The Tasmanian Healthy Brain Project

Ageing is no barrier for engagement in university education: A potential intervention in middle to later life to reduce risk of dementia

Professor James Vickers
Modifiable Risk Factors for Dementia

• Approximately a third of Alzheimer’s disease cases worldwide can be attributed to seven modifiable risk factors (Population Attributable Risk (PAR), Norton et al, 2014)
  • Low educational attainment (PAR 19%)
  • Smoking (PAR 14%)
  • Physical inactivity (PAR 13%)
  • Depression (PAR 8%)
  • Midlife hypertension (PAR 5%)
  • Diabetes (PAR 3%)
  • Midlife obesity (PAR 2%)
Protective Effect of Early Life Education: The ECLipSE Study (Brayne et al. 2010)

- Epidemiological Clinicopathological Studies in Europe
- Harmonised three longitudinal studies
- 872 brain donors, 56% demented at death
- Longer years in education (Yrs 1-12) = reduced dementia risk
- Dose-related
- **BUT**, education itself had no effect on brain pathology
- Education = greater capacity to resist brain pathology before symptoms appear - ‘Cognitive Reserve’ or ‘Neural Resilience’
The Tasmanian Healthy Brain Project

Can tertiary education later in life protect the brain from ageing-related cognitive decline and dementia in later life?
Commenced in 2010, 520 participants
Age at recruitment: 50-79 years
Annual assessments to year 4, then biennially
Blood/saliva collected (genetic studies)
Skin samples (adult stem cells - neurons)
Exclusion criteria at time of recruitment:
- Dementia
- MS
- Previous significant TBI requiring hospitalisation
- Epilepsy
- History of cerebrovascular complications
- Poorly controlled diabetes
- Other significant neurological disorders
- COPD
- Heart disease
- Sensory loss (visual or hearing)

**SCREENING MEASURES**
- Medical Health Status questionnaire

**COGNITIVE RESERVE MEASURES**
- Premorbid cognitive reserve
  - WTAR (Wechsler Test of Adult Reading)
  - LEQ (Lifetime Experience Questionnaire)
- Current cognitive reserve
  - WAIS-III-SF1 (WAIS-III, short-form)
  - WRAT4-PMV (Wide Range Achievement Test 4th edition, Progress Monitoring Version)

**OUTCOME MEASURES**

**Cognitive/Neuropsychological**

- **Global**
  - DRS-2 (Mattis Dementia Rating Scale, 2nd edition)

- **Memory**
  - PAL (Paired Associates Learning Test, CANTAB)
  - RAVLT (Rey Auditory Verbal Learning Test)
  - LM (Logical Memory Test, WMS-III)
  - RCFT (Rey Complex Figure Test)

- **Working memory**
  - SSP (Spatial Span test, CANTAB)
  - DSP (Digit Span test, WAIS-III)
  - SWM (Spatial Working Memory test, CANTAB)
  - LNS (Letter-Number Sequencing test, WAIS-III)

- **Language**
  - VOC (Vocabulary test, WAIS-III)
  - COM (Comprehension test, WAIS-III)
  - BNT (Boston Naming Test)

- **Executive function**
  - COWAT (Controlled Oral Word Association Test)
  - RVP (Rapid Visual Processing test, CANTAB)
  - MTS (Match to Sample Visual Search test, CANTAB)
Baseline - APOE/BDNF and Memory

- 407 participants
- Avg age – 62.2 years, SD 6.8
- Apolipoprotein E (APOE) – major risk factor gene for Alzheimer’s disease
- Brain Derived Neurotrophic Factor (BDNF) linked to neuron health and plasticity
- No individual effects of BDNF or APOE polymorphisms on memory function at baseline
- Significant interaction between APOE and BDNF genotype in declarative memory function

David Ward and Mathew Summers
Most ‘at risk’ group?
BDNF genotype, Cognitive Reserve and Executive Function

David Ward and Mathew Summers
33% of variance linked to Grade Point Average (GPA) associated with 3 main factors:
• Intelligence
• Internal motivation
• Conscientiousness
THBP - Predictors of Academic Success

