IS MOLECULAR IMAGING REALLY HELPFUL IN DIAGNOSING PD? YES

Angelo Antonini
IRCCS San Camillo Venice Via Alberoni 70 Venice Italy

The clinical diagnosis of Parkinson's disease (PD) is based on the presence of characteristic motor symptoms: bradykinesia, rigidity, postural instability and resting tremor but neuropathology is still considered the gold standard for definite diagnosis.
Differentiating PD from other movement disorders (e.g. essential tremor and atypical parkinsonism) can be challenging throughout the disease course, when signs and symptoms overlap. Indeed, neuropathology studies revealed that clinical diagnosis of PD can be confirmed with an accuracy of about 75%. Good response to levodopa is often used to support the diagnosis of PD. However, cases of pathologically proven PD with poor response to levodopa have also been reported.
Misdiagnosis of PD can occur for several reasons. In a community-based study of patients taking antiparkinsonian medication, the most common causes of misdiagnosis were essential tremor, Alzheimer's disease and vascular parkinsonism. In addition, some of the prominent features of PD (e.g. rigidity, gait disturbance, bradykinesia) may also occur as a result of normal aging or from comorbid and multifactorial medical conditions (e.g. diabetes, cancer).
In recent years SPECT imaging has shown to be helpful in supporting the clinical diagnosis in early PD and the differential diagnosis with essential tremor and atypical parkinsonism. Single Photon Emission Tomography (SPECT) with radioligands binding selectively to striatal dopamine nerve terminals provides an objective and reproducible measurement of the nigrostriatal dopaminergic system in early PD patients with additional high sensitivity to disease progression. Uncertainty about an interaction between therapeutical drugs and tracer binding have raised debate on whether imaging proves a valid biomarker for progression of nigrostriatal pathology in PD [25-30]. These issues need to be clarified in appropriate studies.
The effectiveness in evaluating changes in presynaptic DAT sites in vivo in PD patients has been demonstrated particularly using either [^{123}I]β-CIT or [^{123}I]FP-CIT.
When cardinal motor signs required for a clinical diagnosis of PD appear, as many as 58–64% of dopaminergic neurons in the substantia nigra (SN) have been lost and striatal dopamine content has been reduced by 60–80%. Imaging studies of the dopaminergic system and postmortem cell counts of pigmented neurons in the SN, suggest that the onset of dopaminergic neuronal loss seems to precede by approximately 4-6 years the clinical diagnosis of PD. Abnormalities have been shown in individuals at risk for the disease years before disease onset.
It is worth mentioning that in some large clinical drug trials of PD where patients were enrolled based on their clinical diagnosis of early "untreated" PD, a significant proportion of patients has normal scans. These individuals have been defined subjects with scans without evidence of dopaminergic deficit (SWEDD) and represented from 5.7 to 14.7% of cases clinically diagnosed as early PD. Uptake values measured by fluorodopa PET (REAL-PET study) and by [^{123}I]β-CIT (ELLEDOPA study) remained normal after 2- and 4-year follow up respectively, thus questioning the diagnosis of a progressive and neurodegenerative disorder as PD. Alternative explanations on false-negative PD at DAT SPECT are the theoretical possibility of scans in the normal range at a very early stages of the disease and greater specificity of quantitative vs. qualitative analysis of the SPECT scans.
Regarding the differential diagnosis between PD and ET both [^{123}I]β-CIT and [^{123}I]FP-CIT showed no evidence of PD-like dopaminergic disruption in ET and [^{123}I]FP-CIT/SPECT proved a specificity of 95% and sensitivity of 80% in discriminating ET from PD patients. Recent evidence suggests that DAT imaging with in the differential diagnosis between PD and ET is cost-efficient.