Emory Brain Talk Live: Healthy Aging
Goizueta Alzheimer’s Disease Research Center

Sharon Horesh Bergquist, MD, FACP
Associate Professor of Medicine, Emory School of Medicine
September 29, 2020
What is normal in aging?

1950’s

"Successful aging"

1980’s

Empiric and epidemiologic ways to age healthily

Baltimore Longitudinal Study on Aging

MacArthur Foundation Study of Successful Aging

Danish twin studies & Blue Zones

1990’s

Founding biomarkers and interventions to slow aging and detect and treat common age-related diseases at an earlier stage

2000 →

ADRC: Emory Healthy Aging Study, Emory Healthy Brain Study & others
As much as 75% of longevity may be due to nongenetic attributes, including psychological and behavioral factors.

Behavioral factors include:
- LIFESTYLE
- GENES
- ENVIRONMENT

Psychological factors include:
- Purpose
- Social connection
- Perception of aging
- Optimism
- Stress resilience

References:
The processes that lead to aging increase our susceptibility to disease.

Five specific processes involved in aging (left) interact with each other and contribute to chronic diseases (right) that become more common with age. (Adapted from GSIG Summit Perspective, Burch et al., 2014)
What can you begin doing today?

- One in five deaths around the world linked to diet
- Meeting the physical activity guidelines reduced mortality 31%
- Less than seven or more than eight or nine hours of sleep shortens lifespan
- Stress resilience significantly contributes to longevity at all ages
- Lack of high quality relationships has been shown to increase risk of premature death from all causes by 50% compared to having strong relationships.
- Feeling a sense of purpose in life may help you live longer, no matter your age
Adding more whole grains, fruits, nuts and seeds, and vegetables was more effective at reducing premature death and illness than reducing fats and sugars.

Greater purpose in life is associated with a reduced risk of all-cause mortality among older persons.

- 1238 older persons without dementia from two longitudinal cohort studies (Rush Memory and Aging Project and Minority Aging Research Study)
- The association of purpose in life with mortality did not differ among men and women or whites and blacks.
- The finding persisted after accounting for depressive symptoms, disability, neuroticism, the number of chronic medical conditions, and income.

The hazard rate for a person with a high score on the purpose in life measure (90th percentile) was about 57% of the hazard rate of a person with a low score (10th percentile).
Life Crafting: Finding your purpose and meaning

Life crafting as a “wise intervention”

• a process in which people actively reflect on their present and future life, set goals for important areas of life—social, career, and leisure time—and, if required, make concrete plans and undertake actions to change these areas in a way that is more congruent with their values and wishes.

In short, life-crafting is about:

(1) finding out what you stand for (i.e., values and passions)
   • Envision and feel best future self
   • Create an autobiographical narrative (more broadly than goals in context of your personal narrative)

(2) finding out how to make it happen (i.e., goal-attainment plans), and
   Gap between current and future state

(3) telling someone about your plans (i.e., public commitment)
It's not the workout but the intensity

John Lewis, CEO
Update on AD Prevention Trials

Reisa Sperling, M.D.
Center for Alzheimer Research and Treatment
Brigham and Women’s Hospital
Massachusetts General Hospital
Harvard Medical School
The continuum of Alzheimer’s disease

- Preclinical
- MCI Prodomal AD
- “Normal” Aging
- Dementia

Sperling R et al *Alz & Dem* 2011
NIA-AA Preclinical Workgroup
Jack C et al *Alz & Dem* 2018
PET Amyloid Imaging Across the Spectrum of AD

Harvard Aging Brain Study

Sperling, Mormino, Johnson  Neuron 2014
Amyloid and Tau PET Imaging

Aβ (PiB)

Aβ− CN  Aβ+ CN  AD Dementia

Tau (T807)

Sperling, Mormino, Johnson *Neuron* 2014
Testing the Right Target and Right Drug at the Right Stage of Alzheimer’s Disease

Abnormal

Aβ accumulation

Cognitive impairment

Primary Prevention
Delay onset of AD pathology
• Decrease Aβ₄₂ production
• Prevent tangle formation

Secondary prevention
Delay onset of cognitive impairment in individuals with evidence of pathology
• Decrease accumulated Aβ burden
• Decrease neurodegeneration with anti-tau or neuroprotective agents

