Tasmanian Healthy Brain Project

An Introduction to the Project

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And our wonderful research assistants!
Dementia Demographics

- In 2011 ~ 298,000 Australians suffered dementia (1.3%)
- By 2050 ~ 900,000 Australians will have dementia (2.8%)
- 2009-10 ~ $4.9 billion of health & aged care budget spent on people with dementia
- By 2060 ~ $83 billion of health & aged care budget on dementia
- Delaying AD onset by 5 months = $6.6 billion saved in health costs by 2040;
- Delaying AD onset by 5 years = $67.5 billion saved in health costs by 2040.
Alzheimer’s Dementia

Alzheimer’s Dementia (AD):

- Cause = unknown
- Treatment = none
- Options?
  1. Identify a cause to develop a treatment
  2. Identify interventions (pharmacological & non-pharmacological) that delay AD onset

Risk factors for AD:

- Age (*single biggest risk factor*)
- Genetic factors – Down syndrome, Apolipoprotein E ε4 gene
- Family history
- Vascular risk factors, head trauma, depression – *may be associated with increased risk*

Risk factors for Vascular Dementia:

- Older age and stroke
Protective Factors

- Potential protective factors against dementia:
  - Cardiovascular health
  - Physical activity
  - Education – *higher level of education = lower risk*
  - Social engagement – *more socially active = lower the risk*
  - Active cognitive engagement – *more mentally active = lower the risk*
Cognitive Reserve Hypothesis

- Age-related decline in cognitive functions
- Aging is associated with pathological changes to the brain
- Considerable inter-individual variability across individuals
- This inter-individual variability may reflect variability in Cognitive Reserve (CR)
- CR Hypothesis: A person with higher CR = more pathology can develop before symptoms become obvious
- Stern (2002, 2009) refers to two components of CR – active and passive
Passive Reserve

**Passive (Brain) Reserve Capacity**

- Individual differences in the brain (e.g., brain size, synaptic density) enabling some to cope better than others with brain damage.
- Dementia occurs when the threshold for damage to neurons surpasses the threshold for clinical symptoms.

![Diagram showing brain reserve capacity and clinical severity](image)
Active Reserve

**Active (Cognitive) Reserve**

- Capacity for the brain to actively compensate for brain damage by using pre-existing cognitive processes or compensatory mechanisms
- Stern’s (2009) hypothetical model – inter-individual CR differences account for inter-individual differences in dementia onset despite same neuropathology load.
Measures of Reserve

Passive (Brain) Reserve:
- Anatomic measures
  - Brain volume
  - Head circumference
  - Synaptic count / dendritic branching

Active (Cognitive) Reserve:
- Lifetime experience
  - Socioeconomic status (income, occupational attainment)
  - Educational attainment
  - Leisure activity
- Literacy
- IQ
- Education
A meta-analysis indicated a protective effect (OR = 0.46) of education in incident dementia (Valenzuela & Sachdev, 2006)

Longitudinal studies indicate education exerts a mediating effect on risk for AD (Bennett et al., 2003)

Population based studies indicate those with a clinical diagnoses of AD have 2-3 years less formal education (Roe et al., 2007)

Education and occupation reduce likelihood of adults with MCI converting to AD (Garibotto et al., 2008)

The effect of educational attainment may be mediated by other factors:
- Academic performance
- Social engagement
- Frequent cognitive activity
Cognitive Reserve

- Fritsch et al (2002) $n = 482$ possible or probable AD
- Tracked MMSE score over time against educational attainment (CR)
Aims

- To examine whether University education in older adults modifies age-related cognitive decline.

- To determine the effect of later-life university education, increased socialisation, lifetime mental activity, mood state, and quality of life on age-related cognitive decline.

- To determine the role of genetic risk factors for AD in mediating the influence of late-life university education on age-related cognitive decline.

- To ascertain if increasing the cognitive reserve of older adults results in a significantly decreased risk, or delayed onset, of neurodegenerative diseases such as AD.
Hypotheses

- Late-life university education in older adults results in a measurable increase in CR in these adults
- Increased CR in older adults is associated with a decreased risk for AD and MCI
- Increased CR in older adults is associated with a reduction in age-related cognitive decline
- Genetic risk factors for AD mediate the relationship between increased CR and age-related cognitive decline
Approach

- Mixed group longitudinal study
- Initial duration 5 years with aim to extend to 10-20 years duration
- 2 main groups:
  - **Control group** - Healthy adults aged 50-79 years who do not engage in any further university education
  - **Experimental group** - Healthy adults 50-79 years of age who undertake a minimum of 12 months of university level education (part-time or full-time, undergraduate or postgraduate). Participants grouped according to the load of study completed:
    - Group 1: 25%-100% EFT
    - Group 2: 101-200% EFT
    - Group 3: 201-300% EFT
Recruitment Parameters

- Up to 1000 participants to be recruited into full study
- Target: $n = 900$ experimental group and $n = 100$ control group
- Age at recruitment: 50-79 years
- Exclusion criteria at time of recruitment:
  - Dementia
  - MS
  - Previous significant TBI requiring hospitalisation
  - Epilepsy
  - History of cerebrovascular complications
  - Poorly controlled diabetes
  - Other neurological disorders (CP, spina bifida)
  - COPD
  - Heart disease
  - Sensory loss (visual or hearing)
Protocol

- Each participant will complete a comprehensive annual assessment of:
  - Neuropsychological/cognitive function
  - Psychological status
  - Quality of life
  - Social interaction
  - Medical health
Assessing CR

- Two separate approaches to assessing CR (Exploratory Factor Analyses)

1. **Premorbid CR:**
   a) WTAR – an estimate of premorbid full scale IQ
   b) LEQ – mental activity across 3 age bands

2. **Current CR:**
   a) Full scale IQ (WAIS-III)
   b) Reading, spelling, comprehension, & mathematical ability (WRAT4-PMV)
Test Battery

- Dementia symptoms (DRS-2)
- Premorbid IQ
- Medical health
- Current IQ
- Short term memory span (verbal and visual)
- Working memory capacity (verbal and visual)
- Learning and recall of new information (verbal and visual)
- Language processing
- Naming ability
- Verbal fluency
- Executive functions (selective attention, sustained attention, divided attention, information processing speed, decision making capacity, mental flexibility, impulse control)
- Symptoms of anxiety and depression
- Social networks
Sample as of 2013

- Recruitment of the sample commenced in 2011
- May 2013 ~ 500 adults have completed T1 assessment
- 80 awaiting T1 assessment
- Males = 162
- Females = 334
**Results**

- Exploratory factor analyses used to identify composite measures of premorbid CR and current CR

- Continuous entry - analyses are run at selected time points

- Preliminary statistics suggest that those undertaking the education intervention are experiencing an increase in cognitive reserve

- Detailed results from this intervention can be expected in the next 24-36 months
Future Directions

- Currently recruiting ~120+ new participants each year
- Genetic studies have commenced – ApoE, BDNF, COMT, KIBRA genes are being analysed from the entire sample
- Protocol paper published in 2013
- PhD projects:
  - Genetic determinants of Cognitive Reserve (David Ward)
  - Changes in neuropsychological function following late-life education (Megan Lenehan)
  - Environmental enrichment in an AD mouse model (Kim Stuart)
  - The effect of KIBRA polymorphism on verbal and visual episodic memory (Katherine Franks)