TRUIST

To: McKnight Brain Research Foundation Trustees
Angelika Schlanger, PhD, Executive Director

From: Melanie Cianciotto

Subject: MBRF Meeting March 19 – 21, 2024

Date: March 8, 2024

Enclosed you will find the meeting package for the March 19 – 21, 2024, Trustees' meeting in Bethesda, Maryland. Included in this package for your review are the following items: the agenda, final draft of the minutes of the October 22, 2023 Trustees' meeting, October 23, 2023 Strategic Planning Meeting, February 20, 2024 Trustees' meeting, minimum distribution calculation and other supporting materials for the agenda items.

I have made hotel reservations at The Bethesda North Marriott Hotel and Conference Center. The hotel is located at 5701 Marinelli Road, North Bethesda.

Following are the room confirmation numbers:

Dr. Patricia Boyle	M6TX0HIA	Dr. John Brady	X21JLBJ2
Dr. Sharon Brangman	259D5909	Dr. Allison Brashear	R372ATA7
Dr. Mike Dockery	RXZV4HHB	Dr. Roy Hamilton	5FS7F1J6
Dr. Sue Pekarske	SHH5IXPM	Dr. Madhav Thambisetty	535M43PN
Dr. Angelika Schlanger	IIWK5NPI	Ms. Valerie Patmintra	W0PU5R4A

The meeting on March 19, 2024, will begin at noon and end at 5:00 p.m. The meeting will be held in the Seneca Boardroom. Here is the wifi information for the Boardroom:

Network Name: MarriottBonvoy_Conference
Password: MBRF2024

Dinner will be at 6:30 p.m. at Seasons 52 which is located at 11414 Rockville Pike (a short walk from the hotel).

McKnight Brain Research Foundation (MBRF)
Meeting of the Board of Trustees
Tuesday, March 19, 2024
Seneca Boardroom
Bethesda North Marriott Hotel & Conference Center
5701 Marinelli Road, North Bethesda, Maryland, 20852
12:00 pm – 5:00 pm EDT

12:00 PM	1.	Call to Order	Dr. Mike Dockery
	2.	Approval of Minutes a. October 22, 2023, Minutes b. October 23, 2023, Strategic Planning Minutes c. February 20, 2024 Minutes	Dr. Mike Dockery
12:15 PM	3.	Investment Review	Mr. Mike Hill
12:45 PM	4.	Chair's Report a. News and Updates b. Trustee Annual Self-Assessments c. UF MBI 25th Anniversary Event	Dr. Mike Dockery
	5.	Executive Director's Report a. Partner Updates b. MBRF 25th Anniversary Celebration – Proposed Plan and Estimated Budget c. 2024 Inter-Institutional Meeting d. Strategic Plan Progress Update	Dr. Angelika Schlanger
1:30 pm	6.	Corporate Trustee's Report a. Minimum Distribution Report b. Gifts and Grants Report c. Travel Award Report d. Operating Expense Report	Ms. Melanie Cianciotto
1:45 pm	7.	Committee Reports a. Membership and Governance 1. Updated Committee Activity Timeline 2. March 4, 2024 Minutes 3. Proposed Amendment to Trustee Term of Service 4. Discussion/Consideration of Adding Public Member(s) 5. Review, Monitor and Build Board Membership to Optimize Trustee Diversity and Skillsets 6. Succession Plan for Trustees	Dr. Sue Pekarske

		b. Finance Committee 1. Updated Committee Activity Timeline 2. January 22, 2024 Minutes 3. 2024 Society for Neuroscience (SfN) Poster Reception Proposal	Dr. Allison Brashear
		c. Education Committee 1. Updated Committee Activity Timeline 2. January 29, 2024 Minutes	Dr. John Brady
2:45 PM	BREAK		
3:00 PM		d. Research Committee 1. Updated Committee Activity Timeline 2. January 29, 2024 Minutes 3. March 4, 2024 Minutes 4. Proposal for MBRF Research Prize/Award in Collaboration with the Foundation for the National Institutes of Health 5. FNIH/NIA Annual Report on the Research Partnership In Cognitive Aging 6. American Federation for Aging Research (AFAR) Renewal Proposal for the Innovator Awards Program 7. American Brain Foundation Clinical Translational Research Scholarship 2025 RFP Update	Dr. Madhav Thambisetty Mr. David Carmel Mr. Matt Slater
		e. Communications Committee a. Updated Committee Activity Timeline b. February 15, 2024 Minutes c. 2023 Q4 Media Tracking Report	Dr. Patricia Boyle Ms. Valerie Patmintra
4:00 PM	8.	Comprehensive Campaign Update and Discussion a. Campaign Launch b. Sustaining Activities c. Anticipated Results d. Look Ahead and Discussion	Mr. Shannon McDaniel Ms. Nicole Grady, Ms. Kate Worthy
4:40 PM	9.	Future Meetings and Events (Attachment 1) a. Summer 2024 Board Meeting b. Fall 2024 Board Meeting c. Q1 2025 Board Meeting	
5:00 PM ACTION	10.	Adjournment	Dr. Mike Dockery

