TRUIST

To: McKnight Brain Research Foundation Trustees
Alice Luo Clayton, Ph.D., CEO
Amy Porter, Interim Executive Director

From: Melanie Cianciotto

Subject: MBRF Meeting May 14 – 16, 2025

Date: May 1, 2025

Enclosed you will find the meeting package for the May 14 – 16, 2025, Trustees' meeting to be held in Miami, Florida. Included in this package for your review are the following items: the agenda, final draft of the minutes of the February 24, 2025, Trustees' meeting, minimum distribution calculation, investment review and other supporting materials for the agenda items.

I have made hotel reservations at the Nautilus Sonesta Miami Beach. The hotel address is 1825 Collins Avenue, Miami Beach, 33139.

Following are the room confirmation numbers:

Mike Dockery	#3926447
Madhav Thambisetty	#3926448
Patricia Boyle	#3926449
John Brady	#3926450
Sharon Brangman	#3926451
Allison Brashear	#3926452
Roy Hamilton	#3926453
Sue Pekarske	#3926454
Alice Luo Clayton	#3926458
Amy Porter	#3926455
Valerie Patmintra	#3926456

The meeting on May 14, 2025, will begin at noon and end at 5:00 p.m. The meeting will be held in the Penthouse. The opening Dinner Reception of the Inter-Institutional Meeting will be held at the hotel from 5:30 – 7:00 followed by a performance by the Miami City Ballet.

MCKNIGHT BRAIN RESEARCH FOUNDATION (MBRF)
Meeting of the Board of Trustees
Wednesday, May 14, 2025
12:00 pm EDT – 5:00 pm EDT
Penthouse
Nautilus Sonesta Miami Beach
1815 Collins Avenue
Miami Beach, FL 33139

12:00 pm	1. Call to Order/Welcome/Lunch	Dr. Michael Dockery
ACTION	2. Approval of Minutes -- February 24, 2025	Dr. Michael Dockery
12:15 pm	3. Investment Review	Mr. Mike Hill
12:45 pm	4. Chair's Report a. MBI Annual Report Response Letters b. Open Positions at the University of Florida MBI	Dr. Michael Dockery
1:00pm	5. University of Miami Interim Report a. Dr. Tatjana Rundek, Director, UM EMBI b. Dr. Bonnie Levin, Co-Associate Director, UM EMBI c. Dr. Ihtsham Ul Haq, Co-Associate Director, UM EMBI	Dr. Michael Dockery
1:45 pm	6. CEO's Report	Dr. Alice Luo Clayton
1:55 pm	7. Interim Executive Director's Report	Ms. Amy Porter
2:00 pm	8. Corporate Trustee's Report a. Minimum Distribution Report b. Gifts and Grants Report c. Travel Award Report d. Operating Expense Report	Ms. Melanie Cianciotto
ACTION	e. Proposed 7/1/25-6/30/26 Operating Budget	
ACTION	9. Trustee Compensation	Ms. Melanie Cianciotto
	--- BREAK ---	
2:40 pm	10. Committee Reports	
	a. Membership and Governance i. Updated Activity Timeline	Dr. Sue Pekarske
	b. Finance Committee i. Updated Activity Timeline	Dr. Allison Brashear
	c. Education Committee i. Updated Activity Timeline	Dr. John Brady
	d. Research Committee i. Updated Activity Timeline ii. April 22, 2025 Meeting Minutes	Dr. Madhav Thambisetty
ACTION	iii. CAMI-Core Pilot Grant Program iv. 2026 RFA for Clinical Translational Research Scholarship v. 2025 FRA for Innovator Awards in Cognitive Aging and Memory Loss	
	e. Communications Committee i. Updated Activity Timelines ii. April 29, 2025 Meeting Minutes	Dr. Patricia Boyle
	iii. Brain Works Campaign Update	Ms. Valerie Patmintra BRG Team

4:00 pm	11. National Institute on Aging (NIA) Update	Dr. Molly Wagster
4:45 pm	12. Future Meetings and Events (Attachment 1)	Dr. Michael Dockery
4:55 pm	13. Other Business	Dr. Michael Dockery
5:00 pm	14. Adjournment	Dr. Michael Dockery

ACTION

Attachment 1

MCKNIGHT BRAIN RESEARCH FOUNDATION (MBRF)
FUTURE MEETINGS AND EVENTS

August 18, 2025	**Trustees' Meeting** **Virtual**
October 19 – 20, 2025	**Trustees' Meeting** **Alexandria, VA**
October 19, 2025	7:00 PM – Dinner
October 20, 2025	8:00 AM – 3:00 PM Trustees' Meeting
November 16, 2025	**Society for Neuroscience (SfN) Poster Session** **San Diego, CA**
February 2026	**Trustees' Meeting** **TBD**

16th Annual Inter-Institutional Meeting
Evelyn F. McKnight Brain Institutes
McKnight Brain Research Foundation and University of Miami MBI
MAY 14 - 16, 2025

BRAIN HEALTH: From Discoveries to Community

Wednesday, May 14th, 2025

Location: **Nautilus Sonesta**
1825 Collins Ave
Miami Beach, FL 33139
Phone 305-503-5700

12:00pm - 4:00pm **PRE-MEETINGS** *in the Bridge Room*

12:00pm - 12:15pm **Welcome and Introduction to Pre-Meetings (Ihtsham Haq and Tatjana Rundek, UM)**

12:15pm - 1:00pm **Buffet Lunch** *in the Bridge Room*

12:30pm - 1:10pm Neuromodulation (*Chairs:* John Williamson, UF; Keith McGregor, UAB)

1:10pm - 1:50pm Precision Aging (*Chairs:* Carol Barnes, UA; Ron Lazar, UAB)

1:50pm - 2:30pm Metabolism & Cardiovascular Function (*Chairs:* Sara Burke, UF; Lee Ryan, UA)

2:30pm - 3:10pm Neuroinflammation (*Chairs:* Tom Foster, UF; Meredith Hay, UA)

3:10pm - 3:50pm AI & Neuroimaging (*Chairs:* Ihtsham Haq, UM; Arne Ekstrom, UA)

3:50pm - 4:00pm **Break**

4:00pm - 4:30pm **MCKNIGHT BRAIN AGING REGISTRY (MBAR)** (*Chairs*: Kristina Visscher, UAB; Bonnie Levin, UM; Ron Cohen, UF) *In the Bridge Room*

4:30pm - 5:00pm **INTER-INSTITUTIONAL PROJECTS AND COLLABORATIONS** - Cognitive Aging and Memory Intervention (CAMI) Core: Ihtsham Haq, UM; Sara Burke, UF) *In the Bridge Room*

5:15pm - 7:15pm **Welcome Reception at Lobby Bar**
Nautilus Hotel

5:45pm - 6:00pm **Welcome**
Tatjana Rundek, M.D., Ph.D.
Director of Evelyn F. McKnight Brain Institute

Guillermo (Willy) Prado Ph.D.
Interim Provost and Executive Vice President for Academic Affairs

Michael L. Dockery, M.D.
Chair, Board of Trustees, McKnight Brain Research Foundation

6:00pm - 7:15pm **Dinner at The Backyard, Nautilus Hotel**

7:30pm - 9:00pm **Miami City Ballet Studios**
2200 Liberty Ave
Miami Beach, FL 33139

Thursday, May 15th, 2025

Location:	**Nautilus Sonesta** **1825 Collins Ave** **Miami Beach, FL 33139** **Phone 305-503-5700**
8:00am - 8:45am	**Breakfast at the Nautilus Cabana Club Terrace**
8:00pm - 8:45am	**YOUNG INVESTIGATOR SESSION: Future Research Directions** (*Leaders*: Bonnie Levin, UM; Carole Barnes, UA; Ron Lazar, UAB; Tom Foster, UF)
9:00am - 9:30am	**Welcome & Introduction in the Bridge Room** **Tatjana Rundek, M.D., Ph.D.** Director of Evelyn F. McKnight Brain Institute **Henri R. Ford, M.D., MHA** Dean and Chief Academic Officer University of Miami Leonard M. Miller School of Medicine **Jose Romano, FAHA, FAAN, FAAN** Chairman, Department of Neurology U Miami **New Direction McKnight Brain Research Foundation** **Michael L. Dockery, M.D.** Chair, Board of Trustees, McKnight Brain Research Foundation (MBRF) **Introduction to Program and Meeting Overview** **Tatjana Rundek, M.D., Ph.D.** Director of Evelyn F. McKnight Brain Institute

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SESSION I	**Biomarkers of Optimal Aging: Potential Intervention Targets**
9:30am - 10:30am	**Moderators: Farah Lubin, UAB and Tom Foster, UF**
9:30am - 9:40am	Consequences of Mitochondrial Defects in Aging Neurons: Carlos Moraes (UM)
9:40am - 9:50am	Imaging and Epigenetic Biomarkers of Brain Health: Yenisel Cruz-Almeida (UF)
9:50am - 10:00am	Characteristics of Exceptional Performers and Resilient Individuals: Matt Huentelman (UA)
10:00am - 10:10am	Biomarkers of Sleep in Aging: Christian Agudelo (UM)
10:10am - 10:30am	**Panel Discussion (Discussion Lead: Farah Lubin)**

10:30am - 10:45am Break

SESSION II **Translation to Practice and Community**

10:45am - 11:45am **Moderators: Ron Lazar, UAB and James Galvin, UM**

10:45am - 11:00am Community Participatory Research: Rosie Curiel (UM)

11:00am - 11:15am Precision Aging in the Community: Education, Engagement, and Participation: Lee Ryan (UA)

11:15am - 11:30am Cognitive Decline Following Transient Ischemic Attack: Victor Del Bene (UAB)

11:30am - 11:50am **Panel Discussion (Discussion Lead: Susan Fox-Rosellini, UM)**

12:00pm - 2:00pm **Lunch at the Nautilus Cabana Club Terrace**

12:45pm - 12:55pm **Introduction of the 1st Ralph L. Sacco Scholars in Brain Health by AAN/AHA**
(Dr. Patrick Devlin, UT Houston and Dr. Cyprien Rivier, Yale) *in the Bridge Room*

1:00pm - 2:00pm **KEYNOTE LECTURE: Updates on Vascular Cognitive Aging and Risk for Dementia**

Charles DeCarli, MD, FAAN, FAHA
Victor and Genevieve Orsi Chair in Alzheimer's Research
Distinguished Professor of Neurology
Co-Director, Alzheimer's Disease Research Center
Chief, Imaging of Dementia and Aging (IDeA) Laboratory
University of California at Davis

SESSION III **Environmental Challenges to Brain Health**

2:00pm - 3:00pm **Moderators: Bonnie Levin, UM and Lee Ryan, UA**

2:00pm - 2:10pm Harmful Algal Blooms and Brain Health: Larry Brand (UM)

2:10pm - 2:20pm PFAS and Brain Health: Hannah Gardener (UM)

2:20pm - 2:30pm Microgravity Effects on the Human Brain and Behavior: Co-occurring Dysfunction and Adaptive Plasticity: Rachael Seidler (UF)

2:30pm - 2:40pm	Environmental Exposures Accelerate Brain Aging and Influence: Ashely Adamson (UAB)
2:40pm - 3:00pm	**Panel Discussion (Discussion Lead: David Davis, UM)**
3:00pm - 3:15pm	Break

SESSION IV	**Machine Learning and Big Data Approaches to Cognitive Aging**
3:15pm - 4:00pm	**Moderators: Ihtsham Haq, UM and Aprinda Queen, UF**
3:15pm - 3:30pm	Digital Twin Approaches to Cognitive Aging: Yelena Yesha (UM)
3:30pm - 3:45pm	Examining the Relationship Between Brain Aging and Cognition With a Machine Learning Approach: Junghee Lee (UAB)
3:45pm - 3:55pm	AI in Oculomics: Jianhua Wang (UM)
3:55pm - 4:15pm	**Panel Discussion (Discussion Lead: Ihtsham Haq, UM)**

SESSION V	**Brain Health: Action & Implementation (from pre-meeting groups)**
4:15pm - 5:30pm	**Moderators: Carol Barnes, UAB and Ihtsham Haq, UM**
4:15pm - 5:00pm	Pre-Meeting Group Leaders Present Action Items and Next Steps
5:00pm - 5:30pm	Discussion

6:00pm - 6:15pm	Board buses
6:30pm - 9:00pm	**Dinner** *(Per invitation only)*

Friday, May 16th, 2025

6:30am - 8:00am	**Breakfast at the Nautilus Cabana Club Terrace** Board of Directors Breakfast with MBI Directors
8:15am - 8:45am	**Board buses to depart for UM**
Location:	**University of Miami** Bascom Palmer Auditorium 900 NW 17th Street Miami, FL 33136
9:15am - 9:30am	**Welcome** Tatjana Rundek, M.D., Ph.D.

SESSION VI	**Translating Discoveries into Action**
9:30am - 10:30am	**Moderators: Carol Barnes, UA and Tatjana Rundek, UM** (10 minute presentations with 5 minutes Q & A)
9:30am - 9:45am	Effect of Genetic Ancestry on APOE Risk for Dementia on the Aging Population: Anthony Griswold (UM)
9:45am - 10:00am	Vascular Health and HIV: Exercise is Medicine: Raymond Jones (UAB)
10:00am - 10:15am	Studying the Aging Social-Cognitive Brain: Bridging Basic Science and Real-World Impact: Natalie Ebner (UF)
10:15am - 10:30am	Transcranial Magnetic Stimulation for Mild Cognitive Impairment and Alzheimer's Disease: Ying-Hui Chou (UA)
10:30am - 10:40am	Break

Session VII	**Blitz Presentations**
10:40am - 11:45am	**Moderators: Christian Agudelo, UM and Natalie Ebner, UF**
10:40am - 10:55am	McKnight Brain Aging Registry (MBAR) Updates: Kristina Visscher (UAB) and Bonnie Levin (UM)
10:55am - 11:10am	Cognitive Aging and Memory Intervention (CAMI) Core Updates: Ihtsham Haq (UM) and Keith McGregor (UAB)
	(6 minute presentations with 3 minutes Q & A)
11:10am - 11:20am	Life Essential 8 and Cognition: Tali Elfassy (UM)

11:20am - 11:30am	Cognitive Intervention and Brain Change: Can These be Applied to Aging: Arne Ekstrom (UA)
11:30am - 11:40am	Understanding Cognitive Health and Health Disparities: Social Determinants of Health Perspective: Kun Wang (UAB)
11:40am - 11:50am	Tinker-FUN (Tinkering activities to Flex Ur braiN): A Cognitive Flexibility Oriented Intervention for Older adults: Vince Wu (UF)
11:50am - 12:00pm	Closing Remarks
12:00pm	**Meeting adjourns** Lunch: Boxed lunches available for pickup on the way out

MINUTES
MCKNIGHT BRAIN RESEARCH FOUNDATION
BOARD OF TRUSTEES MEETING
Via Teams
February 24, 2025

The Trustees' meeting of the McKnight Brain Research Foundation (MBRF) was called to order at 4:00 p.m. EST on February 24, 2025.

The following members were present:
Dr. Michael Dockery, Chair
Dr. Madhav Thambisetty, Vice Chair
Dr. Patricia A. Boyle, Trustee
Dr. Allison Brashear, Trustee
Dr. John Brady, Trustee
Dr. Sharon Brangman, Trustee
Dr. Roy Hamilton, Trustee
Dr. Susan Pekarske, Trustee
Dr. J. Lee Dockery, Chair Emeritus
Ms. Melanie Cianciotto, Corporate Trustee,
Truist Foundations and Endowments Specialty Practice

Others attending:
Mr. Mike Hill, Truist Foundations and Endowments Specialty Practice
Mr. Carson Powers, Truist Foundations and Endowments Specialty Practice
Ms. Amy Porter, Interim Executive Director
Ms. Valerie Patmintra, Senior Communications Advisor

1. Approval of Minutes

The minutes of the October 14, 2024, Board of Trustees' Meeting of the McKnight Brain Research Foundation (Attachment 1) were reviewed and approved as amended:

Item 3. A. – the last sentence of the paragraph has been changed to read "The gift agreement will need to be completed before any new gift from the MBRF. Mr. Roczniak was informed the MBRF would not anticipate making the first payment before early 2025.

Action Item 1: The minutes of the October 14, 2024, Board of Trustees' Meeting of the McKnight Brain Research Foundation (Attachment 1) were reviewed and approved as amended.

2. Investment Review

Mr. Hill presented the investment review and commented on key economic and investment factors through January 31, 2025 (Attachment 2).

A. Market Environment

- Equities were positive for 2024, with U.S. large cap growth stocks outperforming relative to small and mid-cap stocks and international markets.

- Given the uncertainty over fiscal policies and interest rates in 2025, it would be normal to see a few, potentially deeper pullbacks in the market.

- U.S. yields remain high relative to the past two decades. Rising yields are defying the typical reaction to Fed rate cuts for now.

B. Portfolio Review

Asset Allocation: The asset classes of the investments within the portfolio of the MBRF remain within the guidelines established by the trustees in the Investment Policy Statement of the Foundation.

Portfolio Performance: For the one-year period ending January 31, 2025, the total return for the portfolio was 19.45% versus 19.61% for the Investment Policy Statement Index.

3. Chairman's Report

Dr. Dockery shared that he spoke with each of the trustees separately to review their Self-Assessment form. Significant change in the volume of email traffic; grateful to Ms. Porter for coming onboard; and pleased with the CEO search process seemed to be common themes.

Dr. Dockery shared that the CEO Search Committee interviewed 3 candidates in person and there is 1 clear front runner, Alice Luo Clayton, Ph.D. The offer letter has been signed and the contract is being negotiated with hopes it is completed by the end of this week. Ms. Porter will be staying on indefinitely at this time and we do not yet have a start date for Dr. Clayton.

4. Executive Director's Report

A. Update on Activities

Ms. Porter provided the trustees with an update on her activities. Ms. Porter participated in all of the committee meetings held in January and February as well as the CEO Search activities.

Ms. Porter worked with Ms. Patmintra and AFAR on the press release for the 2024 Innovator Award Recipients. Ms. Porter worked with AAN on the notification award for the 2025 Clinical Translational Scholarship Recipients.

Ms. Porter worked with Dr. Sara Burke on the Pilot Grants. Thank you letters and the $200 stipend per reviewer have been mailed.

B. Inter-Institutional Meeting
Ms. Porter shared the latest draft agenda for the May 14 – 16, 2025, Inter-Institutional Meeting (Attachment 3). The trustees shared the agenda is well balanced and the program looks quite comprehensive. The trustees would like to know the outcome of the pre-meetings and what has happened to the to do list from the 2024 pre-meetings.

5. Corporate Trustee's Report

A. The trustees reviewed the projected minimum distribution calculation for information (Attachment 4).

B. The trustees reviewed the Gifts & Grants Report for information (Attachment 5).

C. The trustees reviewed the Travel Award Report for information (Attachment 6).

D. Ms. Cianciotto shared the Operating Expense Report with the trustees (Attachment 7).

Action Item 2: The trustees reviewed, for information, the projected minimum distribution calculation (Attachment 4).

Action Item 3: The trustees reviewed, for information, the Gifts and Grants Report (Attachment 5).

Action Item 4: The trustees reviewed, for information, the Travel Award Report (Attachment 6).

Action Item 5: The trustees reviewed, for information, the Operating Expenses Report (Attachment 7)

6. Committee Reports

A. Membership & Governance Committee

Dr. Pekarske provided the trustees with the updated Membership & Governance Committee Activity Timeline (Attachment 8). The committee met on January 21, 2025. Dr. Pekarske pointed out several highlighted items on the activity timeline:

A draft list of updates to the Orientation Manual were presented to the committee for their review. Once all of the updates are made the updated Orientation Manual will be uploaded to the secure website.

The renewal of terms section has been expanded and there are 4 trustee renewals in 2026.

Trustee Self-Assessments were received from all of the trustees. Dr. Mike Dockery has spoken with each of the trustees separately to review their Self-Assessment form.

B. Finance Committee

Dr. Brashear provided the trustees with the updated Finance Committee Activity Timeline (Attachment 9). The committee met on January 21, 2025.

The committee reviewed the financial information contained in each of the MBI Annual Reports and requested follow up information regarding each institutes' spending policy and university endowment fee.

Dr. Brashear shared the 2025 Society for Neuroscience (SfN) proposal (Attachment 10). The committee recommends approval at the Tier 2 Level of $28,050. The trustees approved the recommendation of the committee.

Action Item 6: The trustees approved the 2025 SfN Proposal at the Tier 2 level of $28,050.

Dr. Brashear shared the 2025 Evelyn F. McKnight Clinical Translational Research Scholars Dinner proposal (Attachment 11). The committee recommends approval of the $4,500 proposal. The trustees approved the recommendation of the committee.

Action Item 7: The trustees approved the 2025 Evelyn F. McKnight Clinical Translational Research Scholars proposal of $4,500.

C. Research Committee

Dr. Thambisetty shared the updated Research Committee Activity Timeline (Attachment 12). The committee met on January 28,2025.

Cognitive Aging and Memory Core (CAMI) Update

Dr. Thambisetty shared the CAMI Core Pilot Grant Review Committee met on January 17, 2025, and recommended 3 proposals for funding (Attachment 13). The research committee reviewed these recommendations during their recent committee meeting and support the funding of the three pilot grants:

1)Effects of age on fear generalization and its underlying neurobiological substrates in female adults: a cross-species investigation

PIs Ashley Huggins, PhD (UA) and Caesar Hernandez, Ph (UAB)

2)Effect of Alcohol Reduction and Probiotic Interventions on Cognition and Brain Glucose Metabolism in Normal Aging Adults who are High Risk Alcohol Drinkers
PIs: Teddy Salan, PhD (UM); Eric Porges, PhD (UF)

3)A novel intervention to address orientation and navigation declines with aging
PIs: Arne Ekstron, (UA); Steve Weisberg, PhD (UF)
(also Hill, Ebner, and Visscher as co-investigators)

The trustees approved funding of the three pilot grants recommended by the CAMI Core Pilot Grant Review Committee.

Action Item 8: The trustees approved funding of the three pilot grants recommended by the CAMI Core Pilot Grant Review Committee.

The 2024 Innovator Awards in Cognitive Aging and Age-Related Memory Loss
Dr. Thambisetty shared that the 2024 MBRF Innovator Awards in Cognitive Aging and Memory Loss were announced in a press release on December 17, 2024 (Attachment 14).

2025 MBRF Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss
Dr. Thambisetty shared that 10 applications were received by the September 10 deadline and they were all focused on cognitive aging. The review meeting was held on November 7, 2024. Awards were made to Giovanna Pilonieta, PhD, (UAB); and Deborah Rose, MD, (Johns Hopkins). Their award letters are included in the material but this is to remain confidential until announced in April at the AAN meeting (Attachment 15).

D. Communications Committee

Dr. Boyle shared the updated Communications Activity Timeline (Attachment 16). The Communications and Research Committees met jointly on February 6, 2025.

Ms. Kate Worthy from BRG, provided a Brain Works Campaign update. The campaign is tracking very well against the year two media goals and has already surpassed the number of media impressions anticipated for the year thanks to several high-profile media placements featuring the MBRF Trustees. The digital coverage is also exceeding expectations.

Ms. Patmintra shared a document outlining recommended resources to add to the Brain Works resource hub. The committee was asked to review and approve the document by February 9, 2025.

Dr. Brangman shared an update on the AARP Brain Health Action Collaborative. She is participating in the quarterly meetings with the goal of finding the MBRF's niche and encouraged Ms. Patmintra to join the meetings going forward.

E. Education Committee

Dr. Brady shared the updated Education Committee Activity Timeline (Attachment 17).

Dr. Brady shared the partnership opportunity with the American Academy of Family Physicians (AAFP) for the Trustees' review. The foundation has the opportunity to reach both AAFP professional members and patients through their various communications channels both with existing Brain Works campaign resources and via new articles and content that would be developed in partnership with AAFP. Ms. Patmintra will work with BRG to secure a contract with AAFP.

Dr. Brady shared he participated in a brainstorming session about the MBRF Education Program with BRG and Ms. Patmintra. The session focused on ideas designed to pinpoint the potential program goals, priority audiences, call to action, measures or success, and more.

7. Review of Annual Reports

a. University of Alabama at Birmingham

The trustees reviewed the annual report concerning the Evelyn F. McKnight Brain Institute at the University of Alabama at Birmingham (Attachment 18).

As a follow-up to the report, the trustees request information on the frequency of the advisory committee meetings with a copy of the minutes and agenda from the March 3, 2025, meeting when available.

Action Item 9: Send thank you letter to Dr. Ron Lazar and Mr. Tom Brannon expressing the trustees' appreciation for the report and requesting information on the frequency of the advisory committee meetings with a copy of the minutes and agenda from the March 3, 2025, meeting when available.

b. University of Arizona

The trustees reviewed the annual report concerning the Evelyn F. McKnight Brain Institute at the University of Arizona (Attachment 19).

As a follow-up to the report, the trustees request succession planning be addressed in future annual reports. The trustees also request the issue around the balance of the unmatched funds be clarified and steps be taken to complete the match.

Action Item 10: Send thank you letter to Dr. Carol Barnes expressing the trustees' appreciation for the report and request succession planning be addressed in future annual reports. The trustees' ask the issue around the balance of the unmatched funds be clarified and steps be taken to complete the match.

c. <u>University of Florida</u>

The trustees reviewed the annual report concerning the Evelyn F. and William L. McKnight Brain Institute at the University of Florida (Attachment 20).

The trustees are concerned with the loss of Dr. Ron Cohen and Dr. Adam Woods from the leadership of the CAM Center and their productivity in the human component of Clinical Translational Research. They are also concerned about Dr. Tom Foster's retirement at the end of June 2025.

Action Item 11: Send thank you letter to Dr. Jen Bizon expressing the trustees' appreciation for the report and sharing their concern about the loss of Dr. Ron Cohen and Dr. Adam Woods and the upcoming retirement of Dr. Tom Foster.

d. <u>University of Miami</u>

The trustees reviewed the annual report concerning the Evelyn F. McKnight Brain Institute at the University of Miami (Attachment 21).

The trustees observed a considerable amount of research effort at the EMBI is devoted to Alzheimer's Disease and Dementia. The trustees understand this research is important and contributes to scientific knowledge. However, the purpose of the MBRF is to support research in age related cognitive decline and memory loss differentiated from all other neurogenerative disease.

Action Item 12: Send thank you letter to Dr. Tatjana Rundek expressing the trustees' appreciation for the report and reminding the EMBI that the purpose of the MBRF is to support research in age related cognitive decline and memory loss differentiated from all other neurogenerative disease.

There being no further business, the meeting was adjourned at 7:20 p.m. EST.

Summary of Action Items:

Respectfully submitted,

Melanie A. Cianciotto
Truist Bank, Corporate Trustee

McKNIGHT BRAIN RESEARCH FOUNDATION

Preserving memory, enhancing life

March 9, 2025

Carol A. Barnes, PhD. Director, Evelyn F. McKnight Brain Institute
Evelyn F. McKnight Chair for Learning and Memory in Aging
University of Arizona Regents Professor

Dear Dr. Barnes,

At the February 24, 2025, meeting of the McKnight Brain Research Foundation (MBRF), the trustees reviewed the 2024 annual report submitted by the Evelyn F. McKnight Brain Institute (EMBI) at the University of Arizona (UA). The report was seen as a well-organized synopsis of the productivity of the EMBI in collaborative research, scientific publications, and new grant awards.

It is impressive that the research completed in the (PAN) Precision Aging Network: Closing the Gap Between Cognitive Healthspan and Human Lifespan" will be recognized with ten of the manuscripts to be published in a SPECIAL Issue of the journal **Gerontology** under the general topic of Precision Aging. Publication of these manuscripts represent important achievements in meeting the objectives of the U19 grant award launched in September 2021.

The trustees note the outstanding accomplishment in the publication of a chapter in **The Hippocampus Book.** The chapter on **Aging and the Hippocampus** coauthored by you and your colleague Dr. Sara Burke is the only chapter featuring normal cognitive aging.

The trustees commend the collaboration with Dr. Matt Huentelman through **MindCrowd,** a web-based testing tool, the Precision Aging network has been able to recruit large numbers of participants. The development of an "MRI" van and lab which can be driven to people's homes and other locations will enable testing of difficult to reach or underserved populations and increase the outreach and the number of participants. The trustees are pleased to note the number of participants recruited for the Precision Aging Network has already exceeded the goal for 2026.

The trustees commend your continued research studies on brains of non-human primates. The establishment experimentally of what is typically expected in brain aging trajectories and the differentiation of the changes due to neurogenerative disease and the aging brain is critical to the understanding of cognitive aging.

The research training and mentoring of research training at the undergraduate, graduate and post-doctoral level are commendable in recognizing the importance of educating future scientists in cognitive aging. The undergraduate program on "insights into Healthy Aging" is an important collaboration with the College of Public Health course on "Aging and Public Health". It is impressive the medical students are given research training in laboratories supported by the College of Medicine Medical Research Program.

It noted in your plans for the future you will continue your immense productivity and valuable contributions to the knowledge and the science of cognitive aging. In the past, the trustees have commented on the importance of succession planning and request this issue be addressed in future reports.

It is noted in the report from the UA Foundation, the balance on the unmatched funds from the gift is $36,482. In a verbal report prior to the receipt of the 2024 Annual Report document the MBRF was informed the match had been met. The trustees ask this issue be clarified and steps be taken to complete the match, so that the contribution expected from the unmatched balance no longer requires monitoring.

The trustees express their collective appreciation for your support and efforts in continuing to advance the research initiatives supported by the McKnight Brain Research Foundation, leading preserving memory and enhancing life through brain health.

Sincerely,

Amy Porter
Interim Executive Director

CC. J.P. Roczniak, President and CEO, UA Foundation; Lee Ryan, PhD, EMBI Associate Director; Peggy Nolty, EMBI Executive Assistant and Administrator; MBRF Trustees

Established by Evelyn F. McKnight to Alleviate Memory Loss in the Aging

McKNIGHT BRAIN RESEARCH FOUNDATION

Preserving memory, enhancing life

March 4, 2025

Established by Evelyn F. McKnight to Alleviate Memory Loss in the Aging

Mr. Tom Brannan
Vice President for Development and Alumni
The University of Alabama at Birmingham
1264 1720 2nd Ave. S
Birmingham, AL 35294-0112

Dear Mr. Tom Brannan

At their meeting on February 24, 2025, the trustees of the McKnight Brain Research Foundation (MBRF) reviewed the 2024 annual report submitted by the Evelyn F. McKnight Brain Institute (EMBI) at the University of Alabama at Birmingham (UAB). The trustees are pleased the report provided a favorable representation of the EMBI with its continued growth with numerous collaborations and publications demonstrating the productivity in advancing the research mission in cognitive aging.

The trustees were impressed with the notable NIH funding that has been secured and the expansion of faculty to 65 members extending the collaborations between the EMBI and **nine** academic and research units within UAB. However, trustees encourage the continued leverage of grant funding opportunities and to develop more publications in high-impact journals and increased faculty leadership in authorship.

It was pleasing to the trustees to learn the plan to develop the Brain Aging and Memory Hub (BHAM), mentioned in earlier annual reports, is now operational with space for both clinical and research for the EMBI and four other affiliated brain aging and memory divisions and the Alzheimer's Disease Center.

The establishment and the progress in the development of the Brain Health Advocacy Mission are very impressive and an important and powerful connection between the primary care providers. The implementation of a process to evaluate brain health leading to the establishment of a Brain Care Score in collaboration with the McCance Center is commendable and has the potential of great clinical value. The extension of BHAM with the Birmingham Fire and Rescue service to evaluate the wellbeing and brain health of this vulnerable occupational population is to be commended.

The McKnight Brain Aging Registry (MBAR) remains one of the most successful collaborative research projects funded by the MBRF. The trustees recognize Dr. Kristina Visscher's leadership in its success and making research data available to all the McKnight Brain Institutes and external research investigators.

The importance of growing the next generation of scientists is confirmed with the establishment of training programs in "Neurobiology of Cognition and Cognitive Disorders" in the Department of Neurobiology. Additionally, the UAB Neuroscience Roadmap Scholars Program directed by Dr. Farah Lubin provides the tools for enhancing the engagement and retention of graduate trainees in neuroscience. Each of the programs shows strong commitment to diversity and trainee support.

As further evidence of developing future scholars, the trustees note the recruitment of Drs. Abbi and Caesar Hernandez to the EMBI who received their training at the University of Florida MBI.

The trustees remain interested in the role of the advisory committee in the operation and management of the EMBI. It is noted the committee was scheduled to meet on March 3, 2025. Please provide the trustees with information on the frequency of the advisory committee meetings with a copy of the agenda and the minutes of the March 3, 2025, meeting when available.

The trustees express their collective appreciation for your support and efforts in continuing to advance the research initiatives supported by the McKnight Brain Research Foundation, leading preserving memory and enhancing life through brain health.

Sincerely,

Amy Porter
Interim Executive Director

Cc: Dr. Ronald M. Lazar; Dr. Kristina Visscher; Dr. Anupam Agarwal; Dr. Ray L. Watts; Dr. David G. Standaert; MBRF Trustees

McKNIGHT BRAIN RESEARCH FOUNDATION

Preserving memory, enhancing life

March 10, 2024

Established by Evelyn F. McKnight to Alleviate Memory Loss in the Aging

Tatjana Rundek, M.D., Ph.D.
Professor of Neurology | Evelyn F. McKnight Chair for Learning and Memory in Aging
Director, Evelyn F. McKnight Brain Institute
University of Miami

Dear Dr. Rundek,

At the February 24, 2025, meeting of the McKnight Brain Research Foundation (MBRF), the trustees reviewed the 2024 annual report submitted by the Evelyn F. McKnight Brain Institute (EMBI) of the University of Miami (UM). The report is an attractive and well-organized comprehensive summary and describes many research initiatives and collaborations as well as the many scientific and educational achievements of the EMBI's activity.