- Cognitive measures
- Sex
- Psychosocial factors (social networks, depression, anxiety)
- Lifetime Experience Questionnaire
- Brain gene polymorphisms (BDNF, APOE, KIBRA, COMT)

<table>
<thead>
<tr>
<th>Cognitive Tests</th>
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<tbody>
<tr>
<td>WAIS full-scale IQ</td>
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<tr>
<td>Working memory</td>
</tr>
<tr>
<td>Digit span</td>
</tr>
<tr>
<td>Letter-number sequencing</td>
</tr>
<tr>
<td>SWM between errors</td>
</tr>
<tr>
<td>SSP length</td>
</tr>
<tr>
<td>Episodic memory</td>
</tr>
<tr>
<td>RAVLT 1-5 total</td>
</tr>
<tr>
<td>LM I immediate recall total</td>
</tr>
<tr>
<td>LM II delayed recall total</td>
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<tr>
<td>PAL first trial memory score</td>
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<tr>
<td>Executive function</td>
</tr>
<tr>
<td>Stroop trial C</td>
</tr>
<tr>
<td>RVP A'</td>
</tr>
<tr>
<td>TMT trial B</td>
</tr>
<tr>
<td>Language processing</td>
</tr>
<tr>
<td>WAIS vocabulary</td>
</tr>
<tr>
<td>WAIS comprehension</td>
</tr>
<tr>
<td>Boston naming test</td>
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## THBP - Predictors of Academic Success

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
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<tbody>
<tr>
<td>Age</td>
<td>334</td>
<td>59.6</td>
<td>6.6</td>
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<tr>
<td>Gender (male/female)</td>
<td>334</td>
<td>29/71 %</td>
<td></td>
</tr>
<tr>
<td>Equivalent full time study load</td>
<td>334</td>
<td>50.9%</td>
<td>33.7</td>
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<tr>
<td>Prior education</td>
<td>334</td>
<td>14.1</td>
<td>2.8</td>
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<tr>
<td>Grade Point Average</td>
<td>334</td>
<td>5.6</td>
<td>1.0</td>
</tr>
</tbody>
</table>
No significant relationship between age and GPA was identified in either males or females

Abbie-Rose Imlach, David Ward and Kim Stuart
All predictor variables (cognitive, psychosocial, genetic, and life experience) entered into a multiple linear regression model.

- Language processing
- Episodic memory
- LEQ midlife nonspecific lifetime experiences

Account for 16.7% of variance in GPA

<table>
<thead>
<tr>
<th>Predictor</th>
<th>B</th>
<th>S.E</th>
<th>β</th>
<th>t</th>
<th>P.value</th>
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<tbody>
<tr>
<td>LEQ midlife nonspecific</td>
<td>.035</td>
<td>.01</td>
<td>.20</td>
<td>3.59</td>
<td>&lt; .001</td>
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<tr>
<td>Language processing</td>
<td>.285</td>
<td>.06</td>
<td>.24</td>
<td>4.33</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Episodic Memory</td>
<td>.175</td>
<td>.06</td>
<td>.18</td>
<td>3.36</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

Summary of regression analysis for final model (N = 331)
Effect of Intervention over Time

Language Capacity - composite measure of z-scores:
- Vocabulary (WAIS-III)
- Comprehension (WAIS-III)
- Boston Naming Test

Language capacity linked to resistance to dementia

Multiple group latent growth curve modelling
Academic Load and Cognitive Function

- High education load
- Medium education load
- Low education load
- No education

Mean estimated language processing (Z score)

Baseline, 12-month, 24-month
Academic Load and Cognitive Function

BDNF Val homozygotes

- High education load
- Medium education load
- Low education load
- No education

BDNF Met carriers

Mean estimated language processing (Z score)

Baseline | 12-month | 24-month

David Ward
Predictors of academic success in older adults
~ 17% of variance
• Language processing
• Lifetime history of engagement in mentally stimulating activities
• Episodic memory

Age and sex did not influence GPA performance

APOE and BDNF genotype interacted to predict episodic memory performance at baseline

BDNF genotype moderates how cognitive reserve affects cognitive function (executive function)

Intervention leads to improvement in language processing
~ Mainly in BDNF Met carriers
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