Attachment 1

MCKNIGHT BRAIN RESEARCH FOUNDATION (MBRF)

FUTURE MEETINGS AND EVENTS

April 15, 2024	McKnight Scholars Dinner at AAN Conference 6:30 PM MT **Denver, CO**
May 15 - 17 2024	Inter-Institutional Meeting hosted by UF **Gainesville, FL**
May 15, 2024	12:00 PM – 5:00 PM MBRF Trustees' Meeting 5:30 PM – 8:00 PM Open Reception & Dinner
May 16, 2024	Scientific Program Casual Reception & Dinner
May 17, 2024	Scientific Program
Summer 2024 Meeting	**TBD**
October 6, 2024	Society for Neuroscience (SfN) Poster Session **Chicago, IL**
Fall 2024 Meeting	**TBD**
Q1 2025 Meeting	**TBD**

MINUTES
MCKNIGHT BRAIN RESEARCH FOUNDATION
BOARD OF TRUSTEES MEETING
ALX Community
Potomac Conference Room (1st Floor)
201 N. Union Street
Alexandria, VA 22314

October 22, 2023

The Trustees' meeting of the McKnight Brain Research Foundation (MBRF) was called to order at 3:00 PM EDT on October 22, 2023.

The following members were present:
Dr. Michael Dockery, Chair
Dr. Madhav Thambisetty, Vice Chair
Dr. Patricia A. Boyle, Trustee
Dr. John Brady, Trustee
Dr. Sharon A. Brangman, Trustee
Dr. Allison Brashear, Trustee
Dr. Roy H. 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 (via Teams)
Dr. Angelika Schlanger, Executive Director
Ms. Valerie Patmintra, Senior Communications Advisor
Mr. Robert Wall, Legal Counsel

1. Approval of Minutes

The minutes of the July 24, 2023, Board of Trustees Meeting of the McKnight Brain Research Foundation were reviewed and approved as amended (Attachment 1). The changes are:

Page 5, Item 6, paragraph 3 – Add "and Memory Loss" after "Cognitive Aging"

Action Item 1: The minutes of the July 24, 2023, Board of Trustees Meeting were approved as amended (Attachment 1).

2. Chair's Report

Trustee Annual Self-Assessment – Dr. Dockery informed the Trustees that Ms. Cianciotto will be sending out the Trustee Annual Self-Assessment. Once returned, the self-assessments will be shared with Dr. Mike Dockery and Dr. Sue Pekarske.

Leadership Council Update – Dr. Dockery shared that the Leadership Council has been meeting regularly and submitted some recommendations for the Trustees' consideration. These recommendations will be reviewed during the Research Committee update.

University of Miami McKnight Brain Institute (MBI) Leadership Update – Previously, it was decided the UM MBI would change their leadership structure from Executive Director and Scientific Director to Director and Associate Director with Dr. Rundek assuming the role of Director. This change creates consistency among the MBIs. Dr. Rundek shared a new update regarding the MBI in her letter dated September 30, 2023 (Attachment). Dr. Bonnie Levin and Dr. Ihtsham Ul Haq have been appointed Co-Associate Directors of the UM MBI.

Legal Counsel – Dr. Dockery introduced Mr. Rob Walls and welcomed him to the meeting. Mr. Walls has assumed the Mr. Hank Raattama's work at Akerman and is now the MBRF Legal Counsel.

3. Executive Director's Report

Dr. Schlanger provided an update on her activities.

Cognitive Aging Summit IV – The Cognitive Aging Summit IV will be held March 20 – 21, 2024. Save the Dates have been sent and the FNIH is putting together the agenda. There will be six scientific sessions each led by a member of the Steering Committee. The FNIH is finalizing the media/branding toolkit. Dr. Schlanger will connect BRG Communications with the FNIH. BRG is planning to attend the Summit and will seek to leverage information from the Summit to develop messaging for the campaign. Dr. Schlanger and Ms. Patmintra will also promote the summit through the MBRF's social media platforms based on a branding toolkit that is being finalized by the FNIH.

Society for Neuroscience (SfN) Poster Session – Dr. Schlanger informed the trustees that 67 Abstracts have been received and will be judged by Dr. Molly Wagster and Dr. Jonathan King from the National Institute on Aging (NIA). Cash awards will be given for First, Second and Third place as well as three Honorable Mentions. Dr. Thambisetty will represent the MBRF at the Poster Session.