Tertiary prevention and treatment
Delay onset or progression of dementia
• Neuroprotection-prevent neuronal loss
• Enhance function of remaining neurons
• Neurotransmitter repletion

Normal

No pathology

Preclinical

MCI

Dementia

Sperling, Jack, Aisen Science Trans Med 2011
Anti-Amyloid Treatment of Asymptomatic Alzheimer’s disease (A4) Study

• Secondary prevention trial in clinically normal older individuals (age 65-85y) elevated Aβ screening PET
• 67 sites in U.S., Canada, Japan, Australia
• Phase 3 randomized, double-blind, placebo-controlled trial of solanezumab vs. placebo – 240 weeks (4.5 years)
• Quadrupled dose of sola mid-study due to outside results
• Enrollment N=1150; 575 per arm, stratified by APOE
• LEARN companion study of Aβ-
• Amyloid Disclosure Ethics Substudy
### A4 PET Screening Demographics

<table>
<thead>
<tr>
<th></th>
<th>Not Elevated Amyloid (Aβ-)</th>
<th>Elevated Amyloid (Aβ+)</th>
<th>P-value Aβ- vs Aβ+</th>
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<tbody>
<tr>
<td></td>
<td>( N = 3163 )</td>
<td>( N = 1323 )</td>
<td></td>
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<tr>
<td><strong>Age</strong> Mean years (S.D.)</td>
<td>71.0 (4.5)</td>
<td>72.1 (4.9)</td>
<td>(&lt;0.0001)</td>
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<tr>
<td><strong>Education</strong> Years (S.D.)</td>
<td>16.6 (2.9)</td>
<td>16.5 (2.8)</td>
<td>0.532</td>
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<tr>
<td><strong>Sex Female</strong> (%)</td>
<td>60%</td>
<td>59%</td>
<td>0.641</td>
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<tr>
<td><strong>Marital Status</strong> (%)</td>
<td></td>
<td></td>
<td>0.655</td>
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<tr>
<td>Married</td>
<td>70%</td>
<td>71%</td>
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<tr>
<td>Divorced</td>
<td>14%</td>
<td>14%</td>
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<tr>
<td>Widowed</td>
<td>10%</td>
<td>9%</td>
<td></td>
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<tr>
<td>Never married</td>
<td>4%</td>
<td>4%</td>
<td></td>
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<tr>
<td>Retired</td>
<td>76%</td>
<td>76%</td>
<td>0.927</td>
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<tr>
<td><strong>Amyloid PET SUVr</strong></td>
<td>(0.99 (0.07))</td>
<td>1.33 (0.18)</td>
<td>(&lt;0.0001)</td>
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### A4 Demographics – Race/Ethnicity

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<tr>
<th></th>
<th>All Amyloid PET N=4486</th>
<th>Not Elevated (Aβ-) N = 3163</th>
<th>Elevated (Aβ+) N = 1323</th>
<th>P-value* Aβ- vs Aβ+</th>
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<tr>
<td><strong>All Diverse Participants</strong></td>
<td>503 (11%)</td>
<td>393 (12%)</td>
<td>110 (8%)</td>
<td>&lt; 0.001</td>
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<td><strong>Race</strong></td>
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<tr>
<td>American Indian/Alaskan</td>
<td>32 (1%)</td>
<td>22 (1%)</td>
<td>10 (1%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Asian</td>
<td>171 (4%)</td>
<td>141 (4%)</td>
<td>30 (2%)</td>
<td>0.002</td>
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<tr>
<td>Hawaiian/Pacific Islander</td>
<td>2 (0%)</td>
<td>2 (0%)</td>
<td>0 (0%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Black/African American</td>
<td>167 (4%)</td>
<td>133 (4%)</td>
<td>34 (3%)</td>
<td>0.029</td>
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<tr>
<td>White</td>
<td>4116 (92%)</td>
<td>2866 (91%)</td>
<td>1250 (94%)</td>
<td>&lt; 0.001</td>
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<tr>
<td><strong>Ethnicity</strong></td>
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<tr>
<td>Hispanic/Latino</td>
<td>142 (3%)</td>
<td>103 (3%)</td>
<td>39 (3%)</td>
<td>0.641</td>
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<tr>
<td>Not Hispanic</td>
<td>4309 (96%)</td>
<td>3040 (96%)</td>
<td>1269 (96%)</td>
<td>0.801</td>
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</table>

*p values not adjusted for multiple comparisons
AHEAD 3-45 Study - Optimal Time to Intervene
Aim to Prevent Tau Spreading and Cognitive Decline

Hanseeuw B, Sperling R, Johnson K JAMA Neurology 2019
How to get involved!

