The Australian Imaging Biomarkers and Lifestyle Flagship Study of Ageing

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Consultant Neurologist, National Ageing Research Institute, NARI.
Sites

Major Sponsor

PERTH

MELBOURNE
18 month follow-up complete

- 25% of MCI progressed to AD
- Large shifts between NMC and SMC
- 25% AD, 23% MCI, 8% HC lost
Addressing population aging and Alzheimer’s disease through the Australian Imaging Biomarkers and Lifestyle study: Collaboration with the Alzheimer’s Disease Neuroimaging Initiative

Kathryn A. Ellis\textsuperscript{a,b,c,\#}, Christopher C. Rowe\textsuperscript{d}, Victor L. Villemagne\textsuperscript{b,d}, Ralph N. Martins\textsuperscript{e}, Colin L. Masters\textsuperscript{b}, Olivier Salvado\textsuperscript{e,g}, Cassandra Szoeke\textsuperscript{g}, David Ames\textsuperscript{a,c}; and the AIBL research group\textsuperscript{h}

Organizational Structure of AIBL

Management committee
D. Ames (Chair, study leader), L. Bevege, K. Ellis (study manager)
R. Martins, C. Masters, A. Milner, C. Rowe, P. Stasinios, C. Szoeke

Neuroimaging stream
C. Rowe (Chair), V. Villemagne, O. Salvado, N. Lenzo

Clinical and cognitive stream
K. Ellis (Chair), P. Maruff, G. Savage

Biomarkers stream
C. Masters, R. Martins (Joint Chairs), A. Bush, B. Wilson

Lifestyle stream
R. Martins (Chair), C. Szoeke
Study Databases

Clinical Cognitive
- PET-PiB
  - Amyloid beta load

Biomarkers
- T1W
  - Anatomy

Genomic
- T2W
  - CSF and structures

Lifestyle Intervention
- SWI
  - Venous tree

Imaging
- FLAIR
  - White matter lesions
- DWI
  - White matter connection
CLINICAL PROGRAM

- Clinical Research – Kathryn Ellis
- Leadership Group – G. Savage, P. Maruff, D. Ames
- Other – C. Szoeke, N. Lautenschlager, D. Darby
- Clinical Classifications – David Ames

BIOMARKERS PROGRAM

- Leadership Group - Colin Masters, Ralph Martins
- --A. Bush, N. Faux
  - Other - B. Wilson, J. Doecke, K. Taddei, S. Laws

IMAGING PROGRAM

- Leadership Group - Chris Rowe
- --V. Villamagne, O. Salvado, N. Lenzo
  - Others - S. Ourselin

LIFESTYLE/INTERVENTION PROGRAM

- Leadership Group - Cassandra Szoeke, Ralph Martins
- --M. Riley, K. Ellis
  - Others – N. Lautenschlager
Early Detection

HC
SMC
NMC

MCI
PRE-MCI

AD
EARLY DIAGNOSIS

INTERVENTION
Early Detection

HC
- Clinical
- Biomarkers
- Imaging

MCI
- Clinical
- Biomarkers
- Imaging

AD
- Clinical
- Biomarkers
- Imaging
- Tissue
Clinical

HC – Truly HC?

n=704

Two classes

59% performed significantly better on 4 tests than the lower 41%

Independent of APO E status.

• Manuscript in preparation – ICAD abstract
Baseline demographics
(n=288)

<table>
<thead>
<tr>
<th></th>
<th>HC*</th>
<th>MCI</th>
<th>AD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>73.6 ± 7.6</td>
<td>77.4 ± 7.5*</td>
<td>74.0 ± 8.7</td>
</tr>
<tr>
<td>MMSE</td>
<td>28.8 ± 1.2</td>
<td>27.1 ± 2.3*</td>
<td>20.5 ± 4.9*</td>
</tr>
<tr>
<td>%ApoE ε4</td>
<td>43%</td>
<td>54%</td>
<td>71%*</td>
</tr>
</tbody>
</table>

*enriched with ApoE ε4

*Significantly different from HC, p <0.05
Age effect on AD, Plaques and PiB+

Prevalence of plaques in HC

(Davies, 1988, n=110)
(Braak, 1996, n=551)
(Sugihara, 1995, n=123)

~15 yrs

Prevalence of PiB+ve PET in HC

Prevalence of AD
(Tobias, 2008)
Influence of ApoE ε4 status on PiB+ in HC

- **ApoE ε4-ve**: 21% PiB+ve, 79% PiB-ve
- **ApoE ε4+ve**: 49% PiB+ve, 51% PiB-ve
Imaging: CHANGE in memory vs baseline PiB

- **PiB+ve only**

18 month data

- **HC**
  \[ r = -0.32 \ (p = 0.02) \]

- **MCI**
  n.s.

- **AD**
  n.s.
Change in memory vs Baseline PiB: Decline >0.5 SD in HC with a 3 year follow-up (n=60)

100%

15% decliners

HC-

58% decliners*

HC+

* Significantly different from HC-, p <0.05
**AIBL Plus**  
**Prediction of Conversion MCI to AD**  
*38 months*  
*(n=65)*

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Accuracy</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neocortical PiB+ve (SUVR &gt;1.5)</td>
<td>0.83</td>
<td>0.95 (CI 0.73-1.00)</td>
</tr>
<tr>
<td>ApoE ε4+</td>
<td>0.77</td>
<td>0.83 (CI 0.60-0.94)</td>
</tr>
<tr>
<td>Composite Memory (&lt;-2.0 sd)</td>
<td>0.77</td>
<td>0.79 (CI 0.59-0.91)</td>
</tr>
<tr>
<td>Hippocampal atrophy (&lt;0.76)</td>
<td>0.74</td>
<td>0.79 (CI 0.54-0.93)</td>
</tr>
<tr>
<td>Plasma Aβ_{42}/Aβ_{40} (&lt;0.17)</td>
<td>0.57</td>
<td>0.69 (CI 0.39-0.90)</td>
</tr>
</tbody>
</table>

NB/ Pilot data analysis
Over Three Years

- 25% of PiB+ HC develop MCI/AD (c.f. 3% of PiB-)

- 71% PiB+ MCI develop AD (c.f. 5% of PiB- but 20% develop other dementias)

- Combination of biomarkers provides better prediction (e.g. if PiB+ and hippocampal atrophy is present the 2 year progression from MCI to AD is 95%)
AIBL – the next 3 years

**Clinical**
- Complete 3 and then 4.5 year follow-up

**enrich**
- Add 200 new subjective memory complainers and MCI

**enrich + midlife risk**
- Add 200 women from a cohort previously assessed in 2002 and 2004

**Imaging**
- Amyloid and MRI imaging in all participants

**Lifestyle Intervention**
- “AIBL Active” – exercise intervention in 150 HC/MCI
AIBL study team

David Ames
Jennifer Ames
Manoj Agarwal
David Baxendale
Kiara Bechta-Metti
Justin Bedo
Carli Bevage
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Pierrick Bourgeat
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Kathleen Crowley
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Victor Villemagne
Stacey Walker
Vanessa Ward
Bill Wilson
Michael Woodward
Olga Yastrubetskaya
Advance notice of Global AD Cohort Congress

Australia, date to be fixed, 2012