2024 Inter-Institutional Meeting – The 2024 Inter-Institutional Meeting will be held at the University of Florida May 15 – 17, 2024. A draft agenda for the Pre-Meeting and Inter-Institutional Meeting (Attachment 2) was shared with the trustees for information. The trustees were asked to send any feedback regarding the draft agendas with Dr. Schlanger to share with Dr. Bizon and the Leadership Council.

University of Florida MBI 25th Anniversary – The UF MBI 25th Anniversary celebration will be held February 1 – 2, 2024. They plan to integrate the Luttge Lecture into the event. The speaker will be Dr. Adam Gazzaley, MD, PhD, from UCSF. Dr. Gazzaley is a neuroscientist, who works at the intersection between technology and cognition.

4. Corporate Trustees' Report

A. The trustees reviewed the projected minimum distribution calculation for information (Attachment 3).

B. The trustees reviewed the Gift & Grants Report for information (Attachment 4).

C. The trustees reviewed the Travel Award Report for information (Attachment 5).

D. Ms. Cianciotto shared the Operating Expense Report with the trustees (Attachment 6).

E. Ms. Cianciotto shared the University of Miami Annual Investment & Growth Pool Report with the trustees (Attachment 7).

Action Item 2: The trustees reviewed, for information, the projected minimum distribution calculation (Attachment 3).

Action Item 3: The trustees reviewed, for information, the Gifts and Grants Report (Attachment 4).

Action Item 4: The trustees reviewed, for information, the Travel Award Report (Attachment 5)

Action Item 5: The trustees reviewed, for information, the Operating Expenses Report (Attachment 6).

Action Item 6: The trustees reviewed, for information, the University of Miami Annual Investment & Growth Pool Report (Attachment 7).

5. Investment Review

Mr. Hill presented the investment review and commented on key economic and investment factors through September 30, 2023 (Attachment 8).

A. Market Environment

- Year-to- date through September 30, 2023, the S&P 500 is up 13.07%. Global stocks and bonds pulled back in September and during the third quarter with rising interest rates and energy prices.

- The lagged effects of higher rates is likely to weigh on U.S. economic growth. The Big 4 Indicators (production, employment, real consumer spending and real income) suggest the U.S. economy is slowing, but not yet in recession. Rates are now above inflation but are likely to stay higher for longer.

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 September 30, 2023, the total return for the portfolio was 12.53% versus 16.38% for the Investment Policy Statement Index.

6. Future Meetings and Events

February Trustees' Meeting

The trustees will meet virtually on February 20, 2024, for ninety minutes to review the MBI Annual Reports.

March Trustees' Meeting and Cognitive Aging Summit IV

The trustees will meet March 19, 2024, in Bethesda, Maryland. The trustees will arrive the morning of March 19, 2024 and the Trustees' Meeting will begin at 12:00 noon. The Cognitive Aging Summit will be held March 20 – 21, 2024.

2024 Inter-Institutional Meeting

The 15th McKnight Brain Research Foundation Inter-Institutional Meeting will be hosted by the Evelyn F. McKnight Brain Institute at the University of Florida May 15 - 17, 2024. The trustees will arrive the morning of May 15, 2024, and the Trustees' Meeting will begin at 12:00 noon.

The Inter-Institutional Meeting will begin with a reception on the evening of May 15, 2024, followed by scientific sessions on May 16 -17, adjourning at noon on May 17, 2024.

7. Committee Reports

A. Membership and Governance Committee

Dr. Sue Pekarske provided the trustees with the updated Membership and Governance Committee Activity Timeline (Attachment 9). The committee last met August 29, 2023. The Trustee Appointment History and Terms (Attachment 10) has been updated to include Drs. Brangman and Hamilton.

The Proposed Amendment to Trustee Terms of Service (Attachment 11) was shared with the trustees. The trustees discussed various options to adjust the wording related to Trustee term limits, with input from Mr. Wall. After discussion, it was decided to table the discussion and have the Membership and Governance Committee review and draft proposed language based on the feedback.

Action Item 7: The proposed amendment will be sent back to the Membership and Governance Committee to work with Legal Counsel to draft renewal terms.

The possible addition of a Public Member was discussed during the August Membership and Governance Committee Meeting. The MBRF Board of Trustees is getting to be a mature board now and believes it is time to consider adding a public member. The board should start to think of people they know who would provide good chemistry and deliberation to the discussions of the board, share the same concerns about brain health, and have connections to different agencies with the ability to advocate and influence the direction of the MBRF. After discussion by the Board, a decision was made to table this item until strategic planning has been completed.

Action Item 8: The topic of Public Members was tabled until strategic planning has been completed.

Trustee Reappointment - The trustees held an executive session to discuss the renewals of the appointments of Dr. Allison Brashear and Dr. Patricia Boyle as trustees for three more years. Their terms expired on October 1, 2023. After discussion, the trustees unanimously agreed to retroactively renew Dr. Allison Brashear and Dr. Patricia Boyle's appointment as trustees for a second three-year term to begin October 1, 2023.

