SPECT and PET in Neurodegenerative Diseases

Isabel Roca, MD
HU VALL HEBRON
Barcelona, Spain
Global prevalence of dementia

Number of people with dementia in developing and developed countries

Ferri et al 2005
1. SPECT: perfusion and metabolism
2. DATSCAN: dopamine transporters
3. IBZM: D2 receptors
<table>
<thead>
<tr>
<th>SPECT</th>
<th>Type of Image/Information</th>
<th>PET</th>
</tr>
</thead>
<tbody>
<tr>
<td>99mTc-HMPAO</td>
<td></td>
<td>15O-H2O</td>
</tr>
<tr>
<td>99mTC-ECD</td>
<td>PERfusion</td>
<td></td>
</tr>
<tr>
<td>99mTC-ECD</td>
<td>METABOLISM</td>
<td>18F-FDG</td>
</tr>
<tr>
<td>123I-ioflupane</td>
<td>DOPAMINE TRANSPORTERS</td>
<td>18F-DOPA</td>
</tr>
<tr>
<td>123I-IBZM</td>
<td>DOPAMINE RECEPTORS</td>
<td>11C-raclopride</td>
</tr>
<tr>
<td>201Thallium</td>
<td>TUMOR VIABILITY</td>
<td>11C-metionine</td>
</tr>
</tbody>
</table>
IMAGING FUNDAMENTALS
Brain Perfusion SPECT

HMPAO  ECD  FDG
DATSCAN  IBZM

HMPAO

FDG

ECD

FDG
IMAGING FUNDAMENTALS

Brain Perfusion SPECT
IMAGING FUNDAMENTALS

Datscan or IBZM SPECT
<table>
<thead>
<tr>
<th>DIFFERENCES</th>
<th>SPECT</th>
<th>PET</th>
</tr>
</thead>
<tbody>
<tr>
<td>RADIOPHARMACEUTICALS</td>
<td>ECD</td>
<td>FDG</td>
</tr>
<tr>
<td></td>
<td>HMPAO</td>
<td>DOPAMINE</td>
</tr>
<tr>
<td></td>
<td>DATSCAN</td>
<td>H2O</td>
</tr>
<tr>
<td></td>
<td>IBZM</td>
<td>METHIONINE</td>
</tr>
<tr>
<td>CUANTIFICATION</td>
<td>relative</td>
<td>relative and absolute</td>
</tr>
<tr>
<td>SPATIAL RESOLUTION</td>
<td>6-7 mm</td>
<td>3-4 mm</td>
</tr>
</tbody>
</table>
PET: Positron Emission Tomography
Perfusion Brain SPECT

‘FROZEN’ IMAGE

99mTc-HMPAO / ECD

METABOLISM – BRAIN PERFUSION AT TRACER INJECTION
DIFFERENTIAL DIAGNOSIS OF PARKINSONISM

SPECT $^{123}$I-FP-CIT DATSCAN

NORMAL
- Non-Organic Parkinsonism

PATHOLOGIC
- Organic Parkinsonism
  - SYMMETRIC / ASSYMMETRIC
  - Left / Right
# Differential Diagnosis of Dementia

