Neuropathology Core

Robert Hevner, MD, PhD
Professor and Director of Neuropathology
Co-Director, ADRC Neuropathology Core
Department of Pathology
UCSD
1. Diagnosis

- Postmortem brain exam and histological studies to evaluate AD and other pathologies
Why is the Postmortem Brain Exam Important?

Positive Predictive Value
bottom row most relevant?

<table>
<thead>
<tr>
<th>Neuropathological AD Definition</th>
<th>Clinically Probable AD N = 526</th>
<th>Clinically Probable or Possible AD N = 648</th>
<th>Dementia N = 919</th>
</tr>
</thead>
<tbody>
<tr>
<td>CERAD NP Freq Braak Stage V or VI N = 427</td>
<td>N = 327 PPV = 62.2%</td>
<td>N = 373 PPV = 57.6%</td>
<td>N = 427 PPV = 46.0%</td>
</tr>
<tr>
<td>CERAD NP Mod or Freq Braak Stage III-VI N = 618</td>
<td>N = 438 PPV = 83.3%</td>
<td>N = 511 PPV = 78.8%</td>
<td>N = 618 PPV = 67.2%</td>
</tr>
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Beach et al., 2012
Neuropathology of AD

- The brain is atrophic in severe AD (right) as compared to the healthy brain (left)
Microscopic Neuropathology of AD

- The main lesions are amyloid plaques and neurofibrillary tangles
- Neuronal cell death is the consequence
Neuropathologists

- Dr. Larry Hansen
- Dr. Annie Hiniker
The Neuropathology Data Form

ADC subject ID: ________________________________  Completed by: ________________________________

1. MDS/UDS patient ID

2. Date form completed (MM/DD/YYYY)  ___ ___ / ___ ___ / ___ ___ ___ ___

3. Neuropath ID

4. Sex (CHECK ONE)
   □ 1 Male
   □ 2 Female

5. Age at death  ___ ___ ___ years

6. Date of death (MM/DD/YYYY)  ___ ___ / ___ ___ / ___ ___ ___ ___

7. Postmortem interval (PMI): time between death and brain removal  ___ ___ . ___ hours  (99.9 = unknown)

8. Fixative
   □ 1 Formalin
   □ 2 Paraformaldehyde
   □ 3 Other
NACC Report

- UCSD results combined with data from ADRCs across the country
- We also report to family via letter

### 11. ALZHEIMER’S DISEASE. Please score AD neuropathologic changes.

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<table>
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<tbody>
<tr>
<td>a. Thal phase for amyloid plaques by immunohistochemistry (IHC)</td>
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<td>A score — CHECK ONE</td>
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<tr>
<td>Use only standard blocks (as described in Montine et al., Acta Neuropathol (2012) 123:1–11) to assign phase (i.e., midfrontal, superior/middle temporal, inferior parietal, hippocampus, entorhinal, basal ganglia, midbrain, cerebellum).</td>
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<td>b. Braak stage for neurofibrillary degeneration</td>
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<td>B score — CHECK ONE</td>
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<tr>
<td>Use standard blocks (as described in Montine et al., Acta Neuropathol (2012) 123:1–11) to assign phase (i.e., midfrontal, superior/middle temporal, inferior parietal, occipital, hippocampus, entorhinal).</td>
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<tr>
<td>c. CERAD score for density of neocortical neuritic plaque (plaques with argyrophilic dystrophic neurites, with or without dense amyloid cores). Score without respect to age or diagnosis.</td>
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<tr>
<td>C score — CHECK ONE</td>
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<tr>
<td>Use only standard blocks (as described in Montine et al., Acta Neuropathol (2012) 123:1–11) to assign phase (i.e., midfrontal, superior/middle temporal, inferior parietal).</td>
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<td>d. NIA-AA Alzheimer’s disease neuropathologic change (ADNC)</td>
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<td>CHECK ONE</td>
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Neuropathology Core
2. Research

- Half of each brain is snap frozen to be available for research
- **Brain tissue** from the ADRC is used in many studies at UCSD and across the country
- Eye tissue, spinal cord, live cells (fibroblasts) also for research. The latter are used to make **stem cells**.
How Can Research Help?

1. Prevent degeneration

• Why is medial temporal lobe (entorhinal cortex) the first area affected in AD?
• The concept of selective vulnerability

NFT stage III

Braak & Del Tredici, 2012
How Can Research Help?
2. Neuroregeneration

- Neural stem cells can be used to make new neurons
- The potential for neuron replacement therapy

hiPSCs: human induced pluripotent stem cells
OKSM: Oct4, Klf4, Sox2, c-Myc
THANK YOU from the Neuropathology Core

Dr. Robert Rissman,
NP Core Director

Dr. Robert Hevner,
NP Core Co-Director

Dr. James Brewer,
ADRC Director