Cerebrovascular Markers in Alzheimer’s Disease Quantifiable with 4D Flow MRI

Leonardo A. Rivera-Rivera
Research Associate
Department of Medical Physics
University of Wisconsin-Madison

https://www.medphysics.wisc.edu/~kmjohnso/
Alzheimer’s disease and cerebrovascular disease

- Cerebrovascular disease manifests in AD but is also an independent cause of dementia.

- AD – CVD hypotheses need testing:
  - Additive, causative, AND/OR combinatorial effects?
  - Will CVD biomarkers improve early diagnosis?

- Need for CVD biomarkers in longitudinal studies of subjects at risk of AD
  - Push to incorporate vascular dysfunction into the AT(N) biomarker system (Responses to the 2018 NIA-AA Research Framework [1,2])
  - Potential for MRI biomarkers of CVD

Neuroimaging of cerebrovascular disease using 4D flow MRI

- 4D flow MRI enables both volumetric angiographic and quantitative assessment of blood flow velocities in a single acquisition
- AD patients showed decreased blood flow
  - low blood pressure
  - elastic arteries
  - neuron loss -> decreased metabolism


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Intracranial PWV

- AD patients or at risk of AD will likely get an MRI
- 4D flow MRI:
  - blood flow, pulsatility, intracranial pulse wave velocity and other markers of vascular health
Study population recruited from WADRC clinical core

- Total number of subjects for this study = 192
- 5 groups

<table>
<thead>
<tr>
<th></th>
<th>AD (n=42)</th>
<th>MCI (n=37)</th>
<th>Older Cognitively healthy (n=50)</th>
<th>Impact (n=29)</th>
<th>Younger cognitively healthy (n=34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>71 ± 9</td>
<td>73 ± 9</td>
<td>73 ± 7</td>
<td>58 ± 3</td>
<td>57 ± 5</td>
</tr>
<tr>
<td>Sex (# females, %)</td>
<td>25, 60</td>
<td>20, 54</td>
<td>28, 56</td>
<td>21, 72</td>
<td>26, 76</td>
</tr>
<tr>
<td>Parental dementia history positive (# positive, %)</td>
<td>18, 43</td>
<td>19, 51</td>
<td>3, 6</td>
<td>29, 100</td>
<td>0, 0</td>
</tr>
<tr>
<td>APOE ε4 positive (# positive, %)*</td>
<td>16, 46</td>
<td>16, 57</td>
<td>0, 0</td>
<td>29, 100</td>
<td>0, 0</td>
</tr>
</tbody>
</table>

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Statistically higher PWV in AD and MCI compared to controls

- Higher PWV in the AD group suggests arterial stiffening of the internal carotid arteries and macrovascular damage

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Statistically higher PWV in APOE ε4 carriers healthy adults

- Higher PWV in the Impact group suggest vascular changes are occurring in a group of otherwise healthy individuals
  - need for longitudinal assessment

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Pathology and age effects

- AD accelerates aging effect
- PWV increases with age in healthy adults
- PWV needs to be correlated pathologic biomarkers associated with AD such as:
  - amyloid burden,
  - tau pathology
  - brain atrophy

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