Reducing Your Risk of Alzheimer's Disease: Building a Better Brain as We Age

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October 11, 2011
Acknowledgments

Study Participants in the Religious Orders Study Memory and Aging Project

Faculty and Staff of the Rush Alzheimer’s Disease Center Study collaborators across the USA and Canada

National Institutes of Health
Alzheimer’s Association
Illinois Department Public Health
Elsie Heller Brain Bank Endowment Fund
Robert C. Borwell Endowment Fund
Objectives

- The case for disease prevention of AD
- Two clinical-pathologic studies of aging and AD
- What’s in an aging brain
- Concept of neural reserve
- Factors that increase brain vulnerability
- How to build a better brain as we age
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Question?
Would you rather:
A. Get Alzheimer’s disease and treat it? or
B. Never get Alzheimer’s disease?
Groucho Marx

“Growing old is something you do…

If you’re lucky.”
Dad, where do old people come from?
Alzheimer Disease in the US Population

Prevalence Estimates Using the 2000 Census

Implication Of Treatments

How do we Prevent AD?

- Identify risk factors for AD
- Determine biologic pathways linking risk factors to disease
- Develop strategies to prevent AD
"That was easy..."
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The Religious Orders Study

• Began in 1993
• > 1,150 older nuns, priests, and brothers without known dementia from across the U.S.
• All agreed to annual clinical evaluation
• All agreed to brain donation
• > 275 have developed dementia
• > 375 have developed MCI
• > 525 brain autopsies
Religious Orders Study: Participating Sites
Queen of the Rosary Chapel, Sinsinawa, WI
Norbertines of Saint Norbert Abbey

De Pere, WI
Capuchin Franciscans

Appleton, WI
The Rush Memory and Aging Project
... because memories should last a lifetime

- Began in 1997
- > 1,500 residents from about 40 retirement communities and senior housing from across the Chicago area
- All agreed to annual clinical evaluation
- All agreed to donate brain, spinal cord, muscle, and nerve at the time of death
- > 275 have developed AD
- > 375 have developed MCI
- > 400 autopsies
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What’s in the aging human brain

- Alzheimer’s disease changes
  - Neuritic plaques and neurofibrillary tangles
- Stroke changes
  - Cerebrovascular disease
- Frontal-temporal lobar degeneration changes
  - TDP-43
- Parkinson’s disease changes
  - Lewy bodies
Alzheimer’s disease

Normal brain
It's a mammoth.
Normal brain

Infarct (stroke)
Nigral Lewy bodies

Limbic Lewy bodies

Cortical Lewy bodies
By Age 85

- Alzheimer’s disease changes
  - Virtually every brain

- Cerebrovascular disease (stroke)
  - More than half of brains

- Frontal-temporal lobar degeneration (TDP-43)
  - About 40% (2 in 5) brains

- Parkinson’s disease changes (Lewy bodies)
  - About 20% (1 in 5) brains
George Burns (1896-1996)

Trout Brook - 1960
Anna Mary Robertson (Grandma) Moses (1860-1961)

Rondanini Pieta - 1564
Michelangelo (1475-1564)
The Centenarian Spirit in Wisconsin
Most research on the treatment or prevention of AD focuses on AD pathology.

**Risk Factors**
- Genetic
- Lifestyle

**Amyloid plaques**
- Neurofibrillary tangles

**Mutations:**
- APP
- PSEN1
- PSEN2

**Polymorphisms:**
- APOE
- CR1
- PICALM

Pick your parents well (Part 1)
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Concept of neural reserve:

- Individual brains differ in their ability to withstand the effects of brain pathology
Concept of neural reserve:

- Individual brains differ in their ability to withstand the effects of brain pathology
- The same amount of brain pathology does not result in the same amount of memory loss in different people
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Increase Brain Vulnerability

- Vulnerable
  - Cerebral infarctions (stroke)
  - TDP-43 (frontal-temporal lobar degeneration)
  - Lewy bodies (Parkinson’s disease)

Risk factors for these pathologies will increase the likelihood of dementia (including AD)
Diabetes Mellitus and Risk of Alzheimer Disease and Decline in Cognitive Function

Diabetes is related to cerebral infarction but not to AD pathology in older persons

Harm Avoidance and Risk of Alzheimer’s Disease

Harm avoidance is a trait associated with a tendency to avoid new situations and aversive stimuli.