• **AHEAD Study** (https://www.aheadstudy.org/)
  – Ages 55-80 (55-64 years old must have strong family history)
  – Screening steps to determine amyloid eligibility
  – 4 year prevention trial with dosing targeted to amyloid burden

• **APT WebStudy** (https://www.aptwebstudy.org/)
  – Internet study to find people for “Trial Ready Cohort”

• **Alzheimer Clinical Trial Consortium (ACTC)**
  – Emory is an ACTC steering committee site – many new trials coming!
Importance of Social Interactions on Cognitive and Emotional Well-being

I-CONECT Project

Hiroko H. Dodge, PhD
Professor of Neurology

Data Core Director
Layton Aging and Alzheimer’s Disease Center
Oregon Center for Aging and Technology (ORCATECH)
Oregon Health & Science University

Goizueta Alzheimer’s Disease Center,
Emory University, Webinar 9/2020
Humans are Social Animals
Human-to-Human Interactions (the Core Component of Social Interaction) and Cognition

- Recent report by the Lancet Commissions (Livingstone, et al., 2020) estimates that 4% of dementia cases can be prevented by eliminating social isolation.
- Same magnitude as smoking (5%) and depression (4%) and higher than other risk factors (physical activity, pollution, diabetes: 2%).

Figure 7: Population attributable fraction of potentially modifiable risk factors for dementia.
Key Research Questions

1. Does increasing social interactions (at advanced ages) lead to improved cognitive function?
2. Mediated by emotional well-being (less lonely)?
3. Who gains?
4. What are the biological mechanisms?
RCT Aimed to Enhance Cognitive Functions Through Social Interactions Using Video Chat

1. NIA R01 AG0033581 (2010-2014) Completed  (ClinicalTrials.gov: NCT01571427)
2. NIA R01 AG051628   (2016-2021) Ongoing (Normal) (ClinicalTrials.gov: NCT02871921)
3. NIA R01 AG056102   (2017-2022) Ongoing (MCI) (ClinicalTrials.gov: NCT02871921)

WWW.I-CONECT.ORG

In this series of RCTs
❖ Participants engage in 30 minutes of semi-structured conversation with trained interviewers (conversational staff).
❖ Requires little motivation (MCI – more apathetic)
❖ Video Chat: Can reach those with chronic illness, home-bound, oldest old
Social Interaction and Cognition

Pilot R01 project (2010 – 2014) results

• Mean age: 80.5 (SD 6.8)
• Adherence: 89% (mean % of days completed)
• Cohen’s D = 0.51 (gains in animal fluency tests compared with control group)

Alzheimer’s & Dementia: Translational Research and Clinical Interventions 2015 V1: 1-12

Web-enabled conversational interactions as a method to improve cognitive functions: Results of a 6-week randomized controlled trial

Hiroko H. Dodge\textsuperscript{a,b,c,*}, Jian Zhu\textsuperscript{d}, Nora C. Mattek\textsuperscript{a,b}, Molly Bowman\textsuperscript{a,b}, Oscar Ybarra\textsuperscript{e}, Katherine V. Wild\textsuperscript{a,b}, David A. Loewenstein\textsuperscript{f}, Jeffrey A. Kaye\textsuperscript{a,b,g}
Video Chat with an automated pop-up of daily picture stimuli (Pilot 2010-2014)

Intense efforts to make the device user-friendly (retention, reduce confounding)
ON-GOING STUDY : ONE TOUCH

Chat

The I-CONECT Study
NEW UI: ONE TOUCH
I-CONECT: Internet-based Conversational Engagement Clinical Trials
(PI: Dodge, NIA R01AG051628; NIA R01AG056102)

ClinicalTrial.gov: NCT02871921

**Isolated 75+ yrs,**

50% African American (AA)

