Cognitive Assessment in the Digital Era

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Framingham Heart Study

- Most renowned epidemiologic study in the world
- Coined “risk factors - basis for Preventive Medicine
- Discovered the primary risk factors for heart disease, which revolutionized treatment
- Created the Framingham Stroke Risk Profile Score and the Framingham Cardiovascular Disease Research Score.
  - Rationale for routine check of blood pressure, cholesterol, blood glucose, family history of disease and smoking status
Framingham Heart Study

Longitudinal Community-Based Family Study

Gen 1 Original cohort
N=5209

Gen 2 Offspring cohort
N=5124

Gen 3 cohort
N=4105

1948 1971 2015

Plus two multi-ethnic cohorts:
Omni Gen 1 (n=506) & Omni Gen 2 (n=410)
FHS Dense Phenotypic Characterization

- Dementia
- Cognitive Aging
- Stroke
- Cardiac
- Pulmonary
- Vascular
- Osteoporosis
- Osteoarthritis
- Reproductive Health
- Aging
- Obesity
- Diabetes
- Alcohol
- Pollution
- Hearing
- Eye
- Renal
- Depression
- Omic
- Genomic
- Epigenomic
- Transcriptomic
- Proteomics
- Metabolomic

Funded grants

Slide courtesy of Emelia Benjamin, M.D.

www.thehumanbody.ecsdnet/ the_human_body.htm
Fostering New Drug Discovery
Multi-Disciplinary, Multi-Institutional

Methylation

miRNA

Risk Factors

Electrical remodeling

Structural remodeling

DNA

RNA

Biomarkers

AF
SD
CHD
CHF
PAD
Stroke

Genome
Epigenome

Transcriptome

Phenome

Tissue
Zebrafish
Mouse
Diverse Cohorts

Slide courtesy of Emelia Benjamin, M.D.
Framingham Cognitive Aging & Dementia Studies
Framingham Heart Study
Dementia Study – Prevalence: Gen 1 Original cohort

1948
Baseline NP

1976-78
MMSE

1981
NINDS-ADRDA
AD Diagnostic Criteria

1984
Framingham Heart Study
Dementia Incidence - Add Gen 2 Offspring cohort

1948
NINDS-ADRDA AD Diagnostic Criteria

1971
1976-78 Baseline NP
1981 MMSE

Gen 1

1984

1991 MMSE

Gen 2
Framingham Heart Study
Incident Dementia + Pre-Clinical

1948
1976-78 Baseline NP
1984 NINDS-ADRDA AD Diagnostic Criteria
1971 1991 MMSE
1999 Brain MRI/NP (n= 331)

Gen 1

1999 1999 Brain MRI/NP (n= 2617)

Gen 2
FHS Cognitive Assessment

WMS Logical Memory – IR & DR & Recogn
WMS Visual Reproductions – IR & DR & Recogn
WMS Paired Associates – IR & DR & Recogn
WAIS Similarities
Digit Span
Controlled Word Association Test – FAS
Category Fluency - Animals
Trails A & B
Boston Naming Test – 30 Item
Hooper Visual Organization Test
Finger Tapping
WRAT III Reading Subtest
Clock Drawing Test
WISC-III Math Fluency
Digit Symbol Substitution Test
Cognitive Impairment Detection Challenge: When Can It Be Detected?

Adapted by Drs. Dana Penney and Randall Davis from Fig 3 of Criteria For Preclinical Alzheimer’s Disease, Alzheimer’s Association report (2010), which in turn cites Jack C R, et al., Hypothetical model of dynamic biomarkers of the Alzheimer’s pathological cascade, The Lancet, 9:1, Jan 2010, pp 119-128.
Cognitive Impairment Detection Challenge: FHS Two-Method Approach

- The Traditional Approach

- Boston Process Approach (BPA)
  - Preserve traditional measures
  - Expand test beyond single score
  - Focus on path to final response
    - Value of incorrect responses
## Logical Memory Error Measures

<table>
<thead>
<tr>
<th>Traditional scores</th>
<th>Qualitative Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>Confabulations – related</td>
</tr>
<tr>
<td></td>
<td>Intrusions – related</td>
</tr>
<tr>
<td></td>
<td>Confabulations – unrelated</td>
</tr>
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<td></td>
<td>Intrusions – unrelated</td>
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</tbody>
</table>
PARTICIPANT #1 - 77 YR OLD WOMAN HIGH SCHOOL GRADUATE

Examined-corrected Errors: 4
Self-corrected Errors: 0

PARTICIPANT #2 - 80 YR OLD WOMAN HIGH SCHOOL GRADUATE

Examined-corrected Errors: 1
Self-corrected Errors: 1
Pen lifts: 9

TIME TO COMPLETION: 2:16
TIME TO COMPLETION: 2:15
Logical memory - # perseverations: IR & DR
Visual Reproductions – perseverations (Y/N per design: IR & DR
Paired Associates – perseveration/pair: IR
Similarities – perseveration/item
FAS - # of perseverations/trial
Animals - # of perseverations
BNT – perseveration/item
BPA on Steroids
Digital Clock Drawing Test - 2011
106 FHS Older controls (60+)
60 Amnestic MCI (aMCI)
79 Alzheimer’s disease (AD)

DCT measures

- Total drawing time
  - Thinking
  - Inking
- Clock Size
aMCI vs. Controls
  Clock Size

AD vs. Controls
  Total Drawing
  Thinking
  Inking
  Clock Size

aMCI vs. AD
  Total Drawing
  Thinking
  Inking
  Clock Size
1350 FHS participants
   Age 67.5 years
15.4 years education
   MMSE - 29

DCT measures
- Total Time to Completion – Command + Copy
  - Total Stroke
- Post clock face circle latencies
  - Pre 1\textsuperscript{st} hand latency
  - Pre 2\textsuperscript{nd} hand latency
  - Inter-digit latency
## Cognitively Intact - Results

<table>
<thead>
<tr>
<th>Command</th>
<th>Copy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Time to Completion</strong></td>
<td><strong>Total Time to Completion</strong></td>
</tr>
<tr>
<td>80+ &gt; 50 &amp; 60 yr olds</td>
<td>70, 80+ &gt; 50, 60 yr olds</td>
</tr>
<tr>
<td>70-79 &gt; 50 &amp; 60s</td>
<td></td>
</tr>
<tr>
<td><strong>Inter-digit latency</strong></td>
<td><strong>Total Strokes</strong></td>
</tr>
<tr>
<td>70s &gt; 60s</td>
<td>80+ &gt; 50, 60, 70; 70 &gt; 50</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Post Clock Face Latency</strong></td>
<td><strong>Post Clock Face Latency</strong></td>
</tr>
<tr>
<td>80+ &gt; 50, 60, 70; 70 &gt; 60</td>
<td>80+ &gt; 50, 60, 70; 70 &gt; 60</td>
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<tr>
<td><strong>Pre 2nd Hand Latency</strong></td>
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<td>80+ &gt; 60</td>
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Cognitively Intact

DCT latency measures
  • ink
  • think
  • intra-component

Results
  • % ink – 35-40%
  • % intra-component – 30% of think time
Our Near Term Directions

- Digital data collection – all cognitive tests
- Integration of state-of-the-art technology into health assessment methods, providing real-time e-health data
- Use “big data” analytics to identify new avenues
- Recruit research partners to expand breadth and depth of cognitive aging research
- Global Aging Well Initiative