The trustees are pleased to note the new and highly qualified leadership of the EMBI that has been established following the death of Dr. Sacco. The trustees look forward to continuing to work with you as the director of the EMBI as well as Dr. Levin and Dr. Haq as Associate Directors. It is also noted Dr. Agudelo has replaced Dr. Sun as the education director and Dr. Sun is now director of the Brain Endowment Bank. The appointment of Dr. Galvin to the Schoeninger Endowed Chair in Memory Disorders as well as Director of the Comprehensive Center for Brian Health (CCBH) provides a strong leadership infrastructure to advance the comprehensive programs in cognitive aging and memory at the UM EMBI.

The trustees applaud the news of the appointment of Dr. Jose Romano as the Chair of the Neurology Department after serving as acting chair and interim chair of the department following Dr. Ralph Sacco's death in 2023. Dr. Romano, a renowned clinical neurologist who is a long-time friend and advocate of the MBRF, has been a highly respected faculty member at the UM Miller School of Medicine for over 25 years.

Other leadership changes in the School of Medicine were noted with the appointment of Dr. Guillermo Prado as Executive Vice President for Academic Affairs and Provost and Mr. Joe Echevarria as the new President and CEO of UM Health

Under Dr. Rundek's leadership, the continued implementation of the 5-year strategic plan scheduled to be completed by the end of 2025 appears to be effective in the efforts to consolidate the cognitive clinical and translational research in all divisions in the Department of Neurology under the EMBI umbrella.

The trustees commend the EMBI on the receipt of 24 new grants in 2024 and 20 special awards for scientific merit and achievement. The report highlights the importance of the two large NIA U19 Programs. In addition, the report reflected the continued robust productivity of the team of seven faculty and 43 staff members under Dr. Galvin's leadership in efforts to innovate and lead brain health and aging research with a particular focus on minoritized populations.

It is impressive that the Annual Report describes collaboration of over 100 clinical and translational scientists in the Collaborative Integrative Translational Trans-Disciplinary Institute (CITTI). The EMBI reflects affiliation with 15 programs located in centers or divisions in the School of Medicine.

The trustees were pleased to observe the partnership of the EMBI in the PAN (Precision Aging Network), the NIA U19 project at the University of Arizona MBI.

With appreciation the trustees recognize Dr. Levin's continued leadership and valued participation in the McKnight Brain Aging Registry (MBAR) Inter-Institutional Research Program designed to evaluate the cognition and memory of individuals older than 85 years of age. The registry now contains over 500 participants followed in the UM cognitive neurology clinics and the data contained in the Registry can be accessed by each of the research scientists at each of the MBIs and external investigators. It is noted that in addition to her many other contributions to the success of the strategic plan for the EMBI, Dr. Levin leads the Neuropsychology Post-doctoral Fellowship Program with six faculty, four post-doctoral Fellows, seven upper-level graduate PhD practicum students, and two volunteer undergraduate assistants.

The trustees commend the establishment of the new compulsory cognitive neurology program as a core requirement for all neurology residents. Under Dr. Agudelo's leadership, twelve students participated in the one-year program which received favorable reviews, and one resident electing to pursue a career in cognitive neurology.

The trustees observed a considerable amount of research effort at the EMBI is devoted to Alzheimer's Disease and Dementia. The trustees understand this research is important and contributes to scientific knowledge. However, the purpose of the MBRF is to support research in age related cognitive decline and memory loss differentiated from all other neurogenerative disease. It is hoped this effort is not sublimated or diluted while other research efforts are pursued.

The trustees are excited and are looking forward to attending the 16th Inter-institutional Meeting hosted by the EMBI on May 14-16, 2025, while remembering the remarkably successful meeting hosted by the UM EMBI held virtually due to the pandemic.

The trustees express their collective appreciation for your support and efforts in continuing to advance the research initiatives supported by the McKnight Brain Research Foundation, leading to preserving memory and enhancing life through brain health.

Sincerely,

Amy Porter
Interim Executive Director

CC: Dean Henri Ford, MD, MHA; Bonnie Levin, PhD; Ihtsham Haq, MD; Susan Fox-Rosellini, MBA; Stacy Merritt, MA, CCRP; Christian Agudelo, MD; James E. Galvin, MD, MPH; MBRF Trustees

McKNIGHT BRAIN
RESEARCH FOUNDATION
Preserving memory, enhancing life

March 5, 2025

Established by Evelyn F. McKnight to Alleviate Memory Loss in the Aging

Jennifer L. Bizon, Ph.D.
Professor and Chair, Department of Neuroscience
Director, Evelyn F. and William L. McKnight Brain Institute | University of Florida

Dear Dr. Bizon,

At their meeting on February 24, 2025, the Trustees of the McKnight Brain Research Foundation (MBRF), reviewed the 2024 annual report submitted by the Evelyn F. and William L. McKnight Brain Institute (MBI) of the University of Florida (UF). The trustees are impressed by the many accomplishments under your leadership of the scientists within and affiliated with the MBI. The expanded services available at the Center for Cognitive Aging and Memory Clinical Translational Research (CAM Center) for investigators to have access to shared behavioral test space for human study participants will be of great benefit in faculty retainment and recruitment.

The expansion of the infrastructure at the UF Jacksonville Campus was noted with the hope collaborations with a clinical department such as Neurology could be developed. In the context of outreach, the report does not mention the Max Planck Institute (MPI). The trustees will appreciate receiving information on if and how the MPI is being integrated with the UF MBI.

The growth of the education and training programs supported by the MBI and the CAM Center is impressive and valuable in sustaining the growth and productivity of the research initiatives for which the CAM Center was created. The NEURON Aging project led by Dr. Sara Burke is particularly impressive.

The scientific program and celebratory activities surrounding the 25th anniversary of the UF MBI were outstanding and distinguished the UF MBI among its peers. Dr. Adam Gazzaley, the speaker for the Luttge Lectureship, was an outstanding success. Likewise, the hosting by the MBI and the CAM Center of the 15th Inter-Institutional meeting was executed perfectly with an excellent scientific program and complemented with enjoyable social functions for informal scientific engagement.

The trustees also note under your leadership, communication within the leadership council has improved among the MBIs. The resolution, with Dr. Burke's assistance, of the problems surrounding the recruitment of investigators for the Cognitive Aging and Memory Interventional Core (CAMI) for funding of the collaborative inter-institutional pilot grants is recognized with appreciation.

The trustees commend the process of evaluating the success of the CAM Center against the originally established six objectives as an ongoing activity of the leadership as outlined by Dr. Sara Burke in her report

The trustees are concerned with the loss of Dr. Ron Cohen and Dr. Adam Woods from the leadership of the CAM Center and their productivity in the human component of Clinical Translational Research. There are further concerns with Dr. Tom Foster's announced retirement by **June 2025**, from the Chair for Research on Cognitive Aging and Memory.

As mentioned, by Dr. Michael Dockery in an email exchange February 23, 2025, the Chair for **Clinical Translational Research** in Cognitive Aging and Memory occupied by Dr. Cohen must return to a clinical department within the College of Medicine. The chair previously occupied by Dr. Cohen and the one by Dr. Foster are both valued at $4 million. It is expected the UF will make every effort to fill each of these positions with distinguished worthy individuals who will advance the clinical translational research in age related cognitive decline and memory loss.

The trustees express their collective appreciation for your support and efforts in continuing to advance the research initiatives supported by the McKnight Brain Research Foundation, leading preserving memory and enhancing life through brain health.

Sincerely,

Amy Porter
Interim Executive Director

Cc: Jennifer Hunt, MD
Thomas C. Foster, PhD
Sara Burke, PhD
MBRF Trustees

The McKnight Brain Research Foundation Announces Alice Luo Clayton, PhD, as Chief Executive Officer

April 28, 2025 -- The McKnight Brain Research Foundation (MBRF) is pleased to announce Alice Luo Clayton, PhD, as its inaugural Chief Executive Officer. Dr. Luo Clayton is a neuroscientist with more than 15 years of programmatic leadership and strategic advising experience in government and private philanthropy.

Most recently, she served as the Senior Science Advisor at the National Institutes of Health (NIH) Brain Research Through Advancing Innovative Neurotechnologies® (BRAIN) Initiative. In this role, she contributed to the overall strategy for BRAIN, a program that transformed neuroscience research in its first 10 years by investing more than $3 billion in tools, technology and foundational knowledge to better understand the mysteries of the human brain. Previously, at the Coalition for Aligning Science, Dr. Luo Clayton spearheaded the initial strategic framework of a new initiative for the Sergey Brin Family Foundation.

Dr. Luo Clayton also served as a Senior Scientist at the Simons Foundation Autism Research Initiative (SFARI), the largest private funder of autism research in the U.S., for over a decade. During her tenure, she developed and oversaw multiple successful programs in systems, behavioral and cognitive neuroscience grant portfolios, in addition to SFARI's Bridge to Independence program.

"Dr. Luo Clayton understands the importance of studying cognitive aging and we are thrilled to welcome her as the first CEO of the McKnight Brain Research Foundation," said Michael L. Dockery, MD, Chair, McKnight Brain Research Foundation. "Her proven scientific acumen and deep expertise in multiple facets of the research ecosystem make her the perfect fit to serve as the Foundation's inaugural CEO. Dr. Luo Clayton's strategic leadership will be critical to expanding and deepening our rich 25-year history of supporting research to better understand and alleviate the effects of age-related cognitive decline and memory loss."

"Understanding cognitive aging is more relevant than ever, and this rapidly growing field is poised for breakthrough discoveries," said Dr. Luo Clayton. "I'm excited to build on MBRF's impressive history, connecting cutting-edge science with practical solutions to help people maintain their cognitive health throughout life."

With cognitive changes due to the normal aging process affecting nearly 87 percent of people age 65 and older to varying degrees, the McKnight Brain Research Foundation is the nation's only private foundation dedicated exclusively to solving the mysteries of the aging brain and helping people achieve a lifetime of cognitive health. The Foundation supports research specifically targeting cognitive aging, age-related cognitive decline and memory loss and works to educate the public on the steps that can be taken to maintain cognitive and brain health.

Dr. Luo Clayton began her research funding career as an AAAS Science & Technology Policy fellow at the National Institute of Mental Health where she focused on programmatic activities in developmental translational research and the Human Connectome Project.

Dr. Luo Clayton was trained as a systems neuroscientist, receiving her Ph.D. from the University of Pennsylvania under the mentorship of Dr. Gary Aston-Jones and completing postdoctoral training at the National Institute on Drug Abuse under the mentorship of Dr. Roy Wise. Her research focused on novel afferent circuitry to the Ventral Tegmental Area and specifying the role of these circuits in circadian rhythms, motivation, and contextual learning.

Working with the Trustees of the McKnight Brain Research Foundation, Dr. Luo Clayton will oversee all strategic planning, operations and administration of the organization's finances, marketing efforts and grants distribution.

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About the McKnight Brain Research Foundation

Founded in 1999, the McKnight Brain Research Foundation is the nation's only private foundation dedicated exclusively to solving the mysteries of the aging brain. By supporting research and investigation, the Foundation works to better understand and alleviate the effects of age-related cognitive decline and memory loss.

McKnight Brain Research Foundation

Projected Minimum Investment Return Calculations

(As of 4/30/2025 for fiscal year ending 6/30/2025)

Average Fair Market Value	$62,221,700.11
Less:	
Cash held for charitable purposes (1 1/2 %)	($933,325.50)
Net value of non-charitable use assets	$61,288,374.61
Minimum Investment Return (5%)	$3,064,418.73

Net Minimum Investment Return Calculation:

Minimum investment return	$3,064,418.73
sub total Qualifying Distributions	($3,398,482.31)
	($334,063.58)
Excess distribution carryover	
(actual for '19, '20, '21, '22, '23)	$2,823,195.00
(estimate for '24)	$334,063.58
	$3,157,258.58

McKnight Brain Research Foundation

Minimum Distribution Calculation
Fiscal years 2000 - 2024

Market Value Dec 1999 -$69,126,583	*Tax Year*	*Distributable Amount*	*Qualifying Distributions*	*Excess Distributions Carryover*	*Undistributed Income*
$51,867,213	7/1/03 - 6/30/04	$2,352,435	$1,665,404	$5,266,241 (last year we could carryover gift to UF	$0.00
$51,898,266	7/1/04 - 6/30/05	$2,450,345	$3,026,049	$575,704	$0.00
$55,777,369	7/1/05 - 6/30/06	$2,620,008	$2,036,659	$0	$7,645.00
$62,782,831	7/1/06 - 6/30/07	$2,843,725	$3,299,931	$448,561	$0.00
$54,753,484	7/1/07- 6/30/08	$2,817,569	$3,110,508	$292,939	$0.00
$39,447,094	7/1/08-6/30/09	$2,016,762	$2,517,340	$500,578	$0.00
$39,991,364	7/1/09-6/30/10	$1,952,550	$3,789,616	$1,837,066	$0.00
$44,648,921	7/1/10-6/30/11	$2,058,313	$3,983,492	$1,925,179	$0.00
$41,206,393	7/1/11-6/30/12	$1,973,938	$2,615,808	$641,870	$0.00
$43,820,218	7/1/12 -6/30/13	$2,020,034	$2,434,496	$414,462	$0.00
$50,408,385	7/1/13-6/30/14	$2,246,743	$2,298,603	$51,860	$0.00
$50,025,982	7/1/14 - 6/30/15	$2,309,295	$3,190,468	$753,267	$0.00

Market Value Dec 1999 -$69,126,583	***Tax Year***	***Distributable Amount***	***Qualifying Distributions***	***Excess Distributions Carryover***	***Undistributed Income***
$43,374,433	**7/1/15 - 6/30/16**	**$2,156,876**	**$4,896,096**	**$2,739,220**	**$0.00**
$45,020,486	**7/1/16 - 6/30/17**	**$2,197,291**	**$3,463,554**	**$1,266,263**	**$0.00**
$48,399,735	**7/1/17 - 6/30/18**	**$2,290,460**	**$2,662,616**	**$372,156**	**$0.00**
$46,247,121	**7/1/18- 6/30/19**	**$2,308,639**	**$2,028,707**	**$0**	**$0.00**
$49,211,422	**7/1/19 - 6/30/20**	**$2,393,971**	**$2,522,157**	**$128,186**	**$0.00**
$65,427,203	**7/1/2020 - 6/30/21**	**$2,728,732**	**$2,018,715**	**$0**	**$0**
$55,517,277	**7/1/2021 - 6/30/22**	**$3,015,394**	**$2,703,592**	**$0**	**$0**
$58,125,334	**7/1/2022 - 6/30/2023**	**$2,774,744**	**$2,424,751**	**$0**	**$0**
$61,342,449	**7/1/2023 - 6/30/2024**	**$2,828,126**	**$5,523,135**	**$2,695,009**	
$59,414,588	**7/1/2024 - 6/30/2025**	**$3,064,418 (estimate)**	**$3,398,482 (estimate)**	**$334,063 (estimate)**	
			$80,980,518.13	**$3,157,198**	**(estimated total excess carryover)**

Part IX **Minimum Investment Return** (All domestic foundations must complete this part. Foreign foundations, see instructions.)

1	Fair market value of assets not used (or held for use) directly in carrying out charitable, etc., purposes:			
a	Average monthly fair market value of securities		1a	57,792,855.
b	Average of monthly cash balances		1b	349,350.
c	Fair market value of all other assets (see instructions)		1c	
d	**Total** (add lines 1a, b, and c)		1d	58,142,205.
e	Reduction claimed for blockage or other factors reported on lines 1a and 1c (attach detailed explanation)	1e 0.		
2	Acquisition indebtedness applicable to line 1 assets		2	0.
3	Subtract line 2 from line 1d		3	58,142,205.
4	Cash deemed held for charitable activities. Enter 1.5% (0.015) of line 3 (for greater amount, see instructions)		4	872,133.
5	**Net value of noncharitable-use assets.** Subtract line 4 from line 3		5	57,270,072.
6	**Minimum investment return.** Enter 5% (0.05) of line 5		6	2,863,504.

Part X **Distributable Amount** (see instructions) (Section 4942(j)(3) and (j)(5) private operating foundations and certain foreign organizations, check here ☐ and do not complete this part.)

1	Minimum investment return from Part IX, line 6			1	2,863,504.
2a	Tax on investment income for 2023 from Part V, line 5	2a	47,764.		
b	Income tax for 2023. (This does not include the tax from Part V.)	2b	82.		
c	Add lines 2a and 2b			2c	47,846.
3	Distributable amount before adjustments. Subtract line 2c from line 1			3	2,815,658.
4	Recoveries of amounts treated as qualifying distributions			4	12,468.
5	Add lines 3 and 4			5	2,828,126.
6	Deduction from distributable amount (see instructions)			6	0.
7	**Distributable amount** as adjusted. Subtract line 6 from line 5. Enter here and on Part XII, line 1			7	2,828,126.

Part XI **Qualifying Distributions** (see instructions)

1	Amounts paid (including administrative expenses) to accomplish charitable, etc., purposes:		
a	Expenses, contributions, gifts, etc. - total from Part I, column (d), line 26	1a	5,523,135.
b	Program-related investments - total from Part VIII-B	1b	0.
2	Amounts paid to acquire assets used (or held for use) directly in carrying out charitable, etc., purposes	2	
3	Amounts set aside for specific charitable projects that satisfy the:		
a	Suitability test (prior IRS approval required)	3a	
b	Cash distribution test (attach the required schedule)	3b	
4	**Qualifying distributions.** Add lines 1a through 3b. Enter here and on Part XII, line 4	4	5,523,135.

Part XII Undistributed Income (see instructions)

	(a) Corpus	(b) Years prior to 2022	(c) 2022	(d) 2023
1 Distributable amount for 2023 from Part X, line 7				2,828,126.
2 Undistributed income, if any, as of the end of 2023:				
a Enter amount for 2022 only			0.	
b Total for prior years: _____, _____, _____		0.		
3 Excess distributions carryover, if any, to 2023:				
a From 2018				
b From 2019	128,186.			
c From 2020				
d From 2021				
e From 2022				
f **Total** of lines 3a through e	128,186.			
4 Qualifying distributions for 2023 from Part XI, line 4: $ 5,523,135.				
a Applied to 2022, but not more than line 2a			0.	
b Applied to undistributed income of prior years (Election required - see instructions)		0.		
c Treated as distributions out of corpus (Election required - see instructions)	0.			
d Applied to 2023 distributable amount				2,828,126.
e Remaining amount distributed out of corpus	2,695,009.			
5 Excess distributions carryover applied to 2023 (If an amount appears in column (d), the same amount must be shown in column (a).)	0.			0.
6 **Enter the net total of each column as indicated below:**				
a Corpus. Add lines 3f, 4c, and 4e. Subtract line 5	2,823,195.			
b Prior years' undistributed income. Subtract line 4b from line 2b		0.		
c Enter the amount of prior years' undistributed income for which a notice of deficiency has been issued, or on which the section 4942(a) tax has been previously assessed		0.		
d Subtract line 6c from line 6b. Taxable amount - see instructions		0.		
e Undistributed income for 2022. Subtract line 4a from line 2a. Taxable amount - see instr.			0.	
f Undistributed income for 2023. Subtract lines 4d and 5 from line 1. This amount must be distributed in 2024				0.
7 Amounts treated as distributions out of corpus to satisfy requirements imposed by section 170(b)(1)(F) or 4942(g)(3) (Election may be required - see instructions)	0.			
8 Excess distributions carryover from 2018 not applied on line 5 or line 7	0.			
9 **Excess distributions carryover to 2024.** Subtract lines 7 and 8 from line 6a	2,823,195.			
10 Analysis of line 9:				
a Excess from 2019	128,186.			
b Excess from 2020				
c Excess from 2021				
d Excess from 2022				
e Excess from 2023	2,695,009.			

McKnight Brain Research Foundation
Active Grant Summary
Fiscal years 2000 - 2029

	FNIH	American Brain Foundation	Innovator Awards in Cognitive Aging and Memory Loss	Innovator Awards in Cognitive Aging and Memory Loss Administrative & Indirect Costs	Evelyn F. McKnight Neurocognitive Clinical Scholar in Brain Health and Aging (UM)	FNIH - CAS IV	MBAR	2025 SfN Poster Session
Total Grant Amount	$5,000,000 (7/2009 - 7/2013) $5,000,000 (7/2014 - 5/2018) $5,000,000 (3/2021 - 3/2025)	$1,650,000 (7/1/2018 - 1/1/2024) $1,650,000 (7/1/2023 - 1/1/2029)	$4,500,000 (11/2021 - 11/2025) $4,500,000 (11/2024 - 11/2028)	$115,000 (4/2021 - 4/2025) $126,500 (4/2025 - 4/2028)	$250,000 payable over 5 years	*$313,573.28 (6/2023 - 5/2024)*	*$58,306 (7/1/2024- 6/30/2025) $31,224 (7/1/2025 - 6/30/2026)*	$28,050
7/1/99 -6/30/00								
7/1/00 -06/30/01								
7/1/01 - 06/30/02								
7/1/02 - 6/30/03								
7/1/03 - 6/30/04								
7/1/04 - 6/30/05								
7/1/05 - 6/30/06								
7/1/06 - 6/30/07								
7/1/07 - 6/30/08								
7/1/08-6/30/09								
7/1/09-6/30/10	$1,000,000							
7/1/10-6/30/11	$1,000,000							
7/1/11-6/30/12	$1,000,000							
7/1/12-6/30/13	$1,000,000							
7/1/13-6/30/14	$1,000,000							
7/1/14-6/30/15	$1,000,000							
7/1/15-6/30/16	$2,000,000							
7/1/16-6/30/17	$1,000,000							
7/1/17-6/30/18	$1,000,000							
7/1/18-6/30/19		$165,000						
7/1/19-6/30/20		$330,000						
7/1/20-6/30/21	$1,000,000	$330,000		$34,500				
7/1/21-6/30/22	$1,000,000	$330,000	$500,000	$34,500	$50,000			
7/1/22-6/30/23	$1,000,000	$330,000	$1,000,000	$34,500		$155,230.20		
7/1/23-6/30/24	$1,000,000	$330,000	$1,500,000	$43,700	$50,000	$158,343.08		
7/1/24-6/30/25	$1,000,000	$330,000	$1,500,000	$43,700	$50,000		$48,306 UAB	$3,500.00
7/1/25-6/30/26		$330,000	$1,500,000	$37,950				
7/1/26-6/30/27		$330,000	$1,500,000	$6,325				
7/1/27-6/30/28		$330,000	$1,000,000	$6,325				
7/1/28-6/30/29		$165,000	$500,000					
7/1/29-6/30/30								
Total	$15,000,000	$3,300,000	$9,000,000	$241,500	$250,000	$313,573.28	$89,530	$28,050
Balance	$0	$1,385,497	$4,500,000	$50,600	$100,000	$0.00	$41,224	$24,550

Total Active Grants
$28,222,653

Active Grants Remaining Balance
$6,101,871

as of 4/30/2025

McKnight Brain Research Foundation Pilot Grants

Active Pilot Grants

	Revitalizing Cognition in Older Adults (Bowers) **$60,000 (5/1/2018)** **$60,000 (5/1/2019)** *4/30/2021 extension approved through 4/30/2022* *3/23/2022 extension approved through 4/30/2023* *5/3/2023 extension approved through 4/30/2024* *6/21/2024 extension approved through 4/30/2025 for Dr. Alexander*	**Feasibility of a Timed Bright Light Exposure Therapy to Improve Circadian Function (Kaur)** **$60,000 (5/1/2023)** **$60,000 (5/1/2024)**	**Cue High-Speed Multidirectional Yoga: Impact on Retinal Microvascular and Cognitive Measures (Signorile)** **$59,997 (5/1/2023)** **$59,742 (5/1/2024)** *3/25/2025 extension approved through 10/31/2025*	**Ketogenic Diet Improvement of Age-Related Memory Impairments Nominates Cell-type Specific O-GicNAc Deficiencies in the Aged Hippocampus (Lubin)** **$57,141 (5/1/2023)** **$64,391 (5/1/2024)**
7/1/18 - 6/30/19	$6,799.94 UF			
7/1/19 - 6/30/20	$14,581.29 UF			
7/1/20 - 6/30/21	$1,694.96 UF $18,363.11 UA			
7/1/21 - 6/30/22	$20,776.94 UF			
7/1/22 - 6/30/23	$3,583.98 UF			
7/1/23 - 6/30/24	$5,593.54 UA $10,677.61 UF	$30,000.00 UM	$26,487.96 UM	$53,281.36 UAB
7/1/24 - 6/30/25	$36,255.93 UA		$58,887.34 UM	$36,095.65 UAB
Total Award	$120,000.00	$120,000.00	$119,739.00	$121,532.00
Unpaid Balance	$13,941.18	$90,000.00	$34,363.70	$32,154.99
	we received a refund from UF of $12,468.18 after Dr. Bowers completed her share of the project. $34,765.04 is balance to be used by Dr. Alexander.			

	Effects of age on fear generalization and its underlying neurobiological substrates in female adults: a cross species-investigation **(Huggins /Hernandez)** **$75,000 (5/1/2025)** **$75,000 (5/1/2026)**	**Effect of Alchol Reduction and Probiotic Interventions on Cognition and Brain Glucose Metabolism in Normal Aging Adults who are High-Risk Alcohol Drinkers** **(Salan/Porges)** **$63,701 (5/1/2025)** **$63,512 (5/1/2026)**	**A novel intervention to address orientation and navigation declines with aging** **(Ekstrom/Hill/Ebner/Visscher)** **$74,138 (5/1/2025)** **$75,758 (5/1/2026)**
7/1/18 - 6/30/19			
7/1/19 - 6/30/20			
7/1/20 - 6/30/21			
7/1/21 - 6/30/22			
7/1/22 - 6/30/23			
7/1/23 - 6/30/24			
7/1/24 - 6/30/25			
7/1/25 - 6/30/26			
7/1/26 - 6/30/27			
Total Award	$150,000.00	$127,213.00	$149,896.00
Unpaid Balance			

McKnight Brain Research Foundation Pilot Grants

Completed Pilot Grants

	A Novel Invention Tool (Levin) $60,000 (5/1/2018) $60,000 (5/1/2019) *completed - remaining balance will not be used*	**Transcutaneous Vagal Nerve Simulation (Williamson) $60,000 (10/1/2019) $60,000 (10/1/2020)** *8/29/2022 extension approved through 10/01/2023* *10/22/2023 extension approved through 10/22/2024* *completed - final invoice received 11/13/2024*	**Reuniting the Brain and Body to Understand Cognitive Aging (Hernandez) $23,600 (5/1/2021) $36,800 (5/1/2022)** *7/2/2023 extension approved through 4/30/2024* *completed - final invoice received 5/31/2024*	**Improving Age Related Cognitive Decline with Exercise in Hypertensive Older Adults (Lazar) $56,144 (5/1/2021) $56,144 (5/1/2022)** *5/3/2023 extension approved through 4/30/24* *no cost extension approved through10/31/2024* *completed - final invoice received 2/4/2025*
7/1/18 - 6/30/19	$11,256.57 UF $6,895.45 UA			
7/1/19 - 6/30/20	$33,845.70 UF $40,000 UM	$9,881.16 UF		
7/1/20 - 6/30/21	$830.52 UF $21,604.96 UA	$12,500.21 UF	$6,801.70 UAB	
7/1/21 - 6/30/22	$3,583.98 UF	$19,472.95 UF $1,231.60 UA	$14,028.50 UAB	
7/1/22 - 6/30/23		$10,391.27 UF $8,276.60 UA	$39,569.80 UAB	$39,734.56 UAB
7/1/23 - 6/30/24		$7,154.71 UF $29,849.90 UA		$34,221.72 UAB
7/1/24 - 6/30/25		$20,641.90 UA		$9,868.59 UAB
Total Award	$120,000.00	$120,000.00	$60,400.00	$112,288.00
Unpaid Balance	$1,982.82	$2,753.63	$0.00	$28,463.13

balances as of 2/4/2025

Travel Award Program

Date	Name	School	Amount
Beginning Balance			**$100,000.00**
5/6/2009	Marsha Penner	University of Alabama	$1,305.43
11/4/2010	Clinton Wright	University of Miami	$1,005.26
11/20/2010	Gene Alexander	University of Arizona	$354.39
7/26/2011	Gene Alexander	University of Arizona	$1,006.74
8/3/2011 - 8/4/2011	Cognitive Test Battery Working Group - Retreat #1	University of Alabama, University of Arizona, University of Florida, University of Miami	$7,505.06
12/1/2011 - 12/2/2011	Cognitive Test Battery Working Group - Retreat #2	University of Alabama, University of Arizona, University of Florida, University of Miami	$10,971.11
4/10/2012 - 4/11/2012	Cognitive Test Battery Working Group - Meeting #3	University of Alabama, University of Arizona, University of Florida, University of Miami	$4,280.42
8/1/2012 - 8/3/2012	MRI Standardization Working Group Meeting	University of Alabama, University of Arizona, University of Florida, University of Miami	$10,540.91
8/8/2012 - 8/9/2012	Cognitive Test Battery Working Group - Meeting #4	University of Alabama, University of Arizona, University of Florida, University of Miami	$4,273.80
8/13/2012 - 8/14/2012	Epigenetics Planning Meeting	University of Alabama, University of Arizona, University of Florida, University of Miami	$7,122.85
1/8/2013 - 1/9/2013	Epigenetics Planning Meeting	University of Alabama, University of Arizona, University of Florida, University of Miami	$10,684.25
	MRI Standardization - Scanning Project	University of Alabama, University of Arizona, University of Florida, University of Miami	$1,735.38
4/8/2013 - 4/10/2013	MRI Standardization Working Group Meeting #2	University of Alabama, University of Arizona, University of Florida, University of Miami	$7,851.43
12/6/2013	MRI Standardization	University of Florida & University of Miami	$1,094.90
8/2016	Brain and Cognitive Health Working Group	University of Alabama, University of Arizona, University of Florida, University of Miami	$10,454.20
3/21/2023	Legal Seafood - AAN Scholars Dinner	Dinner deposit for McKnight Clinical Translational Research Scholars Dinner	$3,878.40
5/10/2023	Tara Tracy IIM Reimbursement	airfare, taxi, meals	$877.42
3/8/2024	Hotel Teatro	Dinner deposit for 2024 McKnight Clinical Translational Research Scholars Dinner	$360.00
4/11/2024	Hotel Teatro	2024 McKnight Clinical Translational Research Scholars Dinner	$2,810.20
6/20/2024	Denise Cai IIM Reimbursement	airfare and taxi	$1,870.78
Remaining Balance			**$10,017.07**
			$89,982.93

MBRF Operating & Communications Budget
7/1/2024 - 6/30/2025

Operating Expenses

	Budget	Actual
Board of Trustee Fees	$400,000.00	$337,500.00
Legal Fees	$27,000.00	$20,900.50
CPA Fees	$20,000.00	$26,551.25
Consulting Fees*	$218,000.00	$135,291.59
Truist Bank Fees	$175,000.00	$157,495.20
Taxes	$107,000.00	$38,000.00
Meetings	$40,000.00	$17,985.91
Website Fees	$840.00	$840.00
Memberships	$5,090.00	$850.00
Conferences/Travel - Executive Director	$3,000.00	$0.00
Insurance	$1,667.00	$1,641.25
Total Operating Expenses	**$997,597.00**	**$737,055.70**
Search Committee Budget**	**$165,000.00**	**$147,604.54**

Communications Expenses

	Budget	Actual
BRG Communications	$500,000.00	$358,797.41
Website Support and Social Media Advertising *Out of pocket expenses for social media promotion, web hosting and support functions*	$6,750.00	$17,375.25
Senior Communications Advisor Consulting Fees	$93,500.00	$76,130.00
Travel	$2,500.00	$513.90
Total Communications Expenses	**$602,750.00**	**$452,816.56**

** represents payment to Executive Director*
approved at the 5.15.2024 Board of Trustees' Meeting
*** approved by Board 8/6/2024*

McKnight Brain Research Foundation

Annual Compensation Survey
April 2025

Exponent Philanthropy's Foundation 2024 & 2025 Operations & Management Reports

Full Time CEO/Top Administrator – Averaging more than 30 hours a week

Annual Survey 2024		Annual Survey 2023	
Average	$199,831	Average	$183,018
Median	$155,000	Median	$190,000
25th Percentile	$201,388	25th Percentile	$145,000
75th Percentile	$230,000	75th Percentile	$217,000

Part Time CEO/Top Administrator – Averaging less than 30 hours a week

Annual Survey 2024		Annual Survey 2023	
Average	n/a	Average	$167,271
Median	n/a	Median	$80,000
25th Percentile	n/a	25th Percentile	$169,564
75th Percentile	n/a	75th Percentile	$249,500

(based on response to Exponent Philanthropy's 2023 & 2024 Foundation Operations & Management Surveys)

C2. Full-time CEO/top administrator annual base salary, by foundation type and asset size

		ASSET SIZE							
	OVERALL	<$1M	$1-4.9M	$5-9.9M	$10-24.9M	$25-49.9M	$50-99.9M	$100-199.9M	$200+M
All foundations									
AVERAGE	$174,793	—	$102,760	$130,409	$135,892	$154,462	$199,831	$220,706	$247,365
25th PERCENTILE	$120,769	—	$84,000	$96,000	$106,000	$121,406	$155,000	$170,000	$188,376
MEDIAN	$156,640	—	$95,000	$112,000	$127,000	$147,983	$201,388	$225,000	$257,000
75th PERCENTILE	$218,458	—	$114,800	$165,000	$154,576	$168,350	$230,000	$265,000	$294,000
(n)	*(174)*	—	*(5)*	*(10)*	*(41)*	*(40)*	*(34)*	*(29)*	*(13)*
Family foundations									
AVERAGE	$178,170	—	—	$126,833	$132,680	$169,600	$203,867	$213,420	$255,900
25th PERCENTILE	$121,656	—	—	$91,000	$95,949	$129,287	$155,600	$199,607	$237,500
MEDIAN	$162,500	—	—	$107,500	$123,328	$155,140	$210,000	$220,000	$268,500
75th PERCENTILE	$225,000	—	—	$165,000	$150,000	$194,481	$226,107	$250,000	$292,600
(n)	*(78)*	—	—	*(6)*	*(14)*	*(18)*	*(17)*	*(10)*	*(8)*
Independent foundations									
AVERAGE	$177,335	—	—	—	$140,015	$141,434	$210,394	$235,133	—
25th PERCENTILE	$125,000	—	—	—	$117,884	$120,000	$157,800	$182,692	—
MEDIAN	$157,500	—	—	—	$141,750	$140,000	$212,395	$242,000	—
75th PERCENTILE	$212,395	—	—	—	$160,000	$158,795	$235,757	$278,000	—
(n)	*(79)*	—	—	—	*(21)*	*(21)*	*(13)*	*(17)*	—
Other foundations (community, corporation, operating, and other organizations)									
AVERAGE	$142,915	—	—	—	$128,960	—	—	—	—
25th PERCENTILE	$102,647	—	—	—	$101,254	—	—	—	—
MEDIAN	$138,474	—	—	—	$105,000	—	—	—	—
75th PERCENTILE	$172,500	—	—	—	$132,000	—	—	—	—
(n)	*(16)*	—	—	—	*(6)*	—	—	—	—

C9. Full-time CEO/top administrator annual base salary, by gender and number of grants awarded[3]

		NUMBER OF GRANTS AWARDED			
	OVERALL	<25	25–49	50–99	100+
All foundations					
AVERAGE	$174,793	$149,406	$156,267	$171,953	$206,593
25th PERCENTILE	$120,769	$105,000	$116,250	$125,000	$155,600
MEDIAN	$156,640	$135,744	$134,350	$156,279	$210,000
75th PERCENTILE	$218,458	$150,000	$167,915	$212,395	$257,000
(n)	*(174)*	*(22)*	*(44)*	*(57)*	*(47)*
Female					
AVERAGE	$163,654	$134,518	$148,116	$166,329	$193,891
25th PERCENTILE	$113,094	$104,000	$110,190	$116,628	$152,500
MEDIAN	$150,000	$120,000	$131,250	$152,780	$186,000
75th PERCENTILE	$205,771	$147,000	$165,000	$213,872	$247,879
(n)	*(124)*	*(17)*	*(35)*	*(40)*	*(28)*
Male					
AVERAGE	$205,569	—	$173,983	$190,333	$226,158
25th PERCENTILE	$154,000	—	$117,884	$140,129	$192,775
MEDIAN	$203,500	—	$170,000	$156,279	$214,182
75th PERCENTILE	$250,000	—	$210,000	$230,282	$257,000
(n)	*(42)*	—	*(7)*	*(13)*	*(18)*

PART-TIME CEO/TOP ADMINISTRATOR COMPENSATION[4]

C10. Part-time CEO/top administrator annual base salary, by asset size

		ASSET SIZE							
	OVERALL	<$1M	$1-4.9M	$5-9.9M	$10-24.9M	$25-49.9M	$50-99.9M	$100-199.9M	$200+M
All foundations									
AVERAGE	$84,418	—	—	$59,620	$53,071	$92,984	—	—	—
25th PERCENTILE	$47,625	—	—	$30,000	$45,483	$57,780	—	—	—
MEDIAN	$65,313	—	—	$32,100	$55,500	$87,800	—	—	—
75th PERCENTILE	$98,500	—	—	$60,000	$65,400	$132,288	—	—	—
(n)	*(33)*	—	—	*(5)*	*(8)*	*(11)*	—	—	—

[3] Participating foundations did not report having a CEO/Top Administrator who identified as nonbinary.
[4] There were insufficient data to report part-time CEO/Top Administrator hourly rate, by asset size.