**WWW.I-CONECT.ORG**

**NORMALS**

- **Non AA**  
  - TX: n=40  
  - Control: n=40

- **Non AA**  
  - TX: n=40  
  - Control: n=40

**MCI**

- **AA**  
  - TX: n=40  
  - Control: n=40

- **AA**  
  - TX: n=40  
  - Control: n=40

**TX**: Video Chat, 4 times/week: 6 months, 2 times/week: 6 months

**Control**: 1/wk phone check.

**Novel Outcome Measures**: MedTracker memory; Conversational Speech & Language Quantification; vMRI, DTI, fMRI
Are U.S. Older Adults Getting Lonelier? Age, Period, and Cohort Differences

Louise C. Hawkley  
The National Opinion Research Center (NORC) at the University of Chicago

Till Kaiser and Maike Luhmann  
Ruhr University Bochum

Kristen Wroblewski  
University of Chicago

L. Philip Schumm  
University of Chicago

- Loneliness decreases in frequency/intensity between 50 and 75 years of age, then increases into oldest old age.
- Women tend to be lonelier than men.
- No evidence of cohort (i.e., birth year) differences
- Small, transient increase in loneliness in 2010, but only in NSHAP.
Translational Effects

**Primary outcomes:** MoCA (National Alzheimer’s Coordinating Center Cognitive battery)

**Secondary outcomes:** Executive functions, Objectively measured IADL (OTDL-R)

**Exploratory outcomes:**
- Changes in Speech utterances/Characteristics
- Medication adherence monitored objectively using electronic medication pill box
- Mediation Effect: Personality
New in On-going Projects

MRI at **baseline**, Apoe 4: Who gains?
fMRI: pre-post **changes** in connectivity for Efficacy Assessment and **Biological Mechanisms**
I-CONNECT  Internet-based Conversational Engagement Clinical Trial

THEME:  World Wonders

National Institute on Aging
Which topic would you like to start with today?

- The Pyramids
- Stonehenge
- Taj Mahal

"Please describe the picture you see."
Topic:
The Pyramids

Picture Caption:
A group of people ride camels on their Egypt Pyramids Tour.

Facts:
- The pyramids were built by paid laborers, not slaves.
- Sudan has more pyramids than Egypt.
- The world's largest pyramid by volume is the Great Pyramid of Cholula in Puebla, Mexico.

Possible Questions:
(SM)
What are some things you associate with Egyptian culture?
What other landmarks are in Egypt (ex: Nile River, Suez Canal, etc.)?
Can you name some famous movies involving Egyptian myths/cultures (ex: The Mummy, Cleopatra, etc.)?

(EP)
Have you ever seen a movie based on the pyramids? What was it? What did you think about it?
Have you ever seen a mummy or Ancient Egyptian artifacts at a museum exhibit? What was that like?
Do you remember learning about King Tut in school? What do you remember about him?

(EX)
How do you think the builders of the pyramids influenced modern technology and construction?
Do you think it's acceptable for archaeologists to remove artifacts from the tombs? Is there information we can gain from this? Why/Why not?

The Ancient Egyptians believed in preparing bodies for the eternal afterlife by artificial mummification and burying them with treasures. What do you think about that?

Source URLs for Facts:
https://www.factslides.com/k-pyramids
http://www.science4us.com/sciencefacts/engineering/pyramids.html

Image Attribution:
Author: Jonathan Look, 03/19/2016.
License: © 2018 LP2. All Rights Reserved.
Usage: I-CONNEクト, which is sponsored by the National Institute on Aging.
Source: https://i-features.com/pictures-of-egyptian-pyramids/
HOW DO CHATS WORK?

- I-PANAS-SF
  - International Positive and Negative Affect Schedule Short Form
  - Serves as a standardization metric across interviewers (pre-post changes)
  - First chat of each week
  - Conducted at the beginning and end of chat

- Semi-structured: Themes & Topic with crafted questions for assistance
  - Over 150 themes, including:
    - Historical events
    - Philosophical ideas
    - Social issues
    - Activities and travel

- Questions aim to utilize/stimulate:
  - Reminiscences
  - Critical thinking skills
I-CONECT  Internet-based Conversational Engagement Clinical Trial

TOPIC: Dancing
"Hello!
It's so nice to talk with you.
You're the first person I've talked to all week and I'm stuck in this house all alone."