<table>
<thead>
<tr>
<th>CONDITION</th>
<th>PATHOLOGY</th>
<th>PERFUSION SPECT</th>
<th>IOFLUPANE SPECT</th>
<th>IBZM SPECT</th>
<th>PRE-POST SYNAPTIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer’s disease</td>
<td>Beta-Amyloid</td>
<td>Temporoparietal bilateral</td>
<td>Normal</td>
<td>Normal</td>
<td>No</td>
</tr>
<tr>
<td>Lewy-bodies’ dementia</td>
<td>Diffuse Lewy bodies</td>
<td>Temporoparietal bilateral +/- occipital</td>
<td>Diminished similar to PD</td>
<td>Normal</td>
<td>Pre</td>
</tr>
<tr>
<td>Fronto-temporal degeneration</td>
<td>Diffuse cortical bilateral</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>. Pick’s</td>
<td>Thaupathy 3R</td>
<td>Frontal bilateral</td>
<td>Normal</td>
<td>Normal</td>
<td>?</td>
</tr>
<tr>
<td>. DCB</td>
<td>Thaupathy 4R</td>
<td>Assymetric</td>
<td>Diminished</td>
<td>Diminished</td>
<td>Pre &amp; Post</td>
</tr>
<tr>
<td>. PSP</td>
<td>Thaupathy 4R</td>
<td>Symmetric</td>
<td>Diminished</td>
<td>Diminished</td>
<td>Pre &amp; Post</td>
</tr>
<tr>
<td>A. Multi-systemic</td>
<td>Astrocytic glyosis</td>
<td>Diffuse hypoperfusion + cerebellum</td>
<td>Diminished</td>
<td>Diminished</td>
<td>Pre &amp; Post</td>
</tr>
<tr>
<td>AMS-C AMS-P</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parkinson’s disease</td>
<td>Lewy bodies (substantia nigra)</td>
<td>Normal</td>
<td>Diminished</td>
<td>Normal</td>
<td>Pre</td>
</tr>
<tr>
<td>Vascular</td>
<td>Multiple Infarcts</td>
<td>Multiple perfusion defects</td>
<td>Normal (often)</td>
<td>Abnormal (often)</td>
<td>Post (often)</td>
</tr>
</tbody>
</table>
- From birth to 2 years old, the brain MATURES

- From 2 to 10 years old, the brain keeps a high metabolic rate

- From 10 years old, regional cerebral blood flow (cortical tracer uptake) progressively decreases

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>CBF (ml/100 g/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10–19</td>
<td>59.6±9.5</td>
</tr>
<tr>
<td>20–29</td>
<td>55.2±2.8</td>
</tr>
<tr>
<td>30–39</td>
<td>47.2±4.5</td>
</tr>
<tr>
<td>40–49</td>
<td>46.6±5.2</td>
</tr>
<tr>
<td>50–59</td>
<td>46.7±4.9</td>
</tr>
<tr>
<td>60–69</td>
<td>44.7±4.6</td>
</tr>
<tr>
<td>70–83</td>
<td>40.8±3.5</td>
</tr>
</tbody>
</table>
Newborn

6 months

80 ys

70 ys

60 ys

50 ys

40 ys

1 y

2 ys

8 ys

MATURING

AGEING
AGEING BRAIN

DIMINISHING ACTIVITY:
- FRONTAL
- POSTERIOR TEMPORAL

INCREASING ACTIVITY:
- OCCIPITAL
<table>
<thead>
<tr>
<th>Cerebral region</th>
<th>Region/cerebellum</th>
<th>Young (n=40)</th>
<th>Aged (n=28)</th>
<th>t test P</th>
<th>Young (n=40)</th>
<th>Aged (n=28)</th>
<th>t test P</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRONTAL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANTERIOR</td>
<td></td>
<td>89.2±4.9</td>
<td>89.7±4.5</td>
<td></td>
<td>89.2±4.9</td>
<td>89.7±4.5</td>
<td></td>
</tr>
<tr>
<td>POSTERIOR</td>
<td></td>
<td>89.1±4.3</td>
<td>86.4±7.7</td>
<td></td>
<td>89.1±4.3</td>
<td>86.4±7.7</td>
<td></td>
</tr>
<tr>
<td>LPF</td>
<td></td>
<td>90.2±4.3</td>
<td>86.8±5.5</td>
<td></td>
<td>90.2±4.3</td>
<td>86.8±5.5</td>
<td></td>
</tr>
<tr>
<td>RPF</td>
<td></td>
<td>89.1±4.3</td>
<td>86.4±7.7</td>
<td></td>
<td>89.1±4.3</td>
<td>86.4±7.7</td>
<td></td>
</tr>
<tr>
<td>RO</td>
<td></td>
<td>95.5±4.2</td>
<td>97.3±4.6</td>
<td></td>
<td>95.5±4.2</td>
<td>97.3±4.6</td>
<td></td>
</tr>
<tr>
<td>LAT</td>
<td></td>
<td>91.5±4.5</td>
<td>92.7±5.1</td>
<td></td>
<td>91.5±4.5</td>
<td>92.7±5.1</td>
<td></td>
</tr>
<tr>
<td>RPT</td>
<td></td>
<td>94.3±4.2</td>
<td>92.1±5.1</td>
<td></td>
<td>94.3±4.2</td>
<td>92.1±5.1</td>
<td></td>
</tr>
<tr>
<td>RWM</td>
<td></td>
<td>66.6±4.1</td>
<td>65.1±7.2</td>
<td></td>
<td>66.6±4.1</td>
<td>65.1±7.2</td>
<td></td>
</tr>
<tr>
<td>LC</td>
<td></td>
<td>–</td>
<td>–</td>
<td></td>
<td>109.2±3.8</td>
<td>109.8±4.4</td>
<td>N.S.</td>
</tr>
<tr>
<td>RC</td>
<td></td>
<td>–</td>
<td>–</td>
<td></td>
<td>110.2±4.1</td>
<td>111.4±4.8</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