C2. Full-time CEO/top administrator annual base salary, by foundation type and asset size

	ASSET SIZE								
	OVERALL	<$1M	$1-4.9M	$5-9.9M	$10-24.9M	$25-49.9M	$50-99.9M	$100-199.9M	$200+M
All foundations									
AVERAGE	$162,860	—	$123,368	$102,588	$135,980	$155,176	$183,018	$200,943	$220,357
25th PERCENTILE	$125,000	—	$108,000	$80,354	$115,750	$133,884	$145,000	$161,817	$175,000
MEDIAN	$153,542	—	$114,480	$92,500	$132,000	$151,594	$190,000	$194,690	$224,771
75th PERCENTILE	$200,000	—	$145,358	$110,000	$149,955	$175,500	$217,000	$245,196	$255,645
(n)	*(175)*	—	*(5)*	*(8)*	*(45)*	*(43)*	*(37)*	*(26)*	*(9)*
Family foundations									
AVERAGE	$172,664	—	—	—	$130,697	$176,918	$191,902	$210,020	$237,083
25th PERCENTILE	$130,544	—	—	—	$110,190	$141,200	$148,000	$175,000	$224,771
MEDIAN	$161,440	—	—	—	$127,772	$160,000	$205,000	$208,649	$225,000
75th PERCENTILE	$217,000	—	—	—	$150,000	$210,931	$225,000	$250,000	$255,645
(n)	*(83)*	—	—	—	*(22)*	*(15)*	*(19)*	*(14)*	*(5)*
Independent foundations									
AVERAGE	$154,787	—	—	$89,200	$138,690	$141,841	$180,530	$192,948	—
25th PERCENTILE	$120,000	—	—	$86,000	$123,000	$106,250	$130,000	$154,000	—
MEDIAN	$147,000	—	—	$90,000	$138,500	$145,500	$160,956	$197,500	—
75th PERCENTILE	$187,000	—	—	$95,000	$149,955	$174,200	$220,000	$238,274	—
(n)	*(79)*	—	—	*(5)*	*(18)*	*(24)*	*(15)*	*(11)*	—
Other foundations (community, corporation, operating, and other organizations)									
AVERAGE	$149,333	—	—	—	$149,470	—	—	—	—
25th PERCENTILE	$132,000	—	—	—	$129,000	—	—	—	—
MEDIAN	$148,837	—	—	—	$132,000	—	—	—	—
75th PERCENTILE	$165,000	—	—	—	$135,000	—	—	—	—
(n)	*(13)*	—	—	—	(5)	—	—	—	—

C9. Full-time CEO/top administrator annual base salary, by gender and number of grants awarded[3]

	NUMBER OF GRANTS AWARDED				
	OVERALL	<25	25–49	50–99	100+
All foundations					
AVERAGE	$162,860	$139,970	$148,208	$163,952	$182,182
25th PERCENTILE	$125,000	$100,000	$110,595	$125,000	$145,000
MEDIAN	$153,542	$140,000	$140,000	$154,271	$175,500
75th PERCENTILE	$200,000	$170,000	$163,978	$197,500	$224,771
(n)	*(175)*	*(19)*	*(48)*	*(58)*	*(47)*
Female					
AVERAGE	$154,267	$133,245	$142,204	$154,926	$173,495
25th PERCENTILE	$120,000	$100,000	$105,095	$120,000	$138,342
MEDIAN	$145,000	$125,000	$135,861	$149,955	$160,909
75th PERCENTILE	$184,500	$157,952	$163,978	$185,220	$222,266
(n)	*(107)*	*(14)*	*(32)*	*(31)*	*(28)*
Male					
AVERAGE	$177,543	—	$162,683	$172,422	$194,705
25th PERCENTILE	$137,270	—	$131,121	$131,020	$161,440
MEDIAN	$174,200	—	$154,000	$151,919	$192,190
75th PERCENTILE	$212,447	—	$189,525	$203,053	$225,000
(n)	*(56)*	—	*(13)*	*(20)*	*(18)*

PART-TIME CEO/TOP ADMINISTRATOR COMPENSATION[4]

C10. Part-time CEO/top administrator annual base salary, by asset size

	ASSET SIZE								
	OVERALL	<$1M	$1-4.9M	$5-9.9M	$10-24.9M	$25-49.9M	$50-99.9M	$100-199.9M	$200+M
All foundations									
AVERAGE	$83,873	—	—	$43,484	$67,249	$88,271	$167,271	—	—
25th PERCENTILE	$47,250	—	—	$28,000	$48,000	$59,184	$80,000	—	—
MEDIAN	$72,500	—	—	$42,839	$60,582	$81,400	$169,564	—	—
75th PERCENTILE	$96,098	—	—	$52,500	$87,000	$102,500	$249,500	—	—
(n)	*(38)*	—	—	*(8)*	*(10)*	*(8)*	*(6)*	—	—

[3] Participating foundations did not report having a CEO/Top Administrator who identified as nonbinary.
[4] There was insufficient data to report part-time CEO/Top Administrator hourly rate, by asset size.

McKnight Brain Research Foundation

Annual Compensation Survey

April 2025

Taken from Council on Foundations Grantmakers 2023 & 2024Salary & Benefits Report

Chief Executive Officer

Annual Survey 2024		**Annual Survey 2023**	
Assets 50 – 100 M		Assets 50 – 100 M	
Average	$266,687	Average	$199,174
Median	$245,000	Median	$183,855
Minimum	$35,568	Minimum	$45,000
Maximum	$1,016,500	Maximum	$549,908

Philanthropy SOUTHEAST
Together for Change

Compensation Summary for Foundation Staff

Position by Asset Size

2024 – National

Assets 50M – 100M

Title	Average	Median	Minimum	Maximum	Number of Positions	Number of Organizations
Executive Staff						
CEO	266,687	245,000	35,568	1,016,500	189	189
Assoc Dir / EVP	182,587	179,064	75,469	291,500	36	31
Executive Assistant	70,235	70,007	35,000	120,872	80	67
Finance Staff						
CFO / Treasurer	173,825	145,596	85,600	559,100	94	94
Controller	109,402	102,590	56,160	171,500	42	42
Director of Impact Investing	103,918	103,300	70,013	136,000	6	6
Manager of Accounting	92,060	93,050	34,938	152,058	14	11
Accountant	70,546	70,000	20,241	123,074	45	42
Accounting Clerk	57,651	55,000	34,406	95,500	35	26
Program Staff						
VP (Program)	149,629	141,000	71,597	281,200	63	57
Program Director	129,975	115,002	56,500	299,000	146	64
Senior Program Officer	127,295	124,913	57,600	230,384	102	69
Program Officer	91,357	91,000	40,000	163,690	189	105
Program Associate	69,623	66,355	32,000	130,000	122	64
Program Assistant	52,877	50,000	35,000	76,548	41	25

Philanthropy SOUTHEAST
Together for Change

Compensation Summary for Foundation Staff

Position by Asset Size

2023 – National

Assets 50M – 100M

Title	Average	Median	Minimum	Maximum	Number of Positions	Number of Organizations
Executive Staff						
CEO	199,174	183,855	45,000	549,908	183	181
Assoc Dir / EVP	182,414	172,564	59,500	380,000	20	20
Executive Assistant	67,271	68,500	16,100	123,919	35	30
Finance Staff						
CFO / Treasurer	142,732	126,228	64,800	333,015	55	54
Controller	96,407	86,275	54,802	192,615	40	40
Manager of Accounting	70,822	64,200	40,000	113,736	9	9
Accountant	70,791	64,597	40,050	150,000	30	23
Accounting Clerk	57,662	55,120	36,500	116,251	11	9
Program Staff						
VP (Program)	153,473	138,580	62,000	341,850	47	34
Program Director	109,781	96,622	30,000	238,000	87	57
Senior Program Officer	106,708	114,400	32,100	189,000	71	46
Program Officer	82,354	77,137	37,440	185,000	146	72
Program Associate	60,488	62,000	36,067	98,606	85	31
Program Assistant	49,394	43,965	33,000	81,993	32	13

Membership & Governance Committee Activity Timeline
2021 to 2026

Updated April 29, 2025

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
"identify, recruit and recommend candidates for appointment or re-election of current Trustees, consistent with applicable qualifications…"	Determine ideal size of Board	Goal Size established as 7 Trustees, plus 1 Corporate Trustee and 1 Chair Emeritus	June 27, 2019	DONE
		Current size is 8 Trustees, plus 1 Corporate Trustee and 1 Chair Emeritus	January 6, 2020	Trust document allows for a maximum of 11 Trustees
	Compile and create an orientation packet that includes the history of the MBRF, in addition to its values, standards, expectations, leadership, gifts and grants, and programs	The orientation packet was compiled, reviewed, and approved by the Trustees	October 5, 2020	The orientation packet became part of the standard information provided to new Trustees. The orientation packet is housed on the MBRF secure site
	Provide ongoing updates to the orientation packet as needed	The orientation packet required the addition of new material, updated trustee information and updated program status and information	January 2022 August 2022 June 2023 January 2025	DONE DONE DONE Draft List of Updates and additions to the orientation packet were presented to the M&G Committee for their review.

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
			April 2025	The updates and changes to the Orientation Manual were completed and posted on the secure site for use by the new CEO.
	Review appointment and retirement dates	Target for Identifying New Trustees to Maintain Board Size of 7 (or more): 1 or 2 in 2020 1 or 2 in 2021 2 in 2023 0 in 2024 Renewal of Terms: 2 in 2023 1 in 2024/25 (Originally Dec. 31, but term changed to begin on January 1) 4 in 2026	 DONE (2) DONE (1) DONE (2) DONE (2) DONE (1)	New Appointments to the Board of Trustees: October 2020 - Dr. Patricia Boyle Dr. Allison Brashear December 2021 Dr. John Brady July 2023 Dr. Sharon Brangman Dr. Roy Hamilton October 1, 2023 to October 1 2026 (2nd Term) Dr. Patricia Boyle Dr. Allison Brashear January 1, 2025 – January 1, 2028 (2nd Term) Dr. John Brady July 1, 2026 – July 1, 2029 (2nd Term) Dr. Sharon Brangman Dr. Roy Hamilton

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
		Renewal of Terms (con't) 4 in 2026		October 1, 2026 – October 1, 2029 (3rd Term) Dr. Patricia Boyle Dr. Allison Brashear
	Review, discuss and determine expertise needed on Board	Behavioral Neurologists; Women; Expertise Needed in 2021 – Geriatric Psychiatrist; Primary Care Physician (Internal Medicine; Geriatrics; Family Practice) Discussed Expertise Needed to round out the Board Trustees approved the appointment of two new candidates in 2023: one with expertise in Behavioral Neurology and one in Internal Medicine with a specialty in Geriatrics Additional Areas of expertise needed – i.e. a public member?	Fall 2020 Summer 2021 Oct 11,2022 October 27, 2022 January/February 2023 At its March 20, 2024 meeting, the board approved the committee's recommendation not to add a public member at this time	DONE DONE DONE DONE DONE DONE

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
"identify, recruit, and recommend…" Continued	Develop Process for Recruiting, Vetting, and Recommending Candidates	Committee reviewed and edited	September 30, 2019 June 1, 2021 July 28, 2021	Document was shared October 2019 Meeting; Document revised; Document was shared July 2021 Trustees Meeting as revised. Document Approved
"oversee annual Board self-evaluations"	Review of the Committee's charge to conduct and monitor the Trustee Self-Assessment Process	Current Self-Assessment form and Commitment Form reviewed New form was distributed for January 2021 Review of Input on Forms and conversations with the Chair	September 2019 October 2019 January 2020 Self-Assessment January 2021 Conversations took place with Chair Feb. 2021	The Committee developed new self-assessment form and process No new changes to form were suggested
		Self-Assessment form distributed to Trustees and Returned to Corporate Trustee	Dec. 2021 January 2022 Dec. 2022 Dec. 2023 Dec. 2024 January/Feb 2025	There were no changes to the form from 2021 Conversations took place with MBRF Chair
"…make recommendations on structure, charters, policies, process and practices…"	Align policy with practice for length of service	Board approved change in policy to allow a "maximum of 9 years" service The Board approved an amendment to the trustee terms of service at its March 20, 2024 meeting.	March 20, 2024	DONE The amendment allows for an extended term of service if desired and approved by the board in unique circumstances.

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
"…structure, charters, policies, process…" Continued	Approve role of first Chair Emeritus	Board developed and approved by unanimous consent in email	July 2019	DONE
	Approve role of Trustee Emeritus/ae	Board approved; Recognition provided	July 31, 2019	DONE
	Review/revise "Qualifications for Trustees"	Expanded to non-MD, non-PhD candidates	July 31, 2019	DONE
	Developed 'Qualifications for Advisory Committee Members'	Trustees approved	2019	DONE
	Develop criteria and process for review of performance of Trustees for Trustee Reappointment. Base criteria on Board Duties and Responsibilities	Summary of Recruitment, Election and Re-Election document developed in July 2020	DONE June 2021	Trustees reviewed Summary of Recruitment, Election and Re-election. Process for Review of Performance for re-election approved
	Develop and implement a formal Trustee Recognition of Appreciation for Service	Discuss notification of Trustees completing their service after one, two or three terms. Retiring Trustees will be recognized with a crystal bowl (or other gift) and proclamation	Jan. 21, 2021 April 30, 2021 July 28, 2021 May 3, 2023	Dr. Gene Ryerson was recognized with gift and proclamation Dr. Robert Wah was recognized with gift and proclamation Dr. Richard Isaacson was recognized with a proclamation

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
	Review concept of developing an Education Working Group vs. establishing an Education Committee Subcommittee	Recommendation to hire a Sr. Advisor, Education, and to follow the Communications model with a working group, was shared with the Board of Trustees Conversation has been paused	Feb. 22, 2022 March 13, 2022 March 23, 2022	TABLED

Finance Committee Activity Timeline
For the One-Year Period July 1, 2024, to June 30, 2025
Updated April 30, 2025

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
"…shall coordinate the Board of Trustee's Financial Oversight Responsibilities (through monitoring of) …financial management, assets, and risks …"	Review Investments and Investment Policy	Asset Allocation Review (Mike Hill)	August 22, 2024	***completed***
		Efficient Frontier Analysis (Shelly Simpson)	August 22, 2024	***completed***
		Monte Carlo Simulation		upon recommendation by Truist or request of the MBRF
		Investment Performance Review	August 22, 2024	***completed***
		Investment Performance & Asset Allocation Review (Mike Hill)	October 14, 2024	***completed***
		Investment Performance & Asset Allocation Review (Mike Hill)	February 2025	***completed***
		Investment Performance & Asset Allocation Review (Mike Hill)	May 14, 2025	

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
Financial Oversight… "…Ensure Compliance with Federal, State and other Financial Reporting Requirements…"	Assess and Maintain IRS Required Distribution Amount	Minimum Distribution Calculation Report	August 22, 2024 October 14, 2024 February 2025 May 14, 2025	***completed*** ***completed*** ***completed***
	Compensation Review	Examples Presented for Comparison	May 14, 2025	
	Tax Filing	Legal Counsel for the MBRF reviews the completed tax form before filing		**7/1/2023 – 6/30/2024 Filed on April 30, 2025**
	Insurance	MBRF carries D & O Insurance	Renewed annually	Premium paid by Corporate Trustee
Financial Oversight " planning, monitoring and evaluation of …funding for the McKnight Brain Institutes… and the MBRF Operations"	Monitor Current and Outstanding Gifts and Grants	Gifts and Grants Report	August 22, 2024 October 14, 2024 February 2025 May 14, 2025	***completed*** ***completed*** ***completed***
		Travel Award Program Report	August 22, 2024 October 14, 2024 February 2025 May 14, 2025	***completed*** ***completed*** ***completed***
	Review MBRF Operating Expenses	Year to Date Operating Expenses Report	August 22, 2024 October 14, 2024 February 2025 May 14, 2025	***completed*** ***completed*** ***completed***
		Review & Approve Annual Operating Budget	May 14, 2025	

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
Financial Review…of reports and requests submitted to the MBRF by the MBIs and Other Partners	Review Financial Reports Submitted with the MBI's Annual Reports		January 2025	***completed***
	Review Financial Information included in Interim and Final Reports for Research Grants		Per terms of the award letter	
	Review Budgets Submitted with Requests for Funding		As submitted	
"…ensure adequacy of MBRF internal controls and compliance with conflict of interest policy…	Review Signing Authority	MBRF policy is minimum of 2 individuals with signing authority	May 14, 2025	*Updated to remove Interim Executive Director and add CEO*
	Conflict of Interest	Conflict of Interest Policy signed by all new and re-elected Trustees and by all Advisory Members of MBRF Committees	ONGOING	

Education Committee Activity Timeline
For the Years 2019 – 2025
Updated April 30, 2025

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
"…shall develop information and resources (for the public and scientific community) on prevalence and impact of age-related cognitive decline and memory loss….	Work toward alignment of messages across the MBIs and MBRF Make substantive judgments on content and quality of educational content/statements developed for or posted on the website	Key Messages Were Approved and Distributed in Spring 2019	July 1 – ONGOING ONGOING	The Education Committee reviews content before it is posted on website, published, or included in print materials or slide presentations, ensuring consistency with key messages. The committee reviews for accuracy, soundness, and alignment with the MBRF mission and current scientific understanding and clinical practice. (The Research Committee also reviews content before making public.)
	A top priority for the committee and MBRF, as approved by the Trustees, is to identify and/or develop educational content for primary care physicians and to oversee the ongoing posting of additional information	The committee approved an outline of resources for the PCP Area on McKnightBrain.org The committee approved content for the Brain Works Microsite, including items featured in the Cognitive	DONE June 30, 2020 DONE Initial content approved between November 2023 and March 2024.	

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
		Aging Resources, Resource Hub, and Hot Topics sections.	ONGOING- Year two of the Brain Works campaign includes identifying partnership and outreach opportunities to reach and engage with healthcare professionals Dr. Brady participated in a brainstorm to discuss potential education program ideas for the MBRF and shared top level ideas as part of the joint Communications and Education Committee meeting on February 6. Moving forward with an education initiative is on hold until Alice is fully onboarded. Dr. Brady reviewed and provided feedback on a partnership opportunity with the American Academy of Family Physicians and, with approval from the Education and	

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
			Communications Committees, the partnership is moving forward. The Education Committee will be asked to review and approve the materials developed in collaboration with AAFP before they are published.	
And…" assist those living with age-related cognitive decline and memory loss"	Website content developed for individuals, families and caregivers of those with age-related cognitive decline and memory loss	Add links to approved articles as appropriate. Development of content is on hold until PCP content is identified and developed. Cognitive Aging Resources section of the Brain Works microsite includes downloadable guides on "How to Talk to Your Doctor About Brain Health" and "What To Do if a Loved One is Experiencing Signs of Memory Loss"	Winter/Spring 2022 March 2024	
Inform "…how to better maintain brain health…"	Website content developed for individuals on how to protect, maintain brain health	Add links to approved publications and articles	July 1 – ONGOING	Committee Reviews before Posting

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
"shall review all educational materials…:	Brochure developed to raise awareness and promote the MBIs and MBRF to individuals, partners, donors Brain Works Microsite developed to feature educational materials on Brain Health and Cognitive Aging.	Review of Brochure was conducted and committee concurs with suggestions by Communications Committee. Microsite launched in March 2024	DONE Posted on website January 2021 ONGOING- Education Committee reviews and approves content for the Brain Works microsite Resource Hub and Hot Topics sections Dr. Brady and the committee reviewed and provided feedback on the Brain Works PSA before it was distributed in mid-December The new partner resources approved by the Education Committee in February have been added to add to the Brain Works resource hub.	
"Identify educational opportunities and implement activities…to encourage MBIs…inspire commitment and shared vision"	12th Annual Inter-institutional Meeting 13th Annual Inter-institutional at UA	2020 Meeting was canceled 2021 Meeting will be virtual Meeting was in-person	April 28 & 29 2021 Mar 23-25, 2022	DONE

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
	14th Annual Inter-Institutional Meeting, UAB McKnight Scholars Will be invited to next Inter-institutional Meeting 15th Annual Inter-Institutional Meeting, UF	Meeting was in-person Innovator Awardees attend 2023 (Dr. Tracy) and 2024 Meetings (Cr. Cai)	May 3-5, 2023 May 15-17, 2024	 Will help promote scholarship and engage scholars
	McKnight Scholars Dinner at AAN	2020 Toronto, AAN Meeting was canceled 2021 Virtual AAN Meeting 2023 AAN Meeting 2024 AAN Meeting	 April 17 – 22, 2021 April 24, 2023 April 15, 2024	Held over - MBRF approved funding of $4,000 to cover travel, hotel for the night, dinner, UM staff travel Hosted by Dr. Thambisetty Co-hosted by Drs. Brashear and Hamilton
	William G. Luttge Annual Lectureship in Neuroscience at the University of Florida	Annual Lectureship by research scientist of National or International prestige in the field of neurosciences	Held in March/April each year in conjunction with Brain Awareness week. 2024 Lecture: February 2, 2024 – Dr. Adam Gazzaley, M.D. Ph.D.	Annual Lectureship established honoring the Founding Director of the Evelyn F. and William L. McKnight Brain Institute at the University of Florida Lecture was part of the UF 25th Anniversary Celebration Event

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
"work to elevate the importance of age-related cognitive decline and memory loss on the national agenda…(work toward) greater investment in research and education by federal health agencies…."	IOM Study	"Public Health Dimensions of Cognitive Health" was released by the IOM (see attached document) MBRF has initiated and implemented several of the IOM recommendations.	DONE April 14, 2015 ONGOING	Study funded by MBRF and federal agencies (NIA,
"work to elevate the importance of age-related cognitive decline and memory loss on the national agenda…" continued		The committee approved content for the Brain Works Microsite, including items featured in the Cognitive Aging Resources, Resource Hub, and Hot Topics sections. The campaign is raising awareness on a national level for the importance of brain health. MBRF Membership in collaborative groups for advocacy and education related to age-related cognitive decline and memory loss	ONGOING July 17, 2024 September 2024	Contact information to contacts at AARP; AAN; and the Milken Institute, as well as Grantmakers in Aging has been transferred to Ms. Cianciotto. Dr. Sharon Brangman was appointed the MBRF representative to the AARP Brain Health Action Coalition and has been attending the group's quarterly meetings.

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
			April 2025	Dr. Brangman will introduce Dr. Luo Clayton to the group as another MBRF representative. (Valerie Patmintra also attends these meetings.)

Research Committee Activity Timeline

2022 - 2026

Updated for the April 22, 2025 Meeting of the Research Committee

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
"Encourage and assess research at the McKnight Brain Institutes (MBIs)"	Review of the Annual Reports of the MBIs	Information for scientific review includes: scientific achievements, publications, presentations, collaborations	Annual Reports were reviewed by the Trustees on February 24, 2025	Reviewers presented at Feb. 2025 Trustees' Meeting. Follow up letters were written and sent to each of the MBIs. Letters are included in the May 14, 2025 trustee meeting material
	Review of all New Funding Requests from MBIs. As a rule, most Funding Requests should be reviewed by the Interventional Core Committee of the MBIs first.	The Leadership Council, by way of the CAMI-Core Chair, Dr. Sara Burke, submitted a proposal to relaunch the Pilot Grant Program.	The board approved the proposal to re-launch the CAMI Core Pilot Grant Program at $75,000 per year for each award at its February 20, 2024 meeting. The CAMI Core Pilot Grant Review Committee met on January 17, 2025 MBRF Research Committee reviewed successful proposals on January 28, 2025 Recommended Funding	The revitalized CAMI-Core Pilot Grant program was officially launched at the 2024 IIM. Dr. Burke shared that 10 LOIs were submitted this year involving 28 faculty from the 4 institutes. Distribution by MBI is as follows: 10 from UAB, 8 from UF, 5 from UM, and 5 from UA. From the 10 LOIs, 8 teams have been invited to submit full proposals due Nov. 1, 2024. (The other 2 LOIs were not appropriate for CAMI-Core pilot funding.) The distribution by Faculty Rank is 9 New Investigators and 19 Established PIs. Trustees reviewed on Feb. 24, 2025 and approved funding of 3 pilot grants

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
"Encourage and assess research at the McKnight Brain Institutes (MBIs)"		Dr. Sara Burke submitted a proposal to renew funding for the 2025/26 Pilot Grant Program and a draft Request for LOIs and Proposals	The Research Committee approved the recommendation to renew support for the 2025/26 Pilot Grant Program	The MBRF Trustees will review for approval on May 14. Dr. Burke hopes to announce the renewal on May 15 at the Inter-Institutional Meeting in Miami
		Dr. Signorile requested a six month no cost extension to his pilot grant "Cued high-speed multidirectional yoga: Impact on retinal microvascular and cognitive measures"	The Research Committee approved the no cost extension by email on March 18, 2025. The Trustees approved it by email.	
		UM submitted a request for $250,000 to co-fund a fellowship over 5 years – The Evelyn F. McKnight Neurocognitive Clinical Scholar in Brain Health and Aging"	A memorandum notifying UM of the approval for funding the Evelyn F. McKnight Neurocognitive Clinical Scholar in Brain Health and Aging for a total of $250,000 ($50,000 over 5 years) to be matched by UM was signed on Nov 10, 2021	There is a balance of $150,000 on this grant commitment

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
"Encourage and assess research at the McKnight Brain Institutes (MBIs)"	Review of Travel Award Fund: Originally established to fund research scholars and faculty to visit other McKnight institutions.	Few applications for travel. The funds allocated for travel have been used to fund the activities of focus groups: Epigenetics, MRI standardization and cognitive test battery working group	Reviewed as needed	Travel funds have been approved to fund travel and lodging for Innovator Award winner(s) to attend the 2024 IIM meeting at UF – Dr. Denise Cai attended.
	Inter-Institutional Block Grants	Cognitive Assessment and McKnight Brain Aging Registry (MBAR) Core	The Leadership Council, by way of Dr. Kristina Visscher, submitted a proposal to support MBAR with remaining dollars. The proposal was approved with minor amendments by the research committee on April 25, 2024 and by the Full Board at its May 15, 2024 Meeting. The Board also approved an additional $88,000 to cover the proposed budget for the MBAR over the next two years, based on a recommendation from the Finance Committee.	

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
"Encourage and assess research at the McKnight Brain Institutes (MBIs)"	Inter-institutional Block Grants	Cognitive Aging Core Working Groups	No Updates	5 Areas: Brain and Cognitive Health Cognitive Aging & Memory Cognitive Testing Battery Epigenetics MRI standardization
	Inter-institutional Block Grants	Bio-Informatics Core (Epigenetics)	No Updates	
	Inter-institutional Block Grants	Neuroimaging Core	No Updates	
"Identify opportunities…to foster greater interest in cognitive aging and age-related memory loss (in the scientific community)"	Research Partnership with the Foundation for NIH and the NIA.	1st cycle-2009, 2nd cycle-2014, 3rd cycle-2019	2023 annual progress report was submitted in January and reviewed by the board on March 19, 2024. 2024 annual progress report is due Jan/Feb 2025.NIA has submitted the information to FNIH per April phone call with FNIH by Amy. FNIH submitted the report and the Research Cmte reviewed on April 22, 2025	History: Established 2009 $5 M over 5 years from MBRF; match from NIA and partners was $23 M for total of $28 M (17 five-year grants funded). The 2014 Partnership renewal funded one 5-year project for $15 million with $5 M from MBRF and $10 M from NIA Current Cycle: NIA committed to provide $15M to be pooled with MBRF's $5M. Two grants were provided from the Research Partnership, led by to Dr. Thomas Perls and Dr. Emily Rogalski.

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
Identify opportunities…to foster greater interest in cognitive aging and age-related memory loss (in the scientific community)"		Cognitive Aging Summit (CAS) IV	Final payment on this round was made in March 2025 Final report on this round of support will be due Jan/Feb 2026 CAS IV, with a theme of "Precision Aging and Brain Health" took place on March 20-21, 2024. There were 170 in-person attendees and up to 449 virtual attendees. Session Chairs, NIA leaders, FNIH and the MBRF met for an Executive Session following the summit.	The FNIH/NIA developed the meeting summaries and the recordings have been posted online (here). Follow-up reflections and takeaways from the Summit and the Executive Session will be shared by NIA, by way of Dr. Molly Wagster and Dr. Jonathan King, later this year. In August, FNIH provided a report on the Cognitive Aging Summit IV. It is included in the material for the September 24, 2024, Research Committee meeting.
	MBRF Innovators Awards in Cognitive Aging and Memory Loss The McKnight Brain Research Foundation committed $4.5 million over the next five years to support outstanding mid-career scientists committed to researching the basic biological mechanisms	AFAR award cycles under the current grant were implemented (2021, 2022, 2023) AFAR presented a renewal proposal to provide two 3-year awards each year for the next three years. It was approved by the MBRF board on March 19, 2024. The MBRF committed to $4,626,500 over the next 5 years.	The research committee reviewed the draft RFA and Institutional Commitment Form at its meeting on April 25, 2024. The committee suggested several edits to the documents. The RFA and application were finalized and posted by AFAR at the end of May, following input from the	AFAR Review Committee: Chair: Dr. Anna Maria Cuervo Members: Dr. Rafa de Cabo Dr. Thambisetty Dr. Boyle and Dr. Roz Anderson Dr. Hamilton (joined in 2023) The Review Committee met on September 30 to review 9

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
Identify opportunities…to foster greater interest in cognitive aging and age-related memory loss (in the scientific community)"	underlying cognitive aging and memory loss. AFAR was invited to submit a renewal proposal for three additional years with updated program guidelines to broaden the applicant pool and able greater access to applicants from institutions with fewer resources AFAR submitted draft RFA and Instruction Sheet for 2025 Innovator Awards		Board at its meeting on May 15, 2024. 2024 grant cycle deadlines include: *July 1: application period opens *August 12: application submission deadline *September 30: review committee meets *Oct 1: Award start date Research Cmte reviewed on April 22, 2025 and provided one edit. AFAR was notified of the edit and approval and is proceeding to post.	applications (11 were submitted). Awards were made to Janine Kwapis, PhD of Pennsylvania State University and Sanaz Sedaghat, PhD, University of Minnesota as 2024 recipients after MBRF Trustee review and support. Having met all institutional requirements, November 2024 Dr. Christopher Thaiss' 2023 Innovators Award was transferred from Penn to the ARC Institute and Stanford
"Encourage young investigators in this area of research"	McKnight Brain Research Foundation Clinical Translational Research Scholarship with American Academy of Neurology (AAN) and American Brain Foundation (ABF)	Seven award cycles have been completed. Two awardees have received the CTRS every year since 2018, with the exception of 2023, when one award was made. Members of the 2022-23 Review Committee include Dr. Madhav Thambisetty and Dr. Patricia Boyle. Dr Hamilton joined in 2023-24.	The Research Committee approved the draft RFA for 2024 with minor amendments at the April 25, 2024 meeting. Upcoming 2024 grant cycle deadlines include: *May: application period opens	<u>2023-24: Seventh Scholarships</u> Two applications were submitted to the MBRF Award mechanism, and one was awarded to Haopei Yang, PhD. The Trustees determined that the other project did not align with the scope or spirit of the award guidelines.