- I-CONECT Participant
March 23, 2020
Hello all,

Yesterday in our team meeting I shared a lovely bit of feedback from our participant XXXX. While calling to cancel her assessor visits and MRI XXXX informed me that her family does not want her out of the house for her safety and she has been trying to order essential groceries online. She also said that meals on wheels has been coming less and less, from 4 days a week down to 2. They now can only leave the food on the doorstep and she can no longer interact with them, even briefly. She wanted to express her gratitude for being a part of the study. She thanked us for the work we do and said she looks forward to getting to speak with us. She wished Tanner, her assessor, well and said her and her little dog Sparky would be waiting for his visit. She wished our whole team health and happiness during these times.

Her words were touching and really shine a light on the impact this study is making and what it could be used for in the future.
My participant really opened up to me today and wanted to express her gratitude for this study and what it has done for her. She had essentially confined herself to her apartment bedroom for years, barely ever coming out of her room. She said that this study has been life changing for her as it has given her a reason to come out of her room/apartment again and her therapist was very excited for her to begin this study. She has since been getting rid of unnecessary things around her apartment and has even begun picking up some of her knitting and crocheting hobbies again. She moved her rocking chair out into the common area and has been able to get to enjoy the sun light coming from the windows and is even going to attend her apartment complex’s Halloween party this afternoon. She is very much looking forward to her continuing participation.
# Loneliness vs. Social Isolation

<table>
<thead>
<tr>
<th>Loneliness</th>
<th>Social isolation</th>
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<tbody>
<tr>
<td>Subjective: feeling isolated</td>
<td>Objective: being isolated</td>
</tr>
<tr>
<td>Mismatch between actual and desired social relationships</td>
<td>Low levels of social contact</td>
</tr>
<tr>
<td>Unpleasant</td>
<td>Need not be unpleasant</td>
</tr>
<tr>
<td>Low sense of control or choice</td>
<td>May be chosen: “solitude”</td>
</tr>
</tbody>
</table>
Likelihood of mortality by type of isolation:
26% increased likelihood of early mortality, on average

Holt-Lunstad, Smith, Baker, Harris, & Stephenson, 2015
Loneliness and health

- Increased risk of hypertension, myocardial infarction, stroke, diabetes, high cholesterol
- Cognitive decline/dementia
- **Systemic inflammation**

Coles et al., 2007, 2011; Gow et al., 2007; Hakulinen et al., 2018; Hawkley et al., 2010; Richard et al., 2017; Valtorta et al., 2016; Wilson et al., 2007
## Acknowledgements: I-CONECT team

<table>
<thead>
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<th>Oregon Health &amp; Science University</th>
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<tr>
<td>Jeffrey Kaye, MD</td>
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<td>Lisa Silbert, MD</td>
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<td>Katherine Wild, PhD</td>
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<tr>
<td>Meysam Asgari, PhD</td>
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<tr>
<td>Mattie MacDonald, MS, CCRP</td>
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<td>Jacob Lindsley, MA</td>
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<tr>
<td>Nicole Fleming, BS</td>
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<td>Colton Scavone, BA</td>
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<tr>
<td>Tanner Dorsey, BS</td>
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<tr>
<td>Avery Richardson, BS, CAN</td>
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<td>Dara Wasserman, BS</td>
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<tr>
<td>Stephanie Bertoli, BA</td>
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<td>Ona Golonka, BA</td>
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<td>Supriya Pandya, BA</td>
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<td>Annie Dillon, BM</td>
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<td>Louis Weisberg, BS</td>
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<td>Deborah Moore, BA</td>
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<td>Brandy Peacock, BA, DAOM</td>
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<td>Delaney McDaniel, BA</td>
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<td>Brennan Heller, BS</td>
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<td>Carissa Thornall, BA</td>
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<td>Sandy Ruhf, BA, BS, MS</td>
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<td>Mary Ziener-McGinn, MA</td>
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<td>Gina Anderson, BS</td>
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<td>Farah Custodio, PTPR, MD</td>
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<td>Diane Farrell, MM</td>
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<td>Desiree’ DuBoise, BA</td>
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<td>Laura Seeton, BS</td>
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<td>Nita Sridharan, BA</td>
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<td>Nicole Sharma, BA</td>
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<td>Khoa Nguyen, BS</td>
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<td>Thomas Riley, BS</td>
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<td>Liu (Sam) Chen, BS</td>
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<td>Nora Mattek, MPH</td>
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<td>Daniel Schwartz, BA</td>
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<td>David Lahna, BA</td>
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<td>Bill Rooney, PhD</td>
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<td>Tracy Zitzelberger, MPH</td>
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<td>University of Michigan (UM)</td>
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<td>Benjamin Hampstead, PhD</td>
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<td>Laura M. Struble, PhD, GNP-BC</td>
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<td>Kathleen Potempa, PhD, RN, FAAN</td>
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<td>Scott Peltier, PhD</td>
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<td>Roger Albin, MD</td>
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<td>Alexis Ellis, BBA</td>
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<td>Jesica Pedroza, MS</td>
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<td>L. D. Nicolas May, MA</td>
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<td>Jonathan Reader, MS</td>
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<td>Krisanne Litinas, MS</td>
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<td>Arijit K. Bhaumik, BA, CCRP</td>
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<tr>
<td>Wayne State University</td>
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<td>Peter Lichtenberg, PhD</td>
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<td>Institute for Human &amp; Machine Cognition (IHMC)</td>
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<td>Kristy Hollingshead, PhD, MS</td>
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<td>National Institute on Aging (Sponsor)</td>
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<td>Kristina A. McLinden, PhD</td>
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<td>Data and Safety Monitoring Board</td>
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<td>Jonathan Mahnken, PhD</td>
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<td>Howard J. Rosen, MD</td>
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<td>Martin J. Sliwinski, PhD</td>
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<td>Ranjan Duara, MD</td>
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---PARTICIPANTS---