Action Item 9: Drs. Allison Brashear and Patricia Boyle were each unanimously appointed to a second three-year term beginning October 1, 2023.

B. Finance Committee

Dr. Brashear provided the trustees with the updated Finance Committee Activity Timeline (Attachment 12). The committee last met August 22, 2023. Dr. Brashear shared the approved 2024 Inter-Institutional Meeting budget (Attachment 13) for information.

C. Communications Committee

Dr. Patricia Boyle provided the trustees with an updated Communications Committee Activity Timeline (Attachment 14). The committee last met September 20, 2023.

Ms. Patmintra provided the trustees with the 2023 3rd quarter Website and Media Tracking Report (Attachment 15). There was a return to normal in the 3rd quarter after the spike from the Mental Health Awareness Campaign. There was a slight drop in the bounce rate after implementing the new navigation bar.

The trustees requested going forward that the update include a report of the Top 5 Visited Pages.

Action Item 10: Include report of the Top 5 Visited Pages in future committee and board meeting material.

The BRG Communications Landscape Analysis (Attachment 16) was shared for information. BRG feels there is an opportunity to establish a niche for the MBRF's public messaging and will present the top 2 campaign initiative for feedback during the Strategic Planning meeting tomorrow, October 23, 2023. BRG has found that no other organizations are working to educate consumer audiences on what cognitive aging is and what can be expected as we age, which will be the focus of the campaign.

D. Education Committee

Dr. Brady provided the trustees with the updated Education Committee Activity Timeline (Attachment 17).

Dr. Schlanger shared a Partner Outreach update, which included highlights of AAN's Brain Health Summit that took place in September, 2023, including the platform, timeline and stated goals. Many ideas expressed during the Summit are reflective of the MBRF's own efforts around educating the public and healthcare providers around brain health. There may be opportunities to get involved as the initiative progresses. Angelika shared the AAN's brain health definition with the Trustees, and they noted the absence of cognition and behavioral neuroscience. It was discussed that the MBRF could potentially advance the "cognitive aging" component within this initiative. Angelika also shared about her engagement with the Milken Alliance for Dementia Care and collaborative opportunities that have stemmed from being

involved in the network, including her being featured on a new healthcare navigation app, called Roon, to share information about the MBRF and cognitive aging.

E. Research Committee

Dr. Thambisetty provided the trustees with the updated Research Committee Activity Timeline (Attachment 18). The committee last met September 20, 2023.

The Leadership Council Consensus Recommendations and the proposed MBRF response letter (Attachment 19) were shared with the trustees. After discussion, the proposed MBRF response letter was approved and will be shared with the Leadership Council.

Action Item 11: The MBRF response to the Leadership Council Consensus Recommendations (Attachment 19) was approved.

The trustees reviewed the "Transcutaneous Vagus Nerve Stimulation and Cognitive Training to Enhance Cognitive Performance in Healthy Older Adults" Pilot Grant no-cost extension request (Attachment 20). The no-cost extension was approved for one year.

Action Item 12: The Transcutaneous Vagus Nerve Stimulation and Cognitive Training to Enhance Cognitive Performance in Healthy Older Adults" Pilot Grant no-cost extension (Attachment 20) was approved for one year.

McKnight Innovator Awards – The committee reviewed the success and progress of the McKnight Innovator Awards, and our partnership with AFAR for which a third grant cycle has just been awarded. While it is acknowledged that the number of applicants has been much less than hoped, it is felt that the concept is still sound and worth continuing to pursue. Suggested communication to AFAR was made, especially around helping to promote and publicize better, as well as several items related to the requirement for matching funds. The committee recommends renewal of this initiative and asked Dr. Schlanger to draft a renewal request letter to share with AFAR (Attachment 21). The trustees reviewed and approved the letter.

Action Item 13: The trustees approved the renewal request letter (Attachment 21) and Dr. Schlanger will share it with AFAR.

MBRF Clinical Translational Research Scholarships – The application window closed on September 14, 2023. There were only two applications that made it through the enhanced screening of the proposals to merit consideration for the MBRF award. The committee will meet in November to review the two applications. Three additional applications listed the MBRF as their second choice award mechanism, but through the screening process were identified as disease-focus and therefore not assigned to the MBRF.

8. Adjournment

There being no further business, the meeting was adjourned at 6:45 PM EDT.

Summary of Action Items:

Respectfully submitted,

Melanie A. Cianciotto
Truist Bank, Corporate Trustee

MINUTES
MCKNIGHT BRAIN RESEARCH FOUNDATION
BOARD OF TRUSTEES
Strategic Planning Meeting
October 23, 2023

The strategic planning session of the Trustee's meeting of the McKnight Brain Research Foundation (MBRF) was called to order at 8:00 AM EDT on October 23, 2023.