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
"Encourage young investigators in this area of research"		ABF submitted a draft 2025/26 RFA for MBRF review	*September 10: application submission deadline *November 7: review committee met *January: notification of awardees *July: Award start date Changes to the draft RFA were submitted to ABF by the MBRF on April 9, 2025 The Research Committee reviewed revised draft on April 22, 2025 ABF was notified of final edits and of approval to proceed	10 applications were received by the deadline of September 10 and they appear to all be focused on cognitive aging. Last year only 2 applications were received; in 2023, 8 were received; and in 2022 there were 5 received. 2025 Recipients (2) were notified by letter on January 5, 2025. An announcement of the 2025 recipients was made at the AAN meeting in April. Names were kept confidential until then.
	Poster Reception at Society for Neuroscience annual meeting	Poster sessions were held in 2008 - 2019, and began again in 2023.		Vicki Hixon submitted a proposal to organize the poster session to take place on October 6, 2024 in Chicago. The trustees approved the proposal at their March 19, 2024 meeting. On June 23rd, Vicki sent a Save-the-Date to MBI leadership and communications teams to announce the event will take place on October 6, 2024 at the Chicago Hilton. Dr. Patricia Boyle will attend as a representative of the MBRF.

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
"Encourage young investigators in this area of research"		A question has been raised – Several posters presented at the 2024 poster reception were not related to cognitive decline or memory loss. The call for abstracts does not specifically require alignment with the MBRF mission. This was discussed and considered to be okay although perhaps subtle wording could be added to encourage research in line with the mission	On April 22, 2025, The Research Committee reviewed the wording of the call for submissions currently used by Vicki Hixon for the Poster Session. They provided an additional sentence to be included in this year's call for submissions. Vicki Hixon was informed of the edit	Ms. Vicki Hixon reported that 48 abstracts have been received with a few more expected before the event. Included in the Sept 24 meeting material are a list of those abstracts, a report and information about the event. There were 64 registered posters and 3 additional posters were added the night of the event. Vicki Hixon has submitted a proposal for the 2025 SfN Poster Session which will be reviewed by the Finance Committee on January 21, 2025. The SfN Poster Session was approved for 2025 by the Finance Committee and the Trustees

**Pending review by chairman*

MINUTES
MCKNIGHT BRAIN RESEARCH FOUNDATION (MBRF)
RESEARCH COMMITTEE
CONFERENCE CALL
April 22, 2025

The Research Committee of the MBRF was called to order at 6:00 pm EST on April 22, 2025, by Dr. Madhav Thambisetty.

The following members were present:

Dr. Madhav Thambisetty, Chair of the Research Committee, Trustee
Dr. Mike Dockery, Chair Emeritus
Dr. Patricia Boyle, Trustee
Dr. Roy Hamilton, Trustee
Dr. Sue Pekarske, Trustee

Others attending:
Ms. Melanie Cianciotto, Corporate Trustee
Ms. Amy Porter, Interim Executive Director
Ms. Valerie Patmintra, Senior Communications Advisor

1. Call to Order

Dr. Thambisetty welcomed the members of the committee to the call.

2. Minutes of the January 28, 2025, Meeting

The minutes of the January 28, 2025, Research Committee Meeting (Attachment 1) were approved as amended.

The changes were:

Item 4 a – "was" should be changed to "were"

Item 5 – add "that" after "question"

Action Item 1: The minutes of the January 28, 2025, Research Committee Meeting were approved as amended (Attachment 1).

3. Updated Activity Timeline

The committee reviewed the updated Activity Timeline (Attachment 2) for information.

4. Current Programs

a. Innovator Awards in Cognitive Aging and Memory Loss

The committee reviewed the 2025 Innovator Award Guidelines, Institutional Commitment Form and Application (Attachment). The committee requests that "with independent research space" be deleted in the first sentence of the Institutional Commitment Letter. The committee feels Question 3 on the Institutional Commitment Form, "Please provide $ amount and details of start-up funds that are provided to cover your *direct costs*" does not need to be revised. The committee recommends approval of the Guidelines, Institutional Commitment Form and Application as amended.

Action Item 2: The committee recommends approval of the Guidelines, Institutional Commitment Form and Application as amended.

b. Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss

The committee reviewed the 2026 RFA (Attachment). A new bullet for "Plan for mentorship and other activities to support and guide candidate's development" should be added to page two, item 4. The committee recommends approval of the RFA as amended.

Action Item 3: The committee recommends approval of the RFA as amended.

c. Cognitive Aging and Memory Intervention (CAMI) Core Pilot Grant

The committee reviewed the Cognitive Aging and Memory Intervention (CAMI) Core Pilot Grant Request for LOIs and Proposals (Attachment 5). The committee recommends approval of the Request for LOIs and Proposals. The full board will vote at the May 14, 2025, Meeting and once approved, Dr. Burke will be able to announce the Request for LOIs and Proposals during the Inter-Institutional Meeting.

Action Item 4: The committee recommends approval of the CAMI Core Pilot Request for LOIs and Proposals.

d. Review of call for submissions for the MBRF/MBI poster reception at SfN 2025

The committee reviewed the Call for Abstracts for the 2025 SfN Poster Session (Attachment 6). The committee would like the wording "The outstanding research in the area of cognitive aging and memory loss will be recognized and awarded monetary awards" added to the Call for Abstracts. Ms. Cianciotto will reach out to Ms. Hixon and ask her to add the wording to the Call for Abstracts.

Action Item 5: Ms. Cianciotto will reach out to Ms. Hixon and ask her to add the wording to the Call for Abstracts.

e. Status of the Research Partnership with FNIH and NIA

The trustees received the report on the Research Partnership in Cognitive Aging (Attachment) for information. The MBRF has completed the commitment to the FNIH. Discussion of renewal of the partnership has been tabled for the time being.

5. Adjourn

Dr. Thambisetty asked if there was any further discussion. Hearing none, he called for adjournment of the meeting at 6:50 p.m. EST.

Summary of Action Items:

Respectfully Submitted,

Melanie A. Cianciotto
Corporate Trustee

Cognitive Aging and Memory Intervention (CAMI) Core Pilot Grant Program

To: Mike Dockery, MD, Chairman of the McKnight Brain Research Foundation (MBRF)

From: Sara Burke, PhD, Chair of the CAMI Core Pilot Grant Program Committee

Subject: Recommendations for 2025-2026 CAMI Core Pilot Grant Program

BACKGROUND: In August 2023 the Inter-Institutional Leadership Council submitted a series of recommendations to the MBRF Trustees for maximizing the impact of MBRF's continued investments in Inter-Institutional efforts. Among these recommendations was "Creating an Infrastructure for the Inter-Institutional Pilot Grant Funding Mechanism." In response to that recommendation, the MBRF Trustees requested the reconstitution of the CAMI Core to run the Pilot Grant Program and recommended that this Core include equal representation of the MBIs and key individuals who will champion and promote this program within and across the MBI sites. The Trustees also asked to engage with the Leadership Council regarding a proposed plan for future implementation of the CAMI Core Pilot Grant Mechanism. The proposal was approved in 2024, and the current CAMI Core Committee would like to propose that we continue to implement this program in the same manner for a 2025-2026 funding cycle.

The primary objective of the CAMI Core Committee is to create a vibrant and impactful intervention hub for the four MBIs that fosters promising multisite collaborations to conduct pre-clinical and clinical intervention studies that will lead to high-profile, extramurally funded, and international recognized research programs. This vision will be actualized with the following objectives that are aligned with the original CAMI Core proposal:

CAMI Core Objectives:

1. Facilitate identifying potential Inter-Institutional collaborations by an enhanced Communications Strategy (see page 3) and leveraging resources from each Institute through the CAMI Core Committee Members who serve as pilot program champions.
2. Generate, and after approval by the MBRF Trustees, distribute Request for Funding Announcements for pilot intervention proposals.
3. Identify high-priority Letters of Intent to invite for full proposal submissions.
4. Prioritize pilot projects for funding through rigorous review by experts in cognitive aging research.

PROPOSED 2025/2026 PILOT GRANT PROGRAM:

Based on the Trustees' recommendation, the CAMI Core will always consist of at least four members representing each of the four MBIs. This facilitates inter-institutional collaboration and communication from the CAMI Core Committee to faculty across all institutes. To promote stability and ensure continuity of leadership within the CAMI Core Committee no more than two members will step down from their role on the committee within the same year. When a committee member decides to longer serve, they will nominate another faculty member from their respective institution to serve as that University's CAMI Core Committee representative and commit to at least 2 years of service. This structure ensures that experienced Core Committee Members, who possess critical historical and institutional knowledge, will always remain on the committee as new members join. For the 2025-2026 funding pilot review cycle, all previous members have graciously agreed to serve again. Sara Burke (UF) has also agreed to serve as the Chair, providing consistent leadership during the second year of the Core. Next year, a Co-Chair will be selected from among the current Core members to ensure a smooth leadership transition, with the Co-Chair stepping into the Chair role thereafter. To further support stability, Dr. Burke has also committed to serving one additional year as a regular member following her term as Chair, facilitating the transfer of institutional knowledge and continuity in leadership.

CAMI Core Members:

Sara Burke, Chair burkes@ufl.edu (UF, Chair 2024-2025, Co-chair 2026, Member 2027)
Ihtsham ul Haq ihaq@med.miami.edu (UMiami, Member, 2024-2026)

Matthew Grilli mdgrilli@arizona.edu (UA, Member, 2024-2027)
Keith McGregor kmmcgreg@uab.edu (UAB, Member, 2024-2026)

The roles of the CAMI Core members will be: 1) assist with drafting the annual request for applications (RFA) at the beginning of each year, 2) serve as a champion of the CAMI Core Pilot Grant Program at their home institution and solicit applications, 3) screen and select letters of intent for full applications annually in July/August, 4) nominate potential external reviewers, 5) review 1-3 applications, and 6) participate in a review panel discussion session over zoom, with other committee members and MBI/external reviewers, as needed.

When the term of a CAMI Core member is complete, if they decide not to volunteer again, there will be two strategies for nominating a successor. Firstly, the Committee Member that is rolling off will nominate 2 potential successors from their home institution. Secondly, any previous Pilot Grant Awardees that are established faculty at the rank of Associate for Full Professor will be identified and nominated. A new CAMI Core Committee member from the same institution as the departing member will then be selected by the Council Leadership from that nomination list.

Role of the Chair: The chair will serve as the liaison between the CAMI Core Committee and Leadership Council to facilitate communication. The chair will also organize CAMI Core meetings, oversee drafting the annual RFA with the CAMI Core Committee based on recommendations from the Leadership Council, invite external reviewers, and organize the zoom review session. The Chair will also serve as the main liaison for the CAMI Core Pilot Grant Program to the MBRF Trustees by providing the annual timeline and updates regarding key steps in the process (for example, how many LOIs were received and how many were advanced). The Chair will also communicate any priority research areas recommended by the CAMI Core Committee and Leadership Council to the MBRF and ensure that the RFA aligns with any areas of focus being prioritized by both groups. Relatedly, the Chair will ensure that the RFA draft language is approved by the MBRF before distribution. Finally, after the scientific review is completed and funding recommendations have been made to the Trustees, the CAMI Core Chair will report to the Leadership Council a summary of the review discussion. This will ensure clear and efficient communication between the CAMI Core, MBRF Trustees, and Leadership Council even if the CAMI Core does not include a member from the Council in future years.

REVIEWERS: We would like to thank the MBRF Trustees for the acknowledgement and honorarium presented to the 4 external reviewers. This support enhanced our ability to recruit experts to participate in the CAMI Core Pilot grant evaluations. We would like to request support to conduct the review process in an identical manner during this 2025-2026 cycle. Details of the review process are included below.

Each pilot grant application requires faculty from at least 2 MBIs to collaborate to be eligible for this funding opportunity. Because it is a conflict of interest to have faculty members review grants submitted from their home institution, it is necessary to recruit reviewers from the MBIs as well as from outside the four institutes to provide an unbiased and expert evaluation of the science in each proposal. The Leadership Council and CAMI Core Committee has discussed how to facilitate the review of grants and has the following recommendations:

1) In addition to the CAMI Core Committee, 2-4 investigators from across the MBI sites will participate in the review. These reviewers will be invited from previous awardees that hold the rank of Associate or Full Professor. The Leadership Council and CAMI Core Committee recommend that the Notice of Award include a clause that awardees will be asked to participate in at least one Pilot Grant Review Panel once they reach the rank of Associate Professor or higher.
2) External reviewers at the rank of Associate Professor or higher will be invited to serve on the CAMI Core Pilot Grant Review Panel when LOIs are selected for full applications. This will ensure that sufficient numbers of reviewers with relevant expertise are available to participate in the review panel discussion and that each grant receives at least 3 independent reviews. Reviewers will be invited by the Chair based on the recommendations of CAMI Core

Committee members. Depending on the number of LOIs selected to submit full grants, it is anticipated that approximately 4 external reviewers will be invited each year.
3) External reviewers will receive an evaluation rubric to score each grant and will be expected to review 3-4 grants and participate in a Zoom review discussion.
4) External reviewers will receive modest monetary compensation of $200 for their service. This is comparable to what the NIH pays investigators who serve on a scientific review panel.
5) The Leadership council also recommends that external reviewers receive a thank you letter from the MBRF to document their service. This will be helpful for investigators seeking promotion because service on review panels is an important metric for showing national recognition of scientific expertise.
6) After the review panel is completed, anonymized reviews will be available to Pilot Grant applicants. These can help with the preparation of future applications, particularly for new investigators.

BUDGET: We thank the MBRF Trustees for their increased budgetary support of the CAMI Core pilot awards to $75,000/year for two years for the last funding cycle. This enhanced commitment to this important initiative was instrumental in the increased interest in this award mechanism and the increase in applications. We would like to respectfully request, that this budget remain for the 2025-2026 cycle.

CAMI CORE PILOT GRANT SCIENTIFIC REVIEW PANEL: The consensus recommendation is that all submitted CAMI Core Pilot Grant applications will be discussed and scored by members of the scientific review panel, comprised of the external reviewers as well as CAMI Core Committee members and other MBI investigators from outside of the PIs home institutions. Scientific review panels will include a chair who runs the meetings and summarizes the discussion. This role will be filled by the CAMI Core Committee Chair, or Co-Chair (selected from the CAMI Core Committee) when a proposal involves the Chair's institution. If both the Chair and Co-Chair have a conflict, then the Chair will choose a review panel chair from among the non-conflicted panelists. These meetings will occur annually over Zoom and will take approximately 4 hours.

To facilitate career development of new investigators (maximum rank of Assistant Professor or Postdoctoral Scholar and no prior funding as a primary PI excepting non-training grants), the Leadership Council and CAMI Core Committee also recommend separate scoring criteria for new and established investigators. New investigators will submit a 1-page mentoring plan and timeline as part of the grant application. Grant funding recommendations will be based on evaluation discussion and scoring. It is recommended that there be no quota for funding a certain number of either junior or established PIs, while taking into account the importance of early support in launching a scientific career.

ROLE OF MBRF TRUSTEES AND GRANT ADMINISTRATION: Following the Scientific Review Panel, the CAMI Core Committee will submit funding recommendations to the MBRF for the final award decision. The MBRF will also collect annual interim reports required before the disbursement of Year 2 funds. The CAMI Core Committee and MBRF will work together to evaluate the annual progress and determine if Year 1 progress was sufficient to release Year 2 funds. The Leadership Council also recommends that the MBRF keep all historical documents regarding submissions, reviews, funding, and final outcomes. The CAMI Core Committee could work with the MBRF to establish a shared repository with this information, with access given to the MBRF and the CAMI Committee Chair.

PROPOSED TIMELINE FOR 2025-2026: Once the Leadership Council and MBRF trustees agree on a new structure for the CAMI Core Pilot Grant Program, we propose the following timeline:

May 14, 2025: Launch RFA at the MBRF Inter-institutional Meeting.

July 1, 2025: LOI due.

August 15, 2025: CAMI Core Committee selects LOIs for full proposal, nominates external

reviewers, and invitations are sent by CAMI Core Chair.

November 5, 2025: Full application due.

November 25, 2025: Review assignments distributed to Committee Members and External Reviewers.

January 5, 2026: Reviews due.

January 2026: Zoom CAMI Core Scientific Review Panel with all committee members, 4-5 external reviewers, the Executive Director, and MBRF Trustee representing the Research Committee.

February 1, 2026: Recommendations for funding to Trustees, meeting with Leadership Council in February to de-debrief funding recommendations and revise RFA for the following year.

March 2026: MBRF will send Notice of Awards and MOUs for funding disbursement.

May 1, 2026: Tentative Grant start date.

April 1, 2027: Year 1 grant progress report due to MBRF Trustees to secure Year 2 funding by May 1, 2026.

The MBRF Cognitive Aging and Memory Intervention Core
Inter-institutional Pilot Program
REQUEST FOR LOI and PROPOSALS

APPLICATION RECEIPT DATE:

LOI Deadline: **July 1, 2025**

Full Application Deadline: **November 5, 2025**
(if invited to submit by the CAMI Core)

PURPOSE: The McKnight Research Foundation (MBRF) Cognitive Aging and Memory Intervention (CAMI) Core invites Inter-Institutional MBI applications for pilot studies related to interventions that aim to reduce age-related memory loss and cognitive decline. The specific goal of these projects will be to facilitate and nurture new Inter-Institute collaborations that will establish nationally renowned and impactful research programs for improving memory and cognition in older adults.

RESEARCH OBJECTIVES: The MBRF Cognitive Aging and Memory Intervention Core was established to facilitate multi-site McKnight Brain Institute cognitive aging and memory interventions, as well as collect and disseminate information important for cross-site study collaborations. The Cognitive Aging and Memory Intervention Core will work with invited applicants to facilitate access to necessary resources for multi-site collaboration.

ELIGIBILITY REQUIREMENTS*:* *Please read carefully.*
Applications are solicited from investigators from the four MBI sites.

- Applications must include principal investigators from at least 2 different MBI sites.
- Applications must propose preliminary or pilot interventions with promise for ameliorating cognitive decline associated with normative aging (that is, non-pathological aging), including memory decline.
- LOI submitted by the Deadline of *July 1, 2025* following the format below.
- Only applications that have not been submitted for review to another extramural funding mechanisms and remain unfunded by any source will be considered.
- Awardees may be asked to serve as a reviewer for 1-2 cycles (2026 & 2027) after completion of their award cycle.
- Young investigators are encouraged to apply and it is strongly suggested that they identify a more senior collaborator/mentor at a different MBI site.
- Both pre-clinical/translational and clinical interventions are eligible for consideration.
- A clear role for principal investigators at both MBI sites must be described in the LOI. This could include data collection at multiple sites, imaging or unique microscopy resources, neurophysiology equipment, data analysis resources, as well as tissue or blood samples.
- Proposals that will leverage resources provided by the McKnight Brain Aging Registry are encouraged.

MECHANISMS OF SUPPORT: Grants will be funded for up to a total of $75,000 per year for 2 years. Year 2 funding is contingent on submission of a progress report that includes specific plans and a timeline for the submission of a multi-investigator application for extramural funding.

APPLICATION PROCEDURES:
1) Pre-proposal Letter of Interest (LOI): A 2-page LOI, a cover sheet, and biosketches for multi-Principal Investigators are required for consideration (***DUE July 1, 2025***). The LOI should use 11 pt arial font with 0.5 inch margins and contain the following information:

- Significance and Innovation
- Brief description of hypothesis for the proposed intervention

- List of specific aims
- Description of the structure and need for multi-site collaboration
- NIH-biosketches for m-PIs (not included in page limit): http://grants.nih.gov/grants/forms/biosketch.htm

The LOI must be sent by July 1, 2025 to Sara Burke (burkes@ufl.edu) and Matthew Grilli (mdgrilli@arizona.edu) via email attachment. LOIs will be reviewed by the MBRF Cognitive Aging and Memory Intervention Core Committee and selected investigators will be notified by August 15, 2025 whether they are invited to submit a full application.

2) Full Application: The full applications must be submitted by the deadline of Nov 5, 2025. The proposal should be sent to Sara Burke (burkes@ufl.edu) and Mathew Grilli (mdgrilli@arizona.edu) *via email attachment in a single file in the PDF format*.

Applications must include:

- Completed Coversheet
- A cover letter with the names and contact information and *5 potential qualified reviewers from outside the Evelyn F. McKnight Institutions.*
- Face Page: Project Title, Senior/Key Personnel, Project/Performance Sites, Contact PI (and Contact PI information), along with the Project Summary (30 lines max).
- Research Plan - limited to 5 pages (not including References, 11 point Arial font, 0.5" margins) and should include:
    a. Specific Aims
    b. Research Strategy (Significance, Innovation, Approach)
    c. Description of Multi-site MBI Collaboration
    d. Timeline and Plans for extramural funding applications
    e. References
- Preliminary data are welcome but not required
- Multi-PI plan and structure of collaboration (1 page maximum)
- For new investigators (at rank of Assistant Professor with no prior R01 or equivalent funding), a 1-page mentoring plan and timeline is also required
- Detailed Budget (Budget limited to $75,000 per year in total costs) and Budget Justification. Indirect costs are not allowable
- Please no appendices
- NIH Biographical Sketches for Key Personnel: http://grants.nih.gov/grants/forms/biosketch.htm

APPLICATION REVIEW CRITERIA: Applications will be reviewed for scientific merit by 2-3 expert reviewers and evaluated by a scientific review panel consisting of CAMI-Core Committee Members and External Scientists. Applications will be rated based on 1) significance, 2) quality, innovation and feasibility, 3) collaboration across the MBI sites, and 4) likelihood of leading to a successful larger grant application. For new investigators, the mentoring plan will also be evaluated.

The rankings and final recommendations provided by the Cognitive Aging and Memory Intervention Core will be reviewed by the MBRF. Awardees will be contacted by email.

The anticipated funding start date of successful applications is May 1, 2026.

INQUIRIES: Inquiries regarding application and review procedures can be directed to the MBRF Inter-Institutional Cognitive Aging and Memory Intervention Core members:

Sara Burke, Chair burkes@ufl.edu (UF)
Ihtsham ul Haq ihaq@med.miami.edu (UMiami)
Matthew Grilli mdgrilli@arizona.edu (UA)
Keith McGregor kmmcgreg@uab.edu (UAB)

McKnight Brain Research Foundation Innovator Awards in Cognitive Aging and Memory Loss

The McKnight Brain Research Foundation (MBRF) and the American Federation for Aging Research (AFAR) will provide up to two 3-year awards of $750,000 (USD) each to advanced Assistant Professors and recently appointed Associate Professors (MDs and PhDs.) One award will be made to support studies focusing on clinical translational research and another award toward understanding basic biological mechanisms underlying cognitive aging and age-related memory loss.

The application deadline is August 12, 2025.

The Program

The major goal of the program is to identify emerging scientific leaders by building a cadre of outstanding research scientists across the United States to lead transformative research in the field of cognitive aging.

The program targets full-time independent investigators at the rank of Assistant Professor or Associate Professor (or equivalent) with established independent research programs who have already demonstrated a firm commitment to cognitive aging research. It will add substantial start-up support for a period of three years to help these investigators develop and/or expand an outstanding research program in cognitive aging and memory loss.

One award will be made to support innovative studies focusing on **clinical translational research** and another will support innovative studies of **basic biological mechanisms** underlying cognitive aging and age-related memory loss. It is expected that the proposed research will yield transformative discoveries and thus proposals are invited that are high risk/high gain in nature and that would be less suitable for conventional sources of funding. For example, this support could be deployed towards conducting a pilot clinical trial, developing proof-of concept interventions to ameliorate age associated cognitive impairment, gather preclinical data to accelerate testing of potential interventions, and further study the mechanistic basis of age-associated cognitive impairment in relevant experimental models with a view to identifying novel treatment targets. Scientists proposing to pursue basic research should clearly articulate the potential of their findings to be translated into clinically relevant strategies, and/or treatments. Research studies at the intersection of age-associated cognitive changes and disease-related cognitive impairment may be considered if a strong case can be made for their relevance to cognitive aging and age-

related memory loss. However, research that is primarily focused on neurodegenerative diseases (e.g., Alzheimer's disease) will not be supported.

Two 3-year awards of $750,000 (USD) each will be made in 2025, of which a maximum of 10% may be used for indirect expenses or institutional overhead.

Eligibility

To be eligible, the applicant must:

- Have completed research training prior to the beginning of this award (October 1, 2025):
  o PhD candidates: no more than 7 years from the completion of formal post-doctoral research training post-PhD,
  o MD or combined degree candidates: no more than 12 years from the date when finished residency.
- Exceptions to the 7 and 12 year limits may be considered for certain life events (e.g. familial, personal commitments or other exceptional circumstances). An exception request can be submitted by emailing an NIH-style biosketch to AFAR at **grants@afar.org** at least one week prior to the deadline date.
- Be an independent investigator at the rank of Assistant Professor or Associate Professor (*promoted to the rank of Associate Professor* no earlier than October 1, 2022), who has received R01 funding (or equivalent funding such as an NIH DP5, R35 or NSF Research awards.)
- Be tenure-track faculty or equivalent in an academic or non-profit institution with evidence of long-term institutional support as indicated by commitment of resources including independent laboratory space, start-up research funds and personnel. Candidates not in a tenure-track position are also eligible and should demonstrate similar evidence of long-term institutional support and not be in a time-limited appointment.
- Have a proven track record of research accomplishments in cognitive aging as indicated by their publications in high-impact journals, awards, and other metrics of peer recognition.
- Provide evidence of institutional commitment as described in a **form completed by the Dean or CEO** and a letter of commitment signed by the Department Chair.
- Be in full time employment at an academic or non-profit research institution in the United States.

The program **does not** provide support for:

- Senior faculty, i.e., at the rank of Associate Professor or higher who have held this position before October 1, 2022.
- Assistant Professors who have not yet received R01 or equivalent extramural independent funding.
- Investigators who are conducting research at a federal government or for-profit institution.

- See comment above about disease specific research.

Questions about eligibility and suitability of research project can be addressed to **grants@afar.org**.

Selection Criteria

Five criteria are used to determine the merit of an application:

- Qualifications of the applicant;
- Quality and promise of the proposed research and its relevance to cognitive aging/age-related memory loss;
- Novelty/impact of the proposed research and potential to have transformative clinical impact;
- Excellence of the research environment;
- The commitment by the institution to the applicant as described in the institutional commitment form and letter.

Application Procedures and Timeline

Please refer to the **application instructions**. Incomplete applications cannot be considered. All applications must be submitted via email to **afarapplication@afar.org**.

The applications will be reviewed by a committee whose recommendations will be presented to MBRF and AFAR for final funding decisions.

Please review **this link** which includes suggestions for submitting an LOI or application to AFAR. Click **here** for our Frequently Asked Questions page. If you are using animals in your research, please review **Principles of Animal Use for Gerontological Research** or this recent webinar recording from the Nathan Shock Centers of Excellence: **https://nathanshockcenters.org...**

MBRF and AFAR will not provide reviewer critiques to any applicants at any review level.

Timeline:
Application deadline: August 12, 2025

Anticipated Award Announcement: September 30, 2025

Award Start Date: October 1, 2025

Reporting Requirements

Investigators will be required to submit a brief **narrative report** annually on the progress of their research. Final narrative and financial reports are required within three months following the end date of the award.

Annual Meeting

Recipients of this award are expected to attend the AFAR Grantee Conference. The purpose of the meeting is to promote scientific and personal exchanges among recent AFAR grantees and experts

in aging research. Grantees are also expected to attend the annual inter-institutional meeting of the MBRF.

McKnight Brain Research Foundation Innovator Awards in Cognitive Aging and Memory Loss

Institutional Commitment Form

Candidates for the McKnight Brain Research Foundation Innovator Awards in Cognitive Aging and Memory Loss must be independent investigators. As part of the review the committee will evaluate the institutional commitment for each applicant in order to ensure that adequate research space and resources are available to the candidate.

To complete the application, this form must be completed by the Dean or the CEO of the institution. In addition, a signed letter from the Department Chair must be submitted, as detailed in the instructions.

The form and the letter are NOT to be included in the application, but must be submitted directly to AFAR by the person/office completing the form (NOT the applicant), to afarapplication@afar.org as a Word or PDF file by the application deadline.

Name, title, and address of official completing this form:

E-mail:
Phone:

Signature of Official: _____

First and Last name of Applicant:_____

1. Does the candidate have independent investigator status at their institution?

☐ YES ☐ NO

2. Has the candidate's institution provided space and equipment specifically dedicated to their research program?

☐ YES
Please Describe:

☐ NO

3. Did the candidate receive intramural start-up funds when offered his/her current position? (AFAR does not consider extramural funds from an outside organization/institution as 'start-up funds'.)

☐ YES
Please provide amount and details of start-up funds that are provided to cover your ***direct costs***:

☐ NO

4. Does the candidate have designated administrative support (e.g. someone who helps with editing and submitting grants, tracks budgets, etc.)

☐ YES ☐ NO

5. What was the start date of the candidate's current position?

Month/Day/Year:

6. Does your institution offer tenure:

☐ YES ☐ NO

a. If yes, is the candidate's current position a tenure track position?

☐ YES ☐ NO

b. If your institution does **not** offer tenure, please provide evidence of long-term institutional support

7. Indicate percentage of the applicant's professional time (FTE) allocated to:
   a. Research: %
   b. Teaching: %
   c. Clinical: %

8. a. Describe overall annual research funding for your institution in 2024.
   b. Describe the overall annual research funding for the department in which the investigator holds their primary appointment.

9. Check any boxes that apply:

☐ Is your institution an undergraduate or graduate-degree granting institution, with at least 35% of undergraduate students supported by Pell grants, that has received less than six million dollars in NIH research project grant (RPG) support per year in three of the last five years?

☐ Does your institution grant doctoral degrees and has it received less than 25 million dollars in NIH RPG support in three of the last five years?

☐ Is your institution's historical and current mission to educate students from historically underrepresented populations in biomedical research?

☐ Other category: Please describe:

☐ None of these categories apply.

10. If there is anything else that may demonstrate the institution's commitment to the candidate please describe here:

AMERICAN FEDERATION FOR AGING RESEARCH
55 West 39th Street, 16th Floor, New York, NY 10018 (212) 703-9977

2025 McKnight Brain Research Foundation Innovator Awards in Cognitive Aging and Memory Loss
Application Instruction Sheet

Instruction Sheet: DO NOT INCLUDE with your grant application!

Please carefully read the application guidelines on the AFAR website, before completing this application. Frequently Asked Questions can be found here, as well as things to consider when applying.

INSTRUCTIONS: The application must be submitted via email to afarapplication@afar.org no later than **August 12, 2025 at 5:00 p.m., EST, as a single PDF application, not to exceed 5MB.** No late submissions will be accepted. The application file should be named as follows: "last name, first name", for example "Lee, Pat.pdf".

The application should start with the title page, and budget pages of the application form, and then include the following five sections in this order:

1. Research proposal in four pages or less, including figures, addressing each of the following (Identify each section by the corresponding letter):
    a. Novelty/impact and relevance to the field of cognitive aging and memory loss, and why the project has the potential to be transformative;
    b. List of specific aims of the research plan;
    c. Background information needed to understand the importance of the problem;
    d. Preliminary data produced by the Principal Investigator;
    e. Experimental design, with key methodologies; include pitfalls;
    f. Brief discussion of implications for future research in your lab and elsewhere;
    g. Relation of this work to current research in your lab and if/why this work is complementary and not overlapping.

2. Scientific Rigor: Describe, when applicable, sample size calculations, rationale for age groups, sex, statistical methods, design as well as power analysis, etc. (not to exceed one page). Statistical analysis should be broken down by aims.

3. Complete titles of essential references (not to exceed two pages).

4. NIH-style biosketch of PI (and collaborators, if applicable), using the new NIH format, not exceeding six pages each. *Include past, pending, and current funding using the NIH 'other support' pages.*

5. One-page letters of commitment should be included from collaborators/co-Investigators, if applicable.

6. Include only the application and required materials. If absolutely necessary for the review, the applicant may include one manuscript of a paper that has been accepted for publication but has not yet been published. Do not include any reprints or papers that have been submitted but not yet accepted for publication. If your manuscript has been placed in a repository this will be considered unpublished.

Sections 1-6 should be submitted with the application as a single PDF File.

7. Your Dean or the CEO of your institution must complete an institutional commitment form, which can be downloaded here: MBRF AFAR Institutional Commitment Form.

8. A letter documenting the institution's commitment to the candidate should be prepared by the Chair of the department in which the candidate holds their primary appointment. The letter should include the following:

- A statement of commitment to the candidate's development into a productive, independent investigator meeting the requirements of this award. It should be clear that the institutional commitment to the candidate is not contingent upon receipt of this award.

