Arterial Stiffness and Cerebral Blood Flow

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Arterial Stiffness is Associated with Dementia-Related Pathology and Impairment\(^{1-3}\)

**Normal Pressure**

- 7 m/s

**High Pressure**

- 12 m/s

**High Pulsatility**

**cfPWV** in m/s

\[
\text{cfPWV} = \frac{d_{\text{IC}} - d_{\text{TC}} - d_{\text{MIC}}}{\tau_{\text{MIC}} - k_1 - k_2 \times d_{\text{MIC}}}
\]

**Sphygmocor XCEL™**

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1. Rabkin. JAD 2012
3. Cui. JAD 2018
6. Maillard, Stroke 2017
11. Hughes. Neurology, 2018
MRI with Cerebral Blood Flow (CBF of GM and WM)

- 3T Siemens Skyra
- Structural metrics (T1-w 3D MPRAGE)
- White matter hyperintensities (WMH, T2 FLAIR)

- CBF by multi-phase pseudo-continuous arterial spin labeling
- Partial volume corrected CBF maps
- Mean total CBF\textsubscript{GM} and CBF\textsubscript{WM}
- Voxel based analysis

\textsuperscript{1}Jung et al. MRM 2010, \textsuperscript{2}Asllani et al. MRM 2008
**Healthy Brain Study: A Clinical Core of WF ADCC**

### Healthy Brain Study Participants (n=145)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>71.3 ±8.2</td>
</tr>
<tr>
<td>Education</td>
<td>15.6 ±2.6</td>
</tr>
<tr>
<td>Women</td>
<td>97 67%</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>124 86%</td>
</tr>
<tr>
<td>African-American</td>
<td>21 14%</td>
</tr>
<tr>
<td>Glucose Tolerance</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>83 57%</td>
</tr>
<tr>
<td>Impaired</td>
<td>62 43%</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>79 55%</td>
</tr>
<tr>
<td>MCI</td>
<td>50 35%</td>
</tr>
<tr>
<td>Dementia</td>
<td>15 10%</td>
</tr>
</tbody>
</table>
Arterial and Cerebral Hemodynamics

<table>
<thead>
<tr>
<th></th>
<th>WMH</th>
<th>CBF&lt;sub&gt;WM&lt;/sub&gt;</th>
<th>CBF&lt;sub&gt;GM&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>beta</td>
<td>SE p-value</td>
<td>beta p-value</td>
</tr>
<tr>
<td>cfPWV (m/s)</td>
<td>0.13</td>
<td>0.05 0.007</td>
<td>0.26 0.13 0.052</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>0.01</td>
<td>0.00 0.026</td>
<td>0.00 0.01 0.812</td>
</tr>
</tbody>
</table>

Adjusted for age, gender, race, glucose tolerance and cognitive status
No interactions with race, glucose tolerance or cognitive status

![Image of brain scan and scatter plot](image.png)

**Figure 2.** Linear fit model between cfPWV and mean CBF in the WM Cluster (age and gender are adjusted)
Implications of Arterial Stiffness in ADRD

- Arteries stiffen with age; changes can precede hypertension and the development of:
  - Cerebral small vessel disease
  - β-amyloid pathology
  - Neurodegeneration

- Greater arterial stiffness is associated with greater $\text{CBF}_{\text{WM}}$ and white matter lesion burden.

- Other studies report arterial stiffness is associated with lower $\text{CBF}_{\text{GM}}$; not observed in Healthy Brain Study.
Next Steps

Vascular Reactivity by hypercapnia
- Breath Hold
- RespirAct™ (CO₂ and O₂)

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- R01 AG058969 (Hughes)
MRI with Cerebral Blood Flow Details

- 3T Siemens Skyra (32-Channel head coil)
- Cortical thickness AD regions (T1 3D MP-RAGE by FreeSurfer 5.3)
- White matter hyperintensities (WMH, T2 FLAIR using lesion prediction algorithm (LPA) by SPM LST)

- Multi-phase pseudo-continuous ASL\(^1\) (3.0×3.0×4.0 mm, 36 slices, labeling duration=1700ms, post-labeling delay=1300ms, TR=4000ms, TE=11ms)
- Quantification into a physiological unit\(^2\)
- Partial volume correction\(^3\) using segmented T1w\(^2\) (Whole brain GM & WM CBF values calculated)
- Normalization into a standard template (i.e. MNI) and atlas (i.e. AAL)

\(^1\)Jung et al. MRM 2010, \(^2\)Buxton et al. MRM 1998, \(^3\)Asllani et al. MRM 2008