The following members were present:
Dr. Michael Dockery, Chair
Dr. Madhav Thambisetty, Vice Chair
Dr. Patricia A. Boyle, Trustee
Dr. John Brady, Trustee
Dr. Sharon A. Brangman, Trustee
Dr. Allison Brashear, Trustee
Dr. Roy H. 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:
Dr. Angelika Schlanger, Executive Director
Ms. Valerie Patmintra, Senior Communications Advisor
Mr. Robert Wall, Legal Counsel
Mr. Stephen Ferrante, Group Victory, LLC
Ms. Jane Barwis, BRG Communications
Mr. Shannon McDaniel, BRG Communications
Ms. Kate Worthy, BRG Communications
Ms. Nicole Grady, BRG Communications

1. Welcome, Introductions & Objective

Dr. Mike Dockery called the meeting to order and welcomed the facilitator, Dr. Stephen Ferrante, Principal Partner, Group Victory, LLC. Dr. Ferrante shared the agenda for today's meeting with all in attendance.

2. Strategic Planning Process & Deliverable

Dr. Ferrante provided an overview of the Strategic Planning Process. The MBRF is in the planning phase. This is the third of three facilitated sessions. The first two facilitated sessions included a subgroup of Trustees who helped draft content for the plan to allow for

an efficient full-board planning meeting. During today's session the foundation's mission, vision, values, goals, objectives, strategies, and success measures will be discussed. This process will yield a 3-year strategic plan for the MBRF.

3. Pre-Planning Assessment Findings

Dr. Ferrante shared an overview of the Pre-Planning Assessment findings with all in attendance (Attachment 1). The key findings included:

- Strengths of the foundation – mission dedication, healthy cognitive aging niche, founding trustees and chair's invaluable work, qualified and accomplished trustees, committee structure, financial stewardship, MBIs, existing partnerships and matching awards, motivated -full-time executive director, thoughtfulness in work and growth, forward-thinking positive direction, longevity;
- History of the foundation – accomplishments of single founding trustee, trustee driven and administered history, increase in board of trustees membership, addition of full-time executive director, interest beyond research agenda, solid foundation with evolving needs;
- Priorities of the foundation – research; education; communication; - health promotion focused/ not disease-based approach; ensure return on investments in all efforts; desire to be visible, distinct, reputable, national, cutting edge, go-to thought leader;
- Education and Communication – need to be integrated and messaging needs to be consistent and informed by consulting firm's work; - don't replicate existing efforts/leverage unique brand and partnerships; promote brand, mission & outcomes; ensure ROI measurement;
- Target audiences of the foundation – general public/consumers/end users, primary care practitioners/health providers, researchers;
- McKnight Brain Institutes – get more from institutes; - relationship & collaboration; increase recognition, visibility & co-branding, application of research/translational science, impact and dissemination of studies; - standard reporting format/ROI measurement; - role in education & communication;
- MBRF Trustees – demanding workload, need to focus on governance, need for role clarity, increase process and decision-making efficiency, diversify and expand board of trustees, succession planning;
- MBRF Executive Director -better use of the position, clearer direction for operations, leverage Executive Director's talent, set Executive Director up for success, leverage contractors

4. Strategic Plan Development & Finalization

Dr. Ferrante shared the initial goals and objectives of the strategic plan as created by the sub-committee of trustees that participated in the first two facilitated sessions. After discussion, the trustees agreed upon two goals and four objectives for the MBRF 2024 – 2026 Strategic Plan.

The agreed upon goals are:

- Advance research and scientific knowledge associated with age-related cognitive decline and memory loss.
- Educate the public and healthcare professionals about age-related cognitive decline and memory loss.

The agreed upon objectives are:

- Invest in and promote research focused on healthy cognitive aging.
- Place understanding about the naturally aging brain and optimal cognition at the forefront of public awareness.
- Position the Foundation as the thought leader, research catalyst, and resource in age-related cognitive decline and memory loss.
- Ensure the organizational structure, resources, and capacity to operate, advance, and sustain the Foundation and its mission.

The trustees discussed and agreed upon strategies, success measures, time frame and responsible parties for each of the objectives. The trustees would like to discuss and further clarify the fourth objective in more detail amongst themselves, and this will be done at an Executive Session at a future date in December or January. Mr. Wall has offered to help facilitate this discussion.

BRG Presentation – Communications Campaign

The BRG team presented an update on the campaign. The overview included sharing the two most popular campaign names and taglines, with options for creative logos. Each of the trustees shared which campaign name, tagline and logo they preferred. The next step is to test the two preferred campaign names, taglines and logos by administering a consumer survey.