| Institute for Human & Machine Cognition (IHMC) |
| Kristy Hollingshead, PhD, MS |

| National Institute on Aging (Sponsor) |
| Kristina A. McLinden, PhD |

FUNDING:
R01 AG051628, R01AG056102, R01AG033581 [www.i-conect.org](http://www.i-conect.org)
JOIN THE COGNITIVE EMPOWERMENT PROGRAM FOR WEEKLY CLASSES

[Emory University Cognitive Empowerment Program Logo]
What is CEP Live Programming?

**Online Healthy Lifestyle Programs**
Healthy brain interventions to help maintain functional independence.

**45 Minute Weekly Zoom Classes**
Join us and participate in live classes with MCI experts, trainers, and teachers.

**Promote Joy, Health and Wellness**
Become a part of our CEP community network and get access to the latest research and support for families experiencing MCI.

**Participate from Home**
All CEP classes are intended to be practiced from home. No special equipment required.
Ayotoni teaching physical fitness to the members in the gym at the Cognitive Empowerment Center at Emory.
Why should you join us for live programming?

01 Virtual Programs including yoga, accessible workouts, and tai chi are fun and neuroprotective.

02 Discover new strategies and ways of thinking about your empowerment journey.

03 All programming is free and open for anyone to join.

04 Programming is approachable and great to do with a loved one.
Physical Activity

Wednesdays at 10:00 am

Functional Fitness

Join us for workouts with Ayotoni to maintain and even improving your functional fitness and range of motion.

Complete Body Workout

Class includes a warm-up with dynamic stretching to prepare you. We will work on upper and lower body strength, balance, and coordination.
Yoga

Wednesdays at 12:00 pm

Accessible and Approachable

Classes are beginner friendly and doable for any age or ability. Benefits of yoga include improved muscle tone, better breathing habits, increase in flexibility and functional movements including joints and stiff tissues.

Combat Stress with Mindfulness

45 minute classes include seated breathwork and mindfulness to reduce stress, aid in better sleep, and support a sense of well-being.
Tai Chi

Wednesdays at 1:30 pm

Why Tai Chi?

Tai Chi forms consist of a series of natural movements or postures that are done slowly and continuously, resulting in full body workout.

Balance and Relaxation

In this process, we incorporate relaxed breathing, focus and seek balance in our movements to generate and energize the body.
Special Sessions

Wednesdays at 2:30 pm

Overview of Mild Cognitive Impairment on October 14

Join the Emory Cognitive Team for a deeper understanding of MCI

Navigating Driving with MCI on October 21

Join Suzette for some great advise about navigating the challenges of driving after a diagnosis.
Type the following into your internet browser to join us each week:

OR

Put your name in the chat to receive our newsletter

[Link]
