A Model for Ethnicity, Diseases of Aging, and Cognitive Impairment

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Overview

• Challenges in assessing cognitive impairment in ethnic minorities
• General model of determinants of cognitive test scores - Implications for cognitive impairment
• Empirical applications of model
  ▪ Separating age, education, and brain effects
  ▪ Deconstructing ethnicity effects
  ▪ Separating demographic and disease effects
Background

• Reasons to study ethnic minorities
  ▪ Practicality - Need for scientific knowledge of diseases affecting cognition in these large (and growing) populations
    • Can be done with homogenous groups
  ▪ Generality - Better understanding of general mechanisms of cognitive impairment that apply across older people of diverse backgrounds
    • Requires heterogeneity
Ethnicity and Cognition

- Well established finding that ethnic minorities have lower average performance on neuropsychological tests
- Cutpoints based upon Caucasian samples result in high false positive rates in minority populations
- Historical context of abuses of IQ testing in minority populations
- Raises important question about measurement bias when using cognitive tests with minority elders
Ethnicity, Cognitive Impairment and Aging

- Context of cognitive assessment in older patients
  - To identify and monitor cognitive impairment associated with diseases of aging
- Questions / Challenges
  - How do we measure cognitive changes of dementing illnesses in ethnically diverse groups?
  - How do non-disease correlates of ethnicity influence sensitivity of cognitive measures to disease effects?
Simple Model of Cognitive Test Performance

- Disease
- Ability
Psychometric Theory

• Definition of ability
  ▪ Capacity to successfully respond to test items
  ▪ Net result of all genetic and environmental influences
  ▪ Measured by scales composed of homogenous items
  ▪ In neuropsychology, domains of interest defined by relationships with brain structure and function
More Complete Simple Model of Cognitive Test Performance

- Disease
  - Ability
    - Item 1
    - Item 2
    - Item 3
    - Item 4
Expanded Model of Cognitive Test Performance

Environment  Disease  Genes

Ability

Item 1  Item 2  Item 3  Item 4
Expanded Model of Cognitive Test Performance

Environment → Disease → Genes → Ability → Item 1 → Item 2 → Item 3 → Item 4
Expanded Model of Cognitive Test Performance with Aging Effects

- Aging
  - Environment
  - Disease
  - Genes
  - Ability
    - Item 1
    - Item 2
    - Item 3
    - Item 4
Model of Ethnicity Effects on Cognitive Test Performance

Ethnicity

Aging

Environment

Disease

Genes

Ability

Item 1

Item 2

Item 3

Item 4

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Implications of Model

- Cognition is complexly determined
- Ethnicity effects are mediated by measurable variables
  - Some known
  - Others to be discovered
- Disease effects can be separated from non-disease influences on cognition
Questions Posed by Model

• Is cognition similarly structured in different ethnic groups?
• Are disease effects on cognition the same in different ethnic groups?
• Are pathways linking environment, genes, disease, and cognition the same in different ethnic groups?
Comparative Study of Determinants of Cognitive Test Performance

Ethnic Group 1

- Aging
- Environment
- Disease
- Genes
- Ability

Item 1 Item 2 Item 3 Item 4

Ethnic Group 2

- Aging
- Environment
- Disease
- Genes
- Ability

Item 1 Item 2 Item 3 Item 4

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Recruitment Plan

Community Screening
Full Range of Cognition

Clinic Referral
Presenting Cognitive Problems

Normal

Memory Impaired

Non-Memory Impaired

Clinical Exam & MRI

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Cognitive Assessment

- Spanish and English Neuropsychological Assessment Scales (SENAS)
  - New Scales
  - Neuropsychologically relevant domains
  - Psychometrically matched
    - English and Spanish
    - Domains within English and Spanish
Age, Education, and Brain Structure

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Age, Education, and Brain Structure
Age, Education, and Test Validity
MRI as Proxy for Disease

- MRI Variables
  - White Matter Hyperintensity Volume
  - Total Brain Matter Volume
  - Hippocampal Volume
Age, Education, and Test Validity

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## Sample* Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Age Mean (s.d.)</th>
<th>Education Mean (s.d.)</th>
<th>Gender % Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>White n = 83</td>
<td>76.8 (8.2)</td>
<td>14.2 (3.1)</td>
<td>51.8</td>
</tr>
<tr>
<td>Minority ** n = 113</td>
<td>72.9 (7.1)</td>
<td>9.4 (5.5)</td>
<td>69.0</td>
</tr>
</tbody>
</table>

* Community dwelling, Normal, MCI, Demented
** Hispanic - n = 69, Black - n = 38, Other - n = 6
MRI Effect Sizes and Age and Education Adjustment - Full Sample (n=196)
MRI Effect Sizes and Age and Education Adjustment - Minorities (n=113)
MRI Effect Sizes and Age and Education Adjustment - Whites (n=68)
Executive Function, MRI, Age & Education
Bivariate Effects (R-Squared)
Executive Function, MRI, & Education
Bivariate and Multivariate Effects (R-Squared)
Executive Function, MRI, Age & Education
Bivariate and Multivariate Effects (R-Squared)
Episodic Memory, MRI, Age & Education
Bivariate and Multivariate Effects (R-Squared)

