The Australian Imaging Biomarkers and Lifestyle Flagship Study of Ageing

(AUSTRAĽIAN ADNI)

July 2013 UPDATE – Imaging
Christopher Rowe MD – Neuroimaging stream leader

October 2006

- 823 not imaged
- 288 imaged MRI + 11C-PiB
  - Funded by CSIRO

1.5 yrs

- 738 not imaged
- 230 imaged MRI + 11C-PiB
  - Funded by CSIRO

3 yrs

- 632 not imaged
- 172 imaged MRI and 11C-PiB
  - Funded by SIEF

4.5 yrs

- 390 not imaged
- 141 participants MRI and 11C-PiB
  - Funded by SIEF

Funded by CSIRO
- 225 imaged
  - MRI + 11C-PiB
  - Funded by CSIRO

Funded by SIEF
- 307 imaged
  - MRI and 11C-PiB
  - Funded by SIEF

Replacement MCI and sMC

- 172 imaged
  - MRI and 11C-PiB
  - Funded by SIEF

Funded by anon
- 390 not imaged
- 105 new participants Florbetaben
  - Funded by Bayer/Piramal

- 102 new participants AV-45
  - Funded anon

Women’s Healthy Aging Program

- 58 new participants AV-45
  - Funded by GE

- 92 participants AV-45
  - Funded by GE

October 2006

- 1112 recruited

June 2013

- 718 remain

- 278 new
3 year Data Release

221 subjects (HC, MCI, AD) with baseline PiB PET and MRI now with 3 year clinical data

- 1.5 and 3 year PiB PET in 173 with MRI in 148

www.adni.loni.ucla.edu

- Data and Samples
  - Access Data
540 research groups granted access to AIBL@LONI through ADNI website

Includes access granted to the following companies:
PiB neocortical SUVR

HC
1.40 ± 0.4
(n = 195)

MCI
1.91 ± 0.6
(n = 92)

AD
2.30 ± 0.4
(n = 79)

31%
68%
99%
Longitudinal PiB PET
6-year follow-up

Neocortical SUVR

Time (months)

73 yo HC female (ɛ3/ɛ3)

78 yo HC male (ɛ3/ɛ3)

74 yo HC female (ɛ3/ɛ3)
Changes in Aβ burden over time

**HC**
(n=152)

**MCI**
(n=36)

**AD**
(n=19)
Relation between baseline Aβ burden and rates of Aβ deposition

3-5 year follow-up

![Graph showing the relation between baseline Aβ burden and rates of Aβ deposition. The R² value is 0.23 (p<0.0001).]
Rate of Aβ deposition vs MMSE
3-5 year follow-up

Baseline MMSE

Rate of Aβ deposition

R² = 0.08 (p=0.0006)
The natural history of Aβ deposition in sporadic AD

Mean SUVR AD+ (2.33)

Mean SUVR HC- (1.17)

0.043 SUVR/yr (95%CI 0.037-0.049 SUVR/yr)

19.2 yr (95%CI 17-23 yrs)

12.0 yr (95%CI 10-15 yrs)
Relationship between “abnormality” and CDR of 1.0

- Aβ deposition
- Hippocampal volume
- Episodic memory
- Grey matter volume
- Non-memory

Biomarker magnitude

Abnormal

Normal

Time (years)

CDR 1.0

Cut-off

Non-demented
Demented
Risk of decline over 3 years: Positive vs negative amyloid scan

**HC**
- (n=183)
- NEGATIVE (n=130)
- 25% to MCI/AD
- POSITIVE (n=53)

**MCI**
- (n=87)
- NEGATIVE (n=27)
- 29% (8/27) to dementia
- POSITIVE (n=60)
- 77% (46/60) to AD

*Odds Ratio 4.8*

\[ p = 0.001 \]

*Odds Ratio 7*

\[ p < 0.001 \]

(OR increases to 14 if non-AD dementia removed)
MCI to **AD** over 3 years (n=87; 59% progressed)

