A Lifecourse Approach to Genetic Endowment and Cognitive Decline

Xuejie Ding

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The Puzzle

- Cognitive status decline with age, but some people experience faster decline than others (Stern, 2009)

- Educational attainment as cognitive reserve is related to better level of cognitive status
  - Improve problem solving, stress coping abilities
  - Improve effectiveness in using brain network

- Mixed evidence on education and rate of cognitive decline

- Education and cognitive ability has shared genetic bases (Okbay et al., 2016; Lee et al., in press)

- Current research seldom account for genetic markers
Research Questions

• How does the association between genetic endowment of education and rate of cognitive decline change with age among older adults (50+) in the US?

• After accounting for genetic endowments, what are the effects of sociodemographic and behavioral factors?
Three competing hypotheses

- Active reserve model:
  - Higher education, slower rate of decline (divergence)
- Passive reserve model:
  - Higher education has no effect on rate of cognitive decline (stable)
- Compensation model:
  - Higher education, faster rate of decline (Convergence)
Sample

• Health and Retirement Survey 1998-2012
  • a biennial, longitudinal survey of a nationally-representative sample of individuals and their spouses aged 50 and above.
  • Genetic information is collected in 2006 and 2008

• 5,005 European and non-Hispanic respondents with at least 4 cognitive interviews
DV – Cognitive Measure

- Episodic Memory (EM)
  - Encodes and retrieves personal experienced events occurred at specific time and place
  - Delayed word recall
- Working Memory (EM)
  - Remember and use memory while in the middle of an activity
  - Serial 7s subtraction test
- Mental status (MS)
  - Knowledge-related cognitive ability
  - Naming the date, month, year and day of the week, backwards counting from 20, object naming, and naming the current president and vice president of the U.S.
- Vocabulary (Vocab)
  - Define 5 words
- Global cognition (GC)
  - Average corrected percentage score: \((\text{score}/\text{maximum score}) \times 100\)
IV

- Polygenic score for education (Okbay et al., 2016), standardised
  - Inverse probability weight (Domingue et al., 2017)
- Years of schooling
- Gender, social interaction, health behavior, chronic diseases

- Analytical Strategy: Linear mixed models

\[
\text{Cognition}_{ij} = \beta_0 + \beta_1 \cdot \text{Age}_j + \beta_2 \cdot \text{PGSedu}_i + \\
\beta_3 \cdot \text{PGSedu}_i \cdot \text{Age}_j + \beta_4 \cdot X_{ij} + \beta_5 \cdot \\
X_{ij} \cdot \text{Age}_j + \mu_{ij} + \mu_{ij} \cdot \text{Age}_j + \epsilon_i
\]

PGS for individual $i$ are calculated as the sum of the allele counts $a_{ij}$ (0, 1, or 2) for each SNP $j = 1, \ldots, M$, weighted by association strength $p_j$:

Polygenic score $= \sum_{j=1}^{M} p_j a_{ij}$
Results
Results – Linear Mixed Models

- Higher education polygenic score is associated with better cognitive performance ($\beta$ Range from 0.08 – 2.44)
- PGS education on rate of cognitive decline varies across domains
  - Strength of association declines for EM, GC (Compensation);
  - Magnifies for MS (Active Reserve);
  - Remains constant for WM, and Vocab (Passive)
Results
Results

- Women performs better in GC, EM, Vocab, worse in WM, no difference in MS. Women also decline faster in GC, EM, WM.
- Years of schooling positively related to cognitive ability, but is associated with faster decline in EM, MS, and slower decline in WM.
- Social interaction: slower decline in GC, EM and MS.
- Smoking: faster decline in MS.
- Multi-morbidity in chronic diseases: faster decline in all measures.
Discussion

• Is the result due to insufficient control? (Keller, 2014)
• Limitations: floor and ceiling effect, mechanisms from a biological angle, other race and ethnicity.