PET and SPECT in Dementia

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Aetiology

- Vascular dementias
  - Multi-infarct dementia
  - Binswanger’s disease

- Vascular dementias and AD

- AD
  - 5%

- AD and dementia with Lewy bodies
  - 10%

- Dementia with Lewy bodies
  - Parkinson’s disease
  - Diffuse Lewy body disease
  - Lewy body variant of AD
  - 65%

- Other dementias
  - Frontal lobe dementia
  - Creutzfeldt-Jakob disease
  - Corticobasal degeneration
  - Progressive supranuclear palsy
  - Others

Epidemiology and Impact

- 8% of population older than 65 years and 20% older than 75 have Alzheimer's Disease (AD).
- 15% of population have Mild Cognitive Impairment (MCI) at age 65, 60% of them will have AD.
- AD is the 3rd most expensive disease in the US.
- There are 4 million people with AD in the US.
- Clinical diagnosis has sensitivity 80%, specificity 70%.
- Late diagnosis in most cases
Epidemiology and Impact

New cases of AD estimated per year in USA (millions)

NIA Alzheimer’s Disease: Unraveling the Mystery
SPECT Brain Imaging in Dementia
Meta Analysis

<table>
<thead>
<tr>
<th>Visual Interpretation</th>
<th>Bilateral Posterior</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sens</td>
<td>Spec</td>
</tr>
<tr>
<td>AD (n = 316) vs. normal (278)</td>
<td>89%</td>
</tr>
<tr>
<td>AD (236) vs. other dementias (235)</td>
<td>75%</td>
</tr>
</tbody>
</table>

Voxel based analysis can improve SPECT diagnostic accuracy

Imabayashi et al. J Nucl Med 2004
Progression of AD

Mild AD. Bilateral posterior parietal/ temporoparietal, precuneus and posterior cingulate hypoperfusion (white arrows).

Moderate-severe AD. Progression to bilateral prefrontal cortex (white). Red arrows indicate preservation of primary sensoriomotor cortex, occipital cortex, basal ganglia, thalami and cerebellum (not shown).
Okada et al. 3D-SSP FDG-PET and MRI. 31 AD vs. 551 normal controls
Evaluating early dementia with and without FDG PET: a comparison of predicted costs and benefits

<table>
<thead>
<tr>
<th>Sensibility</th>
<th>Specificity</th>
<th>Base of Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>66 ±17%</td>
<td>77 ±23%</td>
<td>Clinical evaluation, AD probable</td>
</tr>
<tr>
<td>90.5 ±5.5%</td>
<td>55.5 ±5.5%</td>
<td>Clinical evaluation, AD probable + possible</td>
</tr>
<tr>
<td>91.5 ±3.5%</td>
<td>70 ±3%</td>
<td>FDG-PET, AD pattern</td>
</tr>
</tbody>
</table>

Sensibility and specificity of PET and clinical evaluation compared to histo-pathological confirmation of AD.

Evaluating early dementia with and without FDG PET: a comparison of predicted costs and benefits

<table>
<thead>
<tr>
<th>ALGORITHM</th>
<th>Accuracy</th>
<th>Sensibility</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional</td>
<td>0.69</td>
<td>0.84</td>
<td>0.525</td>
</tr>
<tr>
<td>PET included</td>
<td>0.85</td>
<td>0.94</td>
<td>0.75</td>
</tr>
</tbody>
</table>

Impact of adding PET: 16% less false diagnostic results.

SPECT vs. PET

- 26 AD probable
- FDG vs. HMPAO
- Analysis: SPM
- r = 0.9 for posterior temporoparietal cortex and posterior cingulate
- FDG more intense defects (better contrast)

Correlation of abnormal voxels

SPECT perfusion imaging in the diagnosis of AD

FDG-PET Mild Cognitive Impairment

76 patients with MCI. 3 years follow up.
52 converted to AD, 24 non converters.

Differential diagnosis of Dementia
Differential diagnosis between AD & FTD by the posterior cingulate sign

<table>
<thead>
<tr>
<th>20 patients with AD</th>
<th>20 patients with FTD</th>
</tr>
</thead>
<tbody>
<tr>
<td>PC</td>
<td>No PC</td>
</tr>
<tr>
<td>16 (6 Aut)</td>
<td>4 (4 Aut)</td>
</tr>
<tr>
<td>PC</td>
<td>No PC</td>
</tr>
<tr>
<td>1</td>
<td>19 (7 Aut)</td>
</tr>
</tbody>
</table>

FTD: frontotemporal dementia  PC: posterior cingulate  Aut: autopsy

Vascular Dementia vs. AD

- ~10% of patients.

