Coffee Linked to Lower Dementia Risk

By NICHOLAS BAKALAR

A team of Swedish and Danish researchers tracked coffee consumption in a group of 1,409 middle-age men and women for an average of 21 years. During that time, 61 participants developed dementia, 48 with Alzheimer’s disease.

After controlling for numerous socioeconomic and health factors, including high cholesterol and high blood pressure, the scientists found that the subjects who had reported drinking three to five cups of coffee daily were 65 percent less likely to have developed dementia, compared with those who drank two cups or less.
Reversal Of Alzheimer's Symptoms Within Minutes In Human Study

ScienceDaily (Jan. 9, 2008) — An extraordinary new scientific study, which for the first time documents marked improvement in Alzheimer’s disease within minutes of administration of a therapeutic molecule, has just been published in the Journal of Neuroinflammation. Mayoclinic.com Alzheimer’s Blog  April 23, 2008
‘Miracle cures are hype until proved’

I also understand that during this painful journey, we can become enchanted by news of what appear to be miraculous cures; case in point an arthritic drug you may have heard being touted as a “miracle cure.”

The drug, approved for treatment of immune disorders such as rheumatoid arthritis, is not currently available as a treatment for Alzheimer’s. Keep in mind, this “miracle cure” rests on just a handful of case studies rather than on randomized clinical trials. Before it could become an accepted therapy for Alzheimer’s, it would need to go through the FDA approval process, including randomized, blinded clinical trials.
Comment

• It seems that people like you should simply check out this story and write balanced articles about it. The stories regarding the patients being treated with Enbrel are all over Youtube and the Alzheimer’s forums. Please take a look and see for yourself..... This is so important for so many people that it is negligent for the right people to not investigate this with an open mind.

Another Comment

• Ms Lunde -one more thing and with only respect, why don’t you take a walk away from your desk and go to the Tobrinick center and actually see what is going on. Couldn’t hurt and could provide you with a little more detail for your article. No?

Cures and treatments for AD

Why are emotion reactions so strong?
Maslow's Hierarchy of Needs


We want a sense of control

We need a sense of hope

This makes us vulnerable

Research and Critical Thinking

Be your own scientist, i.e. be skeptical

- Does research meet common sense test?
- Have results been replicated?
- Association does not imply causation
  - The more ambulances at a crash site the more people are injured.
- Are there other ways to explain results?
  - E.g. smoking protects against AD
The AD Vaccine Story

Vaccine: Miracle cure, public health risk or both?

Passive vaccine
Drug Discovery

What are the phases of clinical treatment trials?

- **Phase I trials**, first time, small group of people (20-80)
  - evaluate safety
  - safe dosage range
  - identify side effects

- **Phase II trials**, a larger group of people (100-300)
  - effectiveness and further evaluate its safety

- **Phase III trials**, largest groups of people (1,000-3,000)
  - to confirm its effectiveness
  - monitor side effects
  - compare it to commonly used treatments
  - collect information that will allow the drug or treatment to be used safely

- **Phase IV trials**, post marketing studies additional information including the drug’s risks, benefits, and optimal use

The Story Can Change

- Vioxx
- Estrogen
- Anti-psychotics
Understanding the research

Mechanistic  Treatment

Dementia     Drug Trials

Prevention    Brain Fitness

Coffee       Cognitive

Red wine     Aging

Physical Activity

Associational

Alzheimer's Disease

Senile Plaque  Neurofibrillary Tangle

Secretase Inhibition
**Tau Stabilization**

**Primary prevention of dementia**
-Patterson et al (2007)

<table>
<thead>
<tr>
<th>Prevention Strategy</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control hypertension</td>
<td>↑↑</td>
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<tr>
<td>Statins</td>
<td>--</td>
</tr>
<tr>
<td>Treat diabetes</td>
<td>--</td>
</tr>
<tr>
<td>NSAIDS</td>
<td>--</td>
</tr>
<tr>
<td>Estrogen</td>
<td>↓↓</td>
</tr>
<tr>
<td>Vitamin C and E</td>
<td>↓↓</td>
</tr>
<tr>
<td>Physical or mental activity</td>
<td>--</td>
</tr>
<tr>
<td>Education</td>
<td>--</td>
</tr>
<tr>
<td>Diet (fish, red wine)</td>
<td>--</td>
</tr>
<tr>
<td>Reduce head injury</td>
<td>--</td>
</tr>
<tr>
<td>Reduce chemical exposure</td>
<td>--</td>
</tr>
</tbody>
</table>

**Secondary prevention requires early detection**
Risk factors

- Genetics
  - PS1, PS2, APP
  - Apo E
  - SORL-1

- Biomarkers
  - Serum A-beta
  - Serum homocysteine

- Neuroimaging
  - Morphometry
  - Spectroscopy
  - PET (e.g. PIB)

- Neuropsychological/Clinical
  - Boundary Conditions

*3b* PIB and structural MRI provide complementary information in imaging of Alzheimer’s disease and amnestic mild cognitive impairment

Cognitively Normal vs. Alzheimer’s Disease

PIB (left): SPM of PIB retention ratio.

MRI (right): VBM of MRI grey matter density.

Brain, 2008

Normal

Mild Cognitive Impairment

Dementia
Proposed Model of Episodic Memory Decline (Bondi et al.).