- Assurances that the candidate will be able to devote the required effort and time to complete the proposed project.
- Assurance that the candidate will have access to appropriate office and laboratory space, equipment, and other resources and facilities (including access to clinical and/or other research populations) to carry out the proposed project.
- Assurance that appropriate time and support will be available for any staff needed to complete the proposed project.

Section 7 and 8 are NOT to be included in the application. The form and the letter must be submitted separately by email to afarapplication@afar.org by the person or office who completed the respective document.

This page is the Instruction Sheet: DO NOT INCLUDE IT with your grant application!

2025 McKnight Brain Research Foundation Innovator Awards in Cognitive Aging and Memory Loss

Application

[Title page: should be the first page of your application]

Title of Proposal: **Institution:** **Proposed Start Date:** **Proposed End Date:** **Total Funds Requested:**	**Name, title and address of official authorizing proposal:** **E-mail:** **Phone:** **Signature of Official:**
Applicant: **Title:** **Degree(s):** **Address:** **E-mail:** **Phone:** **Signature of PI:**	**Are you an Assistant Professor? Yes No** **If No, are you an Associate Professor? Yes No If Yes, indicate date of appointment:** **Do you have an R01 or equivalent funding? Yes No**

ABSTRACT: Provide a summary of your research proposal. Do not exceed space provided.

Key words:
Model system used for the proposed research:

2025 MBRF/AFAR Grant Application - Page 3

2. **BUDGET**
Up to $250,000 in total cost per year may be requested.

Category	Year 1 MBRF/AFAR	Year 2 MBRF/AFAR	Year 3 MBRF/AFAR	Grand Total
Personnel				
Equipment				
Supplies				
AFAR Conference			$2,000	
Travel				
Other Expenses				
10% Indirect Cost				

TOTAL

- Personnel funds can be used for P.I., research assistant(s), technician(s), postdoc(s), or graduate student(s)
- $2,000 is budgeted to cover hotel, meals and other meeting incidentals related to attending the AFAR Grantee Conference (not travel) and will be withheld from the final award amount
- Travel line item should include expenses for travel to the AFAR Grantee Conference in year 3 of the award. Allowable travel expenses are limited to reasonable expenses incurred by the grantee for domestic travel to attend a scientific meeting where the grantee is presenting research that has been supported by the award.
- Total budget requested from MBRF/AFAR may not exceed $750,000, including up to 10% for institutional overhead (up to $68,182)

(Note: AFAR does not provide funding for the purchase of personal computers or laptops or other costs not directly related to the research project, such as tuition, 'telecommunications' or similar.)

4. **BUDGET DETAIL AND JUSTIFICATION**

Use as much space as needed

2025 MBRF/AFAR Grant Application - Page 4

5. Does the research plan include use of human subjects? ☐ YES ☐ NO
   Does the research plan include use of animal subjects? ☐ YES ☐ NO

   Applicants should note that IRB certification (for human subjects) and/or Animal Use Committee approval (for animal subjects) must be provided to AFAR before a grant award can be made.

   Applicants are urged to consult the AFAR website at **http://www.afar.org/research/funding/animal-use/** for advice on human and animal usage or this webinar recording from the Nathan Shock Centers of Excellence: https://nathanshockcenters.org/june2021webinar-1. The website includes a helpful set of guidelines for optimal use of rodents in aging research projects.

6. Indicate the candidate's % of time/effort that will be spent on the planned project:

   _____%

7. a. Have you previously applied for an AFAR Grant? Yes____ No_____

   b. If yes, have you previously received any AFAR Grant? Yes_____ No _____

If yes, please provide name of grant, year received and title of project:

[Start text of grant application and additional materials here, in the order as listed on the instructions page. Insert page number and applicant's name at the top of each page and use Arial font that is not smaller than 11 point with at least 1/2-inch margins on all sides. Any figures used must be included in the 4-page proposal.]

McKNIGHT BRAIN RESEARCH FOUNDATION

Preserving memory, enhancing life

Communications Activity Timeline
Updated April 23, 2025

Activity	Date/Status	Action	Responsible Party	Comments
Patient Education Brochures	**Complete**	Drafted content and designed two new patient education brochures	V. Patmintra	The "Cognitive Aging Explained" and "Keeping Your Brain Healthy" brochures are both posted on the Helpful Resources page of the website and on the "About Cognitive Aging" and "Brain Health Tips" pages of the Brain Works microsite. As part of the ongoing relationship with the Gerontological Society of America, the "Cognitive Aging Explained" and "Keeping Your Brain Healthy" brochures were added to GSA's KAER toolkit in July of 2023 along with the Foundation's tip sheet on healthy aging.
MBRF Organizational Brochure	**In Progress**	Updating the MBRF Organizational Brochure to Post for the 25th Anniversary	V. Patmintra	The organizational brochure has been updated to include new visuals, updated metrics and information on the MBRF and updated content for each of the four MBIs. The updated brochure is being posted to the Foundation's 25th Anniversary celebration landing page on the website.
MBRF Anniversary Video	**Complete**	Updating the MBRF Highlights Video for the 25th Anniversary	V. Patmintra BRG	The MBRF's anniversary video is featured on the website and was included in social media promotion efforts as part of the activities commemorating the Foundation's 25th anniversary.

Mind Your Memory Newsletter	**Ongoing**	Quarterly Newsletter with Consumer-Focused News and Highlights	V. Patmintra	The Mind Your Memory consumer newsletter began distribution in September 2022 and is distributed quarterly to the Foundation's organizational contacts list and to consumers who sign-up for distribution on the website. The spring 2025 issue of the newsletter is being drafted and will be distributed in mid-May.
McKnight Brain Website	**Ongoing**	Home Page Refresh and Ongoing Content Development	V. Patmintra	Based on results from the User Testing initiative, the website navigation was updated at the end of July with new headers designed to draw audiences in to the content most relevant to their needs. The organizational content about the Foundation is also now separated across two tabs titled "Our Work" and "About Us." Following completion of the navigation update, new content has been added to the Blog and News pages of the website on a weekly basis. The Brain Works microsite launched on March 22 as part of the campaign kickoff activities and features a Resource Hub with materials from the MBRF as well as other leading cognitive aging and brain health organizations. The Hot Topics section of the microsite is updated regularly to feature campaign news and consumer-friendly research updates from the MBIs. A Brain Works button is featured in the McKnightBrain.org's primary navigation and a hero image highlighting the campaign was added to the homepage carousel to help users flow seamlessly between the two areas of the site.
PCP Education Initiative	**Ongoing**	Develop content to build a dedicated area of the website for PCP education	V. Patmintra	The Brain Works Year Two campaign recommendations include ideas for engaging with healthcare professionals via partnerships with relevant membership organizations.

				A partnership opportunity with the American Academy of Family Physicians has been secured and materials on brain health and cognitive aging are in development to be featured on the AAFP's patient-facing website FamilyDoctor.org and in the physician trade Family Medicine Today.
Social Media	**Ongoing**	Develop monthly content themes and make regular posts to the MBRF Twitter, Facebook and LinkedIn pages	V. Patmintra	Developing themes and drafting content on a monthly basis to make 2-3 posts per week. Leveraging boosted Facebook posts and Google ads to drive additional traffic to the McKnightBrain.org website. Resulting from additional social media advertising and promotion, the MBRF's social media following has increased by more than 500% since the Brain Works campaign launched in March.

Tracking and Quarterly Reports	**Began in 2019 Onngoing**	Conduct media tracking and provide quarterly updates.	V. Patmintra	Tracking media and social media metrics and reach throughout the year and providing quarterly updates to the Trustees. Tracking topics include: brain health, age-related memory loss, cognitive aging, cognitive decline, age-related cognitive decline, McKnight Brain Research Foundation, McKnight Brain Institutes. A comprehensive report of media coverage and website traffic generated from the Brain Works campaign will be included for review with materials for the May 14 Trustees' meeting.
Communications Working Group	**Began in 2019 Ongoing**	Zoom meetings with members of the Communications Working Group	A. Porter V. Patmintra Last Meeting:	Quarterly meetings with members of the Communications Working Group to discuss and engage in ongoing activities, including:

			March 12, 2025	• Identifying core competencies needed for each MBI's communications outreach • Reviewing, vetting and approving materials • Providing input on upcoming studies with relevant consumer/medical media angles • Identifying young researchers and studies of note to highlight on the MBRF website
Brain Works Public Awareness Campaign	**Ongoing**		V. Patmintra A. Porter BRG	The ***Brain Works: Optimize Your Brain Span*** campaign launched on March 22 with a Satellite Media Tour, launch of the Brain Works microsite and ongoing media outreach. Results from the first few months of the campaign were shared with the Trustees during the May meeting, along with high level plans for year two of the campaign. Plans for the campaign's second year will be formalized following the meeting. Year Two Brain Works campaign activities, including ongoing media relations, distribution of an online public service announcement, influencer activation with Dr. Joy and a partnership opportunity with the American Academy of Family Physicians are underway. Updates will be shared with the Communications Committee during the April 29 committee meeting and a full report on year two results and a look ahead to year three will be shared with the Trustees during the May 14 meeting.

Pending chair review

MINUTES
MCKNIGHT BRAIN RESEARCH FOUNDATION (MBRF)
MEETING OF THE COMMUNICATIONS COMMITTEE
TEAMS MEETING
April 29, 2025

The Meeting of the Communications Committee of the MBRF was called to order at 6:00 pm EDT on April 29, 2025 by Dr. Patricia Boyle.

The following committee members were present:
Dr. Patricia Boyle, Communications Committee Chair
Dr. John Brady, Trustee
Dr. Sharon Brangman, Trustee
Dr. Sue Pekarske, Trustee

Others attending:
Dr. Lee Dockery, Chair Emeritus
Ms. Melanie Cianciotto, Corporate Trustee
Dr. Alice Luo Clayton, CEO
Ms. Amy Porter, Interim Executive Director
Ms. Valerie Patmintra, Senior Communications Advisor
Ms. Mandy Byrd, BRG Communications
Ms. Maureen Higgins, BRG Communications
Ms. Kate Worthy, BRG Communications

1. Call to Order

Dr. Boyle welcomed the committee members and guests attending the meeting. She also welcomed Dr. Alice Luo Clayton, the MBRF's new CEO to the meeting and to the Foundation. Dr. Luo Clayton introduced herself to the group and expressed her enthusiasm in learning more about the MBRF's communications efforts and working with the Foundation going forward.

2. Approval of Minutes from the February 6, 2025, Joint Meeting of the Communications and Education Committees

The minutes of the February 6, 2025, Joint Meeting of the Communications and Education Committees were reviewed and approved as presented.

Action Item 1: The minutes of the February 6, 2025, Joint Meeting of the Communications and Education Committees were approved as presented.

3. Communications Activity Timeline

Dr. Boyle reviewed the updated activity timeline, noting that the BRG team would be joining the meeting soon to provide an update on the Brain Works campaign. She also noted that the next issue of the Mind Your Memory newsletter would be distributed in mid-May and that the AAFP partnership, which was approved during the last meeting, is now in progress and materials are being developed with the AAFP. Dr. Brady shared that the co-branded materials will be featured on AAFP's FamilyDoctor.org patient-facing website and in Family Medicine

Pending chair review
Today, the trade publication for family physicians, and should be a great opportunity to reach and engage with the AAFP's family physician and patient audiences.

4. Brain Works Campaign Update

a. Media and Social Outreach and Results to Date

Ms. Kate Worthy, BRG Communications, presented a summary of media coverage secured for the Brain Works campaign to date. Since the campaign launched in March of 2024, more than 2 billion media impressions, 4,200 placements and 57 interviews have been secured. She noted that the campaign is tracking very well against the year two media goals and has already surpassed the number of media impressions anticipated for the year thanks to several high-profile media placements featuring the MBRF Trustees.

Ms. Worthy shared that the campaign's digital coverage is also exceeding expectations. Thanks to influencer activations and an ongoing advertising strategy, the Foundation has increased its followers across all social media platforms by more than 500 percent. She also noted there have been more than 27,000 visits to the Brain Works microsite since July. In response to Dr. Luo Clayton's question about audience demographics, BRG and Ms. Patmintra offered to present the demographic breakdown of web visitors and social followers with the results that will be shared during the May 14 Trustees meeting in Miami.

b. Upcoming Activities

Ms. Patmintra noted that a draft syndicated article was included with the committee materials and has already been reviewed and approved by Dr. Boyle. She asked the committee members to review the article and let her know if it is approved by Monday, May 5, so the article can be distributed to community papers across the country to boost placements for the second year of the campaign. BRG also presented the idea of partnering with Dr. Joy for another influencer activation in May for Mental Health Awareness Month and the committee members approved.

BRG also shared that a deskside interview opportunity with Jon Hamilton, the lead science reporter for NPR, has been secured and they are working with Dr. Roy Hamilton to schedule the interview. The interview will be a great opportunity to introduce the Foundation and its expert spokespeople to NPR with the goal of serving as a resource for future stories and interview requests.

5. Update on the AARP Brain Health Action Collaborative

Dr. Brangman gave an update on the AARP Brain Health Action Collaborative noting that Ms. Patmintra has been invited to join the group's meetings as the Collaborative is also planning a consumer outreach initiative. Now that Dr. Luo Clayton has started as CEO, Dr. Brangman said she would introduce her to the group as another MBRF representative to participate in the AARP Brain Health Action Collaborative.

6. Adjourn

With no additional items for discussion, Dr. Boyle called for adjournment of the meeting at 7:10 p.m. EDT.

Respectfully Submitted,

Valerie Patmintra
Senior Communications Advisor

BRG

McKNIGHT BRAIN RESEARCH FOUNDATION

Preserving memory, enhancing life

Recent Activity & Upcoming Activations

Brain Works

Optimize Your Brain Span

Brain Works

Optimize Your Brain Span

Program Results

Overall Campaign Results to Date

Media Results

2B+
Impressions

4.2K+
Placements

57
Interviews

Digital Results

552%
Follower Increase Across Platforms

36K
Webpage Views

Year 2 Media Results

Media Outreach Year 2 Goals (July 1, 2024 – June 30, 2025)

500M+
Impressions

2.5-5K+*
Placements

**Goal includes press release wire pickup*

30
Interviews

Year 2 Results

1.2B+
Impressions

227+
Placements

On Track to Goal

25
Interviews

On Track to Goal

Year 2 Digital Results by the Numbers

Digital Reach Goals Year 2 (July 1, 2024 – June 30, 2025)

50%
Follower Increase Across Platforms

25-40K
Webpage Views

Year 2 Results

432%
Follower Increase Across Platforms

27K
Webpage Views

Brain Works

Optimize Your Brain Span

Upcoming Activity

May Activity

Media

- ***National Outreach***
  - Mental Health Awareness Month (May)
  - Deskside with NPR

Influencer Activation – Dr. Joy

- *Tie into Mental Health Awareness Month*
  - *Challenge/Giveaway aspect for more engagement*

AAFP Partnership Overview

By leveraging AAFP channels and McKnight Brain Research Foundation resources and information, we can expand the reach of programs such as BrainWorks, empowering more patients to talk with their doctors about cognitive health and equipping more physicians with additional tools for supporting patients as they age.

Activations

- ✓ Brain health article on FamilyDoctor.org
- ✓ News story or blog post highlighting MBRF Q&A
- ✓ Social media promoting co-branded content
- ✓ PSA style video content
- ✓ Online content promoting MBRF resources

AAFP

BRG

McKNIGHT BRAIN
RESEARCH FOUNDATION
Preserving memory, enhancing life

Thank You

BrainWorks
Optimize Your Brain Span

Research Partnership in Cognitive Aging

A report to the McKnight Brain Research Foundation
April 17, 2025

Foundation for the National Institutes of Health
The National Institute on Aging

REPORT SUMMARY

The Foundation for the National Institutes of Health (FNIH) is pleased to present the following Research Partnership in Cognitive Aging 2024 report to the McKnight Brain Research Foundation (MBRF). The report provides an update from the National Institute on Aging (NIA) on the Cognitive SuperAgers Networks, both supported through the Research Partnership in Cognitive Aging.

The current centerpiece of the Research Partnership in Cognitive Aging between the NIA and MBRF, coordinated by the FNIH, is the research supported through the funding opportunity "Network for Identification, Evaluation, and Tracking of Older Persons with Superior Cognitive Performance for Their Chronological Age," RFA-21-015 (https://grants.nih.gov/grants/guide/rfa-files/RFA-AG-21-015.html). Updates to this research are provided below.

Network for Identification, Evaluation, and Tracking of Older Persons with Superior Cognitive Performance for Their Chronological Age (U19 Clinical Trial Not Allowed)

Resilience/Resistance to Alzheimer's Disease in Centenarians and Offspring (RADCO) U19AG073172

The RADCO cooperative agreement (U19AG073172), awarded to Drs. Thomas Perls (Boston University Medical Campus), Stacy Andersen (Boston University Medical Campus), and Susan Bookheimer (UCLA) is in the fourth year of award. The NIA continues to support a multi-year administrative supplement, in the form of a fourth phenotyping and biospecimen core and neuroimaging core site at Georgia State University (GSU). The addition of the GSU site has increased the number of centenarian cognitive Superagers in the network and should increase the Black participant proportion of the RADCO sample from 7.2% to 22.2%. Current enrollment in this network is 290 individuals, 173 of which are cognitive superagers. The website for the project may be found at https://www.bumc.bu.edu/centenarian/radco/.

The abstract for U19AG073172:

DESCRIPTION (provided by applicant): Centenarians delay age-related diseases and disabilities into their mid-nineties. Some remain cognitively intact despite extreme exposure to the strongest risk factor for cognitive impairment and Alzheimer's disease (AD), aging. The overall hypothesis of this study, titled "Resilience/Resistance to AD in Centenarians and Offspring" (RADCO), is: centenarian cognitive SuperAgers and some of their offspring have protective factors that confer such resilience or, in some cases, even resistance against cognitive decline and dementia. RADCO assembles an unprecedentedly large sample of prospectively studied centenarian cognitive SuperAgers (n=495, essentially, centenarians with cognitive function that falls within the norms of septuagenarians) along with offspring (n=600) and offspring spouses (n=120), who, via RADCO cores, undergo careful, comprehensive, and cutting-edge neuropsychological, biomarker, neuroimaging, and neuropathological phenotyping. These data are used by two projects with the overall scientific objective of gauging cognitive resilience in this sample, understanding the underlying protective biology and translating that into therapeutic targets. The Cognitive Resilience and Resistance Phenotypes Project (Project 1) gauges resilience by neuroimaging, plasma AD biomarkers risk and neuropathology, and therefore generates a range of resilience endophenotypes. The Protective Factors and Mechanisms Project (Project 2) is the translation arm of RADCO; it discovers genes, candidate biological pathways and sets of mi-RNA regulators associated with the resilience endophenotypes characterized in

Project 1. In-vitro models of AD incorporate cortical neurons, microglial cells, and astrocytes created from centenarian cognitive superager induced pluripotent stem cell (iPSC) lines are used to test the candidate pathways for how they cause resilience against AD.

PUBLIC HEALTH RELEVANCE: Centenarian cognitive SuperAgers have exceptional cognitive function despite extreme exposure to the strongest risk factor for cognitive impairment and Alzheimer's disease, aging. The RADCO Study gauges cognitive resilience among centenarian cognitive SuperAgers and their offspring using cognitive testing, neuroimaging, blood biomarkers, and neuropathology. Translational studies will identify protective factors and underlying mechanisms that confer resilience or in some cases, even resistance against cognitive decline and dementia.

Study to Uncover Pathways to Exceptional Cognitive Resilience in Aging (SUPERAging) U19AG073153

The SUPERAging cooperative agreement (U19AG073153) awarded to Drs. Emily Rogalski, Marsel Mesulam, and Changiz Geula is in the fourth year of award. Of note, last year saw a change in the locus of the parent award. Dr. Rogalski has transferred from Northwestern University to the University of Chicago. Dr. Mesulam stepped down as one of the Multi-Principal Investigators (MPI) last year but has rejoined as an MPI this year. Both Drs. Geula and Mesulam remain on faculty at Northwestern. Enrollment in the study to date is 300 participants, all of whom are cognitive superagers. The website for this project may be found at https://haarc.center.uchicago.edu/superaging/.

The team published findings in *Brain Communications* in 2024 regarding the relationship between functional connectivity and age-related cognitive decline. Decreases in functional connectivity have been associated with the cognitive impairment seen in individuals with Alzheimer's disease. However, there are inconsistent findings in the literature about this relationship. Using optimized MRI methods, the team sought to explore this relationship in cognitive superagers. They found that functional connectivity within or between brain networks did not appear to drive the exceptional memory performance seen in cognitive superagers. These findings could have relevance for differentiating the role of functional connectivity changes associated with age-related cognitive change from those associated with AD. This publication is attached to this report.

The abstract for U19AG073153:

DESCRIPTION (provided by applicant): The primary goal is to establish a multicenter SuperAging Consortium to identify behavioral, health, biologic, genetic, environmental, socioeconomic, psychosocial, anatomic and neuropathologic factors associated with SuperAging. These goals will be achieved through an organizational structure with 3 Cores (Administrative/Biostatistics, Clinical/Imaging, and Biospecimen/ Neuropathology) and 2 Research Projects. The Consortium will enroll 500 participants across 4 US Sites located in Illinois, Wisconsin, Michigan and Georgia, and the Canadian Site in Southwest, Ontario, with a focus on the enrollment of Black SuperAgers and Cognitively Average Elderly Controls with similar demographics (Controls). The Administrative/Biostatistics Core will provide governance and fiscal oversight, maintain scientific integrity, and create a centralized biostatistics and database infrastructure to harmonize the goals and activities of the Cores, Sites, and Projects, with each other, with the NIA, and with extramural collaborators. The Clinical/Imaging Core will standardize criteria for the uniform cross- site and multidisciplinary characterization of SuperAgers, streamline recruitment including that of Black participants, enter relevant information in the comprehensive database, support co-enrollment into Project 1, and encourage collaborative ventures aiming to understand the factors that promote SuperAging. The

Biospecimen/Neuropathology Core will collect and bank brain tissue and blood products from SuperAging and Control cases, according to optimized procedures. It will render pathological diagnoses, quantitate selected markers of neurodegeneration and neuronal structure, coordinate the analyses of plasma biomarkers for Alzheimer's disease, and make specimens available for collaborative investigations. Project 1 will use state-of-the-art wearable technology to obtain real-time measurements in the course of everyday life to characterize quantitative parameters related to sleep, physical activity, autonomic responsivity, and social engagement to determine whether SuperAgers have relatively preserved and quantitatively determined physiologic and behavioral "complexity" compared to Controls. Project 2 will use transcriptomic, genetic, and protein profiling approaches to test the hypothesis that SuperAgers will demonstrate significant molecular differences in their central and peripheral immune and inflammatory system parameters compared to matched Control and Alzheimer's disease participants. By identifying neurobiologic features that contribute to superior memory performance in old age, outcomes from this Consortium will help isolate factors that promote successful cognitive aging and perhaps also prevent age-related brain diseases such as Alzheimer's disease.

PUBLIC HEALTH RELEVANCE: The proposed Consortium offers optimal organization for the accelerated recruitment of a racially diverse cohort of SuperAgers so that they can be more fully characterized neuropsychologically, neuropathologically, psychophysiologically, and molecularly. The planned activities of the Consortium will help isolate factors important for promoting successful cognitive aging and potentially also for avoiding age-related brain diseases such as Alzheimer's disease.

Update on findings from the MEDEX Clinical Trial (R01AG049369)

Findings continue to be published from the MEDEX ("Remediating Age-related Cognitive Decline: Mindfulness-based Stress Reduction and Exercise"; R01AG049369) clinical trial that received past support through the Research Partnership in Cognitive Aging. Focusing on those individuals in MEDEX who received the exercise intervention (n = 225) or a nonexercise comparison condition (n = 260), they estimated for each a physiological age of the brain and derived a predicted age difference compared with chronological age, which they termed BrainPAD. The researchers found that for cognitively normal older adults, exercise did not appear to impact BrainPAD but was effective in improving fitness, body composition, and total sleep time. Changes in body composition, but not fitness, physical activity or sleep, impacted BrainPAD. They concluded that a focus on weight control, particularly central obesity, could be an interventional target for healthier brains.

Update on an Additional Initiative Stemming from the Cognitive Aging Summit III

One of the recommendations from the 2017 Summit was to support a longitudinal study of rats that would closely track the animals throughout their lives. NIA's Intramural Research Program (IRP) implemented that recommendation via a longitudinal study in rodents, "Successful Trajectories of Aging: Reserve and Resilience in Rats" (STARRRS). The award was made to Dr. Peter Rapp in the IRP. The study is on track to generate state-of-the-art neuroimaging, along with phenotypic results, non-invasive biological samples, plus other indicators that should yield insights into the mechanisms of healthy neurocognitive aging. The overarching goal of STARRRS is to establish an open resource of longitudinal data from male and female rats, including detailed behavioral characterization and neuroimaging, tissues and other biospecimens, for research on mechanisms of reserve and resilience in aging, and to inform resilience to Alzheimer's disease and related dementias. As of the end of 2024, approximately 200 animals have completed the

longitudinal study. Brain MRI scans and phenotypic data (motor activity, memory, attention, olfaction, frailty, and anxiety assessments), as well as biosamples have been collected on these 200 animals and deposited in the Aging Research Biobank (https://agingresearchbiobank.nia.nih.gov/). Processing is continuing to make data and samples accessible to researchers in the near future.

APPENDIX

- *Medicine & Science in Sports & Exercise*: Fatness but Not Fitness Linked to BrainAge: Longitudinal Changes in Brain Aging during an Exercise Intervention
- *Brain Communications*: SuperAging functional connectomics from resting-state functional MRI
- *New York Times*: A Peek Inside the Brains of ‘Super-Agers’
- *Chicago Sun Times*: 'Enjoy just being here' — At almost 110, she's still baking pie, with a little help
- *Boston Globe*: Who gets to live to 100? The answer may surprise you.
- Additional 2024-2025 Media Coverage
- Example Recruitment Materials
- RADCO Brain Donation Flyer

Fatness but Not Fitness Linked to BrainAge: Longitudinal Changes in Brain Aging during an Exercise Intervention

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ABSTRACT

WING, D., L. T. EYLER, E. J. LENZE, J. L. WETHERELL, J. F. NICHOLS, R. MEEUSEN, J. G. GODINO, J. S. SHIMONY, A. Z. SNYDER, T. NISHINO, G. E. NICOL, G. NAGELS, and B. ROELANDS. Fatness but Not Fitness Linked to BrainAge: Longitudinal Changes in Brain Aging during an Exercise Intervention. *Med. Sci. Sports Exerc.*, Vol. 56, No. 4, pp. 655-662, 2024. Purpose: Fitness, physical activity, body composition, and sleep have all been proposed to explain differences in brain health. We hypothesized that an exercise intervention would result in improved fitness and body composition and would be associated with improved structural brain health. Methods: In a randomized controlled trial, we studied 485 older adults who engaged in an exercise intervention (n = 225) or a nonexercise comparison condition (n = 260). Using magnetic resonance imaging, we estimated the physiological age of the brain (BrainAge) and derived a predicted age difference compared with chronological age (brain-predicted age difference (BrainPAD)). Aerobic capacity, physical activity, sleep, and body composition were assessed and their impact on BrainPAD explored. Results: There were no significant differences between experimental groups for any variable at any time point. The intervention group gained fitness, improved body composition, and increased total sleep time but did not have significant changes in BrainPAD. Analyses of changes in BrainPAD independent of group assignment indicated significant associations with changes in body fat percentage (r(479) = 0.154, P = 0.001), and visceral adipose tissue (VAT) (r(478) = 0.141, P = 0.002), but not fitness (r(406) = −0.075, P = 0.129), sleep (r(467) range, −0.017 to 0.063; P range, 0.171 to 0.710), or physical activity (r(471) = −0.035, P = 0.444). With linear regression, changes in body fat percentage and VAT significantly predicted changes in BrainPAD (β = 0.948, P = 0.003) with 1-kg change in VAT predicting 0.948 yr of change in BrainPAD. Conclusions: In cognitively normal older adults, exercise did not appear to impact BrainPAD, although it was effective in improving fitness and body composition. Changes in body composition, but not fitness, physical activity, or sleep impacted BrainPAD. These findings suggest that focus on weight control, particularly reduction of central obesity, could be an interventional target to promote healthier brains. Key Words: VISCERAL ADIPOSE TISSUE, MAXIMAL CARDIOVASCULAR FITNESS, SUCCESSFUL AGING, EXERCISE INTERVENTION, BRAIN HEALTH

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Changes in brain structure are clearly associated with advancing age. These changes include reduced cortical thickness (1), volumetric decline of both gray and white matter (2,3), and an increase in the absolute number and total volume of white matter hyperintensities (4). However, there is substantial individual variability in the prevalence of these declines (5), as well as the rate at which they progress when observed (3). Better understanding of the mechanisms underlying, and the behaviors that contribute to or inhibit, these changes could help inform interventions targeted at slowing brain structural and functional declines.

High levels of physical fitness, regular engagement in formal exercise, and high levels of overall physical activity have all been hypothesized to explain some of the observed individual differences in brain health. Indeed, several large observational studies have found associations between levels of physical activity and both brain volume and the risk of developing cognitive dysfunction (6). Furthermore, systematic reviews of observational studies have observed that both higher levels of fitness and engagement in regular moderate to vigorous physical activity are often associated with higher volume of gray matter across key regions of the brain, including the hippocampus and prefrontal cortex as measured by magnetic resonance imaging (MRI) (7). Longitudinally, multiple studies have found associations between increased physical activity and changes in brain volume in key regions among both healthy individuals (6) and those with mild cognitive impairment (8), Furthermore, meta-analyses of interventional studies suggest that increasing the number of minutes of moderate- to vigorous-intensity physical activity improves cognitive function in older adults (9) particularly in individuals who are cognitively and physically healthy at baseline (10). In general, these observed improvements are further enhanced by the presence of multimodal instruction that includes strength training (10). However, positive associations both cross-sectionally and longitudinally are not universally observed depending upon clinical status and the presence of comorbidities (2), and some studies have found no association between cardiorespiratory fitness and brain volume in healthy (11,12) and cognitively impaired (13) populations.

Independent of fitness and activity levels, body composition, particularly body fatness, has also been hypothesized to contribute to changes in brain volume and cognitive function. For example, higher BMI has been associated with decreased gray matter volume across multiple brain regions (14), and links between central adiposity, as measured by waist circumference, and executive function have been observed both in children (15) and older women (16). Recent systematic reviews of cross-sectional studies have indicated that obesity, particularly central obesity, is commonly correlated with reduced cortical thickness and gray matter volume (17) and with cognitive impairment in older adults (18). However, prospective longitudinal studies in both children (15) and midlife adults (19) have observed a bidirectional predictive relationship between cognition and central obesity indicating that there may be a common causal pathway contributing to the development of both conditions. Kullmann et al. (20) may have identified at least some portion of this shared pathway, noting that insulin sensitivity in the brain is strongly associated with volume of visceral fat, and insulin (in)sensitivity is associated with cognitive capacity. Beginning in the early 2010s, tools utilizing the capabilities of machine learning algorithms to provide a comprehensive assessment of structural changes within the brain have emerged. These algorithms are applied to MRI images to use volumetric measures of multiple brain regions drawn from large samples that range widely in age to provide an estimation of the *physiological* age of the brain (commonly termed BrainAge). The difference between this BrainAge and chronological age can be calculated to provide a brain-predicted age difference (BrainPAD). Using this, we can determine if an individual's brain structure is younger (negative BrainPAD) or older (positive BrainPAD) than expected. These tools have successfully predicted age across the human lifespan, including in healthy adolescents (21) and older adults (22). In addition, these algorithms show very good test/retest reliability (23) and have correctly identified larger BrainPAD (i.e., higher values/older brains) in populations with expected negative changes in brain structure and/or with evident cognitive decline including multiple sclerosis (24), stroke (25), and Traumatic Brain Injury (26). As such, BrainAge (and the associated BrainPAD) may offer meaningful public health research applications, although there has been little longitudinal research into predictors of BrainPAD or the likelihood of changes in BrainPAD in response to changes in modifiable behaviors.

Our research question(s) centered on how BrainPAD was affected by an exercise intervention and associated changes in fitness, fatness, activity, and sleep. We hypothesized that a 6-month moderately intense multimodal exercise intervention focused on a combination of aerobic exercise, traditional resistance training, and functional movements would result in improved physical fitness and body composition (i.e., greater aerobic capacity, less body fat and visceral adipose tissue (VAT), and greater lean mass). We further hypothesized that this intervention would improve BrainPAD, and that those improvements would be associated with changes in the metrics of interest. As a secondary but associated research question, we explored changes in fitness and/or body composition independent of their experimental grouping, with a hypothesis that beneficial changes over 6 months (i.e., greater fitness, less fat) would be associated with changes in BrainPAD indicating brains that are growing "younger" compared with chronological age. We had a final hypothesis that changes in sleep would be associated with changes in BrainPAD (with more sleep leading to a more negative/younger BrainPAD value), although likely minimally affected by the intervention.

METHODS

Participants. Data were drawn from a multicenter randomized interventional clinical trial approved by Institutional Review Boards at both the University of California, San Diego, and Washington University in St. Louis, and informed consent to participate in the research study was obtained from all participants. This group has been described in depth

elsewhere (27). In brief, participants were sedentary adults aged 65 to 84 yr, not currently using glucocorticoid or diabetes medications, and without diagnosed cognitive impairment or neurodegenerative or cardiovascular disease.

