Molecular Imaging in Movement Disorders

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Disclosures

None
Objectives

• To review anatomy & physiology of the brain
• To review the following Movement disorders, and various imaging techniques of such disorders:
  • Parkinson’s Disease/ Essential Tremors
  • Epilepsy
  • Primary Dystonia & Gilles de la Tourette Syndrome

• To review possible future applications of PET in:
  • Huntington’s Disease
  • Amyotrophic Lateral Sclerosis
Basal Ganglia

+ Glutamate
-GABA
Direct Motor Pathway

Motor Cortex → Striatum
- Glutamate

Striatum → Globus Pallidus Int.
- GABA

Globus Pallidus Int. → Movement

Excited Thalamus → Movement
What Are Movement Disorders

“Movement disorders are a collection of neurologic syndromes characterized by deficits in the execution of voluntary movement, but in the absence of significant muscle weakness or paralysis, loss of sensation or proprioception, or of spinal cord or peripheral nerve lesions.”
Why Use MI for Diagnosing Movement Disorders?

- Direct visualization of Brain Function
- Identifying disease in its earliest stages
- Treatments & Surgical Planning
Essential Tremor & Parkinson’s Disease
Essential Tremor & Parkinson’s Disease

Healthy patient

Transmitting neuron
Dopamine
Receptor cell

Parkinson’s patient

Transmitting neuron
Dopamine
Receptor cell
ET Vs PD Methods of Imaging

Presynaptic nerve terminal

Dopamine synthesis

Vesicle containing dopamine

Synaptic cleft

DaT

Dopamine

D_2 receptor

 Postsynaptic nerve terminal
DaT Scan Protocol

**Prep**
- Thyroid blocking agent 1 hr pre-injection
  - Equivalent to 100mg Iodine

**Injection**
- 5 mCi I-123 Ioflupane (DaT Scan) IV

**Imaging**
- 3-5 hour post injection
- 30-35 min SPECT using LEHR or Fan Beam

**I-123 Ioflupane (DaT Scan)**
- **Dose:** 5 mCi
- **Delay time:** 3-5 hrs
### Normal DaT Scan Values

<table>
<thead>
<tr>
<th>Structure</th>
<th>Z-Score</th>
<th>L-Sc</th>
<th>R-Sc</th>
<th>L-R % Diff</th>
<th>R-L % Diff</th>
<th>Z-Score</th>
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<tbody>
<tr>
<td>DaTscan Atlas</td>
<td></td>
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<tr>
<td>Caudate</td>
<td>1.05</td>
<td>1.27</td>
<td>0.77</td>
<td>6.54</td>
<td>0.9</td>
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<tr>
<td>Anterior Putamen</td>
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<td>1.12</td>
<td>1.02</td>
<td>1.5</td>
<td>0.34</td>
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<tr>
<td>Striatum</td>
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<td>1.13</td>
<td>3.75</td>
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<tr>
<td>Putamen</td>
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<td>1.34</td>
<td>1.3</td>
<td>0.52</td>
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<td></td>
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<tr>
<td>Posterior Putamen</td>
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<td>1.44</td>
<td>1.51</td>
<td>0.91</td>
<td>0.09</td>
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<tr>
<td>Occipital Lobe</td>
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<tr>
<td>Anterior Putamen/Posterior Putamen</td>
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<td>-0.64</td>
<td>-1.1</td>
<td>0.58</td>
<td>0.24</td>
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<tr>
<td>Caudate/Putamen</td>
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<td>-0.48</td>
<td>-1.08</td>
<td>6.02</td>
<td>0.44</td>
<td></td>
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</tbody>
</table>
DaT Scan for Dementia Vs PD

Normal DaT

+ for PD

Suggestive of DLB
Conclusion I-123 DaT Scan for ET vs PD

Diagnostic tool
- ET vs PD
- DLB vs AD

Treatment Planning
- Surgical Planning
- Optimal medication treatment
Epilepsy
Epilepsy

A neurological disorder marked by sudden recurrent episodes of sensory disturbance, loss of consciousness, or convulsions, associated with abnormal electrical activity in the brain.
Epilepsy with SPECT

| Ictal scan (blood flow during a seizure) | Interictal scan (blood flow between seizures) |

[Images of two brain scans side by side]
Epilepsy Imaging: SPECT Tc99m

**Tc99m HMPAO (Ceretec)**
* Dose: 15mCi-30mCi
* Delay time: 40-90 min

**Tc99m EDC (Neurolite)**
* Dose: 30 mCi
* Delay Time: 20-45 min

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**Prep**
* Monitor Seizure Activity

**Inj**
* Inj Rapid bolus at first onset

**Scan**
* Position comfortably
* SPECT w/ fan beam collimators
* 128x128 continuous scan
Epilepsy SPECT Images

Intractable epilepsy with normal MRI

Ictal

Interictal
Subtle asymmetric decreased metabolic activity in the right medial temporal lobe suggests mesial temporal lobe sclerosis, when correlated with recent MRI.
Epilepsy Imaging PET Protocol

F-18 fluorodeoxyglucose (FDG)
Dose: 5 mCi
Delay time 30-60 min

Prep
• NPO 4-6 hr
• Blood Glucose 150 mg/dL
• Rest ~ 30 min in dimly lit, quiet room