LAF, Left anterior frontal; RAF, right anterior frontal; LPF, left posterior frontal; RPF, right posterior frontal; LP, left parietal; RP, right parietal; LO, left occipital; RO, right occipital; LAT, left anterior temporal; RAT, right anterior temporal; LPT, left posterior temporal; RPT, right posterior temporal; LBG, left basal ganglia; RBG, right basal ganglia; LWM, left white matter; RWM, right white matter; LC, left cerebellum; RC, right cerebellum; N.S., non-significant
DEMENTIA – UTILITY of SPECT and PET

- Early detection
- Differential diagnosis
- Follow-up
Natural History of the Neurodegenerative Process

- Symptoms
- Amyloid deposits

NORMAL MCI DEMENTIA

- COGNITION
- GLUCOSE METAB.
- NEURONAL FUNC.
Natural History of the Neurodegenerative Process

- **Diagnosis**
  - PET-SPECT

- **Symptoms**
  - Amyloid deposits

- **Cognition Tests**

- **Phases**
  - NORMAL
  - MCI
  - DEMENTIA
Natural History of the Neurodegenerative Process

- **Diagnosis**
  - PET-SPECT
  - PIB

- **Symptoms**
  - Amyloid deposits

- **Cognition Tests**

- **NORMAL**

- **MCI**

- **DEMENTIA**

- COGNITION
  - GLUCOSE METAB.
  - NEURONAL FUNC.
Voxel-by-voxel quantitative analysis is superior to visual evaluation.

Slice Presentation

3D-SSP Presentation

Burdette et al. Radiology 1996

X-axis: 1 - Specificity, Y-axis: Sensitivity

Tatsch, K
Quantitative methods:
3D-SSP

Voxel-by-voxel quantitative analysis is superior to visual evaluation

Tatsch, K
**Quantitative methods:**

**SPM- Statistical Parametric Mapping**

- **SPM** determines the voxel differences between groups based on the level of significance. It is necessary to transform original space to MNI space (proportional to Talairach space) by registering to a template.
**Quantitative methods: Neurogam**

- **Neurogam** allows the individual comparison with a normal database, very useful when analyzing patients individually and correlating to clinical data.
- **Neurogam** determines abnormal voxels between the patient and the normal or reference database. It is necessary to transform original space to Talairach space by adjusting the limits of the brain.

![Image of brain scans and activity levels](image-url)
Differential diagnosis
Multi-infarct dementia
Dementia of Alzheimer’s type

- Characterized by:
  - Slowly progressing memory loss.
  - Cortical degeneration with:
    - amyloid plaques (fibers of beta-amyloid peptide).
    - neurofibrillar tangles (hyperphosphorylated tau protein).
- It is considered the most prevalent (60%) of cortical dementias.
Progression pattern of Alzheimer’s disease
Causes of Alzheimer’s disease

- Beta-amyloid plaques
- Neuronal damage by vicinity
- Tau protein tangles
- Axonal damage

NIA Alzheimer’s Disease: Unraveling the Mystery
Alzheimer’s disease

Neuropathologic changes

- Amyloid plaque
- Tau protein
- Neurofibrillar tangle

Metabolic changes
Alzheimer’s disease

Tatsch, K
Progression pattern of Alzheimer’s disease
Brain SPECT

→ Initial stage
  • hipoactivity - parietal and/or posterior temporal cortex
  • unilateral or bilateral