5. <u>Strategic Plan Approval</u>

The MBRF Strategic Plan as amended (Attachment 2) was approved unanimously.

There being no further business, the meeting was adjourned at 3:00 PM EDT.

Respectfully Submitted,

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Melanie A. Cianciotto
Truist Bank, Corporate Trustee

MINUTES
MCKNIGHT BRAIN RESEARCH FOUNDATION
BOARD OF TRUSTEES MEETING
Via Zoom
February 20, 2024

The Trustees' meeting of the McKnight Brain Research Foundation (MBRF) was called to order at 6:30 p.m. ET on February 20, 2024.

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:
Dr. Angelika Schlanger, Executive Director
Ms. Valerie Patmintra, Senior Communications Advisor
Mr. Shannon McDaniel, BRG Communications
Ms. Kate Worthy, BRG Communications
Ms. Nicole Grady, BRG Communications

1. Review of the Annual Reports of the McKnight Brain Institutes

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 1). The report was well organized and provided a good summary of the progress made over the last year. The trustees were pleased to learn that enrollment in the Brain Health Advocacy Mission (BHAM) met the initial pilot project goal and that the BHAM team is conducting an impressive amount of community outreach as part of the project. Although the EMBI's membership fell to the lowest level since 2017, the recruitment efforts that resulted in 13 new faculty members in 2024 are reassuring, and their backgrounds impressive.

As a follow-up to the report, the trustees request some information, including:

- an updated organizational chart of the administrative structure of the EMBI and further explanation as to why EMBI membership fell so dramatically;
- more information concerning the training program for graduate students and post-docs, including the areas of focus and structure;
- an update on the advisory committee for the EMBI.

Action Item 1: Send thank you letter to Dr. Ron Lazar and Mr. Tom Brannon expressing the trustees' appreciation for the report and requesting the organizational chart of the administrative structure of the EMBI and other items, as noted above.

b. <u>University of Arizona</u>

The trustees reviewed the annual report concerning the Evelyn F. McKnight Brain Institute at the University of Arizona (Attachment 2). The report was well organized and the trustees were impressed with the many achievements of the EMBI during the year. The UA EMBI continues to thrive under Dr. Barnes' leadership, and her international presence and oversight of many exciting initiatives, including the Precision Aging Network (PAN) and the Resiliency and Reserve Collaboratory, which held its final workshop this year. The trustees are impressed by the great progress made with the MindCrowd participants surpassing 447,000 test takers. The Trustees raised questions about the structure of the mentorship program for trainees and the success plan for the EMBI's leadership. The trustees also noted the significant progress made this past year to meet the balance of the match requirement for the EMBI's endowment, which is approximately $174,061.

As a follow-up to the report, the trustees request some information, including:

- an organizational chart of the administrative structure of the EMBI and the university's administration;
- an update from the associate director of the EMBI;
- clarification on who oversees the trainees and K awards;
- a description of the EMBI's leadership structure supporting the Director and any pathways or opportunities for leadership development for more senior members of the EMBI;
- a description of the plans to meet the balance of the match requirement.

Action Item 2: Send thank you letter to Dr. Carol Barnes expressing the trustees' appreciation for the report and requesting an organizational chart of the administrative structure of the EMBI and the university's administration, an update on the associate director of the EMBI, and

clarification on who oversees the trainees and K awards as well as other items, as noted above.

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 3). The report is a comprehensive overview of the productivity and impressive accomplishments of the UF MBI during 2023. The trustees noted that significant leadership transitions have taken place this year that pave the way for an exciting next chapter for the UF MBI. A remarkable level of productivity, collaboration, and mentorship of trainees has continued to take place.

As a follow-up to the report, the trustees request some information, including:

- information about what CAM Center trainees (e.g. R25 and T32 scholars) have accomplished, a better understanding of the outreach plan, and whether programs designed to enhance the diversity of the field have been effective;
- about Dr. Woods' findings related to the impact of non-invasive brain stimulation on iADL's and the consequences for the onset of dementia;
- ask UF to respond to the following statement from last year's letter, "Looking to the future, we request that your annual reports will incorporate reports from the Deans of the College of Medicine and of the College of Public Health and Health Professions";
- information from Dr. Hunt and Dr. Nelson concerning Dr. Cohen's transition to Professor Emeritus status and that the recruitment process for the new occupant of the Evelyn F. McKnight Chair for Clinical Translation in Cognitive Aging be returned to a clinical department in the College of Medicine;
- request an organizational chart of the administrative structure of the UF MBI.

Action Item 3: Send thank you letter to Dr. Jen Bizon expressing the trustees' appreciation for the report and requesting an organizational chart of the administrative structure of the UF MBI and responses to the other follow up items.

