Pathways to Prevention: Maximizing Brain-Healthy Behavior to Decrease the Risk of Cognitive Decline

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I. **Background: Normal Cognitive Aging vs. Dementia**

II. Brain Health Champion Study: Research

III. Brain Healthy Behaviors: What You Can Do Now!

IV. Get Involved! AHEAD
• **Subjective Cognitive Decline (SCD)** is the experience of worsening memory loss or cognition.
• Though this experience of memory or thinking problems does not affect performance on cognitive tests, SCD is a risk factor for Alzheimer’s disease and other dementias.
• Many people with SCD will not develop MCI or dementia, but others will.

Mild Cognitive Impairment (MCI) is a term used to describe the condition of people whose cognition lies between the normal cognitive changes of aging and early dementia.

Cognition (or memory) is abnormal for what is expected at their age, but their memory changes have not caused an interruption in their daily activities or functioning.


People with **dementia** have significant memory problems that impact their ability to perform daily activities such as cooking, grooming or shopping.

Recent estimates show that **14% of people in the United States over age 71** have dementia.

The annual rate of conversion from MCI to dementia ranges from between **5-15% per year** for any one individual.


Normal Cognitive Aging: “Senior Moments”

• Common experiences include:
  – Forgetting why you walked into a room
  – “Word-finding” difficulty in conversation
  – Making wrong turns while walking or driving
  – Misplacing items around the house

Senior moments ≠ Alzheimer’s Disease!
BUT if frequent, they may be cause for concern.

• Neurologists and psychologists can do detailed testing to determine the cause of your memory concerns
• Many additional factors can cause or contribute to memory problems, including medications, head trauma, psychiatric disorders, alcohol or substance use, hypothyroidism, vitamin B-12 deficiency, fatigue
Normal Cognitive Aging: “Senior Moments”

<table>
<thead>
<tr>
<th>Cause for Concern</th>
<th>vs.</th>
<th>Likely Harmless</th>
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<tbody>
<tr>
<td>Symptoms:</td>
<td>Alzheimer’s disease</td>
<td>Normal aging memory changes</td>
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<td>Forgetting recently learned information</td>
<td>Forgetting things like names or appointments</td>
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<td>Difficulty performing familiar tasks such as preparing a meal</td>
<td>Occasionally forgetting reasons for entering a room</td>
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<td>Forgetting simple words or substituting unusual words</td>
<td>Sometimes having trouble finding the right word</td>
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<td>Disorientation; getting lost in familiar locations</td>
<td>Forgetting the day of the week or where you were going</td>
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<td>Poor or decreased judgment; difficulty with complex mental tasks</td>
<td>Making a questionable or debatable decision from time to time</td>
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<td>Misplacing items or putting them in unusual places</td>
<td>Temporarily misplacing keys or a wallet</td>
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<td>Rapid mood swings</td>
<td>Sometimes feeling sad or moody</td>
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<td>Extreme changes in personality</td>
<td>Slight change in personality</td>
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<td></td>
<td>Loss of initiative</td>
<td>Feeling weary of work or social obligations</td>
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SOURCE: Alzheimer’s Association

Talk to your primary care doctor or neurologist if you or family members are concerned about memory and thinking.
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Research: Modifiable Risk Factors

- A 10-25% reduction in each of seven major risk factors could potentially prevent 1.1-3.0 million AD cases worldwide and 184,000-492,000 cases in the USA
- **Smoking, physical inactivity, and depression** were among the top 3 contributors in the US and worldwide
Research: Modifiable Risk Factors

- **Physical inactivity** is associated with many other AD risk factors, including depression, mid-life obesity, mid-life hypertension and diabetes.
- **Depression** contributed to the second-largest proportion of AD cases in the USA and was the fourth-largest contributor globally.
Brain Health Champion (BHC) Study - 1.0

- **6-month, randomized, controlled trial** of 40 patients from an academic, sub-specialty memory clinic, with mild dementia (15), MCI (21), or subjective cognitive decline (4)

- **Active intervention (BHC) arm**: Health coach
  Patients/caregivers worked with an additional clinical team member, the “brain health champion” (BHC)
  1) Weekly motivational interviewing phone calls
  2) In-person visits every six weeks (updated personalized, attainable goals)
  3) Focused counseling session with a dietician at 6 weeks

- **Control arm (Standard of Care; SOC)**: Usual care
  1) Continuation of usual neurologic care, including some counseling by neurologists about optimal lifestyle/brain health
BHC Study: Outcomes

- **Primary outcomes**: Validated questionnaires assessing changes in physical activity, dietary pattern, and cognitive/social engagement (FCAS)

- **Secondary outcomes** included: Quality of life (QOL), general cognition/memory, neuropsychiatric status, sleep quality, social network size
Coaches Curriculum - Study Flow