Exercise intervention. The exercise intervention was designed with the goal of integrating progressive aerobic and resistance training with functional movement and balance training and has been described in detail previously (28). In short, minimal heart rate targets during aerobic training were generated, personalized resistance training goals were established, and a comprehensive manual was developed to ensure consistency across sites and cohorts. All sessions were led by a trainer licensed by a nationally accredited organization (either The American College of Sports Medicine, The American Council on Exercise, or The National Academy of Sports Medicine) with extensive (>2 yr) on-the-job experience working with older adults. In addition to demonstrated experience working with the target population, trainers went through a 12-h training specific to the intervention during which the goals of the intervention, the exercise prescription and progression plans, and the specific exercises to be utilized were discussed and practiced in detail using team members and "friends and family" as example participants. Across the course of the intervention, a total of five (three at one location and two at the other) trainers were engaged, with one "lead" trainer at each location leading ~60% of all classes at that intervention site. Classes were 90 min and were held twice weekly for 6 months. Classes started with a 30-min warm-up period that included integrated movement designed to warm the body and raise the heart rate to a level at (or above) 55% of heart rate reserve. After the warm-up, classes were split roughly in half, with one group beginning aerobic exercise and the other beginning strength training. After 30 min, the groups switched training positions.

It is worth noting that the larger study was designed with a 2 × 2 factorial design in which approximately half of the individuals within the exercise intervention also received a mindfulness-based stress reduction (MBSR) intervention. Similarly, approximately half of the individuals within the control condition also received MBSR training, whereas the other half received a series of lectures aimed at health promotion. These lectures specifically avoided topics related to exercise and/or mindfulness. All individuals were included in these analyses without differentiation between those receiving or not receiving MBSR.

Neuroimaging acquisition. Neuroimaging was gathered at baseline and following the 6-month intervention period. All baseline scans were acquired >1 d, but <30 d before intervention initiation and ±2 weeks from intervention completion. For individuals involved in the exercise intervention, neuroimage scanning was completed on a nonexercise day (i.e., not on a day where formal training occurred), and participants were asked to report to the scanning location well rested. Although all scans were acquired during standard operating hours (8 AM to 5 PM), time of day and day of the week were not controlled.

MRI scanners (3 T) were used to acquire high-resolution (1 × 1 × 1 mm) T1-weighted sagittal, magnetization-prepared rapid gradient echo with one scanner used at one site (GE, Signa—MP-RAGE; repetition time (TR) = 2300 ms; inversion time (TI) = 900 ms, echo time (TE) = 2.95 ms, flip angle = 9°; acquisition time = 5 min) and two used at another (Siemens Prisma and Tim Trio—MP-RAGE TR = 2400 ms, TI = 1000 ms TE = 3.16 ms, flip angle = 8°). Both used real-time motion correction (PROMO). Scans were processed using FreeSurfer (version 6.0) to provide quantitative measures of image quality. All images were reviewed for incidental findings or excessive head movement by the study neurologist(s).

BrainAge processing of T1-weighted MRI images. The BrainAge model developed by James Cole, commonly called BrainAgeR, was used for these analyses (22). This model was deemed to be the most appropriate available model as the algorithm training was done on a group that contained a comparatively large number of individuals over the age of 65 yr. To derive the BrainAge score, T1-weighted MRI scans were segmented and normalized using SPM12. Vectors with mutually exclusive compartments for Grey Matter, White Matter, and Cerebral Spinal Fluid were established using the Rnifti package in R. The Kernlab package was then applied to provide a BrainAge score using the 435 established input variables. To provide visual quality control beyond the point-of-acquisition review described below, multiple slices of the brain were provided as visual images in .html format using an FMRIB Software Library program. These images were reviewed for obvious object or movement artifact by a specially trained researcher. BrainPAD scores were calculated by subtracting chronological age from the BrainAge score provided by the algorithmic scoring. Positive values reflect brains that are older than chronologically expected, whereas negative scores indicate brains that are younger than the chronological age of the individual.

Assessment of BrainAge values and images for inclusion. Study neurologist's recommendations regarding image usability were applied so that individuals who had uninterpretable findings were not analyzed. The Euler number, which is derived from the FreeSurfer algorithm and provides a quantified description of the number of holes in an image, was applied to further exclude individuals whose scans were poorly visualized and likely to be subject to error. In addition, individuals who had a change in BrainPAD from baseline to the end of the intervention >3 SD from the group change calculated in absolute values were excluded on the presumption that one (or both) of their scans had features that led to inaccurate scoring.

Physical measures (graded exercise test, dual x-ray absorptiometry, accelerometry). These physical measures have been presented in greater detail by Wing et al. (28) and Wetherell et al. (29). However, we have provided key elements of the physical measures below.

A graded exercise test to 85% of age-predicted maximal heart rate (220-age—APMHR) was conducted on either a treadmill (Quinton QStress; Cardiac Science, Chelmsford, MA) or a cycle ergometer (LODE Excalibur Sport, the Netherlands) using 2-min stages that increased by 2.5% elevation (treadmill) or 0.33 $W \cdot kg^{-1}$ (cycle) per stage and continued until the participant reached the predetermined 85% value or the study physiologist ended the test based on physiological changes. Exercise capacity was

calculated in metabolic equivalents of task (METs) using formulas published by the American College of Sports Medicine based upon speed and grade. METs were chosen as the metric of interest based on its common usage in clinical contexts, but changes in estimated oxygen uptake ($\dot{V}O_2$) normalized for body weight at 85% of APMHR could be calculated by multiplying the METs value by 3.5 $mL \cdot kg^{-1} \cdot min^{-1}$.

Body composition was assessed by dual x-ray absorptiometry (DXA) images gathered using a GE Lunar Prodigy densitometer at one site and an iDXA (GE/Lunar, Madison, WI) at the other. Both scanners utilized EnCore software (versions 14.1 and 16.1, respectively) for estimation of body composition. Values of body fat, lean tissue, bone, and VAT were generated. Body fat percentage was derived by dividing the total body fat by the sum of fat, lean, and bone components. Appendicular lean muscle index (ALMI) was derived to control for differences in lean tissue attributable to differences in height. This variable was derived using the sum of the lean tissue (in kilograms) in the arms and legs divided by the participant's height in meters squared.

A triaxial accelerometer, the Actigraph GT9X+ Link (Actigraph Inc., Pensacola, FL), was used to objectively measure physical activity and sleep. Participants were asked to wear the device on their nondominant wrist continuously for 10 d except while bathing or swimming. This location and duration of wear are consistent with best practice as they result in a high degree of wear compliance and have been shown to capture sufficient wear time to be indicative of normal activity (30). After participant wear, devices were downloaded and screened for sufficient wear and potential device malfunction using commonly accepted methods (30) and algorithms (31) with acceleration data process into vector magnitude counts per minute (VM CPM). This metric incorporates intensity, frequency, and duration of movement and has been recognized as a reliable method to assess total volume of physical activity across 24-h (or longer) periods of observation (32) as well as being able to distinguish between sleep and wakefulness (33). Participants were asked to maintain sleep journals recording the time they tried to fall asleep and the time that they first woke during the period(s) of accelerometer wear. These time windows were analyzed on a minute-by-minute basis to determine sleep time using an algorithm designed for use in healthy adults (33). In addition to total sleep time, sleep efficiency and wake after sleep onset (WASO) (both in terms of number of events and total time of events) were calculated.

Statistical analysis. Power calculations were conducted *a priori* to answer the primary research questions of the larger study that these data are drawn from. Specifically, based upon prior investigations completed by the primary investigators of the larger study, power calculations were completed to detect changes in performance-based assessments of cognition and hippocampal volume. Further analysis of power was not conducted for the specific outcomes analyzed here as these data were drawn from the available participant pool. Participants were excluded from any analysis for which they had missing values. SPSS version 27 was used to complete all statistical analysis. Descriptive statistics (percentages, means, and SD) were used to characterize demographic variables and identify potential outliers. Change scores were derived by subtracting baseline values from follow-up values on an individual level. Independent *t*-tests were conducted to assess differences across groups at baseline, and 2 × 2 (time × group) mixed measures ANOVAs were conducted to evaluate the effects of the intervention on BrainPAD, aerobic fitness, body composition, activity levels, and sleep. When there were significant effects for both the interaction and time, groups were split with the effect of time evaluated independently using paired sample *t*-tests.

Independent of the intervention group, associations between changes in BrainPAD and changes in fitness, body composition, activity, and sleep were examined using Pearson's correlation without controlling for any covariates. When associations between change scores were observed, univariate linear modeling was conducted with sex, site, and chronological age included as covariates. These were included based on the known systematic bias in BrainAge estimation toward younger-appearing brains in older individuals, the possibility of systematic differences across sites, and the substantial differences in absolute values for body composition and fitness associated with sex. Years of education were also initially included as a covariate, but excluded when it did not contribute at all to model fit.

RESULTS

After excluding individuals without sufficient imaging (n =1 at baseline, and n = 47 at follow-up), those with suboptimal scans (n =8 at baseline and n = 1 at follow-up), individuals with BrainPAD changes >3 SD of absolute change (n = 10; 5 positive and 5 negative), and those missing all comparator values for aerobic capacity, accelerometry, and body composition (n = 1), a total of 485 participants were included. Because of partially missing data, an additional 77 participants were excluded from analysis of fitness, 4 from body composition, 12 from accelerometry-based physical activity, and 16 from accelerometer-based sleep. Overall, the sample was 72.6% female and showed some racial diversity (365 (75.3%) non-Hispanic White, 54 (11.1%) Black, 33 (6.8%) Hispanic, and 23 (4.7%) Asian, with the remaining 10 (2.1%) claiming either more than one category or declining to answer). Descriptive data and results of 2 × 2 (intervention group × time) mixed measures ANOVA are detailed in Table 1.

There were no significant differences at baseline between those randomized to exercise versus nonexercise conditions for any variables (P range = 0.075 to 0.947), nor were there any cross-sectional group differences at 6 months (P = between 0.118 and 0.944). Variables that were the closest to significant at baseline were total body percentage fat (P = 0.075) with those in the intervention group having an average body fat percentage of 40.5% versus 39.3%, and BrainPAD (P = 0.119) with those in the exercise group having a BrainPAD of −2.5 yr versus −1.6 yr in the nonexercise group.

Changes over time were significant, and the degree of change also differed significantly between the exercise and nonexercise intervention groups for cardiovascular fitness

TABLE 1. Descriptive of key variables at baseline and 6 months.

	Total Group		Exercise Group		Nonexercise Group		
Variable	Baseline Mean (SD)	6-Month Mean (SD)	Mean (SD)	6-Month Mean (SD)	Mean (SD)	6-Month Mean (SD)	*P* for Time by Group Interaction
BrainAge (yr)	69.2 (7.6)	70.0 (7.4)	69.1 (8.1)	69.8 (8.0)	69.4 (7.0)	70.1 (6.9)	0.959
n	485	485	225	225	260	260	
BrainPAD (yr)	−2.0 (6.3)	−1.9 (6.2)	−2.5 (6.6)	−2.4 (6.6)	−1.6 (5.9)	−1.5 (5.9)	0.996
n	485	485	225	225	260	260	
Fitness (METs)	4.7 (1.5)	5.2 (1.5)	4.6 (1.4)	5.3 (1.4)	4.8 (1.6)	5.1 (1.5)	0.001
n	471	414	216	192	255	222	
Body fat (%)	39.8 (7.6)	39.2 (7.8)	40.5 (7.0)	39.0 (7.5)	39.3 (8.0)	39.4 (8.1)	0.001
n	485	481	225	224	260	257	
Lean tissue (kg)	43.7 (9.2)	43.8 (9.0)	43.0 (8.8)	43.6 (8.8)	44.2 (9.6)	43.9 (9.2)	0.001
n	485	481	225	224	260	257	
ALMI (kg·m^{-2})	6.97 (1.24)	6.93 (1.35)	6.94 (1.18)	7.01 (1.26)	6.99 (1.30)	6.86 (1.43)	0.004
n	484	481	224	224	260	257	
VAT (kg)	1.32 (0.93)	1.28 (0.88)	1.32 (0.91)	1.24 (0.83)	1.33 (0.95)	1.32 (0.92)	0.001
n	480	476	224	223	256	253	
Sleep efficiency (%)	84.2 (6.8)	84.2 (6.5)	84.1 (6.6)	84.1 (6.7)	84.3 (6.9)	84.3 (6.4)	0.806
n	483	471	225	221	258	250	
Time asleep (min)	384.6 (56.3)	384.9 (58.8)	382.9 (59.9)	388.9 (60.6)	386.1 (53.1)	381.4 (57.0)	0.011
n	483	471	225	221	258	250	
WASO (min)	72.5 (33.2)	71.8 (30.4)	72.4 (31.4)	72.7 (31.0)	72.6 (34.8)	71.1 (29.8)	0.608
n	483	471	225	221	258	250	
VM (CPM)	1937 (506)	1952 (539)	1935 (484)	1964 (533)	1938 (525)	1941 (545)	0.385
n	483	475	225	222	258	253	

BL, baseline.

(METs, $P \le 0.001$ for both time and group × time interaction), body fat percentage ($P \le 0.001$ for both time and group × time interaction), total lean tissue ($P = 0.003$ for time and <0.001 for group × time interaction), and VAT ($P = 0.002$ for time and <0.001 for group × time interaction). Follow-up tests indicated that the intervention group gained fitness and improved body composition by lowering body fat percentage and visceral adiposity and increasing lean tissue, whereas the nonexercise group had a significant decrease in lean tissue and nonsignificant changes in body fat and VAT. Somewhat unexpectedly, the nonexercise group also evidenced increased fitness, although not by as large a margin as the exercise group. There was also a significant effect of the intervention on total sleep time (group × time interaction, $P = 0.011$), with small increases in the exercise group and nonsignificant decrease in the nonexercise group; the main effect of time was not significant ($P = 0.485$). Specific results and confidence intervals of follow-up tests are shown in Table 2.

As would be expected with over an approximately 6-month period, there was a significant effect of time for BrainAge ($P = 0.001$) with BrainAge increasing 0.709 yr on average (CI, 0.502 to 0.916). However, there was no significant group by time interaction ($P = 0.959$). In addition, there was no significant effect for time or group by time interaction for BrainPAD ($P = 0.345$ for time and $P = 0.996$ for interaction), nor for sleep efficiency ($P = 0.870$ for time and 0.806 for interaction), number of minutes awake during sleep periods (WASO, $P = 0.096$ for time and 0.608 for interaction), or overall daily physical activity (VM, $P = 0.503$ for time and 0.385 for interaction).

As with many interventions, changes in the metrics of interest were not universal, and some individuals within the nonexercise group also experienced meaningful changes, particularly in fitness. With this in mind, we explored the correlations between changes in BrainPAD and changes in fitness, fatness, activity, and sleep without consideration of the group. These analyses revealed that changes in BrainPAD were significantly associated with changes in body fat percentage ($r(479) = 0.154$, $P = 0.001$) and VAT ($r(478) = 0.141$, $P = 0.002$), but not fitness ($r(406) = -0.075$, $P = 0.129$), metrics of sleep ($r(467)$ range, −0.017 to 0.063; P range, 0.171 to 0.710), or physical activity ($r(471) = -0.035$, $P = 0.444$).

When significant associations were explored independently (while controlling for chronological age at baseline, gender, and location) via linear regression, changes in both body fat percentage and VAT significantly predicted changes in BrainPAD ($P = 0.002$ and 0.003, respectively), although when both are included in the model, neither remains significant ($P = 0.054$ and 0.089, respectively), likely because of a moderate amount of collinearity. The regression model including changes in VAT is included in Table 3, which indicates

TABLE 2. Significant interaction effects from the exercise intervention.

Variable	Units	Exercise		No Exercise	
		Estimate (CI)	*P*	Estimate (CI)	*P*
CRF	METs	0.695 (0.571 to 0.820)	<0.001	0.313 (0.189 to 0.437)	<0.001
Body fat	%	−1.433 (−1.158 to − 1.709)	0.001	−0.095 (−0.331 to 0.142)	0.432
Lean tissue	kg	0.584 (0.418 to 0.751)	<0.001	−0.237 (−0.397 to −0.077)	0.004
ALMI	kg·m^{-2}	0.72 (0.004 to 0.140)	0.039	0.133 (−0.019 to −0.247)	0.022
VAT	g	−84 (−46 to − 123)	0.001	4 (38 to -30)	0.803
TST	min	6.4 (0.7 to 12.1)	0.028	-3.7 (-8.9 to 1.6)	0.171

Significant results in bold.
ALMI, Appendicular Lean Mass Index; CRF, cardiorespiratory fitness; TST, Total Sleep Time; VAT, Visceral Adipose Tissue.

TABLE 3. Linear regression analysis of the association between changes in VAT and changes in BrainPAD.

Model Summary	*R*	R^2	Adjusted R^2	SEE	*P*
	0.203	0.041	0.033	2.258	<0.001

Predictors	Unstandardized *B*	SE	Standardized *B* Coefficient	*T*	*P*
Constant	4.388	1.639		2.677	0.008
VAT mass[a]	0.948	0.316	0.137	2.996	0.003
Covariates					
Chronological age at baseline	−0.054	0.022	−0.110	−2.424	0.016
Sex[b]	0.258	0.237	0.050	1.087	0.278
Site[c]	−0.468	0.208	−0.102	−2.246	0.025

Values for VAT and BrainPAD are change scores based on the difference between values gathered at the 6-month visit minus values gathered at baseline.
[a]VAT derived from DXA measured in kilograms.
[b]Female = 1, male = 2.
[c]UCSD = 1, WUSTL = 2.
UCSD, University of California, San Diego; WUSTL, Washington University of St. Louis.

that for each 1-kg change in VAT, there is a corresponding change of 0.948 yr in BrainPAD when chronological age at baseline, sex, and location are controlled for.

DISCUSSION

As expected, it appears that the multimodal exercise intervention was successful in increasing the cardiovascular fitness of the participants, as well as improving body composition by both decreasing fat and increasing lean tissue. Furthermore, the intervention appeared to have a small but potentially meaningful effect on visceral fat, which is strongly negatively implicated in several chronic disease states common among older adults (34). However, this 6-month exercise intervention did not appear to have a meaningful impact on BrainPAD. In addition, the increased fitness experienced in the nonexercise group suggests that there may have been larger factors at play in this population that encouraged a focus on fitness regardless of the intervention. We have previously observed cross-sectional associations between visceral adiposity, but not fitness and/or physical activity, and BrainPAD (29) in this sample of older adults, and now we show that, when changes in metrics of fitness, fatness, and sleep and their relationship(s) to changes in BrainPAD are explored independent of group assignment, there is a clear association between increased/faster aging brains and increased fatness, particularly increased VAT. However, there was no association between changes in BrainPAD and changes in either fitness or overall physical activity. Given the recent evidence presented by Vidal-Pineiro et al. (35) suggesting that early life behaviors have a strong(er) influence on brain structure, and consequently, BrainPAD, with only minimal contributions from behaviors during middle and older adulthood, it is notable that we found links between BrainPAD change and fatness, but not fitness, change later in life in the context of an intervention study.

These data contrast with published evidence linking fitness and brain health, both in terms of the volume of various brain structures (6) and cognitive performance (10). A possible explanation for this may be that the relatively modest changes in fitness observed in this study (increase of 0.5 METs at 85% of Age Predicted Maximal Heart Rate) were too small to elicit meaningful changes in brain structure (and thus, BrainPAD), and that an intervention that was either longer or more intense might elicit significant changes. Similarly, the combination of strength and aerobic training within the same intervention may have reduced the effectiveness of structural changes that have been observed with interventions more focused on aerobic training exclusively (6,8,9). However, it is worth noting that many of the studies that have found positive associations between fitness and brain structure have looked at individual segments of the brain (i.e., the hippocampus or frontal lobe exclusively); when the whole brain is examined, data have indicated variable levels of association and have generally had small effect sizes (8,36). Furthermore, the data here extend cross-sectional data showing no association between fitness and/or physical activity and BrainPAD in a nearly identical population (29). Given the large number of brain regions/features contributing to the BrainAge score, it is possible that subtle changes to small regions within the brain are not sufficient to meaningfully impact the score. Thus, although BrainAge has proven itself potentially useful in a number of clinical populations (i.e., Traumatic Brain Injury, multiple sclerosis, etc.) to provide a relatively easily understood metric of brain health, it may not be sufficiently sensitive to be useful in evaluating changes that are expected to affect localized regions within the brain, particularly if those regions are ones that are not particularly age related and thus contribute less to the prediction of BrainAge. Interestingly, the observed relationship between body fatness and BrainPAD does offer some evidence to suggest that BrainAge (and the associated BrainPAD) may have utility in evaluating interventional changes in brain health, provided that those changes are occurring across a number of age-related brain regions. Indeed, the results from these analyses match recent research that has identified links between high levels of body fatness and reduced brain health (17,18). Combined with recent scholarship indicating associations between central obesity and declines in whole brain structure (29) and cognitive function (37), these data offer additional evidence to suggest that VAT is particularly deleterious to health and has downstream effects across multiple systems.

Several mechanisms have been proposed to explain the detrimental impact of VAT. For instance, VAT has been linked to reduced immunity secondary to increased levels of inflammation (38) and to increased oxidative stress resulting from upregulated cytokine activation (39). However, potentially most compelling

given the observed links between brain insulin resistance and decreased cognitive function and brain structure (32) is the fact that increased VAT contributes to decreased insulin sensitivity *systemwide* (40). Although these data do not confirm a causal relationship between VAT and insulin (in)sensitivity in the brain, and there is a possibility of shared etiology that affects both independently, they do suggest the possibility of a causal pathway in which increased insulin resistance and visceral adiposity are linked both to each other and to structural brain health.

Although total sleep time was modestly affected by the intervention, neither changes in sleep time nor changes in sleep efficiency were associated with changes in BrainPAD. Because this population was nearly exclusively composed of normal sleepers, both in terms of time and efficiency, and the changes over the observation window were quite small, it is possible that the modest changes in sleep time did not elicit structural changes, or that there was no sufficient variation within the group to detect meaningful differences in brain structure. Furthermore, the lack of association is supported by evidence that suggests that it is only with an amount of sleep substantially above or below the recommended amount (for instance, <4 or >10 h per night) that structural and functional decline is observed (41).

Given the many important positive health outcomes associated with increased fitness and larger volumes of physical activity (particularly moderate to vigorous physical activity), it is tempting to see it as a panacea that can promote good health across all organ systems, including the brain. Interestingly, the role of exercise in weight control is also often overstated (42), further suggesting a desire for one mechanism of intervention to work to promote health in all areas. Unfortunately, likely even more than weight control, brain health is made up of many complementary and interconnected factors that are affected both independently and in coordination with each other. Although these data do not preclude the possibility of positive adaptation in the brain with increased exercise, they do suggest that the physiological aging of the brain as a whole cannot be slowed/changed simply by increasing exercise levels by a moderate amount over a short period. However, these findings do contribute to a substantial literature that suggest that a focus on weight control, particularly reduction/prevention of central obesity, even in the short term, may be a useful target to promote healthier/younger brains, as well as benefiting other physiological systems.

Strengths of this study include the use of high-quality measurement tools in a large population of (presumptively) healthy older adults. Specifically, the use of whole brain MRI imaging for BrainAge calculation, graded exercise testing to estimate aerobic capacity, accelerometry to provide objective measures of physical activity and sleep, and DXA to estimate body composition and visceral adiposity mean that there are likely fewer sources of error compared with proxy measures, self-report, or epidemiologically derived estimation algorithms. However, there are some limitations that should be considered when applying these findings to intervention development or as a guide for future research. In particular is the possibility of a (n unmeasured) shared etiology that accounts for the observed changes in visceral adiposity, and BrainPAD. Furthermore, it is possible that BrainAge, and consequently BrainPAD, is affected not just by the amount of VAT and body fatness, but also by the length of time those metrics are above "safe" levels. In addition, because the BrainAgeR algorithm uses a large number of structural features drawn from multiple brain regions, it is possible that it is insensitive to isolated changes in areas that are less age related and yet make meaningful contributions to cognition and/or function. Furthermore, although 6 months is a reasonably long intervention period, it may be that it was not long enough with an intervention of the intensity used in this investigation to elicit changes in fitness sufficient to manifest as changes in brain structure. Similarly, a 6-month window for observation may not be long enough to see changes in BrainPAD that might be associated with small changes in fitness, fatness, or sleep that are maintained over time. Finally, the degree to which changes in BrainPAD are explained by changes in VAT is small, accounting for less than 4% of the total variance. However, given the potentially modifiable nature of VAT, and the possibility of benefiting multiple other systems through systematic reduction in VAT levels, further research is warranted. In particular, research that better elucidates the causal pathways linking VAT and brain health, or that identifies novel or particularly effective ways to reduce VAT, has the potential to lead to substantial public health benefit, likely including improved structural brain health.

CONCLUSIONS

Brain health as described by the difference between the biological age of the brain versus the chronological age of the individual appears to be modifiable with changes in body composition. Specifically, reducing body fatness in general, and visceral adiposity in particular, is associated with positive changes in BrainPAD consistent with brains growing younger compared with chronological age over time. However, changes in fitness levels, volume of physical activity, and sleep are not associated with changes in BrainPAD. This contributes to the body of evidence that suggests that body composition should be a primary target for behavioral interventions aimed at promoting brain health.

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The results of this study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. The results of the present study do not constitute endorsement by the American College of Sports Medicine. The authors have no conflicts of interest to disclose.

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BRAIN COMMUNICATIONS

SuperAging functional connectomics from resting-state functional MRI

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Understanding the relationship between functional connectivity (FC) of higher-order neurocognitive networks and age-related cognitive decline is a complex and evolving field of research. Decreases in FC have been associated with cognitive decline in persons with Alzheimer's disease and related dementias (ADRD). However, the contributions of FC have been less straightforward in typical cognitive aging. Some investigations suggest relatively robust FC within neurocognitive networks differentiates unusually successful cognitive aging from average aging, while others do not. Methodologic limitations in data processing and varying definitions of 'successful aging' may have contributed to the inconsistent results to date. The current study seeks to address previous limitations by optimized MRI methods to examine FC in the well-established SuperAging phenotype, defined by age and cognitive performance as individuals 80 and older with episodic memory performance equal to or better than 50-to-60-year-olds. Within- and between-network FC of large-scale neurocognitive networks were compared between 24 SuperAgers and 16 cognitively average older-aged control (OACs) with stable cognitive profiles using resting-state functional MRI (rs-fMRI) from a single visit. Group classification was determined based on measures of episodic memory, executive functioning, verbal fluency and picture naming. Inclusion criteria required stable cognitive status across two visits. First, we investigated the FC within and between seven resting-state networks from a common atlas parcellation. A separate index of network segregation was also compared between groups. Second, we investigated the FC between six subcomponents of the default mode network (DMN), the neurocognitive network commonly associated with memory performance and disrupted in persons with ADRD. For each analysis, FCs were compared across groups using two-sample independent *t*-tests and corrected for multiple comparisons. There were no significant between-group differences in demographic characteristics including age, sex and education. At the group-level, within-network FC, between-network FC, and segregation measurements of seven large-scale networks, including subcomponents of the DMN, were not a primary differentiator between cognitively average aging and SuperAging phenotypes. Thus, FC within or between large-scale networks does not appear to be a primary driver of the exceptional memory performance observed in SuperAgers. These results have relevance for differentiating the role of FC changes associated with cognitive aging from those associated with ADRD.

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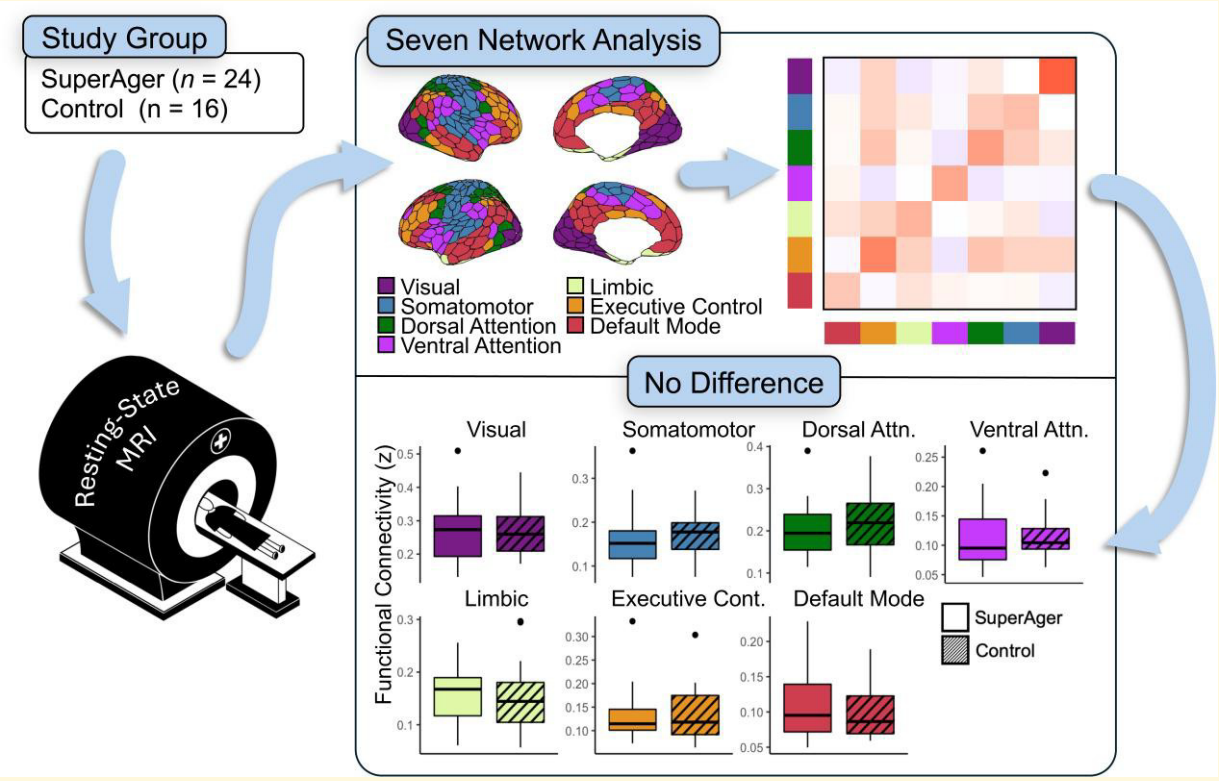
Graphical Abstract



Introduction

The global population is rapidly aging and the proportion of adults aged 85 or older is growing faster than younger generations.[1] These adults are at the highest risk for both age-related memory decline[2] and the onset of amnestic dementia due to Alzheimer's disease (AD).[3] However, significant memory decline is not inevitable. A growing literature on 'successful aging'[4,5] has aimed to describe and investigate older adults with unusually high physical,[6-8] social,[7,9] or cognitive functioning.[6,8] Understanding mechanisms of successful cognitive aging promises to inform the development of interventions to prevent or slow cognitive decline.

One well-established phenotype of successful cognitive aging is *SuperAging,* defined by age and cognitive performance as individuals 80 years and older with episodic memory performance equal to or better than 50− to 60-year-olds.[10] The multicenter SuperAging Research Initiative (R01AG045571, R01AG067781, and U19AG073153) was launched to understand what factors underlie this memory-specific phenotype and, by comparison, to inform our understanding of normal cognitive decline and AD. Initial results show that SuperAgers share unique neuropsychological,[11,12] psychosocial,[13] genetic,[10,14] and biologic[15-19] features. Post-mortem studies have identified neurobiological features of the SuperAger phenotype, such as relatively large neurons in the entorhinal cortex,[15] a lower AD neuropathologic burden, and a greater density of von Economo neurons in the anterior cingulate cortex.[16] Structural MRI studies have found brain features of the SuperAging phenotype that appear more like middle-aged-controls than older-aged-controls (OACs), such as relatively slow atrophy rates[20] and thick cingulate cortices.[18] To date, studies of the SuperAger phenotype have focused on brain morphometry. Less is known about the brain functional connectivity (FC) that supports their extraordinary memory abilities.

The brain is thought to be subdivided into distinct brain networks composed of highly interconnected neural regions that communicate to manifest complex behaviours and cognitive abilities.[21] Resting-state functional MRI (rs-fMRI) has emerged as a proxy method for exploring the FC of these distributed neurocognitive networks[22] by capturing intrinsic temporal correlations in neural activity[23] indirectly measured from blood-oxygen-level-dependent (BOLD) signal. Exploratory rs-fMRI studies have identified resting-state networks that correspond to major networks previously established by neuroanatomical experiments[21,24] and others with unclear neural connections.[25] Some resting-state networks are thought to be involved in unimodal sensory processing, such as the visual[26] and somatomotor networks.[23] Other resting-state networks are thought to modulate indistinct higher-order cognitive functions, such as the frontoparietal,[27] ventral attention,[28-30] dorsal attention,[28] and default mode networks (DMN).[31]

Resting-state networks have become a focus of cognitive aging research because they undergo a complex

reorganization during development and in older adulthood[32,33] and within-network FC has been directly related to cognitive performance.[29,34-36] An age-related decrease in within-network FC has been demonstrated in regional activation during task-based fMRI comparing young and older adults[37,38] and in cross-sectional studies of rs-fMRI over the normal lifespan as measured by independent component analysis[39] and seed-based connectivity.[40-42] The significance of these age-related changes is unclear. Some have suggested that a gradual shift away from 'youthful' functional patterns indicates progressive dysfunction and signifies or precipitates cognitive decline.[41,42] One rationale for this hypothesis is that the topography of resting-state networks overlaps with regional activation during specific cognitive tasks. For example, commonly identified regions of the DMN, such as the inferior parietal lobe (IPL), posterior cingulate cortex (PCC), medial prefrontal cortex (MPC), parahippocampal cortex (PHC), medial temporal gyrus (MTG), reliably demonstrate greater BOLD activity during task-based fMRI involving episodic memory encoding and retrieval.[43-45] The DMN is also commonly thought to include the hippocampus,[31] the brain region most commonly associated with episodic memory.[46] In some cases, within-network FC has also been related to composites of neurocognitive performances, such as persons with relatively strong within-network FC in the DMN performing better on episodic memory tasks.[34,39,41] Nearly all higher-order resting-state networks display a similar pattern.[32] As such, the overall degradation of within-network FC may be more closely related to the severe cognitive decline associated with ADRD.