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 4). The report is very well written and serves as a tribute to Dr. Ralph Sacco and his impact on the EMBI. Carrying on his legacy, significant leadership transitions have taken place this year that pave the way for an exciting next chapter for the EMBI. The trustees noted the tremendous depth and breadth of mentorship and training opportunities for early career clinicians and

scientists. The trustees request that the EMBI team please share any recordings, handouts, or resources that have been developed for the purpose of community outreach and education.

Action Item 4: Send thank you letter to Dr. Tatjana Rundek expressing the trustees' appreciation for the report and requesting additional information.

e. MBRF Trustee Review Form for the MBI Annual Report and Annual Report Template

The Trustees discussed the MBRF Trustee Review Form for the MBI Annual Report as well as the Annual Report Template. The overall feeling is the MBRF Trustee Review Form is helpful for reviewing by subsections but the use of quantitative scales is challenging because there is no understanding for what it means to meet expectations. Instead, an overall score to compare to the prior year was suggested by one of the Trustees. Several suggestions for changes to the Annual Report Template were made including asking for an organizational chart, and populating a table with information about publications and grants, that would be laid out in a consistent format with pertinent information being sought by the MBRF. Dr. Schlanger will compile the suggestions and add review of the annual report template to the upcoming Research Committee agenda.

2. Leadership Council Proposal to Relaunch the Cognitive Aging and Memory Intervention (CAMI) Core Pilot Grant Program

Dr. Thambisetty provided the trustees with an overview of the revised proposal to relaunch the Cognitive Aging and Memory Intervention Core Pilot Grant Program (Attachment 5). Dr. Lee Dockery shared edits that help strengthen the specifications of the communications strategy for the CAMI Core to solicit high quality inter-institutional collaborative proposals. After discussion, the trustees approved the revised proposal, to include Dr. Lee Dockery's edits, at a funding level of $75,000 per year for two years, per award. Dr. Schlanger will inform the Leadership Council of the trustees' decision as well as provide them with a clean version of the document.

Action Item 5: The trustees approved the revised proposal, to include Dr. Lee Dockery's edits, at a funding level of $75,000 per year for two years, per award.

Action Item 6: Dr. Schlanger will inform the Leadership Council of the trustees' decision as well as provide them with a clean version of the document.

3. Evelyn F. McKnight Clinical Translational Research Scholars Dinner at the 2024 AAN Annual Meeting

Dr. Brashear shared the proposal for the Evelyn F. McKnight Clinical Translational Research Scholars Dinner to be held at the 2024 AAN Annual Meeting with the trustees. The Finance Committee recommends funding the dinner at the proposed cost of $4,400. The trustees approved funding the dinner at the proposed cost of $4,400. The expected MBRF Trustees who will attend the Scholars Dinner on behalf of the MBRF are Dr. Brashear, Dr. Hamilton and Dr. Thambisetty.

Action Item 7: The trustees approved funding the Evelyn F. McKnight Clinical Translational Research Scholars Dinner to be held at the 2024 AAN Annual Meeting at the proposed cost of $4,400.

4. Comprehensive Campaign Update

Ms. Nicole Grady, BRG Communications, shared a preview of the BrainWorks microsite with the trustees and asked for feedback. Dr. Brangman shared that the language is at the college level and should be at a different level of education. Dr. Lee Dockery shared the font is too small and needs to be easier for older eyes to read. The use of contrast should be considered. Dr. Mike Dockery suggested adding a footnote to the survey to add credibility. The icons should be changed to make it clearer that they need to be clicked on to continue to the information. Ms. Grady shared BRG is reviewing accessibility and comprehension level as well as vison friendly fonts. They are also considering contrast but are trying to keep the colors in line with the colors of the MBRF.

5. Adjournment

There being no further business, the meeting was adjourned at 8:15 p.m. ET.

Summary of Action Items:

Respectfully submitted,

Melanie A. Cianciotto
Truist Bank, Corporate Trustee

LUTTGE LECTURE SPEAKER

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

Adam Gazzaley, MD, PhD

David Dolby Distinguished Professor of Neurology, Physiology, and Psychiatry at the University of California, San Francisco, and the founder and executive director of Neuroscape, a translational neuroscience center engaged in technology creation and scientific research. He designs and develops novel brain assessment and optimization tools to impact education, wellness, and medicine practices. This novel approach involves the development of custom-designed, closed-loop video games integrated with the latest advancements in software (brain computer interfaces, GPU computing, cloud-based analytics) and hardware (virtual/augmented reality, motion capture, mobile physiological recording devices, transcranial electrical brain stimulation). These technologies are then advanced to rigorous research studies that evaluate their impact on multiple aspects of brain function and physiology.