• **Significant** evidence that certain behaviors can decrease the chance developing new or worsening cognitive problems.
• A **set of behaviors** is more effective at slowing the rate of conversion from SCD and/or MCI to dementia than a single lifestyle change.
Intervention Effect on Composite Behavioral Score

Change in brain-healthy behavior also strongly predicted improvement in QOL
\( r=0.75, r^2 = 0.56, p<0.00001 \)
Brain Health Champion (BHC) Study 2.0 - Mobile technologies-augmented

• **6-month, randomized, controlled trial** of ~45 patients (27 completers to-date; 34 enrolled), age 60-79, from BWH Behavioral Neurology and BWH Primary Care, with either MCI due to AD/Vascular/Mixed or cognitive normal (CAIDE dementia risk)

• **Active intervention (BHC) arm**: *Health coach*

   Patients/caregivers worked with an additional clinical team member, the “brain health champion” (BHC)

   1) Weekly video-based motivational interviewing calls/ongoing mobile messaging on mobile platform; Use of wearable fitness tracker; Photographed food log (at assessments)

   2) Focused video-counseling session with a dietician at 6 weeks

• **Control arm (Standard of Care; SOC):** *Usual care*

   1) Continuation of usual neurologic care, including some counseling by neurologists about optimal lifestyle/brain health
Preliminary results for Study 2.0

• All participants successfully operated the mobile technology by themselves or with study partner (caregivers) assistance.

• Current trends show BHC participants increased participation in cognitive activities and adherence to a Mediterranean diet based on photographed food logs compared to CE.

• Participants in both arms show significantly increased scores on the composite neuropsychological assessment (pre- and post-study), quality of life (QOL) measures, and an increase in active minutes from pre-to post-assessments.
Future: The Vision of the BHC Program

Develop flexible, replicable, scalable programs, utilizing different groups of health coaches, and applied to diverse groups (patients; community members), across all SES strata.
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“Healthy Heart, Healthy Brain”

Heart Health Is Linked to Brain Health: Study

Protect Your Heart, Protect Your Brain

What’s Good For The Heart Is Good For The Brain
Brain Healthy Behaviors: Diet

- In many studies, **anti-inflammatory diets** are shown to be both brain and heart healthy.

- Greater adherence to the diet is associated with a **lower risk of conversion from MCI to Alzheimer’s dementia**, and **lower mortality** in Alzheimer’s dementia patients.

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**Mediterranean-Style Diet**

**Every Day:**
- Fresh fruits and vegetables
- Beans, lentils and nuts
- Fish
- Whole grains
- Olive oil

**In Moderation:**
- Poultry
- Eggs
- Dairy
- Alcohol (wine)

**Avoid:**
- Sweets with refined sugars
- Red meat
- Saturated fats (butter)

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Cognitive reserve may make the brain more resilient to neurodegenerative changes, and delay the onset and reduce severity of cognitive symptoms. Many factors can contribute to cognitive reserve, including high educational attainment, participation in cognitively challenging activities, and maintenance of a large and active social network.

Brain Healthy Behaviors: Cognitive Reserve

- Cognitive Reserve
- Normal Aging
- Modifiable Health Factors (e.g. diet, exercise, substance use)
- Education
- Social Support
- Positive Affect
- Stimulating Activities/Novel Experiences
- Cognitive Training

IFA Copenhagen Summit
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Prevention Trials based on Alzheimer’s risk

• Anti-Amyloid Treatment in Asymptomatic AD (A4 Study) (Sperling 2013, Sperling 2020)
  – 1167 asymptomatic older adults with elevated amyloid on PET; ages 65-85; 4.5-year trial (with OLE); drug: solanezumab; ongoing

• AHEAD (A3/45) Trials:
  – 1400 asymptomatic older adults (planned); A45 elevated amyloid (similar to A4); A3 intermediate amyloid (lower threshold); ages 55-80 (55-64 additional risk factor); 4-year trial; drug: BAN2401/lecanemab; launched Summer 2020
**AHEAD – 2 Trials in 1**

- **AHEAD (A3-45) Prevention trials**
  
  - Lecanemab (BAN2401), anti-amyloid monoclonal antibody
  
  - **A3**: 4-year phase 2 trial in 400 participants ages 55-80 with preclinical AD (cognitively normal with intermediately elevated amyloid on PET); infusion every 4 weeks
  
  - **A45**: 4-year phase 3 trial in 1,000 participants ages 55-80 with preclinical AD (cognitively normal with elevated amyloid on PET); infusion every 2 weeks x2 years, then every 4 weeks x4 years
Research Needs YOU

- Nearly 6.5 million people in the United States have Alzheimer’s disease
- Communities of color are especially at risk
- Treatments are needed now to help all people at risk for Alzheimer’s disease
Who is Eligible?

- Healthy adults, ages 55 - 80
- Have not been diagnosed with Alzheimer’s disease, but may be worried about memory loss in the future
- Agree to a four-year commitment
- Have a study partner
Thank you!
Questions, Discussion....