Case discussions in movement disorders

Dr. Piyush Chandra, MD., DNB
Dept. of Nuclear Medicine
MIOT Hospitals
Chennai

Society of Nuclear Medicine
India
(Southern Chapter)
AUGUST 12 & 13, 2017
‘Almost half of all Parkinson's cases misdiagnosed’

‘Thousands of Parkinson's disease sufferers wrongly diagnosed, report claims’

‘Calls to scrap diagnosis of 'Parkinson's disease', with one in four misdiagnosed’
Why
misdiagnosis?
Parkinson's disease mimics!

- Tremor
  - Dystonic tremor
  - Isolated rest tremor
  - Indeterminate tremor
  - Essential tremor
  - Fragile X tremor–ataxia syndrome

Primary gait disorders
- Progressive supranuclear palsy
- Vascular parkinsonism/frontal gait disorder
- Normal pressure hydrocephalus

Atypical parkinsonian disorders
- Multiple system atrophy
- Corticobasal degeneration
- Dementia with Lewy bodies

Drug-induced parkinsonism
- Neuroleptics
- Dopamine blocking antiemetics
- Sodium valproate

Depression

Early-onset and genetic parkinsonian disorders
- Wilson’s disease
- Juvenile Huntington’s disease
- Spinocerebellar ataxias
- Fronto-temporal dementia with parkinsonism
- Pallido-pyramidal syndromes/neurodegeneration with brain iron accumulation

I May Be Shakin’... But It Ain’t A Seizure!
Synuclein or Tau

- **Alpha-synucleinopathies**: PD, PD with dementia (PDD), Diffuse lewy body dementia, Multisymmetic atrophy (MSA)

- **Tauopathies**: Progressive supranuclear palsy (PSP), Coticobasilar degeneration/syndrome (CBD/CBS)
Why differentiate PD from APS??

- Levodopa or No levodopa
- Newer treatments: Deep brain stimulation for PD
- Prognostic: Survival in PD- Avg. 10 years from diagnosis, Survival in MSA, PSP and CBD 7-8 yrs from symptom onset and 3-4 years from clinical diagnosis.
- Reducing the overall treatment costs.
Nuclear Imaging of Parkinsonism

- **SPECT:** 123I-CIT, 99mTc-TRODAT-1, 123I-IBZM, 123I-MIBG

- **PET:** 18F-DOPA, 18F-FDG, 18F-B-CFT, 18F-DTBZ, 18F-AV-1451, 18F-FDDNP, 11C- PK11195
<table>
<thead>
<tr>
<th>PET Tracers</th>
<th>PSP</th>
<th>MSA</th>
<th>CBD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FDG</strong></td>
<td>Bilateral medial frontal cortex, premotor areas, prefrontal areas, striatum (caudate in particular), thalamus, and brainstem</td>
<td>bilateral putamen, cerebellum, and brainstem</td>
<td><strong>CONTRALATERAL</strong> to the most affected side involving parietal cortex, primary sensorimotor cortex, the medial and lateral premotor areas, striatum, and thalamus.</td>
</tr>
<tr>
<td><strong>DOPA</strong></td>
<td>caudate, putamen</td>
<td>caudate, putamen, ventral striatum, globus pallidus</td>
<td>caudate and the putamen <strong>CONTRALATERAL</strong> to the most affected side</td>
</tr>
<tr>
<td><strong>TAU (18F-FDDNP)</strong></td>
<td>Sub-thalamic area, midbrain region, and cerebellar white matter.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neocortical regions (frontal lobe, temporal lobe and posterior cingulate gyrus) with more severe disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MICROGLIAL ACTIVATION [11C]- PK11195</strong></td>
<td>Caudate, putamen, pallidum, substantia nigra, midbrain, thalamus, cerebellum, and frontal lobe</td>
<td>dorsolateral prefrontal cortex, caudate, putamen, pallidum, thalamus, substantia nigra, and pons</td>
<td>caudate, putamen, substantia nigra, and fronto-parietal cortex</td>
</tr>
</tbody>
</table>
TRODAT-1 brain SPECT + FDG brain PET for evaluation of parkinsonism???
72 patients with parkinsonism (age 34–80 years). FDG-PET diagnosis assigned at the time of imaging was compared with the final clinical diagnosis made by the movement disorder specialists after ≥2 years follow up.

Concordance between the FDG-PET and clinical diagnoses was 92% (IPD 93%, MSA 90%, PSP 91% and CBS 100%).

Evidence- FDG PET and Parkinsonism

136 patients with parkinsonism, gold standard 2 years follow up

Concordance of visual evaluation of fluorodeoxyglucose-PET with clinical diagnosis was achieved in 91.7% of patients scanned, 97.6% IPD, 80% MSA, 76.6% PSP, and 100% CBS.

Blinded computer assessment using SPM was concordant with the clinical diagnosis in 91% of cases evaluated (90.4% IPD, 80% MSA, 93.3% PSP, and 100% CBS).