Four subscales:
- anticipatory worry
- fear of uncertainty
- shyness
- fatigability


Increase Brain Vulnerability

- Vulnerable
  - Depressive symptoms
  - Distress proneness
  - Anxiety
  - Loneliness
Depressive symptoms

I felt like everything I did was an effort
My sleep was restless
I felt sad
I could not get going

Neuroticism refers to the disposition to experience psychological distress

I am a worrier
I often feel tense and jittery
I often get angry at the way people treat me
I often feel helpless and want someone else to solve my problems

Feelings of anxiety thought to be relatively stable over time

I feel nervous and restless
I wish I could be as happy as others seem to be
I feel like a failure
I get in a state of turmoil as I think over my concerns

Loneliness is a measure of the feeling of social isolation

I experience a general sense of emptiness,
I miss having people around,
I feel like I don’t have enough friends,
I often feel abandoned,
I miss having a really good friend

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Midway through the exam, Allen pulls out a bigger brain.
Building a Better Brain

• Resilient
  – Years of education
  – Cognitive activities
  – Pick your parents well (Part II)
  – Physical activities
  – Sleep
  – Social activities
  – Conscientiousness
  – Social networks
  – Purpose in life
  – Life Space
  – Novelty seeking
Education modifies the relation of AD pathology to level of cognitive function in older persons.

Participation in Cognitively Stimulating Activities and Risk of Incident Alzheimer Disease

Time spent in 7 common activities that involve information processing

Viewing television
Listening to the radio
Reading newspapers
Reading magazines
Reading books
Playing games
Going to museums

The relation of cognitive activity to risk of developing Alzheimer’s disease

<table>
<thead>
<tr>
<th>Activity</th>
<th>Age 6</th>
<th>Age 12</th>
<th>Age 18</th>
<th>Age 40</th>
<th>Current</th>
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<tr>
<td>Read to</td>
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<td>Told stories</td>
<td>X</td>
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<tr>
<td>Play games</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Time reading/day</td>
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<td></td>
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<tr>
<td>Time on homework/day</td>
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<tr>
<td>Visit library</td>
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<td>X</td>
<td>X</td>
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<tr>
<td>Read newspaper</td>
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<tr>
<td>Read magazine</td>
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<tr>
<td>Read books</td>
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<td>Write letter</td>
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<td>X</td>
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<td>Music instruction</td>
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<td>Kept a diary</td>
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<td>X</td>
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<tr>
<td>Visit museum</td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
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<tr>
<td>Attend concert, play</td>
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<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

Pick your parents well (Part II)

Household and county level early life socioeconomic status

Household:
- parental education
- parental occupation
- number of children in family

County level:
- Duncan socioeconomic status for head of household
- Literacy rate for those over age 6
- Proportion of children age 6-13 in school

Total Daily Activity is Associated With Cognition in Older Persons


Total Daily Physical Activity and the Risk of AD and Cognitive Decline in Older Adults
Quantification of the Fragmentation of Rest-Activity Patterns in Elderly Individuals using a State Transition Analysis

Increased Fragmentation of Rest-Activity Patterns Is Associated With a Characteristic Pattern of Cognitive Impairment in Older Individuals

Lim ASP, et al. Pending revisions.
SOCIAL ENGAGEMENT AND COGNITIVE FUNCTION IN OLD AGE

How often during the past year did you

Go to restaurants, sporting events, play bingo
on day trips or overnight trips
do unpaid community/volunteer work
visit relatives or friends houses
participate in groups, such as senior center, social club

Conscientiousness refers to a tendency to be self-disciplined and scrupulous

I am a productive person who always gets the job done
I am a very active person
I have a lot of intellectual curiosity
I strive for excellence in everything that I do

Number of relatives (besides spouse and children) and other friends that they saw each month that they felt close to and at ease with and could talk to about private matters and could call upon for help.

Purpose in life refers to the psychological tendency to derive meaning from life’s experiences and possess a sense of intentionality and goal directedness that guides behavior.

I feel good when I think of what I’ve done in the past and what I hope to do in the future; I am an active person in carrying out the plans I set for myself.

Six zones in the past week


CORRELATES OF LIFE SPACE IN A VOLUNTEER COHORT OF OLDER ADULTS

Life space and risk of Alzheimer’s disease, mild cognitive impairment, and cognitive decline in older adults: prospective cohort study
Novelty seeking is a broad trait indicating behavioral activation in response to novel stimuli.

Four subscales:
- exploratory excitability versus stoic rigidity
- impulsiveness versus reflection
- extravagance versus reserve
- disorderliness versus regimentation

Genes, Lifestyles, and Crossword Puzzles:
Can Alzheimer’s Disease be Prevented?
What can you do to prevent AD?

• Control vascular disease risk factors
  – Diabetes, high blood pressure, cholesterol
• Relax, be happy
• Engage in regular:
  – Cognitive, physical, and social activities
• Strengthen and maintain social ties
• Get a good night’s sleep
• Be diligent
• Spend time engaged in meaningful, goal directed activities
• Get out more, and explore new things
• And even if you do all of this…
Groucho Marx

“Growing old is something you do… If you’re lucky.”
Start early –
you can’t pick
your parents,
but you can pick
your activities.