The DMN has become a major focus of cognitive aging research because of its high detectability, topographical overlap with memory-related regions, and enigmatic association with AD dementia. The DMN is one of the most commonly studied resting-state networks.[47] It demonstrates unique functional patterns in persons with mild neurocognitive impairments[48] and amnestic dementia due to AD.[49] The pathogenesis of AD amyloidopathy appears to selectively accumulate within regions of the DMN[50,51] early in the disease course. Given these findings, some have argued that preserved DMN integrity in old age supports optimal memory abilities. However, DMN functional anomalies emerge prior to amnestic symptoms of AD.[49,52-55] In addition, decreases in DMN cannot distinguish persons with amnestic AD from persons with non-amnestic variants of AD.[56-58] Furthermore, functional changes in the DMN are also implicated in non-AD diagnoses including depression, autism spectrum disorder and schizophrenia[44] where memory impairments are not core features. As such, the relationship between the DMN and memory decline in AD is complex, with evidence suggesting the network may be vulnerable to change in multiple disease-related states rather than being specific for AD.

Given the age and AD-related findings, it has recently been proposed that relatively robust FC within neurocognitive networks may support successful cognitive aging. Research differs in the terminology and classification of successful cognitive aging,[59,60] specifically the age range of cohorts, which limits the generalizability of findings. Nonetheless, one recent study of adults aged 60 and over with exceptional episodic memory abilities found that these individuals had relatively strong FC within the DMN and ventral attention neurocognitive networks compared to similar aged cognitive controls.[34] They also reported a positive association between FC and performance on a task of episodic memory. However, another recent study using the same methods in a separate but equally sized cohort from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database was unable to replicate their findings.[61] Two recent studies have used machine learning to differentiate rs-fMRI signal from successful cognitive agers and controls in participants 60 and older[62] and 80 and older.[63] However, results are difficult to interpret because neither study has longitudinal data to ensure that participants were free from emergent neurodegenerative disease.

In summary, the role of resting-state networks in memory and aging is not well defined and the SuperAger phenotype provides a unique opportunity to understand its role in memory preservation beyond the eighth decade. The few studies that have investigated rs-fMRI in successful cognitive aging have had mixed results and no study has longitudinally monitored progressive cognitive decline. This study includes carefully characterized groups of cognitively stable SuperAgers and OACs over two or more visits to investigate the baseline functional integrity of seven canonically defined resting-state networks and subregions of the DMN.

Materials and methods

Participants

Retrospective data used in this project were obtained from the SuperAging Research Initiative database. The goal of the SuperAging Research Initiative is to identify factors that contribute to SuperAgers' uniquely youthful memory function. Participants are community-dwelling, English speaking adults 80 years or older and without significant neurological or psychiatric illness. While enrolled, participants returned every two years for follow-up research visits. At each visit, participants receive a neuropsychological evaluation and, when feasible, MRI scans. Participants were recruited through community lectures, advertisements, word of mouth, community engagement and outreach activities, clinician referral and from the healthy control sample in the Clinical Core of the Alzheimer's Disease Research Center (ADRC) at Northwestern University. This study was approved by the Institutional Review Boards of Northwestern University and the University of Chicago and informed consent was provided by all participants at enrolment.

Neuropsychological evaluation

At each visit, we administered a battery of neuropsychological tests sensitive to detect cognitive aging and incipient amnestic AD dementia[64] that capture both episodic memory

Table 1 Participant demographic and cognitive characteristics

	SuperAgers (n = 24)	Older-aged controls (n = 16)	Statistic (t-test or x^2)	P-value
Demographic characteristics				
Age (SD), y	84.7 (2.89)	84.27 (3.67)	−0.4	0.69
Sex (F,M), no.	16, 8	10, 6	0.00	1.00
Handedness (R, L, A)	22, 1, 1	15, 1, 0	0.75	0.69[a]
Education (SD), y	16.79 (2.23)	15.88 (3.7)	−0.89	0.38
Follow-up time (SD), y	1.78 (0.31)	1.65 (0.3)	−1.31	0.2
Neuropsychological measures				
WTAR Est. FSIQ, (SD), SS	116.75 (6.24)	113.81 (8.83)	−1.15	0.26
RAVLT delay (SD), raw	11.25 (1.68)	6.13 (1.09)	−11.85	<0.001
CFT (SD), raw	22.29 (5.18)	18.25 (4.93)	−2.49	0.02
BNT-30 (SD), raw	28.71 (1.3)[b]	26.63 (3.36)	−2.36	0.03
TMT-B (SD), s	85.36 (33.48)	106.47 (53.01)[c]	1.38	0.18
MRI quality checking				
Mean FD (mm)	0.17 (0.05)	0.17 (0.04)	−0.12	0.91
Volumes after scrubbing (%)	94.31 (3.85)	93.55 (4.92)	−0.53	0.6

[a]One SuperAger was ambidextrous and not included in the x^2 analysis. [b]One SuperAger met all SuperAging criteria with the exception of the BNT-30, but scored within expectation in a subsequent visit, 6 months later. [c]One older-aged control was missing the TMT-B at the MRI visit. SD = standard deviation; y = years; F = female; M = male; d = days; R = right; L = left; A = ambidextrous; SS = standard score (mean = 100; SD = 15); WTAR = Wechsler test of adult reading; FSIQ = Full-Scale Intelligence Quotient; RAVLT = Rey Auditory Verbal Learning Test; CFT = Category Fluency Test; TMT-B = Trail Making Test - B; BNT-30 = 30-item Boston Naming Test; FD = Framewise Displacement.

Table 2 Group classification criteria according to neuropsychological test scores

Cognitive domain	Neuropsychological assessment	SuperAger	Older-aged control
Episodic memory	RAVLT	ss ≥ 10[a]	ss = 7–11
Executive Functioning	Trail Making Test: Part B	ss ≥ 7	ss ≥ 7
Verbal fluency	Semantic Fluency: Animals	T ≥ 40	T ≥ 40
Picture naming	BNT-30	ss ≥ 7	ss ≥ 7

[a]Scaled scores for SuperAgers are compared to 56–64-year-olds (midpoint age = 61); all other standardized scores are compared to same-aged peers. Standardize score summary statistics: ss (mean = 10; SD = 3), T (mean = 50; SD = 10). Reference norms: Rey Auditory Verbal Learning Task, Trail Making Test: Part B, Semantic Fluency, Boston Naming Test. SD = standard deviation; ss = Scaled Score; T = T-Score.

and non-memory domains. Tests included the Rey Auditory Verbal Learning Test (RAVLT) for episodic memory, 30-item Boston Naming Test (BNT-30)[65] for picture naming, Trail Making Test Part B (TMT-B)[66] for executive functioning and Category Fluency Test[67] for verbal fluency. Participant neuropsychological performance is summarized in Table 1.

Group criteria

In accordance with the criteria operationally defined for SuperAgers in the study by Harrison *et al.*, 2012, SuperAgers performed above the average range for their peer age normative group on the RAVLT delayed recall (raw score, ≥ 9), at least as good as normative scores for adults in their 50s and 60s,[68] and at least in the average range compared to same-aged peers on the three other tests loading on non-memory cognitive domains (BNT, TMT-B and Category Fluency Test). OAC scored within one standard deviation of average compared to same-aged peers on the memory measure (RAVLT delayed recall score between 3 and 7) and at least in the average range on other cognitive tests. Group classification criteria are summarized in Table 2. Participants maintained group status at consecutive study visits occurring approximately two years apart (mean = 1.7 years; range = 1.16–2.29 years).

Inclusion criteria

Participants with T_1-weighted (T1w) scans and rs-fMRI scans were considered for this study. Of these participants, we identified those with stable neuropsychological profiles over two visits and excluded those whose group status changed over that interval of time (e.g. participants who developed mild cognitive impairment). MRIs were collected during both visits. Data from the baseline MRI were used in our analysis where possible; data from the second MRI was used only if the baseline scan was unavailable or unusable. We excluded participants with scans containing artefacts in both scans (e.g. magnetic susceptibility, motion, aliasing). In total, 40 participants [mean age (SD): 84.5 (3.2)] were identified for inclusion in the present study. Participant demographics are summarized in Table 1 and a flow chart detailing cohort selection is shown in Fig. 1.

Imaging protocol

MRI scans were acquired for all participants with a standard 12-channel birdcage head coil on a Siemens 3T

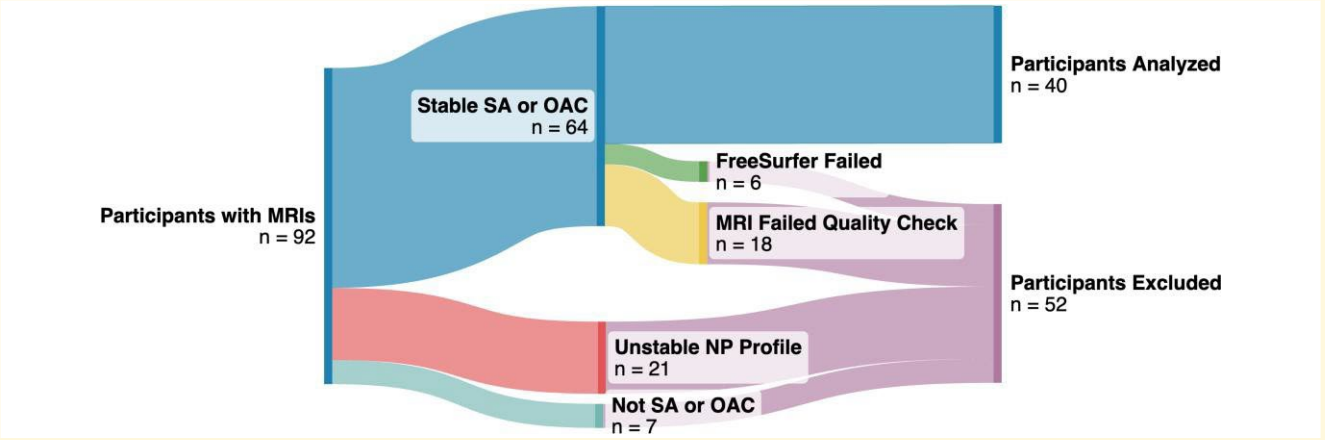


Figure 1 Flow chart of cohort selection. T1w = T1-weighted; rs-fMRI = resting-state functional magnetic resonance imaging; NP = neuropsychological; SA = SuperAger; OAC = older-aged control.

MAGNETOM TIM Trio scanner (Erlangen, Germany). For surface reconstruction, we acquired structural T1w MP-RAGE sequences (repetition time [TR] = 2300 ms, echo time [TE] = 2.86 ms and flip angle = 9°, 1 mm^3). The functional scan was un-directed and participants were instructed to stay awake, keep their eyes open and let their minds wander. Runs were 11.5-minute long and consisted of a spin echo/echo planar imaging sequence with 244 volumes (TR = 2800 ms, TE = 20 ms, 1.7 × 1.7 × 3 mm^3).

MRI processing

Structural imaging

T1w images underwent volumetric segmentations and surface reconstruction by FreeSurfer (v7.2). Trained technicians visually inspected and made iterative edits to optimize FreeSurfer processing. Volumetric segmentations and surface reconstructions were used for registration during rs-fMRI processing.

fMRI quality assessment

Motion artefacts in rs-fMRI are concerning for confounds in older populations.[69,70] Quality checking measures were used to censor time series motion artefacts by accounting for deviation in frame-to-frame motion and signal. Respectively, framewise displacement (FD) is a six-dimensional metric of instantaneous head motion calculated from frame-to-frame and DVARS is the relative change in signal from frame-to-frame. We used the eXtensible Connectivity Pipeline[71,72] (XCP; v3.2) to calculate FD using the formula from Power *et al*. (2014), with a head radius of 50 mm. Volumes with filtered FD greater than 0.4 mm were flagged as outliers and excluded from nuisance regression. The filtered versions of the motion traces and FD were not used for denoising. DVARS and the correlation between DVARS and FD decreased following motion scrubbing. Scans with fewer than 80% interpretable frames (total scan-time, ≥ 9 minutes) were excluded. Quality reports produced by fMRIPrep[73] (v22.1.1) and XCP[71,72] were inspected to ensure suitable completion of preprocessing steps. Quality checking metrics are summarized in Table 1.

fMRI processing

Minimal functional MRI preprocessing was performed using fMRIPrep[73] with custom methodologies. fMRIPrep preprocessing included slice-time correction, motion correction using affine registration to the middle time-point, co-registration to the T1w image and resampling into standard space using a single interpolation step. Following minimal MRI preprocessing, XCP[71,72] was used to post-process rs-fMRI. XCP post-processing includes the removal of initial rs-fMRI volumes, outlier detection and filtering, de-spiking and interpolation and a bandpass filter (0.01–0.1 Hz) to reduce low-frequency drift and high-frequency noise in the signal. Global signal, the first principal components from cerebral spinal fluid and white matter, and frame-to-frame motion in six degrees of freedom calculated during motion correction were regressed out to reduce physiologic noise.[74] The use of global signal regression is controversial and may remove real neural signal.[75] Therefore, all analyses were replicated using rs-fMRI without global signal regression. The processed BOLD was smoothed on the surface using Connectome Workbench[76] with a Gaussian kernel size of 3.0 mm in agreement with best practices.[77-80]

To calculate within-network FC of the DMN, executive control, limbic, ventral attention, dorsal attention, somatomotor and visual networks, Connectome Workbench was used to extract residual signal from all parcels of a seven network (see Fig. 2A), 400 region-of-interest (ROI) parcellation (Schaefer *et al*., 2018), of a common group-level resting-state atlas (Yeo *et al*., 2011), resulting in 400 time-series.[25,81] Subsequently, pair-wise FC (i.e. Pearson's r converted to Fisher's z) between all ROI time-series were computed to create connectivity matrices (400 × 400). Within-network FC was defined as the average z-value for all pairs within a given

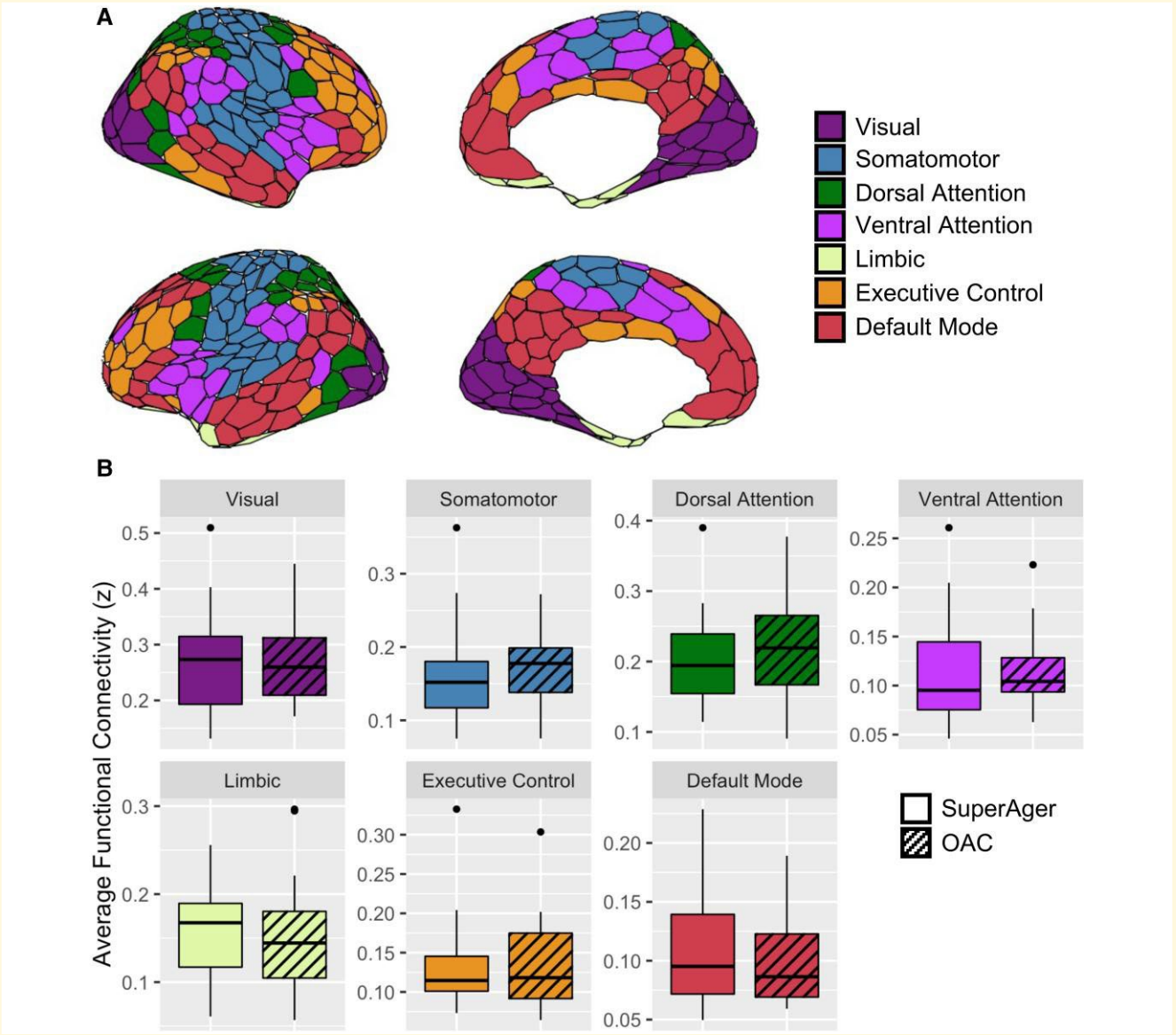


Figure 2 Within-network resting-state functional connectivity does not differ between groups. (**A**) 400-parcel cortical parcellation of seven large-scale resting-state networks from Schaefer *et al.* (2018) used for within-network analysis. (**B**) Average within-network functional connectivity across resting-state networks did not differ between SuperAgers and older-aged controls; OAC = older-aged controls. Wilcoxon signed-rank test; $P > 0.05$ for all comparisons.

network. The seven network parcellation from Schaefer *et al.* (2018) is freely available online.[81]

To calculate the DMN subcomponent FC, ROI-ROI correlation coefficients were calculated from six bilateral DMN canonical regions: the IPL, PCC, MPC, PHC, MTG and hippocampus. Correlations were calculated between each possible pair, for a total of 30 correlations (15 unique correlations) per person. To ensure that ROIs were completely confined to their predefined regions, cortical areas of interest were defined as the central polygon for each DMN region from the seventeen network parcellations subdivided into 600 parcels[81] (Supplemental Fig. 1). The hippocampal ROI was taken from the Human Connectome Project (HCP) subcortical CIFTI atlas.[78] All ROIs were chosen to include homologous regions on both hemispheres. ROI placement is shown in Fig. 3A and cortical ROI identification values (corresponding to the atlas CIFTI metadata) are provided in Supplemental Table 1. Code to generate the custom CIFTI parcellation of cortical ROIs used in the DMN analysis is provided in the Supplemental Material.

Statistical analysis

Independent sample two-tailed *t*-tests and x^2 tests were used to examine group differences in demographic factors, MRI quality metrics and neuropsychological measures. One ambidextrous SuperAging participant was excluded from

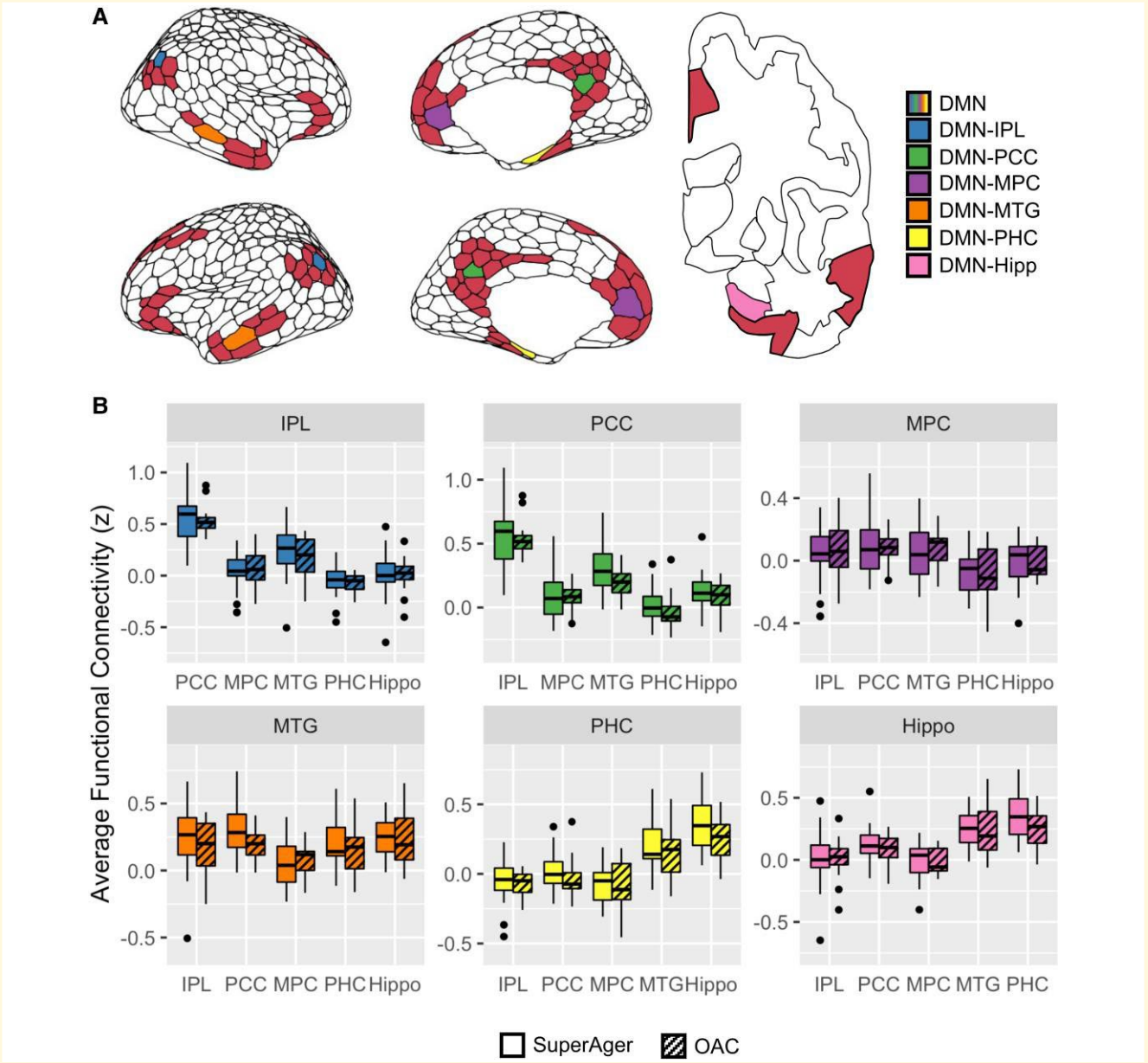


Figure 3 Functional connectivity between subcomponents of the DMN do not differ between SuperAgers and controls.
(A) Regions-of-interest (ROIs) used for functional connectivity of the default mode network (DMN); Left: Five central polygons from DMN clusters of the 600-parcel cortical parcellation from Schaefer *et al.*, 2018; Right: Hippocampus (Hipp) seed from Glasser *et al.*, 2013.
(B) Two-sample independent *t*-tests found no significant between-group difference in functional connectivity; IPL = inferior parietal lobe; PCC = posterior cingulate cortex; MPC = medial prefrontal cortex; PHC = parahippocampal cortex; MTG = middle temporal gyrus. Wilcoxon signed-rank test; $P > 0.05$ for all comparisons.

the handedness x^2 analysis because no OACs were ambidextrous. The Pearson correlation was calculated between the time-series for each possible pair of ROI. For the 400-parcel atlas, this generated 79 800 unique coefficients which were averaged within-network to create seven average within-network coefficients for every participant. Average between-network connectivity was also computed for each participant (Supplemental Fig. 2). Average within-network FC was defined for each participant as the average of all coefficients between two ROIs of the same network (2618 coefficients per participant). For each participant, average between-network FC was defined as the average FC of all ROIs belonging to separate networks (77 182 coefficients per participant). Finally, system segregation was defined for each participant as the difference between within-network FC and between-network FC divided by within-network FC.

For subcomponents of the DMN, we generated 15 unique coefficients for every participant. Pearson's coefficients were converted to Fisher's z-transformed values for all analyses.

After ensuring normality within groups,[82] each within-network coefficient and DMN subcomponent z-value was compared across groups using two-sample independent t-tests with α's adjusted for multiple comparisons using the Benjamini–Hochberg false discovery rate (FDR) at $q = 0.05$.[83] All statistical analyses were performed within RStudio (version 2023.06.1 + 524).

Results

Data inclusion

At the time of our analysis, the SuperAging Research database included 92 participants with T1w scans and rs-fMRI scans from a Siemens 3T MAGNETOM TIM Trio scanner. Of those, 28 were excluded from our analysis due to unstable neuropsychological profiles across two research visits ($n = 21$) or unclear neuropsychological group profile ($n = 7$). An additional 24 were excluded due to artefacts in T1w data that made FreeSurfer segmentation fail ($n = 6$), contained rs-fMRI motion that surpassed FD thresholds ($n = 17$), or had insufficient useable imaging data ($n = 1$). Twenty-four SuperAgers and 16 OACs ($n = 40$) had MRI data and longitudinal neuropsychological profiles that met inclusion criteria for analysis in the present study (Fig. 1).

Demographic and neuropsychological profiles

There were no significant between-group differences in demographic characteristics (all P-values > 0.05) including age, sex, handedness, education or time between research visits. Performance on neuropsychological measures was significantly different between SuperAgers and OACs for episodic memory as measured by the RAVLT delay ($t = -11.85$; $P < 0.01$), generative fluencies as measured by category fluency test ($t = -2.49$; $P = 0.02$) and confrontation naming as measured by the BNT-30 ($t = -2.36$; $P = 0.03$). The between-group difference in RAVLT delay performance is expected due to predefined group classification criteria. There were no significant between-group differences in the overall premorbid functional abilities as measured by the WTAR estimated Full-Scale Intelligence Quotient [FSIQ ($t = -1.15$; $P = 0.26$)] or executive functioning as measured by TMT-B ($t = 1.38$; $P = 0.18$). Statistical tests for group differences in demographic and neuropsychological profiles are summarized in Table 1.

Functional connectivity analysis

After motion scrubbing, there were no significant between-group differences in mean FD or scan length. Group summary values are included in Table 1.

Average within-network FC of seven resting-state networks were compared between SuperAgers and OACs. There were no significant differences between SuperAgers and OACs in within-network FC of the resting-state networks, including the DMN, executive control, limbic, ventral attention, dorsal attention, somatomotor and visual networks (P-values > FDR adjusted α; Fig. 2B). Similarly, there were no significant group differences in between-network FC (Supplemental Fig. 3). Additionally, broader measures of FC compared between SuperAgers and OACs, including average within-network FC from all networks, average between-network FC from all networks, and system segregation, did not differ significantly between groups (P-values > 0.05; Fig. 4).

FC between subregions of the DMN, including the IPL, PCC, MPC, PHC, MTG and hippocampus, were compared between SuperAgers and OACs. There were no significant between-group differences in FC of the four DMN ROIs after adjusting for FDR (P-values > FDR adjusted α; Fig. 3B). Notably, even before adjusting for FDR, we were unable to find significant between-group differences. Replication of all analyses without global signal regression similarly did not reveal significant group differences. Figures contain results from analyses with global signal regression.

Discussion

The present study compared FC within seven canonical resting-state networks and between major regions of the DMN in SuperAgers and OACs. Results showed no significant group differences in FC between groups for any networks or regions of the DMN. The relationship between the large-scale resting-state networks and the spectrum of cognitive aging is complex and group-based average measurements of FC do not appear to explain the exceptional memory performance observed in SuperAgers. Potential contributors to these results, including the discrepancy between our findings and those that have found relatively strong within-network FC of successful cognitive agers,[34] are likely multifactorial.

One possible contributor to the difference between our results and those of previous studies is our longitudinal inclusion criteria to reduce the risk of undiagnosed neurodegenerative processes among our participants. Of the 92 participants from the SuperAging Research Program with MRI considered for our study, 21 exhibited unstable neurocognitive profiles and were excluded. Participants with unstable neurocognitive profiles are not commonly accounted for in alternate successful cognitive aging rs-fMRI studies[59] in part because the studies only have access to cognitive data from a single time-point. Participants with declining neurocognitive profiles could inadvertently drive differences in within- or between-network FC due to underlying ADRD. As such, group differences observed in prior studies may have been driven by ADRD. This highlights the importance of careful consideration of participant profiles in future studies aiming to elucidate the role of FC in cognitive aging.

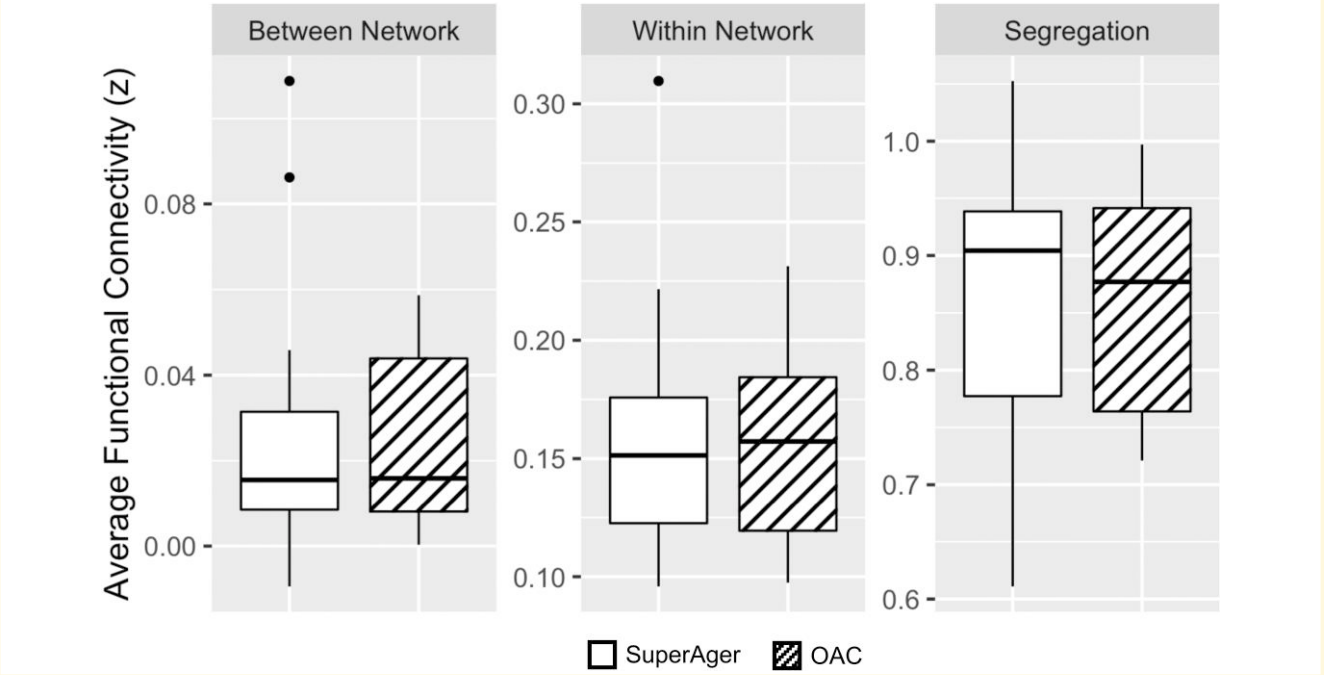


Figure 4 Whole-brain measures of functional connectivity do not differ between SuperAgers and controls. Network-wide average within-network functional connectivity and between-network connectivity did not differ between groups. A measure of network segregation (the difference between within-network FC and between-network FC divided by within-network FC) also did not differ between groups; OAC = older-aged controls. Wilcoxon signed-rank test; $P > 0.05$ for all comparisons.

It is also plausible that differences in rs-fMRI between SuperAgers and OACs are subtle and require highly precise measurements to detect. Subtle differences may be confounded by the relatively superior health of our OACs. Nonetheless, high-precision instruments are capable of identifying even the most nuanced group differences.[84,85] For example, recent machine learning studies have successfully differentiated SuperAgers from OACs, albeit with limited generalizability due to sample overlap. Leveraging similar machine learning techniques in expanded datasets with more robust methods could potentially unveil significant and reliable findings. Furthermore, additional high-precision methods, such as adopting person-specific approaches for rs-fMRI metrics, may help capture subtle nuances that may differentiate SuperAgers from OACs.[35,86,87]

The present study of SuperAgers applies advanced neuroimaging methods, is the first to ensure participants maintain stable cognitive profiles and includes a cohort matched in size to similar studies[34,61,88]; however, it is limited in participant size. Nonetheless, at least one study[61] was recently unable to detect previously reported group differences in FC of successful cognitive agers and controls observed with equivocal group size.[34] Given the publication bias,[89] there may also be unpublished studies with similar null results. Looking forward, the recent expansion of SuperAging Research Initiative (U19AG073153) into a multisite initiative will provide increased enrollment and greater power for future analyses. Future research may also make use of MRI scanners with higher magnetic field strength (e.g., 7 Tesla) or employ high-precision machine learning methods, both of which have been demonstrated to improve sensitivity[90,91] and detect subtle group differences and have shown promise in recent studies.[62,63]

In conclusion, this study serves as a foundational step in exploring the complexity of large-scale neurocognitive networks and their relationship to cognitive aging. At the group-level, within-network FC of large-scale networks and between subcomponents of the DMN were not a primary differentiator between cognitively average aging and SuperAging phenotypes. Recognizing the complexity of this field, future research may benefit from considering the role of undiagnosed neurodegenerative processes and employing high-precision rs-fMRI measurements including those that allow for consideration of individual rather than group-based statistics. These efforts will undoubtedly enhance our understanding of the contributions of resting-state network integrity to cognitive aging trajectories and the factors that underlie the exceptional cognitive abilities of SuperAgers.

