Overview and Objectives
1. Introduction to Parkinson's Disease
2. Understand how the DaTscan can aid in the diagnosis of Parkinson's Disease
3. The DaTscan
Parkinson’s Disease

• Chronic and progressive movement disorder
• Malfunction and death of neurons particularly dopaminergic neurons in the substantia nigra that project to the striatum (basal ganglion)
• Reduction in dopamine, a neurotransmitter used to control movement and coordination
• Clumps of a protein in the cytoplasm of neurons termed alpha synuclein (Lewy Bodies)

Parkinson’s Disease

• Second most common neurodegenerative disorder behind AD
• Estimated prevalence of 0.5-1% aged 65-69, 1-3% aged >80
• 500,000 people in the US, with 50,000/new cases per year
Parkinson’s Disease and the Neurologist

- Movement disorder characterized by hypokinetic movements
  - Tremor at rest (hands, arms, legs, jaw and face)
  - Bradykinesia/hypokinesia – slow movement
  - Rigidity or stiffness in the limbs and trunk
  - Flexed posture of the neck, trunk and limbs
  - Loss of postural reflexes
  - Freezing

Accuracy of Clinical Dx of PD

- 76% in the early 90’s (Hughes et al, 1992)
- 90% in the early 2000’s (Hughes et al, 2001)
  - High sensitivity by specialist ~99%, however, the specificity is only 91%.
  - Increased awareness/specialization by neurologist
  - Publication of consensus criteria for diagnosis of parkinsonian disorders
- 74% by nonexperts, 84% by movement disorder specialists (Rizzo 2016)

Importance of Early Diagnosis

- Correct prognostication and treatment
- Avoidance of unnecessary tests, examinations and therapies and their side effects, costs and safety risks.
- Critically important for recruitment into a clinical trial
- Early prevention of motor progression, psychotic symptoms, and dementia might be the most promising strategies to increase life expectancy in Parkinson’s disease.
The Neurologist’s Office

Hyperkinetic Movements Hypokinetid Movements

Tremors

- Neurologic DO – Neurodegenerative, MS, TBI, stroke
- Drug-induced
- Thyroid Disease
- Alcohol abuse/withdrawal
- Heavy metal poisoning (Hg)
- Liver failure
- Familial
- Idiopathic

Parkinson’s Disease Tremor

- Tremor at rest
- Often is the first symptom of Parkinson’s disease
- Pill-rolling hand action
- Can affect the chin, lips, legs and trunk
- Markedly increased by stress
- Onset typically after age 60
- Typically starts unilaterally, progresses to involve the contralateral side
Essential Tremor

• Benign Essential Tremor
• Typically an action tremor
• Most common
• Often mild and non-progressive, but can be progressive
• Hands most often affected
• Mild gait disturbance is not uncommon
• Exacerbated by stress
• Onset after age 40
• Familial predisposition

Types of Parkinsonism

• Clinical syndrome characterized by tremor, bradykinesia and postural rigidity
  — Idiopathic Parkinson's disease
  — Parkinsonism Plus Syndromes (atypical PD)
    • Multiple systems atrophy, progressive supranuclear palsy, corticobasilar degeneration and Dementia with Lewy Bodies
  — Secondary Parkinsonism
    • Drug-induced Parkinsonism
      — Neuroleptic antipsychotics
        » Tardive dyskinesia
Common Drugs Associated with Drug induced parkinsonism

<table>
<thead>
<tr>
<th>Drug categories</th>
<th>Drugs frequently causing parkinsonism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical antipsychotics</td>
<td>Promethazine, chlorpromazine, prochlorperazine, perphenazine, fluphenazine, thiothixene</td>
</tr>
<tr>
<td>Atypical antipsychotics</td>
<td>Clozapine, quetiapine</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>Imipramine, amitriptyline, doxepin</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>Propranolol, timolol</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>Nifedipine, verapamil</td>
</tr>
</tbody>
</table>

Diagram:
- Tyrosine
- Dopamine
- Monoamine oxidase B (MAO-B)
- Dopamine transporter
- Signal transduction
- Postsynaptic neuron
- Pre-synaptic neuronal axon
- Degeneration
Striatal Dopamine Transporter Imaging

