The Role of Cognitive Reserve in Normal and Abnormal Aging

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DISCLOSURES

• Consulting / Scientific Advisory Boards
  – Eli Lilly Pharmaceutical Company
  – Neurotrack
  – Biogen Idec
  – Janssen Pharmaceuticals

These disclosures are not relevant to the work presented today
More and more people are living vibrant lives into old age.
Who lives to 100+?

People who…

- Drank moderate amounts of alcohol or coffee
- Were overweight in their 70s
- Stopped smoking
- Ate plant-based diets
- Kept up constant low-level exercise
- Had family & social support

Claudia Kawas, MD

The 90+ Study
PET Amyloid Imaging in Clinically Normal Older Individuals

Sperling, Mormino, Johnson *Neuron* 2014
Theories of Reserve

Two Proposed Models of Reserve

1. Brain Reserve – Neuroplasticity
Reserve Hypothesis

Neuroplasticity and cognitive reserve

– **Positive neuroplasticity** refers to the physiological ability of the brain to form and strengthen dendritic connections, produce beneficial morphological changes and increase cognitive reserve.

Whalley, L. Ageing Research Reviews, 2004
Is Neuroplasticity Helpful?

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doi:10.1017/S1355617712000847

**BRIEF COMMUNICATION**

Superior Memory and Higher Cortical Volumes in Unusually Successful Cognitive Aging

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Red and yellow represent significantly thinner cortex in elderly controls compared to SuperAgers. SuperAgers perform similarly to middle-aged controls on a memory test.
Theories of Reserve

Two Models of Reserve

2. Cognitive Reserve- Compensation
How Cognitive Reserve May Mediate Between AD Pathology and Clinical Expression

Stern Y, Neuropsychologia. 2009:47; 2015-2028
Old-High Adults were matched on a composite memory score with Young Adults. PFC activity during source memory was right lateralyzed in Young and Old-Low participants but bilateral in Old-High participants. Old-Low recruited similar network as Young, but used it inefficiently.
Cognition, Reserve, and Amyloid Deposition in Normal Aging


Cognitive Performance vs. Precuneus Aβ is Modified by Cognitive Reserve

$\beta = 0.087, p = 0.027$

Cognitive Performance vs. Precuneus Aβ is not modified by CR in Amyloid Positive

$\beta = 0.052, p = 0.2969$

Cognitive Performance is not related to Aβ but is modified by Cognitive Reserve

$\beta = 0.208, p = 0.0002$

Cognitive Performance is Related to Aβ and Modified by CR on a challenging test only

$\beta = 1.931, p = 0.014$
Cognitive resilience in clinical and preclinical Alzheimer’s disease: the Association of Amyloid and Tau Burden on cognitive performance

Dorene M. Rentz1,2 · Elizabeth C. Mormino1 · Kathryn V. Papp1,2 · Rebecca A. Betensky3 · Reisa A. Sperling1,2,4 · Keith A. Johnson1,2,4,5

<table>
<thead>
<tr>
<th></th>
<th>CN Mean (SD) or count (n)</th>
<th>MCI/AD Mean (SD) or count (n)</th>
<th>Mean Difference</th>
<th>p</th>
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<tbody>
<tr>
<td>n</td>
<td>133</td>
<td>17/6</td>
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<tr>
<td>Age</td>
<td>76.17 (6.23)</td>
<td>69.41 (9.97)</td>
<td>6.76</td>
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<tr>
<td>Sex (M/F)</td>
<td>59/74</td>
<td>19/4</td>
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<tr>
<td>Education (years)</td>
<td>15.91 (2.96)</td>
<td>16.29 (3.38)</td>
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<td>Inferior Temporal T807</td>
<td>1.20 (0.09)</td>
<td>1.61 (0.44)</td>
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<tr>
<td>PiB</td>
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<td>1.50 (0.26)</td>
<td>0.28</td>
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<td>MMSE</td>
<td>29.18 (1.02)</td>
<td>26.61 (3.06)</td>
<td>2.57</td>
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<tr>
<td>AMNART</td>
<td>121.59 (8.75)</td>
<td>121.22 (8.01)</td>
<td>0.37</td>
<td>0.850</td>
</tr>
<tr>
<td>Global CDR (1/0.5/0)</td>
<td>0.03 (0.13)</td>
<td>0.41 (0.05)</td>
<td>0.38</td>
<td>0.001</td>
</tr>
</tbody>
</table>

* MMSE Mini Mental Status Exam, CDR Clinical Dementia Rating, MCI Mild Cognitive Impairment, AD Alzheimer’s disease, AMNART American National Adult Reading Test
CR modifies Aβ & Tau burden on PACC over time

PIB*VIQ*Time $\beta = 0.007$ $p = 0.09$

T807*VIQ*Time $\beta = 0.24$ $p = 0.010$

Unpublished data
Reserve Hypothesis

– **Negative neuroplasticity** refers the same physiological ability of the brain to atrophy and weaken dendritic connections, produce detrimental morphological changes and decrease cognitive reserve.

Whalley, L. Ageing Research Reviews, 2004
Reserve Hypothesis

Factors that promote negative neuroplasticity and decreases in cognitive reserve:

- Poor health
- Poor sleep hygiene
- Poor nutrition
- Substance abuse
- Depression
- Anxiety/ stress
Don’t become President of the US!!
What Can I Do to Delay the Onset of Dementia
Cognitive Changes with Age: What’s normal????

Who’s that movie star?  What’s that word?

Where did I park the car?  What did I come in here for?  What was I going to do?
When to Worry?

- **Memory loss** - not just forgetfulness
- **Problems with language** - not just word finding
- **Getting lost** or disoriented in familiar places
- **Misplacing things** - not just your glasses or keys
- **Loss of initiative** - for previously enjoyed activities
What Can I Do?

- **Volunteer** for a research study
- **Become an Advocate**
  - Generate action from elected officials
  - Elevate Alzheimer’s from a disease to a cause
- **Support** a Walker or Rider to End Alzheimer’s Disease
- **Help a caregiver**
Thank you to our Funding Sources:

NIA/ NIH
Alzheimer’s Association