Education 0.06 MRI 0.34 Age 0.00

Episodic Memory

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Age and Education Influences on MRI - Cognition Relationships

• It is possible to separate disease effects from extraneous influences
• MRI effects on cognition can obscured by demographic effects on test performance, especially when
  • Demographic relationship with test score is larger than relationship with disease
  • Substantial heterogeneity of demographic variable in population of interest
Demographic Influences on Cognition
## Sample Characteristics - Community Sample

<table>
<thead>
<tr>
<th></th>
<th>Age Mean (s.d.)</th>
<th>Education Mean (s.d.)</th>
<th>Gender % Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>White N = 272</td>
<td>73.3 (7.5)</td>
<td>14.2 (3.2)</td>
<td>60.6</td>
</tr>
<tr>
<td>Black N = 277</td>
<td>73.0 (7.3)</td>
<td>13.2 (3.0)</td>
<td>62.5</td>
</tr>
<tr>
<td>Hispanic N = 355</td>
<td>70.3 (7.1)</td>
<td>6.1 (4.7)</td>
<td>67.0</td>
</tr>
</tbody>
</table>
Background

- Average differences between Blacks and Whites can be explained by group differences in education and reading
  - e.g. Manly et al., 2002, 2004
  - Reading a proxy for quality of education
    - Small acculturation effects independent of reading
- Average differences between Hispanics and Whites can be explained by education and language use
  - Mungas et al., 2005
  - English --> higher test scores, Spanish --> lower scores
    - Small acculturation effects independent of language
Determinants of Cognitive Test Performance

Ethnic Group 1
- Aging
- Environment
- Disease
- Genes
- Ability
  - Item 1
  - Item 2
  - Item 3
  - Item 4

Ethnic Group 2
- Aging
- Environment
- Disease
- Genes
- Ability
  - Item 1
  - Item 2
  - Item 3
  - Item 4
Semantic Memory
Mean Ethnic Group Differences

Age + Gender

Ability Score (Standard Deviation units)

White (n=272)  Black (n=277)  Hispanic (n=355)

Ethnicity

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Semantic Memory
Mean Ethnic Group Differences

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Semantic Memory
Mean Ethnic Group Differences

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Semantic Memory
Mean Ethnic Group Differences

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Episodic Memory
Mean Ethnic Group Differences

- Age + Gender
- Age + Gender + Educ + Lang
- Age + Gender + Educ + Lang + Read

Ability Score
Standard Deviation units

- White (n=272)
- Black (n=277)
- Hispanic (n=355)

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Ethnicity, Diagnosis, and Cognition
Determinants of Cognitive Test Performance

Ethnic Group 1

Environment → Disease → Genes

Ability → Item 1 → Item 2 → Item 3 → Item 4

Ethnic Group 2

Environment → Disease → Genes

Ability → Item 1 → Item 2 → Item 3 → Item 4
## Sample Size - Clinical Evaluation

### Community + Clinic

<table>
<thead>
<tr>
<th></th>
<th>White</th>
<th>Black</th>
<th>Hispanic</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>56</td>
<td>45</td>
<td>55</td>
<td>156</td>
</tr>
<tr>
<td>MCI</td>
<td>64</td>
<td>33</td>
<td>32</td>
<td>129</td>
</tr>
<tr>
<td>Demented</td>
<td>23</td>
<td>14</td>
<td>27</td>
<td>64</td>
</tr>
<tr>
<td>Total</td>
<td>143</td>
<td>92</td>
<td>114</td>
<td>349</td>
</tr>
</tbody>
</table>
Semantic Memory by Diagnosis
(Age, Gender, Education, Language, Reading Adjusted)

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Episodic Memory by Diagnosis
(Age, Gender, Education, Language, Reading Adjusted)
Ethnic Differences and Test Validity

• Sensitivity to diagnostic group differences is a prerequisite for a measure of cognitive impairment
  ▪ Equivalent sensitivity across ethnic groups is an added advantage for comparative studies
  ▪ Differences in mean scores across ethnic groups can lead to differential validity (bias) for detecting cognitive impairment in cross-sectional assessment
  • Importance of understanding and deconstructing ethnic difference
Conclusions

- Cognition in older persons is complexly determined
- Cognitive impairment associated with disease occurs in the context of remarkable heterogeneity of normal cognitive function
- Ethnicity contributes substantially to normal heterogeneity
- Appropriate studies can separate disease effects from demographic heterogeneity
Collaborators

• UC Davis
  ▪ Charles DeCarli, M.D.
  ▪ Bruce Reed, Ph.D.
  ▪ Sarah Tomaszewski Farias, Ph.D.
• UC Berkeley
  ▪ William Jagust, M.D.
• University of Michigan
  ▪ Mary Haan, Dr. Sc.

• University of Washington
  ▪ Paul Crane, M.D.
• Hebrew Center for Rehabilitation of the Aged
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