- **I-123 ioflupane** (N-w-fluoropropyl-2B-carbomethoxy-3B-(4-123I-iodo-phenyl)nortropane)
  - US FDA approved in 1/2011 (Europe since 2000)
  - Available everywhere through GE (DaTscan)
  - Also abbreviated as ^123^FP-CIT
- **I-123 iometopane** – (123 I-B-CIT) – available largely for research
- **Tc-99m Trodat**
- **PET imaging agents** – C^11^  
- Correlates with loss of presynaptic dopamine

DaTscan SPECT with ^123^I-ioflupane

- **Indications**
  - Essential tremor versus Parkinson’s Disease
  - Early diagnosis of Parkinson’s disease
  - Parkinson’s disease versus parkinsonism
  - Dementia with Lewy bodies versus Alzheimer’s disease
- **Contraindications**
  - Pregnancy
  - Inability to cooperate
  - Known hypersensitivity (not iodine allergy)
  - Breastfeeding (relative)
Patient Preparation

• Off medications that interfere with dopamine
  – Cocaine, amphetamines, methylphenidate
  – Ephedrine and phentermine (CNS stimulants)
  – Bupropion, fentanyl and some anesthetics
• Medications that do not interfere with visual interpretation
  – SSRI’s, cholinesterase inhibitors and neuroleptics
  – Anti-parkinsonian drugs

Patient preparation

• One hour before radiotracer administration
  the patient should receive one of the following:
  – Single dose of 400mg potassium perchlorate
  – Single dose of SSKI (potassium iodide)
  – Lugol’s solution – 100mg
• Blocks the thyroid from receiving significant I-123

\(^{123}\text{I}-\text{ioflupane}\)

• Cocaine analog, no longer classified as a schedule II narcotic (2015)
• Delivered from GE ready to use
• 3-5 mCi IV, over 20 seconds, followed by a saline flush
• Renal excretion, primarily
• SE’s are uncommon (>1%), but include headache, nausea, vertigo, dry mouth and dizziness
• Advise pt’s to stay well hydrated for 2 days
• No significant radiation safety precautions
Protocol

- Brain SPECT imaging 3-6 hours post injection
- Supine, with head centered and secured
- Sedation is optional (benzodiazepines)
- Include entire brain in FOV
- Smallest rotational radius (11-15 cm)
- Photopeak set to 159 keV +/- 10%
- 128 x 128 matrix
- Step and shoot mode with 3 degree increments for 30-40 seconds
- 360 degree coverage
- Minimum of 1.5 million counts
- Takes 30-45 minutes typically

Image Processing

- Check cine mode and sinograms for scan quality
- Flash 3-D (iterative reconstruction)
- Low-pass filter (Butterworth or Gaussian)
- Attenuation correction recommended, but not required
- Reformatted in the 3 standard planes
- Reorientation often necessary for symmetry

Interpretation

- Semi-quantification using the striatal binding ratio
  - Manual region of interest
  - Manual volume of interest
  - Automated tools using VOI
  - Parametric mapping
- Image quality
- Visual interpretation – symmetric, crescent or comma shaped striata are typically normal
  - Abnormal show decreased striatal activity
Healthy Volunteer

Newly diagnosed Parkinson’s disease

7-yr history of Parkinson’s disease
12 year history of Parkinson’s disease

Radiation Safety

- Urinary bladder wall receives the largest radiation dose
- The effective dose from 5mCi I-123 is 3.89 – 4.44 mSv in adults (389-444 mrem).
- Stay well hydrated for 2 days
- Men can consider sitting to void for 1 day
- No other restrictions

Summary

- Parkinson’s disease is associated with decreased dopamine transporter in the basal ganglion and substantia nigra
- Many conditions may mimic Parkinson’s disease
- I-123 Ioflupane (DaTscan) targets the dopamine transporter density
- Brain SPECT imaging following SSKI
- Iterative reconstruction using Flash 3D
- Visual interpretation where a crescent shaped striatum is normal and a dot indicates disease
Questions?

Resources