→ Intermediate stage
  • hipoactivity - extensive, parietal and temporal, bilateral
  • hipoactivity – posterior frontal

→ Advanced stage
  • diffuse cortical hipoactivity
  • less/not affected: motor areas, occipital, BG, cerebellum
Dementia of Alzheimer’s type

Normal Controls vs. AD (P ≤ 0.001 uncorrected)

SPM
Statistical Parametric Mapping
Dementia of Alzheimer’s type

Results - SPM

Significant differences in several Brodmann areas localized in:

- Cingulate
- Temporal lobe
- Parietal lobe
- Frontal lobe
- Especially in right hemisphere
Normal DB > DAT

Significant differences (hypoactivity $\leq 2$SD):

- Cingulate 100%
- Parietal 80%
- Anterior temporal 60%
- Anterior frontal 60%
- Posterior temporal 50%
## Dementia of Alzheimer’s type

Comparison SPM - Neurogam

<table>
<thead>
<tr>
<th></th>
<th>concordant Brodmann areas</th>
<th>SPM - NEUROGAM</th>
</tr>
</thead>
<tbody>
<tr>
<td>CINGULATE</td>
<td></td>
<td>24, 32</td>
</tr>
<tr>
<td>FRONTAL</td>
<td></td>
<td>10, 46</td>
</tr>
<tr>
<td>TEMPORAL</td>
<td></td>
<td>21</td>
</tr>
<tr>
<td>PARIETAL</td>
<td></td>
<td>7, 37, 39, 40</td>
</tr>
<tr>
<td>PARIETAL-OCCIPITAL</td>
<td></td>
<td>19</td>
</tr>
</tbody>
</table>
Dementia of Alzheimer’s type

surface projections

right lateral view  left lateral view  view from above

comparison to normal database

Tatsch, K
Diagnosis of AD (n=54)

- Sensitivity: 89.5%
- Specificity: 81.5%
- Positive Predictive Value: 93.2%
- Negative Predictive Value: 73.3%

Bonte FJ, Weiner MF, Bigio EH, White CL III.

Brain blood flow in the dementias: SPECT with histopathologic correlation in 54 patients.

The OPTIMA Study

SPECT perfusion imaging in the diagnosis of Alzheimer’s disease

A clinical-pathologic study

W. Jagust, MD; R. Thisted, PhD; M.D. Devous, Sr., PhD; R. Van Heertum, MD; H. Mayberg, MD; K. Jobst, MD; A.D. Smith, DPhil; and N. Borys, MD

NEUROLOGY 2001;56:950–956

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Age, y, mean (SD)</th>
<th>Sex, M/F</th>
<th>MMSE score, mean (SD)</th>
<th>Time from SPECT to death, mo, mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>70</td>
<td>77.1 (8)</td>
<td>35/35</td>
<td>13.2 (8.5)</td>
<td>29.3 (15)</td>
</tr>
<tr>
<td>Autopsied controls</td>
<td>14</td>
<td>80.4 (8)</td>
<td>9/5</td>
<td>27.9 (2.0)</td>
<td>22.9 (18.6)</td>
</tr>
<tr>
<td>Nonautopsied controls</td>
<td>71</td>
<td>73.3 (11)</td>
<td>28/43</td>
<td>28.8 (1.3)</td>
<td>NA</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPECT</td>
<td>68</td>
<td>98</td>
<td>78</td>
<td>86</td>
</tr>
<tr>
<td>Clinical Dx (Probable)</td>
<td>59</td>
<td>95</td>
<td>84</td>
<td>86</td>
</tr>
</tbody>
</table>
Conversion from Mild Cognitive Impairment (MCI) to Alzheimer’s disease

\[ ^{99m}\text{Tc-ECD} \]

Conversion: 52/76 patients with MCI in 3 years

Hirao et al. Neuroimage 2005;28:1014-21
FDG-PET changes in brain glucose metabolism from normal cognition to pathologically verified Alzheimer’s disease

Eur J Nucl Med Mol Imaging
Received: 22 August 2008 / Accepted: 28 November 2008
© Springer-Verlag 2009
Normal cognition                                            Alzheimer’s (necropsy diagnosis)

