WHIMS Update

Steve Rapp
for the WHIMS Team

WHI Annual Scientific Meeting
NIH Neuroscience Center
Rockville, MD
May 7, 2015
## WHIMS: Status Update

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N (current; contributing any cognitive data)</strong></td>
<td>2880</td>
<td>1337</td>
</tr>
<tr>
<td><strong>Age (yr.)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>82.3</td>
<td>67.1</td>
</tr>
<tr>
<td>Range</td>
<td>72 – 95</td>
<td>62-71</td>
</tr>
<tr>
<td><strong>Cognitive Assessments</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total # administered</td>
<td>12,626</td>
<td>5,634</td>
</tr>
<tr>
<td>Mean # admin.</td>
<td>4.38</td>
<td>4.21</td>
</tr>
<tr>
<td>Range</td>
<td>1-7</td>
<td>1-6</td>
</tr>
<tr>
<td><strong>Cognitive Functions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attention:</td>
<td>Digit Span-Forward;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Oral Trail Making Test-Part A</td>
<td></td>
</tr>
<tr>
<td>Memory:</td>
<td>East Boston Memory Test;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>California Verbal Learning Test</td>
<td></td>
</tr>
<tr>
<td>Language:</td>
<td>Verbal Fluency-Animals</td>
<td></td>
</tr>
<tr>
<td>Working Memory:</td>
<td>Digit Span-Backward</td>
<td></td>
</tr>
<tr>
<td>Executive Function:</td>
<td>Oral Trail Making Test-Part B</td>
<td></td>
</tr>
<tr>
<td><strong>Additional variables</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression:</td>
<td>Geriatric Depression Scale-15</td>
<td></td>
</tr>
<tr>
<td>Insomnia:</td>
<td>WHI Insomnia Rating Scale</td>
<td></td>
</tr>
<tr>
<td>Dementia:</td>
<td>Dementia Questionnaire</td>
<td></td>
</tr>
</tbody>
</table>
WHI Cognition Program - Driving Data

Women's Driving and Mobility Study (AS380)

• Data Collection: August 2013 – present
  – WHIMS-ECHO and WHIMS-Y women
  – Questionnaire administered during annual telephone follow-up
  – Broad coverage of WHI Regions and US states
  – <2% of women are never-drivers, >80% of women have driven within 1 year

• Current Driving Questionnaire Data Set: May 2015
  – N ~ 2,700 women: 1,700 WHIMS-ECHO and 1,000 WHIMS-Y
  – >1,200 have 2 consecutive annual interviews with driving data

• Main Driving Exposures/Outcomes
  – Miles and # trips in typical week
  – Total and types of moving violations in past year
  – Total accidents in past year
  – Related injuries and damage
  – Age at driving cessation

• Other Data from the Driving Questionnaire
  – Driving habits and conditions (driving less, not at nighttime, out-of-town, highway, bad weather, etc.)
  – Providing transportation for others, and for whom
  – Alternate modes of transportation used, and provided by whom
WHI Cognition Program - Driving Data

WHIMS-ECHO Driving Data: Women with mild cognitive impairment (MCI) or probable dementia

- **Data Collection**
  - Telephone-administered cognitive test battery
  - Dementia Questionnaire: Telephone-administered, semi-structured interview of proxies
    - Dementia-related cognitive and behavioral status, and relevant medical history
    - Driving status, problems, reasons for driving problems/cessation
  - Adjudicated MCI, probable dementia, no cognitive impairment

- **WHIMS-ECHO Driving Data Set: Follow-up Years 1-4**
  - Women with either MCI or probable dementia and driving data from proxy
  - N = 385 women
    - 178 MCI, 207 Probable dementia
    - 200 Current drivers, 185 Former drivers
Other Proposed Objectives

- To identify key cognitive, health, and other factors predictive of adverse driving events and driving cessation.
- To examine relationships among: (1) WHIMS-MRI brain volumes, lesion volumes, and changes in these markers; (2) trajectories of cognitive functioning; and (3) adverse driving events and driving cessation.
WHI Cognition Program – Genetic Data