Supplementary material

Supplementary material is available at *Brain Communications* online.

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Competing interests

The authors report no competing interests.

Data availability

All codes used to conduct analyses are made available in the Supplemental Material. Atlases used for analyses are open source and publicly available: Schaefer cortical atlases (https://github.com/ThomasYeoLab/CBIG/) and HCP subcortical atlas (https://github.com/Washington-University/HCPpipelines/blob/master/global/templates/91282_Greyordinates/Atlas_ROIs.2.nii.gz). Data are available through a collaborative request to the SuperAging Research Initiative (superagingdata@uchicago.edu or emily.rogalski@bsd.uchicago.edu).

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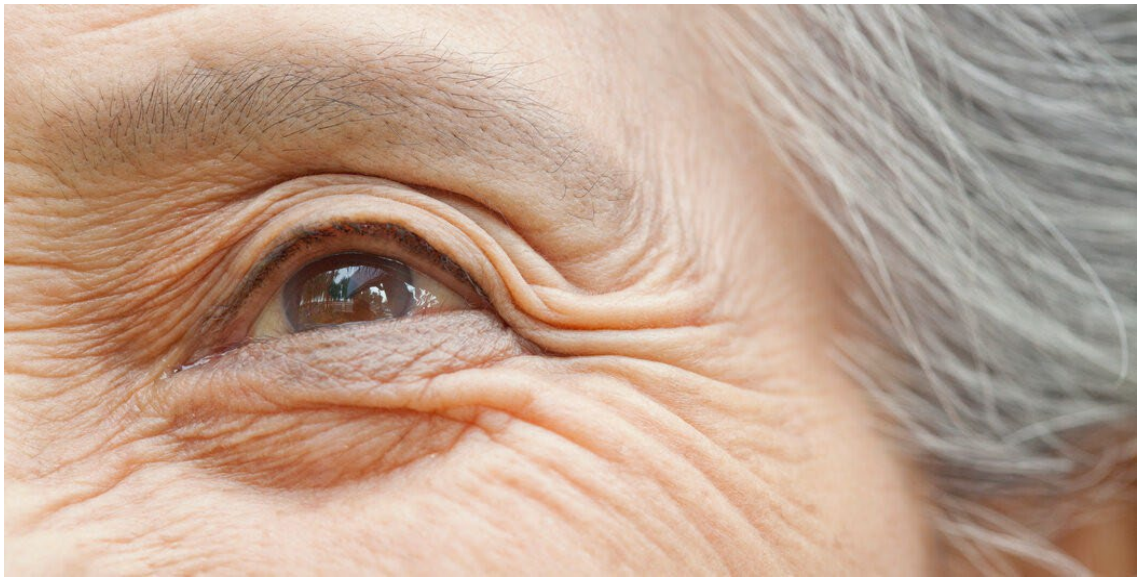
A Peek Inside the Brains of ‘Super-Agers’

nytimes.com/2024/04/29/well/mind/super-agers-study.html



When it comes to aging, we tend to assume that cognition gets worse as we get older. Our thoughts may slow down or become confused, or we may start to forget things, like the name of our high school English teacher or what we meant to buy at the grocery store.

But that’s not the case for everyone.

For a little over a decade, scientists have been studying a subset of people they call “super-agers.” These individuals are age 80 and up, but they have the memory ability of a person 20 to 30 years younger.

Most research on aging and memory focuses on the other side of the equation — people who develop dementia in their later years. But, “if we’re constantly talking about what’s going wrong in aging, it’s not capturing the full spectrum of what’s happening in the older adult population,” said Emily Rogalski, a professor of neurology at the University of Chicago, who published one of the first studies on super-agers in 2012.

A paper published Monday in the Journal of Neuroscience helps shed light on what’s so special about the brains of super-agers. The biggest takeaway, in combination with a companion study that came out last year on the same group of individuals, is that their brains have less atrophy than their peers’ do.

The research was conducted on 119 octogenarians from Spain: 64 super-agers and 55 older adults with normal memory abilities for their age. The participants completed multiple tests assessing their memory, motor and verbal skills; underwent brain scans and blood draws; and answered questions about their lifestyle and behaviors.

The scientists found that the super-agers had more volume in areas of the brain important for memory, most notably the hippocampus and entorhinal cortex. They also had better

preserved connectivity between regions in the front of the brain that are involved in cognition. Both the super-agers and the control group showed minimal signs of Alzheimer's disease in their brains.

"By having two groups that have low levels of Alzheimer's markers, but striking cognitive differences and striking differences in their brain, then we're really speaking to a resistance to age-related decline," said Dr. Bryan Strange, a professor of clinical neuroscience at the Polytechnic University of Madrid, who led the studies.

These findings are backed up by Dr. Rogalski's research, initially conducted when she was at Northwestern University, which showed that super-agers' brains looked more like 50- or 60-year-olds' brains than their 80-year-old peers. When followed over several years, the super-agers' brains atrophied at a slower rate than average.

No precise numbers exist on how many super-agers there are among us, but Dr. Rogalski said they're "relatively rare," noting that "far less than 10 percent" of the people she sees end up meeting the criteria.

But when you meet a super-ager, you know it, Dr. Strange said. "They are really quite energetic people, you can see. Motivated, on the ball, elderly individuals."

Experts don't know how someone becomes a super-ager, though there were a few differences in health and lifestyle behaviors between the two groups in the Spanish study. Most notably, the super-agers had slightly better physical health, both in terms of blood pressure and glucose metabolism, and they performed better on a test of mobility. The super-agers didn't report doing more exercise at their current age than the typical older adults, but they were more active in middle age. They also reported better mental health.

But overall, Dr. Strange said, there were a lot of similarities between the super-agers and the regular agers. "There are a lot of things that are not particularly striking about them," he said. And, he added, "we see some surprising omissions, things that you would expect to be associated with super-agers that weren't really there." For example, there were no differences between the groups in terms of their diets, the amount of sleep they got, their professional backgrounds or their alcohol and tobacco use.

The behaviors of some of the Chicago super-agers were similarly a surprise. Some exercised regularly, but some never had; some stuck to a Mediterranean diet, others subsisted off TV dinners; and a few of them still smoked cigarettes. However, one consistency among the group was that they tended to have strong social relationships, Dr. Rogalski said.

"In an ideal world, you'd find out that, like, all the super-agers, you know, ate six tomatoes every day and that was the key," said Tessa Harrison, an assistant project scientist at the University of California, Berkeley, who collaborated with Dr. Rogalski on the first Chicago super-ager study.

Instead, Dr. Harrison continued, super-agers probably have "some sort of lucky predisposition

or some resistance mechanism in the brain that's on the molecular level that we don't understand yet," possibly related to their genes.

While there isn't a recipe for becoming a super-ager, scientists do know that, in general, eating healthily, staying physically active, getting enough sleep and maintaining social connections are important for healthy brain aging.

CHICAGO SUN-TIMES

COLUMNISTS HEALTH

'Enjoy just being here' — At almost 110, she's still baking pie, with a little help

Edith Renfrow Smith, Grinnell College class of '37, is a rare "supercentenarian." In the fall her alma mater is naming a new dorm after her.

By Neil Steinberg | Jul 9, 2024, 12:18pm CDT

Edith Renfrow Smith, who will celebrate her 110th birthday on July 14, is the first Black graduate of Grinnell College in Iowa. She's planning to return to her alma mater later this year for the dedication of a dormitory named in her hono[illegible]. Ashlee Rezin/Sun-Times

Edith Renfrow Smith is baking a sour cherry pie.

"I just love sour cherry," she confides. "My father planted a sour cherry tree in the yard. He was a cook ... all the fruit; he had peaches, he had plums, he had gooseberries,

currants and grapes. Everything that momma could can, because we were poor."

That yard was in Grinnell, Iowa, where Smith was born on July 14, 1914, two weeks before the start of World War I. Regular readers might remember meeting her in 2021 for her 107th birthday and learning her down-to-earth world view, "Nobody's better than you." I figured, if 107 was noteworthy, how could 108 not be? Or 109, for that matter? The year she got COVID-19 and weathered the deadly disease so easily she didn't even mention that she'd had it.

For her 110th, this Sunday, I wondered how to shake things up. Such "supercentenarians" are an extreme rarity. Researchers estimate one person in a thousand who reaches age 100 will live to see 110, which makes Smith one woman out of a million, maybe out of 5 million.

I asked her daughter, Alice Smith, 78, if her mother still makes homemade jelly and wine.

She does, Alice said, inviting me to come by and watch production of a cherry pie last Friday, an offer I suspect she had reason to regret.

Edith Renfrow Smith, who turns 110 on July 14, bakes a cherry pie at her North Side home last week.|Ashlee Rezin/Sun-Times

“It takes 45 minutes to pit a quart of cherries,” says Alice, arriving at her mother’s apartment with a bag from a farmer’s market. “I won’t be doing that ever again.”

Alice is late, and perhaps not in the best mood, having had to fight NASCAR traffic from the South Side. “I’m only bringing this stuff,” she says. “I’m not making the cherry pie. That’s not something I want to make.”

But as daughters know, what you want to do, and what you end up doing, are two different things when your mother enters the equation. Alice is pressed unwillingly into the role of de facto pastry sous chef.

“Open the cookbook right there and check,” Edith says, gesturing to a 1960s-era Better Homes &lightttttt Gardens ring binder cookbook on the floor.

“Mother, I don’t need to open the cookbook,” snaps Alice. “I understand how to bake.”

Not easy as pie

The cookbook surprises me — I had anticipated cherished family baking traditions dating back to the 19th century, which is why it's always good to check your imagined notions against the yardstick of reality. Edith sets me right.

"Momma didn't make pies," she explains. "She didn't give us dessert. She said children should have apples and peaches. 'No garbage.' She called cookies and doughnuts and what have you 'garbage' because they were not good for you. She didn't give us cookies. She didn't bake pie. She made bread, three times a week, and she only used graham flour."

A pie needs sugar, and Edith directs her daughter to fetch it.

"The sugar's right there on the counter," she says. "Turn the light on."

"Mother, I don't need the light on," replies Alice. "I'm not blind!"

Edith Renfrow Smith (left), gets a spoon from her daughter, Alice, as they make a pie in Smith's North Side home last week. She turns 110 on July 14| Ashlee Rezin/Sun-Times

Edith flips the switch anyway.

“Mother, turn the light off,” says Alice. “I don’t need the light. I can see perfectly fine without it.”

“Excuse me,” says Edith, with formality.

“I found the sugar. I knew where the sugar was,” Alice says, then, as an aside to me: “This is why we don’t cook together. Or live together.”

I decided to share the sometimes messy process of pie-making, not to embarrass anybody, or because it is in any way unusual, but because it is so ordinary. The relationship between mothers and daughters is often fraught, and if there are daughters in their 20s reading this, thinking about their own mothers in their 50s, wondering if it will be any different half a century hence, the honest answer is: probably not.

“Mother, mother, *mother!*” exclaims Alice. “I will mix it … never mind, I’ll let you dirty up all you want, because I’m not cleaning up.”

Edith stands at a small table, assembling the pie. For maybe 20 minutes. Alice stands in the kitchenette of her one-room apartment. Communication is called back and forth, at a distance.

“It’s better that I walk away, ‘cause I have a bad habit of doing it myself,” says Alice.

“How much sugar?” asks Edith.

“One and a half cups,” calls Alice. “And you need three cups of cherries. That’s barely two cups. So you need one more cup of cherries.”

Edith Renfrow Smith adds sugar to the sour cherry pie she and her daughter Alice were making last week. Ashlee Rezin/Sun-Times

Flour is requested.

“Why are you putting flour in there? You’re already using corn starch?” asks Alice.

“May I have the flour, please?” asks Edith, coolly.

“I’m handing it to you, mother,” Alice says.

‘That’s just how we are’

One of the preconceptions I had was that the pie would be made for others — and the guard at the front desk did say that Mrs. Smith is known to regularly show up with a slice for whomever is on duty. But Edith is making this pie for herself. Why? Aren’t bakery pies adequate?

“‘They don’t make ‘em like I like,” she says.

Alice certainly isn’t touching it.

“It’s her pie,” she says. “I don’t eat that stuff.”

“I need half a cup of sugar,” says Edith, abruptly.

“*Why*?” asks Alice. “I’m asking ‘Why’? You don’t need it.”

“Because they’re sour cherries,” says her mother.

“They’re not that sour,” says Alice.

As the process winds up, credit is given.

“She does a much better job than anybody I know on crimping, making it look pretty,” says Alice. “That looks nice, mom.”

But that doesn’t last long. Cream is requested.

“I will get the cream for you,” says Alice. “I will take the brush and brush cream across the top.”

“No, you will give it to me,” says Edith.

“Why, don’t you trust me?”

“No,” replies Edith, who previously pressed down on each cherry with a spoon, to make sure her daughter hadn’t missed a pit. She shrugs off Alice’s suggestion of a pastry brush and egg white and massages the cream onto the top of the crust with her fingertips. “This will make it a pretty golden brown,” she says.

Alice leaves. A few days later, not wanting to cause anybody any unease by sharing the sticky pie-making process, I phone her to sound her out. She doesn’t mind.

“That’s just how we are,” Alice says. “We still love each other.”

‘Don’t let life pass you by’

Her mother’s 109th year, by the way, was unexceptional — except maybe for the publication of a children’s book about her life, “No One Is Better Than You” by Monique McLay Shore, with illustrations by Erica Lauren Butler.

“I feel great,” Edith says. “Very good. Not sick one day. I’m very, very fortunate.”

She does need a caregiver when she goes out, which she plans to do to mark her 110th

birthday.

“My daughter and I are going to tea,” she adds, with the regal lilt such a sentence demands. “I haven’t been to tea for a good while. The last time we went to tea was at the Peninsula. It’s a very lovely place. It’s very nice to have such nice places to go.”

Who gets to live to 100? The answer may surprise you.

In old age, life expectancy among the races shifts in dramatic ways, a new study shows.

By Kay Lazar Globe Staff, Updated December 4, 2024, 3:01 a.m.

Dr. Tom Perls, a Boston University researcher who runs the largest study of centenarians and their families in the world, sat last year with Herlda Senhouse, who was 112 at the time. Senhouse, who died last month at 113, was the second oldest person in the United States. JESSICA RINALDI/GLOBE STAFF

Imagine two neighbors, both in their mid-to-late 80s. One is Black and the other is white. Which one might have a better chance of reaching 100 years old?

Conventional wisdom would suggest the white octogenarian would have a leg up on that climb to 100, because of the mountains of research showing better access to health care and other opportunities for white Americans. Additionally, Black people in the United States generally have higher death rates at younger ages.

But a new study from Boston and Canadian researchers adds important depth to an unusual reversal of that death equation — that Black octogenarians in the United States have significantly better odds of living to 100 than their white counterparts. And those odds get better with age.

The study, published in the Journal of Internal Medicine, found that white women at 80 years old have a 4 percent chance of living to 100, while the odds are 6 percent for Black women. By the time they hit 90, that stretches to 9 percent for white women — and 13 percent for Black women.

The survival odds are lower for males, but the pattern is the same; a roughly 3 percent chance for Black men at age 80 to make it to 100, but just 2 percent for white men. By age 90, it was 5 percent for white men and 9 percent for Black men.

The researchers also studied survival patterns among Hispanics and Asian Americans and both showed even better longevity odds. They found a roughly 8 percent chance for Hispanic women, and 10 percent for Asian women to make it to 100 from age 80. That expanded to roughly 15 percent for both groups at 90. The researchers did not have sufficient data to analyze survival patterns for American Indian or Alaska Native populations.

“There is a tremendous amount to be learned from these different groups in what they have in common and don’t have in common,” said study coauthor Dr. Tom Perls,

professor of medicine and geriatrics at Boston University's school of medicine and director of the New England Centenarian Study.

"By studying this, we will solve this puzzle, which is, what are the environmental and genetic underpinnings of exceptional longevity and healthy aging," Perls said.

The study also acknowledged the significant disparities between Black and white populations at birth, showing a life expectancy of 78 years in 2019 for Black people, but 81 for whites. Hispanic and Asian American life expectancies were even greater, with Hispanics projected to live to 84 and Asians to 87.

But it also dramatically highlights a long-debated phenomenon known as the Black-white mortality crossover: Up until roughly their mid-80s, Black people have higher mortality rates than whites, but then decline in comparison to whites, and their life expectancy becomes greater.

The phenomenon was first noted by researchers more than a century ago, and it has been debated and investigated ever since. Skeptics have long said that the "crossover" was not real, and that the phenomenon of Black people outliving whites in their later years was merely a reflection of inaccurate birth and death records, especially from decades ago for Black people.

That concern remains but has eased as record-keeping has improved. The data Perls and his coauthor, Nadine Ouellette, an associate demography professor at the University of Montreal, used to calculate survival rates came from the US National Center for Health Statistics and are considered reliable.

Nadine Ouellette, an associate professor of demography at the University of Montreal, and coauthor of the new study on the Black-white crossover. NADINE OUELLETTE

Today, most researchers say the crossover phenomenon likely reflects what they call "select survival," meaning that many Black people die at younger ages because of social, economic, and other disadvantages, leaving the hardiest to live on. Or, as Ouellette puts it: "Those who survived to these great old ages are probably the most robust and this is what we are seeing in terms of survival."

In their study, the Black-white crossover occurred between the ages of 86 and 88, depending on gender, and persisted to age 100 and beyond.

Researchers not involved in the study said it is the first to demonstrate the Black-white crossover continued a decade longer than previous studies have shown.

But it wasn't just the persistent Black-white crossover that was intriguing, they said. The study also demonstrated that at age 100, estimated additional life expectancy for the Black population was similar to that of the Hispanic and Asian populations, and all three were significantly greater than for the white population.

"It's interesting how all the minority groups were together in terms of their probability of survival. They are very similar to each other, and all of them together are very different than the white population, and that's news," said Mark Hayward, a sociology professor at the University of Texas at Austin who studies population health and mortality rates of older adults.

Those greater odds of survival, even at age 100, translated to a life expectancy that was roughly six months longer for Black people compared to white people in 2019, the study showed. And for the Hispanic and Asian populations, it added up to about four to five additional months, compared to the white population.

Perhaps one of the most dramatic illustrations of Black longevity came in the life of Herlda Senhouse of Wellesley, who died last month at age 113. A petite woman with a firecracker personality, she was the second oldest person in the United States whose age was verified. The oldest is Naomi Whitehead, a 114-year-old in Pennsylvania, who is also Black.

The research by Perls and Ouellette did not try to answer the question of why Black, Hispanic, and Asian-American populations have longer life expectancies once they hit old age.

But the researchers noted other ongoing work by Perls at the New England Centenarian Study has demonstrated that combinations of certain genes appear to play an increasingly stronger role in survival to very old ages.

Even so, as the researchers point out, behavariol and environmental factors are the main drivers of mortality rates up to about age 90. For example, studies of Seventh Day

Adventists in California, whose members typically don't smoke, showed their life expectancies were roughly four to seven years longer than the California population as a whole. And Adventists who were vegetarian, did not smoke, engaged in high physical activity, and were not overweight lived roughly 10 years longer than their white California peers.

Lowell Taylor, an economics professor at Carnegie Mellon University who has studied the Black-white crossover phenomenon, said the Perls and Ouellette study will help researchers and the general public focus on similar ways to live better longer.

"Learning about the forces that shape mortality at a very old age would give us really good ideas about what we theoretically can do ourselves to make us have longevity," Taylor said.

Kyriakos Markides, a pioneering sociology professor at the University of Texas Medical Branch, said the new study confirms and adds to the research he has done. Markides is credited with coining the term the 'Hispanic paradox,' where Hispanic people in the United States live longer than white people, despite generally lower socioeconomic levels and health-care access.

Back in 1984, Markides coauthored a study about the Black-white crossover and found the phenomenon in the United States then happened at around age 75 — when overall life expectancies were lower. The study suggested that having a greater proportion of Black people who are more robust at very old ages, compared to white people, might have explained the lower rates of suicide among older Black people and fewer living in nursing homes at that time.

But Markides notes that often overlooked in discussions of the Black-white crossover are the great disadvantages Black populations often face earlier in life, hurdles that often lead to proportionately more deaths at younger ages, compared to white people.

"When you get to be very old," he said, "and you enjoy certain advantages, it's nice to see."

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Additional Media Coverage

1. **Unlocking the Secrets of SuperAgers** – *Michigan Today*, February 2024
2. **Bio and the Brain** – *Wittenberg University – Next Why Witt?,* February 2024
3. **What We Can Learn from SuperAgers** – *BottomLine Inc.*, March 2024
4. **SuperAging Research Initiative** – *Senior Talk Radio*, *Podcast/Video*, April 2024
5. **Maximizing Healthy Aging & Alzheimer's Research Care** – *University of Chicago HAARC Center - Video spotlight at American Academy of Neurology annual conference*, *Video*, April 17, 2024
6. **Why this 110-year old's brain is exciting scientists** – *BBC Sounds*, *Podcast*, June 2024
7. **Is an 80-year-old brain fit for the Presidency?** – *Men's Health Australia*, July 2024
8. **What's happening inside an 80-year-old brain?** - *Fortune Well*, July 2024
9. **How to increase your odds of becoming a 'SuperAger'** – *Fortune*, August 2024
10. **All the right moves: Middle Tennessee woman shares secrets to SuperAging** – *WSMV4*, August 2024
11. **Unlocking the Secrets of 'SuperAgers,' with Emily Rogalski** – *Big Brains Podcast*, October 2024
12. **The Future of Aging** - *AARP*, November 2024
13. **Episode 21: Dr. Emily Rogalski on Neurodegenerative Diseases and Brain SuperAging** – *Backed by Science Podcast*, November 2024
14. **Western researchers unlocking secrets to healthy aging** – *Western News*, November 2024

15. **Unlocking secrets to healthy aging** – *The Globe and Mail*, November 2024
    a. Western University SuperAging Awareness Campaign in partnership with the Globe and Mail

16. **The 10 habits to keep your brain young** – *The Telegraph*, February 9, 2025

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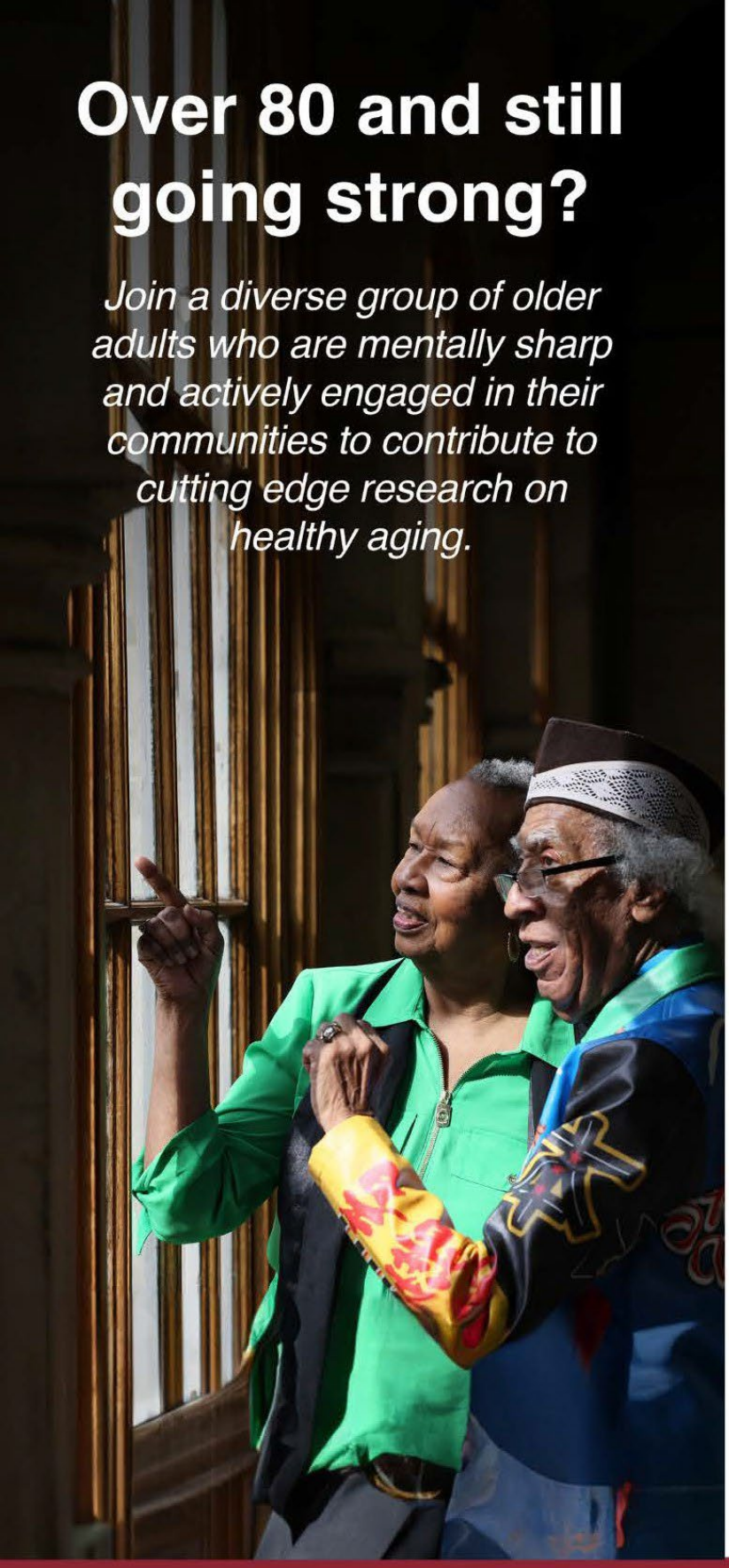

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SuperAgers are adults who have the memory capacity of someone 20-30 years younger.

What's involved?

About 8 hours of study visits broken up in 2-3 visits every 2 years, including:

- Pen, paper, and computerized memory and thinking tests
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Study funded by: National Institute of Aging and the McKnight Brain Research Foundation
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IRB NUMBER: 2021-13250
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To become a brain donor, consider enrolling in the brain donation program through the Resilience/Resistance against Alzheimer's Disease in Centenarians and Offspring (RADCO) study. Call the RADCO study program manager, Cristian Ibarra, at **617-353-0919** to discuss the program and have your questions answered.

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Anyone over age 18 who has a brain disorder or a healthy brain can donate. Many brains are needed from diverse populations and ages.

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Brain Donation: A Gift for Future Generations

Frequently Asked Questions

One donated brain can make a huge impact, potentially providing information for hundreds of studies on brain disorders, such as Alzheimer's and related dementias. Learn about the brain donation process and how to get started.

Why is brain donation important?

Brain donation helps researchers better understand the causes and potential treatments for brain disorders that affect millions of people.

Who can donate?

Anyone over age 18 who has a brain disorder or a healthy brain can donate. Many brains are needed from diverse populations and ages.

What happens to the brain after donation?

A specialist carefully removes the brain through the back of the head in a way that does not affect a person's appearance. The brain is sent to our brain bank, which distributes tissue samples to qualified researchers. The body remains with the family or funeral home for burial or cremation and related ceremonies.

Are there any fees to me or my family?

No, when donating as part of our study, there is no cost to the family for the donation procedure.

How do I donate?

Brain donation is different from other organ donation. You can donate by enrolling in our brain donation program as part of the RADCO research study.

What do my family and friends need to do?

Agree on who will contact the brain donation center at the time of death.

How do I talk with my family and friends about brain donation?

Tell them why you want to donate your brain and share what you've learned. Talk with them early in your decision-making process. Contact us to help answer questions.

Ready to take the next step?

To become a donor, consider enrolling in the brain donation program of the Resilience/Resistance against Alzheimer's Disease in Centenarians and Offspring (RADCO) study. Call the RADCO study program manager, Cristian Ibarra, at **617-353-0919** to discuss the program and have your questions answered.

BRAIN DONATION A GENEROUS GIFT #braindonation

Resilience/Resistance against Alzheimer's Disease in Centenarians & Offspring

EINSTEIN
Albert Einstein College of Medicine
IRB NUMBER: 2021-13250
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Be the **Brain** Behind the **Breakthroughs**

Volunteering to donate your brain could help lead to better understanding, treatment, and prevention of brain diseases, such as Alzheimer's disease and related dementias.

Why do people donate their brains to research at the end of life?

- Help researchers better understand the causes and potential treatments for brain diseases that affect millions of people.
- Have a broad, positive impact on public health and future generations.
- Help family members learn more about any diagnosis of brain diseases that may run in the family.

How does brain donation work?

To volunteer, register ahead of time through the RADCO brain donation program. At the time of death, a designated loved one or health professional will call the program manager. A specialist will carefully remove the brain through the back of the head in a way that does not affect the person's appearance. The brain is then sent to our brain bank and with researchers working to understand brain diseases. The body remains with the family or funeral home for burial, cremation, or related ceremonies.

What do I do next?

Although topics around life and death matters can be difficult to address, the best time to think about brain donation is now. Learn more about our brain donation program. Talk with your family and friends early in your decision-making process. If you choose to donate, consider registering for the brain donation program soon.

To become a brain donor, consider enrolling in the brain donation program through the Resilience/Resistance against Alzheimer's Disease in Centenarians and Offspring (RADCO) study. Call the RADCO study program manager, Cristian Ibarra, at **617-353-0919** to discuss the program and have your questions answered.

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Use su **cerebro** para ayudar a las **generaciones futuras**

Ofrecerse como voluntario para donar el cerebro podría ayudar a mejorar la comprensión, el tratamiento y la prevención de trastornos cerebrales, como la enfermedad de Alzheimer y las demencias relacionadas.

¿Por qué donar el cerebro a la investigación al llegar al final de la vida?

- Ayuda a los investigadores a comprender mejor las causas y los posibles tratamientos de las enfermedades cerebrales que afectan a millones de personas.
- Tiene un impacto amplio y positivo en la salud pública y en las generaciones futuras.
- Ayuda a sus familiares a aprender más sobre cualquier enfermedad cerebral hereditaria que puede haber sido diagnosticada en su familia.

Cómo funciona el proceso de donación del cerebro?

Para ser voluntario, regístrese con anticipación en el programa de donación de cerebros de RADCO. En el momento de la muerte, un ser querido designado o un profesional de la salud llamará al centro de donación de cerebros. Un especialista extraerá cuidadosamente el cerebro a través de la parte posterior de la cabeza de manera que no afecte la apariencia de la persona. Luego, el cerebro se envía a un banco de cerebros para su análisis . El cuerpo permanece con la familia o en la casa funeraria para su entierro o cremación y las ceremonias afines.

¿Cuál es el siguiente paso?

Aunque los temas relacionados con la vida y la muerte pueden ser difíciles de abordar, el mejor momento para pensar en ser un donante de cerebro es ahora. Obtenga más información sobre nuestro programa de donación de cerebro. Hable con su familia y amigos al comienzo del proceso de toma de decisiones. Si decide donar, considere registrarse con tiempo en el programa de donación de cerebro de RADCO.

Para convertirse en un donante de cerebro, considere inscribirse en el programa de donación a través del estudio de Resiliencia/Resistencia contra la Enfermedad de Alzheimer en Centenarios y sus descendientes (RADCO, por sus siglas en inglés) . Si tiene dudas o desea más información del programa, contacte al coordinador del estudio RADCO, Cristian Ibarra al **617-353-0919**

BRAIN DONATION · A GENEROUS GIFT

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Resilience/Resistance against Alzheimer's Disease in Centenarians & Offspring

La donación del cerebro: Un regalo para las generaciones futuras

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Preguntas Frecuentes

La donación de un cerebro puede generar un gran impacto ya que tiene el potencial de ofrecer información para cientos de estudios de trastornos cerebrales, como la enfermedad de Alzheimer y las demencias relacionadas. Aprenda más sobre el proceso de donar el cerebro y cómo comenzar.

¿Por qué es importante?

La donación del cerebro ayuda a los investigadores a comprender mejor las causas y los posibles tratamientos de los trastornos cerebrales que afectan a millones de personas.

¿Quién puede donar?

Cualquier persona mayor de 18 años, tanto con un trastorno cerebral como con un cerebro sano, puede donar el cerebro. Se necesitan muchos cerebros de diferentes poblaciones y edades.

¿Qué le sucede al cerebro después de la donación?

Cuando el donante fallece, un especialista extrae cuidadosamente el cerebro por la parte posterior de la cabeza de manera que no afecte la apariencia de la persona. El cerebro se envía nuestro banco de cerebros, que distribuye muestras de tejido a investigadores calificados. El cuerpo permanece con la familia o en la casa funeraria para su entierro o cremación y las ceremonias afines.

¿Hay algún costo para mí o para mi familia?

No, cuando se dona un cerebro como parte de un estudio , no hay ningún costo para la familia por el proceso de donación del cerebro.

Cómo puedo donar?

La donación de cerebros es diferente a la donación de otros órganos. Usted puede ser un donador de cerebro inscribiendose en el programa de donación del estudio RADCO.

¿Qué deben hacer mi familia y mis amigos?

Deben decidir quién se comunicará con el centro de donación de cerebros en el momento de su muerte.

¿Cómo puedo hablar con mi familia y amigos sobre la donación del cerebro?

Explíqueles por qué quiere donar el cerebro y comparta lo que ha aprendido sobre este tipo de donación. Hable con ellos desde el inicio de su proceso para tomar una decisión. Si tienen preguntas, comuníquense con nosotros.

¿Listo para dar el siguiente paso?

Para convertirse en un donante, considere inscribirse al programa de donación de cerebro a través del estudio de Resiliencia/Resistencia contra el la Enfermedad de Alzheimer en Centenarios y sus Descendiente (RADCO, por sus siglas en inglés) Si tiene dudas o desea más información del programa, contacte al coordinador del estudio RADCO, Cristian Ibarra al **617-353-0919**

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