FDG-PET changes in brain glucose metabolism from normal cognition to pathologically verified Alzheimer’s disease

Eur J Nucl Med Mol Imaging
Received: 22 August 2008 / Accepted: 28 November 2008
© Springer-Verlag 2009
Pittsburgh compound B

Imaging Technology for Neurodegenerative Diseases

Progress Toward Detection of Specific Pathologies

Chester A. Mathis, PhD; William E. Klunk, MD, PhD; Julie C. Price, PhD; Steven T. DeKosky, MD

Arch Neurol. 2005;62:196-200
Imaging Brain Amyloid in Alzheimer’s Disease Using the Novel Positron Emission Tomography Tracer, Pittsburgh Compound-B

Klunk et al. Ann Neurol 2004
Imaging Technology for Neurodegenerative Diseases

Progress Toward Detection of Specific Pathologies

Arch Neurol. 2005;62:196-200
$^{11}$C-PIB PET imaging in Alzheimer disease and frontotemporal lobar degeneration

*Neurology* 2007;68:1205-1212
<table>
<thead>
<tr>
<th>Brain area</th>
<th>MCI</th>
<th>Control</th>
<th>%</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frontal cortex</td>
<td>1.50 (0.46)</td>
<td>1.08 (0.10)</td>
<td>139</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Posterior cingulate</td>
<td>1.92 (0.58)</td>
<td>1.38 (0.16)</td>
<td>139</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Parietal cortex</td>
<td>1.49 (0.40)</td>
<td>1.14 (0.12)</td>
<td>131</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Temporal cortex</td>
<td>1.59 (0.45)</td>
<td>1.24 (0.13)</td>
<td>128</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Caudate</td>
<td>1.50 (0.48)</td>
<td>1.20 (0.08)</td>
<td>125</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Putamen</td>
<td>1.68 (0.39)</td>
<td>1.43 (0.12)</td>
<td>117</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Thalamus</td>
<td>1.33 (0.30)</td>
<td>1.22 (0.07)</td>
<td>109</td>
<td>=0.19</td>
</tr>
<tr>
<td>Occipital cortex</td>
<td>1.46 (0.20)</td>
<td>1.37 (0.11)</td>
<td>107</td>
<td>=0.19</td>
</tr>
<tr>
<td>Hippocampus</td>
<td>1.43 (0.21)</td>
<td>1.37 (0.12)</td>
<td>104</td>
<td>=0.36</td>
</tr>
<tr>
<td>White matter</td>
<td>1.94 (0.21)</td>
<td>1.88 (0.24)</td>
<td>103</td>
<td>=0.51</td>
</tr>
</tbody>
</table>

PET amyloid ligand [\(^{11}\text{C}\)]PIB uptake is increased in mild cognitive impairment

*Neurology* 2007;68;1603-1606
## Alzheimer’s Disease
### Amyloid and hypometabolism

<table>
<thead>
<tr>
<th>Demography</th>
<th>AD</th>
<th>Controls</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no.</td>
<td>19</td>
<td>14</td>
<td>—</td>
</tr>
<tr>
<td>Age, y, mean ± SD</td>
<td>66.8 ± 5.6</td>
<td>64.8 ± 6.2</td>
<td>NS</td>
</tr>
<tr>
<td>Male</td>
<td>9/19</td>
<td>8/14</td>
<td>—</td>
</tr>
<tr>
<td>Duration of diagnosis, months</td>
<td>5 ± 6.5</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>MMSE, mean ± SD</td>
<td>2.2 ± 3.9</td>
<td>29–30</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PIB uptake RATIO, mean ± SD</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hippocampus</td>
<td>1.26 ± 0.19</td>
<td>1.16 ± 0.14</td>
<td>NS</td>
</tr>
<tr>
<td>Amygdala</td>
<td>1.24 ± 0.22</td>
<td>1.05 ± 0.09</td>
<td>NS</td>
</tr>
<tr>
<td>Parahippocampus</td>
<td>1.36 ± 0.22</td>
<td>1.11 ± 0.10</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Primary motor cortex</td>
<td>1.70 ± 0.33</td>
<td>1.26 ± 0.10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Primary sensory cortex</td>
<td>1.76 ± 0.38</td>
<td>1.21 ± 0.09</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Primary visual cortex</td>
<td>1.63 ± 0.33</td>
<td>1.17 ± 0.10</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Increased PIB**