18F-FDG PET Is an Early Predictor of Overall Survival in Suspected Atypical Parkinsonism

Sabine Hellwig1,2, Lars Frings2,3, Florian Amtage1, Ralph Buchert4, Timo S. Spehl3, Michel Rijntjes1, Oliver Tüscher1,5, Cornelius Weiller1, Wolfgang A. Weber6, Werner Vach7, and Philipp T. Meyer3

1Department of Neurology, University Hospital of Freiburg, Freiburg, Germany; 2Centre of Geriatrics and Gerontology, University Hospital of Freiburg, Freiburg, Germany; 3Department of Nuclear Medicine, University Hospital of Freiburg, Freiburg, Germany; 4Department of Nuclear Medicine, Charité, Universitätsmedizin Berlin, Berlin, Germany; 5Department of Psychiatry, University Hospital Mainz, Mainz, Germany; 6Molecular Imaging and Therapy Service, Memorial Sloan Kettering Cancer Center, New York, New York; and 7Clinical Epidemiology, Institute of Medical Biometry and Medical Informatics, University of Freiburg, Freiburg, Germany
FDG Brain - what's normal?
Improving the quality of TRODAT-1 scans

- Injected activity: 740-960MBq (20-25mCi)
- Uptake time: 260 minutes
- Acquisition time: 60s/projection
- Filters: Butterworth, critical frequency around 0.35-0.45/ Metz filter, with attenuation correction

Huang et al, PLoS ONE, 2015
Case 1

- 57 year old man, with rheumatoid arthritis, complaints of slowness of activities since 5 years

- O/E: hypomimia, decreased arm swing, postural instability, right hand tremors, no rigidity
Case 2

- 70 year old with history of psychiatric disturbances, on haloperidol and chlorpromazine.

- c/o Slurring of speech, drooling of saliva since 1 week.

- O/E: Bradykinesia +, Rest tremors+
Case 3

- 54 year female with history of AML in remission, now with complaints of weakness on left side, with gait disturbance and left upper limb tremors since 2 months.

- Treated with syndopa plus for 2 months, no improvement.
Case 4

- 67 year old male, unsteadiness of gate since 1 year with slurring of speech
- O/E: upgaze restriction++, postural instability ++,
- Follow up after 3 months: diminished gag reflex, dysphagia, nasal regurgitation to liquids and emotional incontinence.
Case 5

76 year old male, difficulty in walking since 3 years with emotional incontinence.

O/e: severe gait ataxia and absent vertical gaze, with dysarthria.

MRI- Mid brain atrophy
Pimple sign on PET correlates with mid-brain atrophy

Botha H et al. The pimple sign of progressive supranuclear palsy syndrome. Parkinsonism Relat Disord. 2014
Case 6

- 54 yrs female, on treatment for Parkinson's disease since 2012.

- Now with levo-induced dykinesia of tongue, tendency to repeated falls and lean toward left side, speech unclear by the day

- O/E: bilateral rigidity +++ and postural instability++++, cerebellar dysrthria++, reduced facial expression
Case 7

- 66 yr female with unsteadiness while walking and tendency to fall since 6 months with memory disturbance
- O/E: short shuffling gait, right upper limb rigidity, incoordination
- F/u after 3 months- bladder bowel incontinence.
Case 8

- 58 year old man, on syndopa for PD since 1 year
- Complaints of worsening postural instability and bladder incontinence, reduced speech volume, weakness in both lower limbs
- o/E: diminished facial expression, postural drop in BP, brisk bilateral lower limb reflex.
MRI- Multi-systemic atrophy

Hot cross bun sign of MSA

Case 9

73 year old female, slowness of activities since 2010, with gradual decline in speech and loss of bladder control

O/E: reduced blink rate, very slow saccades, speech apraxia, phonemic aphasia, postural instability++, more involvement of right side
Case 10

- 63 yrs female with gradual worsening of gait since past 4 years

- O/e: severe bradykinesia, dystonia and rigidity, significantly more on the right side

- No response to L-DOPA
Case 11

- 75 Year old lady- on treatment for parkinsonian tremors for 1 year

- C/o irrelevant talks, hallucinations and unconcerned micturition and defecations

- O/E: Hand dystonia, bradykinesia, right hand tremors++
<table>
<thead>
<tr>
<th>Brain region</th>
<th>PD without dementia</th>
<th>PDD/DLB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Striatum</td>
<td>Preserved to ↑</td>
<td>↓ (especially caudate nucleus)</td>
</tr>
<tr>
<td>Thalamus</td>
<td>Preserved</td>
<td>↓</td>
</tr>
<tr>
<td>Parietotemporal cortices</td>
<td>Preserved</td>
<td>↓</td>
</tr>
<tr>
<td>Posterior cingulate cortex</td>
<td>Preserved</td>
<td>↓↓</td>
</tr>
<tr>
<td>Frontal cortex</td>
<td>Preserved</td>
<td>Variable ↓</td>
</tr>
<tr>
<td>Occipital cortex</td>
<td>Brodmann area 17 ↓</td>
<td>Brodmann areas 17, 18 and 19 ↓↓</td>
</tr>
</tbody>
</table>
Towards a biomarker....

The Future

NEXT EXIT
Tau imaging- for PSP using 18F-FDDNP

Issue with TAU PET

- What is the best tracer?

- Different TAU isoform for different disease (4R isoforms for CBD/PSP)

- High off target binding in basal ganglia and mid-brain.

- Quantification of the uptake.
Take home message

- FDG PET has a very good concordance with clinical diagnosis for atypical parkinsonism.
- FDG PET in addition to TRODAT scans may probably improve the specificity of the clinical diagnosis and help to predict treatment outcomes.
- FDG PET with APS or PDD/DLB pattern have significantly reduced survival. Prediction is equal or better than using 1 year clinical follow up.
- Research with biomarkers such as Tau-imaging would give earlier and more specific diagnosis.
Thank you!

God gave me Parkinson's syndrome to show me I'm not 'The Greatest' - he is.

— Muhammad Ali