Timeline of clinical definitions and criteria and developments in diagnostic biomarkers for AD

Review of AD Research in 2010

"2010 will be viewed as an important year in Alzheimer disease (AD) research. Reports from clinical trials of anti-amyloid-β (Aβ) drug candidates were disappointing; however, many studies published this year provide information that might aid the development of novel drug therapies for AD or enable the early diagnosis of individuals at risk of developing this condition."
TABLE 2. Ongoing Age-Related Cognitive Decline Clinical Trials Funded by NIA

<table>
<thead>
<tr>
<th>Trial Name</th>
<th>Principal Investigator(s)</th>
<th>Institution</th>
<th>Intervention</th>
<th>Population</th>
<th>Enrollment Start Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Action Activities for the Aging Mind</td>
<td>Dennis Ramsay, University of Texas, Dallas</td>
<td>Cognitive enrichment through physical activity</td>
<td>Healthy adults, age 65+</td>
<td>2012</td>
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<tr>
<td>Dorm-Based Approach to Enhancing Cognitive Function in Old Age</td>
<td>Mark D. Espinosa, University of California, Berkeley</td>
<td>Cognitive training</td>
<td>Healthy adults, age 65+</td>
<td>2012</td>
<td></td>
</tr>
<tr>
<td>Expanding the Effectiveness of an Effective Cognitive Aging Intervention</td>
<td>Nejla Noto, Emory University</td>
<td>Cognitive enrichment through training</td>
<td>Healthy adults, age 65+</td>
<td>2010</td>
<td></td>
</tr>
<tr>
<td>Exercise and Improving Health in Older Populations Through Exercise Interventions</td>
<td>George Farkas, Johns Hopkins University</td>
<td>Exercise training</td>
<td>Healthy adults, age 65+</td>
<td>2011</td>
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<tr>
<td>Foster Memory and the Alzheimer's Disease of Cognitive Reserve</td>
<td>Elizabeth Stroop, University of Illinois at Urbana-Champaign</td>
<td>Cognitive enhancement through participation in the memory of the mind program</td>
<td>Healthy adults, age 65+</td>
<td>2012</td>
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TABLE 3. Ongoing Age-Related Cognitive Decline Clinical Trials Funded by NIA

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<tr>
<td>Estrogen Effects on Cognitive Function in Older Women</td>
<td>Paul Mather, University of Illinois at Urbana-Champaign</td>
<td>Estrogen therapy</td>
<td>Healthy women, age 50-65</td>
<td>2014</td>
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<tr>
<td>Estrogen Use in Protection from Cognitive Decline</td>
<td>Natalia Proven, Stanford University</td>
<td>Estrogen therapy</td>
<td>Healthy women, age 65-75</td>
<td>2011</td>
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<tr>
<td>Harmone and Cognitive Processing in Everyday Contexts</td>
<td>Kathleen Smith, University of Michigan</td>
<td>Estrogen and tocopherol</td>
<td>Healthy women, age 65-75</td>
<td>2011</td>
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<tr>
<td>NEXUS (Exercise and Sleep)</td>
<td>Stanley Fischman, University of Wisconsin, Madison</td>
<td>Exercise and sleep intervention</td>
<td>Healthy women, age 65-75</td>
<td>2012</td>
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<tr>
<td>Mechanisms of Estrogen on Cognitive Function in Aging</td>
<td>J. Leo, Duke University, Durham Health and Science</td>
<td>Estrogen therapy</td>
<td>Healthy women, age 50-65 and 65-75</td>
<td>2009</td>
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<tr>
<td>Sex Steroids and Estrogen Use in Postmenopausal Women</td>
<td>Ellen Frazier, George Washington University</td>
<td>Estrogen therapy</td>
<td>Healthy women, age 50-65 and 70-85</td>
<td>2011</td>
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</tr>
</tbody>
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TABLE 4. Ongoing Age-Related Cognitive Decline Clinical Trials Funded by NIA

<table>
<thead>
<tr>
<th>Related Trial</th>
<th>Principle Investigator(s)</th>
<th>Institution</th>
<th>Intervention</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer's Disease</td>
<td>Peter S. Snyder, University of Pennsylvania</td>
<td>Testosterone gel</td>
<td>Testosterone gel</td>
<td>Older men</td>
</tr>
</tbody>
</table>

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TABLE 5. Ongoing Age-Related Cognitive Decline Clinical Trials Funded by NIA

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<tr>
<th>Related Trial</th>
<th>Principle Investigator(s)</th>
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<tbody>
<tr>
<td>Across the Lifespan</td>
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<tr>
<td>Exercise Program for Exercise in Older Adults</td>
<td>Jeffrey Burns, Johns Hopkins University</td>
<td>Aerobic exercise</td>
<td>Aerobic exercise</td>
<td>Healthy older adults, age 65-80</td>
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<tr>
<td>Exercise, Age, and Memory Function</td>
<td>Scott Small, Richard Sloan, Columbia University</td>
<td>Exercise training</td>
<td>Exercise training</td>
<td>Healthy adults, age 20-80</td>
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<tr>
<td>Physical Activity and Exercise in Older Adults</td>
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<tr>
<td>Exercise and Cognition Changes after Pregnancy or Physical Training in Older Women</td>
<td>Sarah Chapman, University of Texas, Dallas</td>
<td>Cognition training</td>
<td>Cognition training</td>
<td>Adults, age 60-75</td>
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<tr>
<td>Combined Exercise and Cognition Training</td>
<td>Todd Storl, Columbia University</td>
<td>Aerobic exercise and cognitive training</td>
<td>Aerobic exercise and cognitive training</td>
<td>Healthy adults, age 65-75</td>
</tr>
</tbody>
</table>
Prevention?

Function

Disability

Death

Time

“Ideal”

“Prevention”

“Delay”

“Current AD”

Conclusions

- Great deal of media attention to association studies
- Association doesn’t imply causation
- Drug development process is lengthy
- Recent secretase inhibitor studies disappointing
- Prevention focus continues