### Amyloid, hypometabolism, and cognition in Alzheimer disease

An [11C]PIB and [18F]FDG PET study

*Neurology 2007;68;501-508*
Alzheimer’s Disease

β-Amyloid deposits

Alzheimer’s Disease
In vivo and post-mortem amyloid correlates

Ikonomovic et al. Brain 2008
Post-mortem correlates of in-vivo PiB-PET amyloid imaging in a typical case of AD
β-Amyloid deposit and memory in non-demented individuals

Pike KE et al. Brain 2007; 130:2837-2844
11C-PIB uptake
(Pittsburgh Compound-B)

Edison et al. Neurology 2007;68:501-8
generic denomination proposed at the First International Workshop on Lewy Body Dementia (Newcastle upon Tyne, 1995)

• diffuse Lewy body disease
• senile dementia of Lewy body type
• Lewy body variant of Alzheimer's disease

it is considered second in prevalence of cortical dementias after AD:

15 - 20% of all dementias
1. ↓ dopamine transporters uptake
2. ↓ diffuse cortical uptake, ↓ occipital
3. ↓ MIBG myocardial uptake

Table 1 Revised criteria for the clinical diagnosis of dementia with Lewy bodies (DLB)

1. **Central feature** (essential for a diagnosis of possible or probable DLB)
   
   Dementia defined as progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational function. Prominent or persistent memory impairment may not necessarily occur in the early stages but is usually evident with progression.

2. **Supportive features** (commonly present but not proven to have diagnostic specificity)
   
   Repeated falls and syncope
   Transient, unexplained loss of consciousness
   Severe autonomic dysfunction, e.g., orthostatic hypotension, urinary incontinence
   Hallucinations in other modalities
   Systematized delusions
   Depression
   Relative preservation of medial temporal lobe structures on CT/MRI scan
   
   **Low dopamine transporter uptake in basal ganglia demonstrated by SPECT or PET imaging**
   **Generalized low uptake on SPECT/PET perfusion scan with reduced occipital activity**
   **Abnormal (low uptake) MIBG myocardial scintigraphy**
   Prominent slow wave activity on EEG with temporal lobe transient sharp waves

3. A diagnosis of DLB is less likely
   
   In the presence of cerebrovascular disease evident as focal neurologic signs or on brain imaging
   In the presence of any other physical illness or brain disorder sufficient to account in part or in total for the clinical picture
   If parkinsonism only appears for the first time at a stage of severe dementia

4. **Temporal sequence** of symptoms
   
   DLB should be diagnosed when dementia occurs before or concurrently with parkinsonism (if it is present). The term Parkinson disease dementia (PDD) should be used to describe dementia that occurs in the context of well-established Parkinson disease. In a practice setting the term that is most appropriate to the clinical situation should be used and generic terms such as LB disease are often helpful. In research studies in which distinction needs to be made between DLB and PDD, the existing 1-year rule between the "onset of dementia and Parkinson disease" continues to be recommended. Adoption of other time periods will simply confound data pooling or comparison between studies. In other research settings that may include clinicopathologic studies and clinical trials, both clinical phenotypes may be considered collectively under categories such as LB disease or alpha-synucleinopathy.
**Lewy body dementia**

$^{123}$I-FP-CIT SPECT allows differential diagnosis between dementia of Alzheimer’s type (DAT) and diffuse Lewy body disease (LBD).

<table>
<thead>
<tr>
<th>LBD</th>
<th>DAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased uptake</td>
<td>Normal uptake</td>
</tr>
</tbody>
</table>

Brain perfusion scintigraphy with 99mTc-HMPAO or 99mTc-ECD and $^{123}$I-β-CIT single-photon emission tomography in dementia of the Alzheimer-type and diffuse Lewy body disease.

*Eur J Nucl Med, March 1997*
Lewy body dementia

Occipital hypoperfusion in brain SPECT

LBD  DAT

Kaufer DI et al. Rev Neurol 2003;37:127-30
A comparison of 99mTc-HMPAO SPET changes in dementia with Lewy bodies and Alzheimer’s disease using statistical parametric mapping.

