Molecular Imaging for Differential Dementia Diagnosis 10:07-10:30

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# Faculty Disclosure

<table>
<thead>
<tr>
<th>Company Name</th>
<th>Honoraria/Expenses</th>
<th>Consulting/Advisory Board</th>
<th>Funded Research</th>
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<tbody>
<tr>
<td>General Electric Health</td>
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<td>Eli Lilly</td>
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<td>Avanir</td>
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<td>Abbvie</td>
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<td>ALS Association</td>
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<td>NIH (NIA)</td>
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<td>Novartis</td>
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Learning Objectives

☐ List what imaging modalities are useful for the study of dementia

☐ Indicate why and how molecular imaging may help detect brain changes in neurodegenerative dementia before MRI does

☐ Describe the positron emission tomography patterns of the most common neurodegenerative dementias
Imaging Modalities for Neurodegenerative Dementias

- **MRI**
  - Volume (atrophy)
  - Anatomical (DTI) & functional connectivity (BOLD)
  - Blood flow (ASL)

- **PET** (Positron Emission Tomography)
  - Metabolism
  - β-amyloid load
  - pTau load
  - Inflammation

- **SPECT** (Perfusion)

**Metabolism (FDG) PET**
- Regional pattern (space)
  - Alzheimer Disease (AD)
  - Frontotemporal Dementia (FTD)

**Disease stage** (time)

Alzheimer Disease (2 years later)
# Neuroimaging in the Diagnosis of Degenerative Dementias

<table>
<thead>
<tr>
<th></th>
<th>Atrophy (MRI)</th>
<th>↓ metabolism, perfusion (PET, SPECT)</th>
<th>Amyloid</th>
<th>Tau</th>
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</thead>
<tbody>
<tr>
<td>Alzheimer’s</td>
<td>Medial temporal, other limbic</td>
<td>Parieto-temporal association cortex, retrosplenial</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Semantic dementia</td>
<td>Both temporal tips (L&gt;&gt;R)</td>
<td></td>
<td>Yes (20%)</td>
<td>20%</td>
</tr>
<tr>
<td>Behavioral type FTD</td>
<td>Frontotemporal poles</td>
<td></td>
<td>No</td>
<td>50%</td>
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<tr>
<td>Progressive non-fluent aphasia</td>
<td>Left perisylvian association cortex</td>
<td></td>
<td>No</td>
<td>80%</td>
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<tr>
<td>CBD</td>
<td>High fronto-parietal association cortex</td>
<td></td>
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<td>Yes</td>
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</table>

Why PET to Diagnose Neurodegenerative Dementias?

- Patients and families prefer PET to lumbar puncture ("spinal tap")
  - Orthostatic headache

While some dementias such as Creutzfeldt-Jakob disease have accurate CSF biomarkers, other disease types such as dementia with Lewy bodies, vascular dementia, and frontotemporal dementia lack reliable biomarkers for their specific clinical diagnosis.

**Amyloid-Positive Dementias**
(FDG-PET is enough!)

**Alzheimer’s disease**
Affected (in red or yellow above):
- Precuneus and posterior cingulate gyrus
- Parieto-temporal association cortex


**Diffuse Lewy body disease**
Similar pattern on the lateral aspect but the posterior cingulate not affected (“cingulate island sign”)

Masdeu JC et al. *Brain* 2012;135:2440
Frontotemporal Dementia Variants (Amyloid Negative)

Healthy Control

Behavioral Tau or TDP43
Frontotemporal Dementia Variants

Healthy Control

Semantic Dementia TDP43
Frontotemporal Dementia Variants

Healthy Control

Agrammatic PPA Tau
FDG Metabolism vs MRI in Fronto-temporal Dementia

One year after symptom onset

Three years after symptom onset
FDG PET: Is Abnormal Before Cortical Thickness Becomes Abnormal

Decade in life: 30 50 70 90

Why FDG PET to Diagnose Neurodegenerative Dementias?

- Patients and families prefer PET to lumbar puncture ("spinal tap")
  - Orthostatic headache

- More information than CSF for non-AD disorders
  - Fronttemporal lobar degeneration
  - Diffuse Lewy body disease
Clear-cut, quantifiable worsening in about 15 months
Misfolded tau: Linked to neurodegeneration
Brain Metabolism Versus Brain Tau: Yin-Yang Relationship

Where Tau is High, Metabolism is Depressed
Logopenic Aphasia (Alzheimer disease)

- Areas of normal metabolism
  - Have no tau

- But areas with high amyloid
  - May have normal metabolism

- Areas with high tau
  - Have reduced metabolism

Tau more closely linked to neurodegeneration than amyloid

Pascual et al. *Neurology* 2016;85:487
Tau Propagation Along Natural Brain Networks
Tau deposits in anterior and posterior neuronal nodes of the syntactic network

These neuronal nodes are connected by the arcuate fasciculus, abnormal near the anterior node, where the disease begins

\(^{18}\text{F-AV}1451\) Tau PET in Non-fluent Primary Progressive Aphasia (nfvPPA)

Arcuate Fasciculus Tractography

Fractional Anisotropy of Arcuate Fasciculus

\(P < 0.001 \quad ***\)
\(P < 0.05 \quad *\)

Pascual et al. *JNM.* 2019

Left hemisphere

Right hemisphere

\(P < 0.05\) FWE-corrected cluster-level
References


