Modeling the Transition from Cognitive Health to Dementia

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Overview

• Categorical versus continuous outcomes
• Influences across the spectrum from intact cognition to dementia
Data Source

Rush Memory and Aging Project
- Annual clinical evaluations and brain autopsy at death
- Began in 1997, ongoing
- >1350 completed baseline evaluations
  - Age 80.1 (7.5)
  - Education 14.4 (3.3)
  - Women, % 72.6
  - NCI, % 67.5
  - MCI, % 27.0
  - Dementia, % 5.5
- >200 incident dementia
- >275 brain autopsies
Data Source

Rush Religious Orders Study

• Annual clinical evaluations and brain autopsy at death
• Began in 1994, ongoing
• >1150 completed baseline evaluations
  
  Age 75.7 (7.5)
  Education 18.1 (3.4)
  Women, % 69.1
  NCI, % 68.7
  MCI, % 24.3
  Dementia, % 7.0

• > 250 incident dementia
• > 500 brain autopsies
Data Source

• Annual clinical evaluations
  -Battery of 17 cognitive performance tests
  -Clinical classification of MCI, dementia, and AD
• Blinding of clinical staff to previously collected data
Statistical Approach

- Logistic Markov model
  - treats outcomes as a transition between different stages
  - transition probability specified through polychotomous logistic regression
  - correlation of within-subjects measurements accounted for by random effects

- Mixed-effects model
  - rate of change in cognitive function over time is primary outcome
  - allowed rate of cognitive change to shift when MCI and AD were first diagnosed
Summary Measure of AD Pathology

• Uniform neuropathologic examination blinded to all clinical data
• AD pathology quantified in 5 brain regions (modified Bielschowsky silver stain)
• Raw counts of neuritic plaques, diffuse plaques, and neurofibrillary tangles converted to standard scores and averaged
Apolipoprotein E ε4 allele

- Association with cognitive loss before and after dementia onset
- Association with cognitive impairment mediated by AD pathology
Personality

• Neuroticism
• Conscientiousness
Social Engagement

• Frequency of social interaction
• Perceived connectedness
• Purpose in life
Conclusions

• Categorical vs continuous outcome
• No cognitive impairment – dementia spectrum
  - AD pathologic burden
  - APOE ε4 allele
  - Psychosocial variables
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