ABSTRACT

INTRODUCTION

PPMI is an observational multi-center study to assess progression of clinical features, imaging and biological biomarkers in Parkinson's patients and healthy controls. PPMI is a five-year natural history study of de novo idiopathic PD patients and healthy controls.

Subjects are assessed at baseline and every 3-6 months thereafter.

Clinical assessments: motor, non-motor and cognitive

Imaging assessment: dopamine transporter imaging, MRI

Biologic collection: blood, CSF, urine and tissue.

Clinical data: Biologic data and clinical data and samples collected under standard protocols and analyzed in laboratories.

Study synopsis

Study population: 400 de novo PD subjects (newly diagnosed and treated with PD treatment: can participate in clinical trials after 12 months). Subjects will be followed for a minimum of 3 years and a maximum of 8 years.

Study measures: each imaging center performs an uncalibrated 57Co Phantom acquired each day a subject is imaged, spatial normalization of image performed for consistent image acquisition, central SPECT core lab performed reconstruction from raw projection data for subsequent uniform analyses. The objective of this study is to confirm the presence or absence of a DAT deficit for enrolled PD and healthy volunteers, respectively, 2) rigorous standardization of the single center measurement process to allow for direct and meaningful comparison across the set of right and left caudate and putamen. Striatal binding ratios (SBR) were calculated using the occipital lobe reference region. Average SBRs, lowest 5th percentile and 95th percentile summary statistics were calculated and across the three centers. Linear regression of SBR as function of age in HV showed reduction of 0.4% per decade.

METHODS

123I-iodopropylamphetamine (123I-IAAP) SPECT Standardization and Quantitative Analysis

1. Each imaging center underwent a technical visit to establish a uniform imaging protocol.

2. Central SPECT Core lab performed reconstruction from raw projection data, including attenuation correction based on protocols acquired during the site visit.

3. Clinical SPECT Core lab performed randomization of order and assignment of information for consistent orientation.

4. Vanishingly small standard of interest template on caudate, putamen, occipital regions

RESULTS

Fig. 1a 57Co calibration phantom is acquired each day a subject is imaged

Fig. 1b DICOM format of the SPECT tomograph and portal images of 57Co data

DISCUSSION

Creating standardized, poolable, multicenter quantitative measures of dopamine transporter SPECT in PD subjects and healthy volunteers is feasible. SBR data are similar to single center reports. PD subjects demonstrate on average 50% SBR signal loss relative to controls.

SBRDx allows for easy implementation and is feasible.

SBRDx装 is similar to healthy volunteers, cross-sectional data across an age range show a similar age-related reduction as healthy volunteers.

Normal aging is associated with about 6% signal loss per decade (0.6%/y).

First longitudinal data suggests SBRDx reduction over one year is approximately 20% the rate of signal loss seen in normal aging.

There is significant subject variability in SBRDx reduction over one year, consistent with both PD and longitudinal imaging and clinical course.

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Baseline Neuroimaging Characteristics of the Parkinson’s Progression Marker Initiative (PPMI) Parkinsons and Healthy Cohorts

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