Cognitive Reserve: Developing a model of the social processes that influence age-related cognitive decline

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Outline

• What is Cognitive Reserve?
• Methodological Issues
• Cognitive Reserve and Noradrenaline
• Research plan and protocol
• Progress to date
• Potential impact
Pathology → Mismatch? → Clinical Manifestation

Reserve
What is this reserve?

Brain Reserve

Cognitive Reserve
Brain Reserve

‘Passive’ (Stern, 2009)

- Structural proxies such as:
  - Brain size
  - Brain volume
  - Neuronal count
  - Synaptic density
Cognitive Reserve

‘Active’ (Stern, 2009)

• Brain’s active attempt to cope with damage
• Pre-existing and compensatory processes
• Neural reserve
• Neural compensation
Cognitive Reserve Variables

- Educational attainment
- Occupational attainment
- Premorbid IQ
- Mentally stimulating activity
- Social engagement
Epidemiological Evidence

- Educational attainment
- Leisure activity participation
- Degree of social engagement
- Occupational complexity

- Risk of dementia
- Risk of AD
- Rate of age-related decline

e.g. Bezerra et al, 2012; Scarmeas et al, 2001; Stern et al, 1994; Yaffe et al, 2011
Pathology doesn’t always equal disease

A tale of two brains:
Both brains have the pathology but only individual died with dementia

e.g. Bennett et al, 2003; Bennett et al, 2006
Epidemiological Evidence

Stern, 2012, Lancet Neurology

e.g. Helzner et al, 2007; Scarmeas et al, 2006; Stern et al, 1999
Imaging Evidence

Resting regional cerebral blood flow (rCBF)

Statistical parametric map and its 3-dimensional brain rendering representation depicting areas of significant (some \(P<.001\), some \(P<.01\), and some \(P<.05\), as presented in Table 4) inverse correlations between cerebral blood flow and activities score in the Alzheimer group, controlling for age and Mini-Mental State Examination score.

Scarmeas et al, 2003, Arch Neurology
Measuring Cognitive Reserve

The Problem:

• Inconsistent use of several proxy indicators
  • Limits comparability
  • Raises concern about construct validity

• Possible confounding factors

A Possible Solution:

• Multiple Indicator Method (Jones et al, 2011)
Multiple Indicator Method: Advantages

- May avoid bias from non-reserve pathways
- May provide a more precise measure
- Single coefficient to summarise the relationship between reserve and function
Cognitive Reserve and Noradrenaline

Currently little understanding as to how protective effects associated with cognitive reserve occur. Robertson (2013) Noradrenaline hypothesis
Measuring Noradrenergic Function

- Pupillometry
  - Murphy et al (2011)

- Sustained Attention to Response Task (SART)
Project Outline

Cognitive Reserve: Multiple Indicator Model

Mental Stimulation
Occupation
Education
Premorbid IQ
Social Engagement

Noradrenaline

SART
Pupillometry

Age related cognitive performance

Cross-sectional data (Study 1)
Longitudinal data (Study 3)

Cross-sectional (Study 2)
Expected Outcomes

• Address methodological issues
• Contribute to standardisation of CR measurement
• Add to knowledge of the role of cognitive reserve in age related cognitive performance
• Increase understanding of the biological mechanisms underlying CR
Step 1
Systematic review of cognitive reserve indicators
Study 1

Aims
• Develop and test multiple indicator model
• Baseline measures
• Examine relationship between CR and age-related cognitive performance

Participants
• N = 200 healthy over 50s – NEIL Memory Research Unit

Measures
• Neuropsychological Measures
• Cognitive Measures
• Self-report questionnaires and scales – lifestyle factors
Cognitive Measures

• Literacy/dyslexia screen WRAT-3 Reading
• Premorbid IQ NART
• Overall function MMSE; MOCA
• Processing speed Colour Trails; CRT
• Attention SART; ACAD
• Working memory Letter number sequencing (WMS-III)
• Visual reasoning CAMCOG task
• Episodic memory/recall WMS-4 Logical Memory; FCSRT
• Recognition memory ACAD
• Executive function Verbal Fluency; Colour Trails
• Prospective memory TILDA task
• Self-rated memory
• Study partner report IQCODE
Cognitive Reserve Proxy Indicators

- Premorbid IQ **NART**
- Educational attainment **Years; Highest level completed**
- Occupation **Categorical occupation history**
- Mental stimulation **Scarmeas et al (2003) self-report scale**
- Social Engagement **Berkman Social Network Index**
Study 2

Aims
• Test Robertson (2013) Noradrenaline hypothesis

Participants
• Subset (N = 60) of participants from Study 1

Measures
• Pupillometry under a variety of conditions (resting; task)
• SART
• Cognitive function and CR measures collected during study 1
Study 3

Aims

• Longitudinal data – cognitive reserve and change in cognitive function over time

Participants

• All consenting participants from Study 1

Measures

• Subset of baseline assessment battery
• Follow up at least 1 year after baseline
Potential Impact

**Population by Age Group**

- **2050**
  - 0-19: 16%
  - 20-64: 27%
  - 65+: 27%

- **2000**
  - 0-19: 7%
  - 20-64: 39%
  - 65+: 54%

- **1950**
  - 0-19: 5%
  - 20-64: 54%
  - 65+: 44%

- **2.5 Billion**
  - 0-19: 51%
  - 20-64: 44%
  - 65+: 5%

- **6 Billion**
  - 0-19: 51%
  - 20-64: 44%
  - 65+: 5%

- **9 Billion**
  - 0-19: 51%
  - 20-64: 44%
  - 65+: 5%
Prevalence of Alzheimer’s disease in 2050

Scenario A: No advancements in treatment
Scenario B: Delaying disease onset
Scenario C: Delaying rate of progression
Scenario D: Delaying both disease onset and rate of disease progression

Potential Impact

• Implications for clinical diagnosis
• Development of non-pharmacological interventions
Professor Yaakov Stern

Wednesday 8th May
Academic Seminar 2pm
Public Seminar 6.30pm

www.tcd.ie/neuroscience/neil