The Australian Imaging Biomarkers and Lifestyle Flagship Study of Ageing

(AUSTRAILIAN ADNI)

July 2013 UPDATE – Biomarkers
Samantha Burnham
Fractions and Analytes

serum/plasma

buffy coat

red blood cells

Proteins

Steroids/Hormones

Metalomics

Lipids

Platelets

Exosomes

DNA & RNA

White Blood Cells

Red Blood Cells
## Fractions and Analytes

<table>
<thead>
<tr>
<th>Blood tube type</th>
<th>Fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Serum</td>
<td>Serum</td>
</tr>
<tr>
<td>2. Whole EDTA Blood</td>
<td>WB</td>
</tr>
<tr>
<td>3. EDTA (PGE1)</td>
<td>Plasma</td>
</tr>
<tr>
<td>4. Li/Hep</td>
<td>Plasma</td>
</tr>
<tr>
<td>5. EDTA (PGE1)</td>
<td>Platelet</td>
</tr>
<tr>
<td>6. Li/Hep</td>
<td>Platelet</td>
</tr>
<tr>
<td>7. EDTA (PGE1)</td>
<td>WBC</td>
</tr>
<tr>
<td>8. Li/Hep</td>
<td>WBC</td>
</tr>
<tr>
<td>9. EDTA (PGE1)</td>
<td>RBC</td>
</tr>
<tr>
<td>10. Li/Hep</td>
<td>RBC</td>
</tr>
<tr>
<td>11. PaxGene tube</td>
<td>RNA</td>
</tr>
</tbody>
</table>
Aims and Objectives

Blood-Based Protein Biomarkers for Diagnosis of Alzheimer Disease

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Original Article

Molecular Psychiatry, (30 April 2013) | doi:10.1038/mp.2013.40

A blood-based predictor for neocortical Aβ burden in Alzheimer’s disease: results from the AIBL study

Transition Trajectories
Longitudinal Models

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)
Longitudinal Models
Summary

Validation is imperative
THE AUSTRALIAN IMAGING, BIOMARKERS AND LIFESTYLE STUDY OF AGEING (AIBL): LIFESTYLE PROGRAMME

Stephanie Rainey-Smith, PhD
Edith Cowan University, Western Australia
Lifestyle factors in Alzheimer’s Disease

A healthy lifestyle is associated with reduced cognitive decline and AD risk

Risk Factors
- Genetic Risk Factors
- Socio-Economic Status Factors
- Life Habits (e.g. smoking), hypertension, occupation, depression, head trauma

Protective Factors
- High Education
- Physical Activity & Diet
- Rich social networks
- Mental Activities

Protective factors at mid-life and late-life
Aβ40 is associated with cognitive function, body fat and physical fitness in healthy older adults

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Effect of Physical Activity on Cognitive Function in Alzheimer Disease

C. Fabre¹
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C. Préfaut³

Im uprovement of Cognitive Function by Mental and/or Individualized Aerobic Training in Healthy Elderly Subjects

Leisure-time physical activity at midlife and the risk of dementia and Alzheimer's disease

Lifestyle factors and risk of dementia: Dubbo Study of the elderly

Exercise is Associated with Reduced Risk for Incident Dementia Among Persons 65 Years of Age and Older

Capitalizing on cortical plasticity: influence of physical activity on cognition and brain function

Arthur F. Kramer and Kirk E. Erickson

A Prospective Study of Physical Activity and Cognitive Decline in Elderly Women

Women Who Walk

Kristine Yaffe, MD; Deborah Barnes, MPH; Michael Nevitt, PhD; Li-Yung Lui, MA; Kenneth Covinsky, MD

 ORIGINAL INVESTIGATION
AIBL Lifestyle Programme

Led by Professor Ralph Martins

**Aim:** Identification of lifestyle and dietary modifications which prevent or delay onset of AD
Dietary data
Methods

• CSIRO FFQ (online)
• Cancer Council of Victoria (CCV) FFQ
  • Previously validated in multiple epidemiological studies *(Keogh et al., 2010)*
  • Quantifies intake of 74 foods and beverages
  • Data can also be used to examine dietary patterns
Dietary Pattern Analysis

- **Mediterranean diet (MeDi)** - ‘a priori’ method
  - Includes high intake of fruit and vegetables, fish, legumes, cereals and unsaturated fatty acids
  - Low intake of dairy, meat and poultry and saturated fatty acids
  - Regular but moderate alcohol intake

