PPMI Imaging Core

3 May 2012
Working Group Discussions and Future Directions

- VMAT2 imaging
- Resting state MRI
- Refining DAT quantification
- New targets
D2/D3 (raclopride, others)

Vesicular transporter (VMAT2)

DOPA → dopamine

neuronal dopamine metabolism (fluorodopa)

dopamine transporter (β-CIT, others)

dopamine receptors

Adapted from Science 2000; 289: 409-411.
18F-AV-133: Targets VMAT2

Healthy Subject
Mean putamen binding ratio = 3.52

Parkinson’s Subject
Mean putamen binding ratio = 1.36
18F-AV133 PET: possible to image the substantia nigra directly

Healthy Subject

PD Subject

Substantia nigra
SN ratio = 1.59

Substantia nigra
SN ratio = 0.91
PPMI AV-133

PET Imaging sites

- IND
- UPENN
- Johns Hopkins
- Banner
- Baylor
- Sydney- used for enrollment eligibility
VMAT2 Questions

• Will AV-133 PET differ from DAT as an enrollment scan?

• What analyses should be done in subjects with both AV-133 and SPECT DAT, is higher VMAT2 binding associated with slower clinical progression?

• Analyses could also include locus coeruleus, s. nigra, raphe nuclei
PPMI
Resting State MRI Sub-Study

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Resting State Sub-Study

- **Aim:** To acquire resting state functional MRI (rsfMRI) data on a subset of patients with Parkinson’s disease and controls.

- **Background:** rsfMRI examines the brain's intrinsic functional connectivity by measuring the synchrony of low frequency fluctuations of BOLD (blood oxygen level dependent) MR signal.
  
  - Changes in rsfMRI activity has been seen in a number of neurodegenerative disorders including PD.
Methods

- **Sites:** 7 sites with fMRI licenses currently participating in the DTI acquisition.
- **Scanners:** Siemens 3T Trio
- **Subjects:** 30 PD subjects, 30 controls.
- **MR sequence:** TR = 2400 msec, 48 slices, 3 x 3 x 3 mm voxels
- **Quality control:** measures of movement, scan-to-scan and slice-to-slice variance, phantom measurements of noise and stability
Schedule

• **PD participants:** Scanned at entry, then yearly until the end of the study.

• **Controls:** Scanned at entry.
Analyses

• Data analysis is not formally part of this proposal, but potential analyses listed below.
  – Whole brain correlations
  – Seed-based correlations
  – Independent components analysis
  – Amplitude of low frequency fluctuations (ALFF)
  – ReHo (regional homogeneity)
  – Network measures (e.g., small world networks)
ICA of rsfMRI data in PD (n=11)
DATSCAN Analyses

• Normative database(s) for age correction and informing SBR cut-offs for premotor cohort inclusion.

• Biomarker associational analyses, e.g.
  • Does baseline DAT predict rate of change in clinical measures or other biomarkers?
  • Does change in DAT predict longitudinal changes in clinical or other imaging or non-imaging biomarkers?

• Use of 57 Cobalt correction phantoms to reduce variance in within-subject longitudinal SBRs.
Percent change over one year (n=47)

Mean reduction = 12.4 % (%COV= 131%)
57-Co Striatal Phantom
Other Imaging Biomarkers

- If funding were available, what other brain targets should PPMI focus on over the next years?
  - Neuroinflammation (e.g. TSPO on activated microglia)
  - Proteinopathy (e.g. alpha-synuclein, tau, amyloid-b)
  - Metabolism (FDG)
  - Other receptor targets (e.g. A2a, mGluR5, 5HT1a, CB1)
PBR111-01 First series only (0-90 min post injection) 2 tissue
PBR111-03 2T 1\textsuperscript{st} series