WHI Data: Common APOE alleles (ε2, ε3, and ε4) in non-Hispanic whites

- **Genetic Data Collection**
  - Two SNPs used in APOE genotyping were imputed by the CCC in a genome-wide imputation
  - $R^2 = 0.98$ for each SNP in this study population
  - Alleles based on the imputed SNPs were checked against direct genotyping in an available subset

- **APOE (ε2, ε3, and ε4) genotypes in WHI/WHIMS Data Sets – Examples**
  - WHIMS: ~$N = 5,800$
  - WHISCA: $N = 1,900$
  - WHIMS MRI-1: $N = 1,200$
  - WHIMS MRI-2: $N = 600$
  - WHIMS Extension: $N = 3,200$
  - WHIMS-ECHO: $N = 2,400$
WHI Cognition Program – Genetic Data

WHI/WHIMS Ancillary Study AS250: Genetic contributions to cognitive decline in older postmenopausal women and modification by hormone therapy (Ira Driscoll, Ph.D. et al.)

• Primary Objective
  – To investigate relationships between cognitive decline and genetic variation in candidate genes

• Design
  – Case-Control study design within the WHIMS study population
    • All adjudicated cases were eligible: Probable Dementia or Mild Cognitive Impairment (MCI)
    • Controls were selected from those with no cognitive impairment; no individual-level matching

• Genetic Data
  – Candidate genes were selected based on previously shown associations with one or more aspects of cognition and Alzheimer’s disease pathogenesis
  – The gene regions were extended at least 20 kilobases in each direction
  – 96 SNPs were selected in 5 gene regions: **KIBRA, BDNF, SORL1, APOE/TOMM40, COMT**
  – Genotyping used existing DNA from WHI baseline samples and a custom Illumina GoldenGate assay

• Data Set
  – N = 387 Probable Dementia, N = 165 Mild Cognitive Impairment, N = 2305 Controls
WHI Cognition Program – Genetic Data

- **Ongoing and Proposed Objectives – Examples**
  - To employ a neuroimaging–genetics paradigm and examine variation in regional brain volumes as possible intermediate phenotypes in the gene-to-behavior pathway, and to determine whether variation in brain morphometry mediates potential associations between candidate gene variants, cognitive function, and hormone therapy (Ms1714)
  - To measure SNP and haplotype variation in candidate genes with known involvement in different aspects of cognition and to investigate their association with cognitive decline and impairment (Ms1715)
  - To examine (1) the relationship between physical activity and brain tissue and white matter lesion volumes, and in the hippocampal formation, parahippocampal gyrus, and caudate nucleus; and (2) whether these relationships are moderated by \text{APOE} allele status (Ms1498)
  - To evaluate (1) whether physical activity at WHI baseline is predictive of changes in regional gray matter volume between WHIMS MRI scans; and (2) whether changes in physical activity between the first MRI assessment and 2005 is moderated by the \text{APOE} genotype (Ms1631)
  - To evaluate associations between mitochondrial ribosomal protein genes and (1) time to a major health event, and (2) cognitive decline (Ms2609)
  - To profile genetic modifiers of potential benefits of dietary patterns on cognitive outcomes in the Alzheimer’s Drug Discovery Foundation CAPA Consortium (Ms2648)
Recent WHIMS Publications


Recent WHIMS Publications


Acknowledgments

- Sally Shumaker, PhD
- Mark Espeland, PhD
- Laura Coker, PhD
- Bev Snively, PhD
- Dan Beavers, PhD
- Iris Leng, PhD
- Laura Baker, PhD
- Leslie Vaughan, PhD
- Kate Hayden, PhD
- Susan Resnick, PhD
- And the WHIMS staff

WHIMS ECHO and WHIMS-Y are supported by the National Institute of Aging (HHSN271-2011-00004C). The WHI program is funded by the National Heart, Lung, and Blood Institute, National Institutes of Health, U.S. Department of Health and Human Services.