- **Prudent diet** - ‘a posteriori’ (factor analysis)
  - Heavily loaded with vegetables, fruits and nuts

- **Western diet** - ‘a posteriori’ (factor analysis)
  - Heavily loaded with red and processed meats, high fat dairy products, chips, refined grains, potatoes, sweets and condiments.
Higher Adherence to MeDi in Healthy Controls compared to MCI and AD Groups

Mean ± SEM. *p<0.05; ***p<0.001; multinomial logistic regression models. Controlling for age, gender, education, APOE genotype, country of birth, BMI, total caloric intake, smoking status, history of hypertension, angina, stroke, diabetes and heart attack.

Higher MeDi and prudent diet adherence is associated with improved cognitive performance at baseline

<table>
<thead>
<tr>
<th>Cognitive Domain</th>
<th>MeDi Score</th>
<th>Prudent score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted</td>
<td>Adjusted</td>
</tr>
<tr>
<td>Verbal Memory</td>
<td>0.143**</td>
<td>0.138*</td>
</tr>
<tr>
<td>Visual Memory</td>
<td>0.077</td>
<td>0.081</td>
</tr>
<tr>
<td>Executive Function</td>
<td>0.135*</td>
<td>0.127*</td>
</tr>
<tr>
<td>Language</td>
<td>0.139*</td>
<td>0.128*</td>
</tr>
<tr>
<td>Visuospatial Function</td>
<td>0.131*</td>
<td>0.135*</td>
</tr>
</tbody>
</table>

Linear regression analysis; standardised β values shown. p < 0.01 = statistical significance. Fully adjusted model includes age, gender, YOE, APOE ε4 allele carriage, country of birth, BMI, energy intake, past/current smoking status, and history of hypertension, angina, stroke, heart attack and diabetes as covariates.

From: Gardener, Rainey-Smith et al 2013, Neurology (under review).
Higher western diet adherence at baseline is associated with greater cognitive decline at 36 months

- Global cognitive function (MMSE score)
- Visuospatial functioning and memory (RCFT, 3 min delay)
- Language, attention, fluent productivity and executive function (Fruit and furniture total and switching)

Linear regression analysis; standardised β values; p < 0.01 = statistical significance. Fully adjusted model includes age, gender, YOE, APOE ε4 allele carriage, country of birth, BMI, energy intake, past/current smoking status, and history of hypertension, angina, stroke, heart attack and diabetes as covariates.

From: Gardener, Rainey-Smith et al 2013, Neurology (under review).
Linear models show association between western dietary pattern and change in clinical classification

• Higher western diet adherence at baseline $\rightarrow \uparrow$ number of transitions from HC to MCI or AD at 36 months ($p < 0.001$).

• When analysis was stratified by APOE ε4 allele carriage, association was seen only in non APOE ε4 allele carriers.

From: Gardener, Rainey-Smith et al 2013, Neurology (under review).
Physical activity data
Physical Activity and AD

• Physical activity has previously been associated with:
  – Reduced cognitive decline and AD risk
  – Enhanced cognitive functioning

• Most mechanistic studies have been animal studies

• AIBL array of biomarkers and comprehensive neuropsychological battery
  – Potential to investigate association of physical activity with a number of AD-related factors in one cohort.
Methods

• **International physical activity questionnaire**
  – Answers used to calculated metabolic equivalent score (METs·min/wk⁻¹)

• **Actigraph**
  – Total counts (volume of activity)
  – Peak counts (intensity of activity)

• To date all analyses have been on cognitively healthy controls only
Cross-sectional analyses

Peak counts and cognitive function

Raw and adjusted (for age, gender and YOE) of cognitive test score means (+ standard error) for each actigraphy intensity (peak count) tertile. \(^1\)RCFT, Rey figure complex test.

*Brown et al (2012), Translational Psychiatry,*
Cross-sectional analyses

Physical activity (IPAQ) and PiB SUVR

Adjusted means ± standard error (corrected for age, gender and years of education) of PiB SUVR for each self-report IPAQ tertile; after stratification by APOE ε4 allele carriage.

From: Brown et al 2012, Molecular Psychiatry.
Cross-sectional analyses

Physical activity (IPAQ) and blood biomarkers

Adjusted means ± standard error (corrected for age and gender) of blood biomarkers across each self-report IPAQ tertile

From: Brown et al 2012, Molecular Psychiatry.
Acknowledgements and Thanks

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