist class drugs may slow the progression.

Upon analysis, a standardized effect was estimated from an ordinal logistic regression of the absolute deviation in symptom ratings on age, the use of dopamine agonist, the duration of disease, and dummy variables indicating the sequential observation number (1-5 years of follow up). Standardized effects indicate the difference in the underlying propensity to have a higher or lower absolute difference in R and L sided symptoms. The standardized effect is the difference in log odds of being in a higher or lower category per standard deviation difference in the predictor variable for continuous predictors (age, duration of disease) and the differences between factor present versus absent for binary predictors (dopa agonist and observation dummies). Estimates that are significantly different (p=.05) are emboldened. Values greater than 0 suggest a tendency toward asymmetry, while negative values reflect more symmetry, with increasing strength of effect as the value is further away from 0.

Conclusions

The negative standardized effect supports a progression toward motor symmetry, but a significant change appears to only occur after 3 years for bradykinesia and 4 years for tremor and rigidity. Since progression was not associated with age, disease progression, or use of dopaminergic agonists, it can be said that most patients with asymmetric Parkinson's disease should expect their bradykinesia, tremor, and rigidity to become more symmetric over the next four years. As a progressive neurologic disease, it is likely that this symmetry represents a worsening of the initially less effected side, rather than amelioration of the effected side.

Due to the substantial variability between patients, it remains to be investigated how much change, in absolute terms, should be expected, and whether statistically significant change is clinically significant change for an individual patient.

This observation may be of use in evaluating purported mechanisms of disease progression. Since the pathological process of PD is thought to be present in the brain many years before clinical manifestations are present the tendency for motor asymmetry at presentation followed by progression toward motor symmetry, but a significant change appears to only occur after 3 years for bradykinesia and 4 years for tremor and rigidity. Since progression was not associated with age, disease duration, or use of dopamine agonists, it can be said that most patients with asymmetric Parkinson's disease should expect their bradykinesia, tremor, and rigidity to become more symmetric over the next four years. As a progressive neurologic disease, it is likely that this symmetry represents a worsening of the initially less effected side, rather than amelioration of the effected side.

References