Cognitive Reserve and Brain Health in Older Women: Implications for Future Research in WHI Sciences

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Outline

• What is cognitive reserve (CR) and why is it important?
• How is CR measured?
  • Methodological challenges
  • Conceptual issues
• Estimating CR in WHIMS participants
  • Analytic approaches
  • Construct validity
• Implications for future studies (including WHI follow-up)
What is cognitive reserve?

Bennett et al., (2012) *Annals of Neurology*

High reserve:
- Lots of neuropathology
- Good cognitive performance

Low reserve:
- Little neuropathology
- Poor cognitive performance
Why is cognitive reserve important?

- Higher reserve = tolerate more neuropathology
- CR is fluid and changes across entire lifespan
- Potential targets for interventions

Stern (2012) *Lancet Neurology*
Measuring cognitive reserve is challenging

• Reliant on both measure of performance and measure of neuropathology
• Traditional method: Proxy approach
  • e.g. years of education, occupational attainment
• Problems with proxy approach
  • Cohort and geographical differences
  • Static measurement

Quantitative approach to estimate cognitive reserve

- Variance decomposition method (Reed et al., 2009)
- Strengths
  - Quantitative model of CR
  - Individual-specific
- Limitations of prior work
  - Local clinical sample
  - Only quantified “memory reserve”
  - General reserve?

Reed et al. (2009) *Brain*
Estimating cognitive reserve in WHIMS

• Can we identify general and cognitive domain-specific cognitive reserve in WHIMS?
• Can we further establish the construct validity of this approach?

Featured Article

General and domain-specific cognitive reserve, mild cognitive impairment, and dementia risk in older women

Andrew J. Petkus\textsuperscript{a,}\textsuperscript{x}, Susan M. Resnick\textsuperscript{b}, Stephen R. Rapp\textsuperscript{c,d}, Mark A. Espeland\textsuperscript{e}, Margaret Gatz\textsuperscript{f}, Keith F. Widaman\textsuperscript{g}, Xinhui Wang\textsuperscript{a}, Diana Younan\textsuperscript{h}, Ramon Casanova\textsuperscript{e}, Helena Chui\textsuperscript{a}, Ryan T. Barnard\textsuperscript{e}, Sarah Gaussoin\textsuperscript{e}, Joseph S. Goveas\textsuperscript{i}, Kathleen M. Hayden\textsuperscript{d}, Victor W. Henderson\textsuperscript{j,k}, Bonnie C. Sachs\textsuperscript{d,l}, Santiago Saldana\textsuperscript{d}, Aladdin H. Shadyab\textsuperscript{m}, Sally A. Shumaker\textsuperscript{l}, Jiu-Chiuan Chen\textsuperscript{a,h}
Sample:

- N = 972 women from WHISCA and WHIMS MRI-1
- 78.1 years old at the time of the cognitive assessment
- Cognitively intact at time of MRI and cognitive assessment
- All-cause MCI and dementia status via WHIMS participation
  - Data available through June 2018
Measures

• Cognitive measures (WHISCA)
  • Attention
  • Verbal memory
  • Figural memory
  • Visuospatial ability
  • Attention/working memory

• Structural MRI (WHIMS MRI-1)
  • Hippocampal volume
  • Total brain volume
  • Small vessel ischemic disease (SVID)

• Covariates
  • Demographics (baseline age, education, ethnicity, employment, geographic region of residence, income)
  • Lifestyle (smoking, alcohol use, exercise, hormone treatment ever)
  • Clinical (cholesterol, hypertension, cardiovascular disease, diabetes)
Variance decomposition approach to quantify reserve

Memory Reserve

Brain Factors
- Total brain volume
- Hippocampal volume
- SVID
- Intracranial volume

Demo Factors
- Education
- Minority status
- Age

Error
- 15% of the variance

Higher memory reserve = performance better than what we would expect given the combination of brain and demographic factors
Is there a “g” cognitive reserve factor?
Domain-specific and general reserve were estimable

- General reserve explained a modest to moderate amount of variance within each domain
  - 20% attention
  - 47% figural memory

Comparative fit index = .97
RMSEA = .056
Tucker Lewis Index = .93
Higher reserve = lower risk of MCI

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Moderating effect of reserve on neuropathology

- Neuropathology measure: Alzheimer’s disease pattern similarity score (AD-PS) (Casanova et al., 2018)
  - Machine learning derived score of capturing AD-related grey matter atrophy
  - Higher score = greater AD-like pattern of brain tissue atrophy
- Aalen additive hazards model to examine the AD-PS x Reserve interaction
Good construct validity of reserve estimates

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All displayed CR x AD-PS interactions p < .05

- AD-PS score and all reserve variables were scaled with mean = 0 and SD = 1
- All models adjust for demographic variables, lifestyle factors, and clinical variables
Summary of findings

• General and domain-specific reserve were identifiable in WHIMS with acceptable model fit
  • General reserve explained a modest amount of variance

• Construct validity of analytic approach
  • Higher reserve was mostly associated with lower risk of MCI and dementia
  • Heterogeneity between domains and across outcomes
  • Reserve moderated the adverse effect of increased neuropathology (AD-PS) on risk of cognitive impairment
What does this mean and implications?

• How do important lifestyle and clinical factors impact reserve?
  • Emotional factors (anxiety and depression)
  • Diet and physical exercise
  • Sleep
• Reserve as an intervention outcome?
• Cognitive reserve in the oldest old?
• Can we apply this approach to study other types of reserve and resilience?
  • Physical functioning reserve
  • Emotional resilience
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