- Random distribution of defects. Diffuse or focal. Cortical and subcortical.

- Usually diffuse small infarcts affecting basal ganglia, thalami, white matter and hippocampus when isolated.

- Usually focal more extent infarcts when associated with AD (~5%).

- Progressive decline depends on severity of AD more than vascular disease.

- Clinical diagnosis + MRI usually overestimate vascular aetiology and underestimate mixed dementia.

*Jellinger KA, 2002*
Late life depression & Hypothyroidism

The two most common causes of reversible dementia in the elderly. May present with similar pattern to AD but basal ganglia and thalami are usually involved.
Differentiation of dementia with Lewy bodies from Alzheimer’s disease using a dopaminergic presynaptic ligand.

<table>
<thead>
<tr>
<th></th>
<th>Cognitive impairment</th>
<th>Extrapyramidal signs</th>
<th>Visual hallucinations</th>
<th>Sensibility to neuroleptics</th>
</tr>
</thead>
<tbody>
<tr>
<td>AD</td>
<td>Progressive</td>
<td>Casual Late</td>
<td>Less common</td>
<td>No</td>
</tr>
<tr>
<td>Parkinson</td>
<td>Slow Dementia 30%</td>
<td>Before cognitive impairment</td>
<td>Casual</td>
<td>Yes</td>
</tr>
<tr>
<td>LBD</td>
<td>Fluctuations Progressive</td>
<td>With cognitive impairment</td>
<td>Recurrent and detailed</td>
<td>Yes</td>
</tr>
</tbody>
</table>
## AD vs. LBD

**Hypoperfusion/hypometabolism**

<table>
<thead>
<tr>
<th></th>
<th>Posterior temporoparietal</th>
<th>Mesial temporal</th>
<th>Frontal</th>
<th>Occipital</th>
<th>BG</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AD</strong></td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>LBD</strong></td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td>++</td>
<td>+</td>
</tr>
</tbody>
</table>
Parkinson vs. Atypical Parkinsonism

-PD- 
NC
MSA

**DAT**
**FP-CIT**

**D2**
**IBZM**

EP (↓)
MSA (↓)

EP (N or ↑)
MSA (↓)

Atypical Parkinsonisms

- *FDG PET* for Parkinson
- *FDG PET* for PSP
- *ECD SPECT* for CBD
- *ECD SPECT* for MSA-OPCA
Huntington’s Disease

A. 7-year evolution with psychiatric symptoms. B. HD with dementia.
C. Cognitive impairment and family history of HD.
Potential impact of treatment to delay AD onset

Brookmayer et al. 1998
Early markers of AD

Cerebral metabolic and cognitive decline in persons at genetic risk for AD.

Small et al. PNAS 2000;97:6037-42.
Imaging brain amyloid in AD using $^{11}$C-PIB PET

Klunk et al. Ann Neurol 2004
$^{11}$C-PIB for differential diagnosis of dementia

Row et al. Neurology 2007
$^{11}$C-PIB as an early marker of AD
Early markers of AD: the search for new treatments in preclinical stages

FDG PET supported in dementia or cognitive decline of at least 6 months when diagnosis remains uncertain after complete clinical evaluation and PET is expected to aid in diagnosis or future treatment.


FDG PET supported in dementia or cognitive decline of at least 6 months when criteria for both AD and FTD coexist and diagnosis remains uncertain after complete clinical evaluation.
Low DAT uptake in SPECT or PET is a *suggestive feature* for DLB.

Low perfusion or metabolism in SPECT/PET with reduced occipital activity is a *supportive feature*.

Alzheimer’s Association & National Institute on Aging. 2010. Recommendations to update diagnostic criteria for AD.


New proposed criteria for AD, MCI/AD and preclinical AD, including PET/SPECT imaging, MRI and CSF assays as biomarkers for AD.
Summary

- Early diagnosis of AD
- Prediction of conversion from MCI to AD
- Differential diagnosis of dementia
- Preclinical diagnosis of AD
- Assessment of new therapeutic interventions
- Progressive incorporation to clinical guidelines