<table>
<thead>
<tr>
<th>MCI positive for marker</th>
<th>Odds Ratio</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>HV</td>
<td>4</td>
<td>0.67</td>
<td>0.65</td>
</tr>
<tr>
<td>ApoE-ε4</td>
<td>5</td>
<td>0.74</td>
<td>0.66</td>
</tr>
<tr>
<td>CVLT&lt;-1.5</td>
<td>11</td>
<td>0.80</td>
<td>0.74</td>
</tr>
<tr>
<td>PiB</td>
<td>15</td>
<td>0.77</td>
<td>0.82</td>
</tr>
<tr>
<td>PiB+ε4</td>
<td>16</td>
<td>0.79</td>
<td>0.81</td>
</tr>
<tr>
<td>PiB+HV</td>
<td>44</td>
<td>0.83</td>
<td>0.90</td>
</tr>
<tr>
<td>PiB+CVLT</td>
<td>na</td>
<td>0.86</td>
<td>1.00</td>
</tr>
</tbody>
</table>
Predictive value of low (<1.4) vs intermediate vs high (>1.9) PiB binding

- HC (n = 183)
- MCI (n = 87)
- AD (n = 79)

Neocortical SUVR

PPV 17%
PPV 35%
PPV 44%
PPV 82%
CVLT-II Delayed Recall over 36 mths

Healthy Older Persons

Baseline

18 months

36 months

PiB -ve

n = 122, SUVR = 1.16

PiB +ve

n = 55, SUVR = 1.95

Mild Cognitive Impairment

Baseline

18 months

36 months

PiB -ve

n = 16, SUVR = 1.18

PiB +ve

n = 32, SUVR = 2.21

Healthy Older Persons

Mild Cognitive Impairment
Initial Aβ burden is a better predictor of progression from MCI to AD than the rate of Aβ accumulation.

\[ OR = 5.4 \]

\[ OR = 15 \]
The image illustrates a graph depicting the progression of Alzheimer's disease from preclinical to clinical stages. The horizontal axis represents the clinical disease stage, ranging from Cognitively Normal to Dementia, with intermediate stages such as MCI. The vertical axis represents the biomarker magnitude, ranging from Normal to Abnormal.

The graph shows a yellow box labeled "Preclinical Stage" with three sub-stages: 1, 2, and 3, each corresponding to different biomarker changes. The sub-stages are marked with time frames: 1-3 years, 5-8 years, and 9-12 years, respectively.

Key biomarkers include:
- Aβ Amyloid
- Neuronal Injury
- Cognitive Symptoms

Cut-points are indicated on the graph, demarcating normal and abnormal biomarker levels. The diagonal lines represent the progression from preclinical to clinical stages, with different markers indicating the onset of disease stages.

The graph highlights the critical transition from preclinical to clinical stages, emphasizing the importance of early detection and intervention.
HC to MCI or AD over 3 years  
(n=183; 13% progressed)

<table>
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<tr>
<th>HC positive for marker</th>
<th>OR</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>HV</td>
<td>46</td>
<td>2.2</td>
<td>0.20</td>
</tr>
<tr>
<td>e4</td>
<td>74</td>
<td>2.1</td>
<td>0.18</td>
</tr>
<tr>
<td>EM&lt;0.5</td>
<td>22</td>
<td>4.2</td>
<td>0.32</td>
</tr>
<tr>
<td>PiB</td>
<td>53</td>
<td>4.8</td>
<td>0.26</td>
</tr>
<tr>
<td>PiB+e4</td>
<td>34</td>
<td>5.7</td>
<td>0.29</td>
</tr>
<tr>
<td>PiB+HV</td>
<td>17</td>
<td>10</td>
<td>0.47</td>
</tr>
<tr>
<td>PiB+EM</td>
<td>10</td>
<td>16</td>
<td>0.50</td>
</tr>
</tbody>
</table>

AIBL composite EM Z-score <-1 (n=49), OR 11, PPV 35%, NPV 96% without correction for age or education.
Future Directions for AIBL Imaging

• Further refine prognostic value and comparative effectiveness of imaging biomarkers

• Replace $^{11}\text{C}-\text{PiB}$ with $^{18}\text{F-NAV4694}$

• Add Tau imaging

• Create a new pool of amyloid scan positive HC and MCI for early intervention trials

• Use AIBL infrastructure to support the A4 and DIAN therapy trials
Tau, Aβ and glucose metabolism in Alzheimer's disease patient

$[^{18}F]$THK-5105  $[^{11}C]$PiB  $[^{18}F]$FDG

SUVR

0  1  2

0  1.5  3

0  0.6  1.2
Acknowledgements and thanks

AIBL is a large collaborative study and a complete list of contributors and the management committee can be found at www.aibl.csiro.au

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We thank all who took part in the study.