Injection
• 5 mCi (+/- 10%) F-18 FDG IV
• Uptake 30-60 min (dimly lit, quiet room)

Imaging
• Position comfortably to image entire brain
• Static Image with CT attenuation
Epilepsy Imaging: F-18 FDG PET
Epilepsy Imaging PET
Conclusion - Epilepsy

Localization

- Provide additional information of the epileptogenic zone

Surgery Planning

- Reduce need for invasive procedures
- Select surgical candidates
Primary Dystonia & Gilles de la Tourette Syndrome
Primary Dystonia (pD) & Gilles de la Tourette Syndrome (GTS)
Motor cortex  Somatosensory cortex

CEREBRAL CORTEX  the entire folded area covering the brain
pD & GTS with PET

**pD+ Uptake**

- *Hypermetabolism* of basal ganglia & sensorimotor pathways

**GTS+ Uptake**

- *Hypermetabolism* at sensorimotor cortex level & *hypometabolism* in the limbic cortex and striatum
Brain PET Imaging Protocol

**Prep**
- NPO 4-6 hr
- Blood Glucose 150 mg/dL
- Rest ~ 30 min in dimly lit, quiet room

**Injection**
- 5 mCi (+/- 10%) F-18 FDG IV
- Uptake 30-60 min (dimly lit, quiet room)

**Imaging**
- Position comfortably to image entire brain
- Static Image with CT attenuation
GTS PET Images

Tourette's Syndrome  Normal Volunteer
Conclusion pD & GTS

- Diagnosing
- Disease Monitoring

Diagnostic Tool

- Personalized treatment therapies
- Treatment monitoring

Treatment Planning
Future PET Applications
Huntington’s Disease
Huntington’s Disease

Repeat expansion mutation

Original DNA code for an amino acid sequence.

DNA bases

CATTCACACAGGTAATCATA

Amino acid

His Ser Gln Val Ile Met Leu

Repeated trinucleotide (CAG).

CATTCACACAGCA

Repeated trinucleotide adds a string of glutamines (Gln) to the protein.

U.S. National Library of Medicine
Huntington's Disease Imaging PET

Normal brain

Huntington's disease

Ventricle

Enlarged ventricles

Basal Ganglia

Atrophy of tissue and Basal ganglia
Huntington’s Disease Uptake

Pre-synaptic  Post-synaptic  F-18 FDG Uptake

Normal Striatum function  Decrease Striatum function  Decreased Striatum uptake & minor decrease in front-temporal cortex uptake
Brain PET Imaging Protocol

Prep
- NPO 4-6 hr
- Blood Glucose 150 mg/dL
- Rest ~ 30 min in dimly lit, quiet room

Injection
- 5 mCi (+/- 10%) F-18 FDG IV
- Uptake 30-60 min (dimly lit, quiet room)

Imaging
- Position comfortably to image entire brain
- Static Image with CT attenuation
Huntington’s Disease Images

Control

HD
Huntington’s Disease Images
Conclusion HD

Promising Outlook

- Diagnostic tool
- Disease Monitoring

Future Research

- Enzyme expression imaging
- Activated Macrophage role
Amyotrophic Lateral Sclerosis
Amyotrophic Lateral Sclerosis

Healthy motor neurons stimulate muscles

Nervous system

Nerve cell

Muscle

ALS kills motor neurons, disrupting the signal between brain and spinal cord and causing muscles to atrophy

Dead nerve cell
Bilateral Frontal Hypometabolism

Bilateral Hypermetabolism of Cerebellum

Heterogeneous frontal, parietal & temporal lobes

ALS with F-18 FDG Uptake Pattern
Brain PET Imaging Protocol

Prep
- NPO 4-6 hr
- Blood Glucose 150 mg/dL

Injection
- 5 mCi (+/- 10%) F-18 FDG IV
- Uptake 30 min (dimly –lit, quiet room, eyes closed)

Imaging
- Position comfortably to image entire brain
- Static Image with CT attenuation
- 15 min single bed, static image
ALS PET Images
ALS PET Images
Conclusion ALS

Promising Outlook

- Diagnostic tool
- Disease Monitoring
  - F18 Amyloid imaging

Research Pit-Falls

- Small number and poor clinical characterization of patients
- Absence of adequate controls
- Scarcity of longitudinal assessments
Conclusion

PD v ET

• I 123 DaT Imaging

Epilepsy

• Tc99m Ictal & Interictal SPECT
• F-18 FDG PET/CT

pD & GTS

• F18 FDG PET/CT
Conclusion

HD

• F-18 FDG PET/CT

ALS

• F-18 FDG PET/CT
• F-18 Amyloid PET/CT
Thank you!
References


References


- Moretti et al. (May 21, 2008). What every psychiatrist should know about PANDAS. Clinical Practice and Epidemiology in Mental Health, Volume 4, (Issue 13).
References


Special Images

- https://www.mayfieldclinic.com/PE-PD.htm
- http://www.alsa.org/about-als/what-is-als.html
- https://www.download.thelancet.com/journals/laneur/article/PIIS1474-4422(14)70167-X/fulltext