Dementia in PD is Due to Diffuse Lewy Body Disease

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Overview

• What is “Diffuse Lewy Body Disease”?  
  - define Lewy related pathology (LRP)  
  - Braak staging of LRP  
  - define “diffuse” Lewy body disease

• What is PDD?

• Is dementia due to coexistent AD?

• Is neocortical LRP associated with dementia in PDD?  
  - Is it presence of diffuse LRP or severity?
What is Lewy Related Pathology (LRP)?

- Classic Lewy bodies
- Alpha-synuclein immunopositive inclusions and neurites
Braak Staging of LRP

- Examination of “incidental” and PD cases with SNCA antibodies
- Proposed “stages” of LRP anatomic progression

What is “Diffuse Lewy Body Disease”?

• Involvement of LRP in all three major anatomic regions “+”
  ◆ brainstem
  ◆ limbic
  ◆ neocortical
  ◆ “more” diffuse
What is PDD?

2007 Clinical Diagnostic Criteria

• Diagnosis of PD

• Dementia syndrome within the context of established PD
  – impairment in more than one cognitive domain
  – decline from premorbid level
  – deficits severe enough to impair daily life

What is PDD?
Interpretation of Neurpathologic Studies

- Case selection
  - PD precedes dementia onset ("1 year rule")
- Neuropathology
  - SNCA immunohistochemistry
  - Up to date AD pathologic criteria
    - Braak stage IV or greater neurofibrillary tangles
    - CERAD neuritic plaque density ≥ moderate
## Is Dementia in PDD due to Coexistent AD?

<table>
<thead>
<tr>
<th>Study</th>
<th># PDD</th>
<th># AD positive</th>
</tr>
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<tbody>
<tr>
<td>Hurtig</td>
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<td><strong>23 (14%)</strong></td>
<td><strong>84 (97%)</strong></td>
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Is Neocortical LRP associated with Dementia?

Two Community Sample Studies

• Honolulu-Asia Aging Study (HAAS)
  ◆ 285 autopsies
  ◆ Logistic regression for AD/Vascular/Cortical LB/HS & dementia
  ◆ Odds ratio for cortical LB = 2.17

• Adult Changes in Thought (ACT)
  ◆ 221 autopsies
  ◆ Multivariate log-linear regression for AD/Vascular/Cortical LB/AA & dementia
  ◆ Odds ratio for cortical LB = 5.08
Is Neocortical LRP Associated with Dementia in PDD?

• Hurtig, Neurology 2000
  - 20 PD & 22 PDD
  - 41/42 with cortical LRP

<table>
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<tr>
<th>Cortical Lewy Body Score</th>
<th>Dementia</th>
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<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Yes, n (%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>No, n (%)</td>
<td>1 (5)</td>
</tr>
</tbody>
</table>

Is Neocortical LRP Associated with Dementia in PDD?

- Apaydin, Arch Neurol 2002
  - 12 PD & 8 PDD

<table>
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<tr>
<th>Region</th>
<th>PDD Mean (SD)</th>
<th>PD Mean (SD)</th>
<th>p value</th>
</tr>
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<tbody>
<tr>
<td>Neocortex</td>
<td>2.3 (2.4)</td>
<td>0.2 (0.2)</td>
<td>.002</td>
</tr>
<tr>
<td>Limbic cortex</td>
<td>6.9 (4.5)</td>
<td>0.7 (0.7)</td>
<td>&gt; .001</td>
</tr>
<tr>
<td>Amygdala</td>
<td>17.5 (18.2)</td>
<td>1.5 (1.9)</td>
<td>.006</td>
</tr>
<tr>
<td>Substantia nigra</td>
<td>5.7 (2.5)</td>
<td>3.3 (2.1)</td>
<td>.05</td>
</tr>
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Is Neocortical LRP Associated with Dementia in PDD?

- Aarsland, Ann Neurol 2005
  - community-based study of PD
  - 4 PD & 18 PDD
  - LRP total score
    - Only LRP score significantly associated with rate of cognitive decline

Is Neocortical LRP Associated with Dementia in PDD?

- Braak, Neurology 2005
  - 9 PD & 79 PDD

![Graph showing PD stage and MMSE scores](attachment:image.png)

Conclusion

• Is dementia due to coexistent AD?  No
• Is presence of *any* neocortical LRP associated with dementia in PDD?  No
• *Is it presence of “more” diffuse LRP associated with dementia?  Yes!*