Lewy body dementia

↓ MIBG myocardial uptake

LBD | DAT
58 patients
- Brain SPECT
- MIBG myocardial scintigraphy

patient with DLB
73-year-old man
MMSE score 22

patient with AD
74-year-old woman
MMSE score 21

Comparative value of brain perfusion SPECT and $[^{123}\text{I}]$MIBG myocardial scintigraphy in distinguishing between dementia with Lewy bodies and Alzheimer’s disease

Eur J Nucl Med Mol Imaging, Nov 2005
Lewy body dementia

Brain SPECT
Medial occipital lobe

Myocardial MIBG
H/M ratio

Comparative value…(cont.)

Eur J Nucl Med Mol Imaging, Nov 2005
Differential diagnosis
DAT vs. FTD
Fronto-temporal degeneration (FTD)
Pick's disease (PiD)
Cortico-basal degeneration (CBD)

Josephs et al. Neurology 2006;66:41-8
Progressive supranuclear palsy (PSP)

Pick Complex

Clinical

CBD-like
PSP-like
FTD

Pathological

Tau-positive
CBD

Tau-negative
FTLD-U
FTLD-MND

Josephs et al. Neurology 2006;66:41-8
PSP and CBD

⇒ SPECT:
Severe bilateral cortical hypoactivity

PSP: symmetric  CBD: asymmetric

Differentiating between progressive supranuclear palsy and corticobasal degeneration by brain perfusion SPET

Nucl Med Comm 2001
Fronto-temporal degeneration (FTD)

Josephs et al. Neurology 2006;66:41-8
Olivo-ponto-cerebellar atrophy (AMS-C)
## DIFFERENTIAL DIAGNOSIS

<table>
<thead>
<tr>
<th>CONDITION</th>
<th>PATHOLOGY</th>
<th>PERFUSION SPECT</th>
<th>IOFLUPANE SPECT</th>
<th>IBZM SPECT</th>
<th>PRE-POST SYNAPTIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer’s disease</td>
<td>Beta-Amyloid</td>
<td>Temporo-parietal bilateral</td>
<td>Normal</td>
<td>Normal</td>
<td>No</td>
</tr>
<tr>
<td>Lewy-bodies’ dementia</td>
<td>Diffuse Lewy bodies</td>
<td>Temporo-parietal bilateral +/- occipital</td>
<td>Diminished similar to PD</td>
<td>Normal</td>
<td>Pre</td>
</tr>
<tr>
<td>Fronto-temporal degeneration</td>
<td></td>
<td>Diffuse cortical bilateral</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>. Pick’s</td>
<td>Thaupathy 3R</td>
<td>Frontal bilateral</td>
<td>Normal</td>
<td>Normal</td>
<td>?</td>
</tr>
<tr>
<td>. DCB</td>
<td>Thaupathy 4R</td>
<td>Assymetric</td>
<td>Diminished</td>
<td>Diminished</td>
<td>Pre &amp; Post</td>
</tr>
<tr>
<td>. PSP</td>
<td>Thaupathy 4R</td>
<td>Symmetric</td>
<td>Diminished</td>
<td>Diminished</td>
<td>Pre &amp; Post</td>
</tr>
<tr>
<td>A. Multi-systemic</td>
<td>Astrocytic glyosis</td>
<td>Diffuse hypoperfusion + cerebellum</td>
<td>Diminished</td>
<td>Diminished</td>
<td>Pre &amp; Post</td>
</tr>
<tr>
<td>AMS-C</td>
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<tr>
<td>AMS-P</td>
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</tr>
<tr>
<td>Parkinson’s disease</td>
<td>Lewy bodies (substantia nigra)</td>
<td>Normal</td>
<td>Diminished</td>
<td>Normal</td>
<td>Pre</td>
</tr>
<tr>
<td>Vascular</td>
<td>Multiple Infarcts</td>
<td>Multiple perfusion defects</td>
<td>Normal (often)</td>
<td>Abnormal (often)</td>
<td>Post (often)</td>
</tr>
</tbody>
</table>
SPECT and PET in Neurodegenerative Diseases

The End