COMMUNITY DAY **AGENDA**

https://mbi.ufl.edu/2024/01/10/25th-anniversary-community-celebration-schedule/

Friday, February 2, 2023

9:00 – 10:00 AM

DeWeese Auditorium

**Breakfast available starting at 8:30 am.*

Entrepreneurship Breakfast with special guest Adam Gazzaley, MD, PhD
David Dolby Distinguished Professor of Neurology, Physiology, and Psychiatry at the University of California, San Francisco, and the founder and executive director of Neuroscape.

Co-hosted by **Neuro(PD)²**, the MBI Postdoc Professional Development Group, and moderated by **Dr. May Khanna**, Assistant Dean of Innovation & Entrepreneurship in the College of Medicine.

10:00 – 10:30 AM

Break

10:30 – 11:30 AM

DeWeese Auditorium

"We Didn't Even Know": Reflections on 25 Years of Progress in Brain Research Blitz

Center directors reflect on the most exciting advances in their respective fields since the inception of the MBI.

- **Sara Burke, PhD,** and **Adam Woods, PhD,** Co-Directors of the Center for Cognitive Aging & Memory Clinical Translational Research (CAM)
- **Gordon Mitchell, PhD,** Director of the Breathing Research & Therapeutics Center (BREATHE)
- **Sara Jo Nixon, PhD,** Director of the Center for Addiction Research & Education (CARE)
- **Mike Jaffee, MD,** Director of the Brain Injury, Rehabilitation, & Neuroresilience Center (BRAIN)
- **Carol Mathews, MD,** Director of the Center for OCD, Anxiety & Related Disorders (COARD)
- **Brandon Zielinski, MD, PhD,** Scientific Director of the Center for Autism & Neurodevelopment Disorders (CAN)
- **Matt LaVoie, PhD,** Director of the Center for Translational Research in Neurodegenerative Diseases (CTRND)
- **Laura Ranum, PhD,** Center for NeuroGenetics (CNG)

- **Roger Fillingim, PhD,** Director of the Pain Research & Intervention Center of Excellence (PRICE)
- **Joanna Long, PhD,** Director of the Advanced Magnetic Resonance Imaging & Spectroscopy Facility (AMRIS)

Moderated by **Jada Lewis, PhD**, Professor and Deputy Director of the MBI.

11:30 – 1:00 PM

Box Lunch & Break

Pick up a box lunch in the lobby and mix with members of the MBI community. *Box lunches must be reserved in advance!*

1:00 – 3:00 PM

DeWeese Auditorium

Luttge Lecture Symposium

Reflections on 25 Years at the MBI

Jen Bizon, PhD, Professor & Chair of Neuroscience Department & Director of McKnight Brain Institute

Michael Dockery, MD, Chair of the McKnight Brain Research Foundation (MBRF)

"A New Era of Experiential Medicine: The Future of Brain Optimization"

Adam Gazzaley, MD, PhD, David Dolby Distinguished Professor of Neurology, Physiology, and Psychiatry at the University of California, San Francisco, and the founder and executive director of Neuroscape.

Introduction by **Sara Burke, PhD,** Professor of Neuroscience & Co-Director of Center for Cognitive Aging and Memory Clinical Translational Research.

3:00 – 3:45 PM

MBI Front Patio

A Silver Celebration

Sweet treats, Photograph on the front patio

3:45 – 4:45 PM

DeWeese Auditorium

New Vistas in Brain Research: Perspectives from MBI Rising Stars

Where will MBI research go in the next 25 years? Panelists will discuss a variety of issues regarding the future of brain research, including potential innovations, new technology, new concepts, and ethics.

- **Ramon Sun, PhD,** Anne and Oscar Lackner Endowed Eminent Scholar & Associate Professor of Biochemistry Molecular Biology
- **Lakiesha Williams, PhD,** Professor of Biomedical Engineering & PI of the Tissue Mechanics, Microstructure, and Modeling Laboratory
- **Shellie-Anne Levy, PhD,** Assistant Professor of Clinical and Health Psychology & PI of the Brain Health Equity and Dementia Prevention Lab
- **Elias Sayour, MD, PhD,** Stop Children's Cancer/Bonnie R. Freeman Professor for Pediatric Oncology Research & PI of the Ribonucleic Acid Engineering Laboratory
- **Lori Knackstedt, PhD,** Associate Professor of Psychology & PI of the Neurobiology of Addiction Research Lab
- **Paola Giusti-Rodriguez, PhD,** Assistant Professor of Psychiatry & Co-Founder of the Latin American Genomics Consortium
- **Eric Wang, PhD,** Associate Professor of Molecular Genetics and Microbiology & PI of the Wang Lab

Moderated by **Jose Abisambra, PhD,** Associate Professor of Neuroscience & Deputy Director of the BRAIN Center, & **Eduardo Candelario-Jalil, PhD,** Associate Professor of Neuroscience.

4:45 – 5:00 PM

DeWeese Auditorium

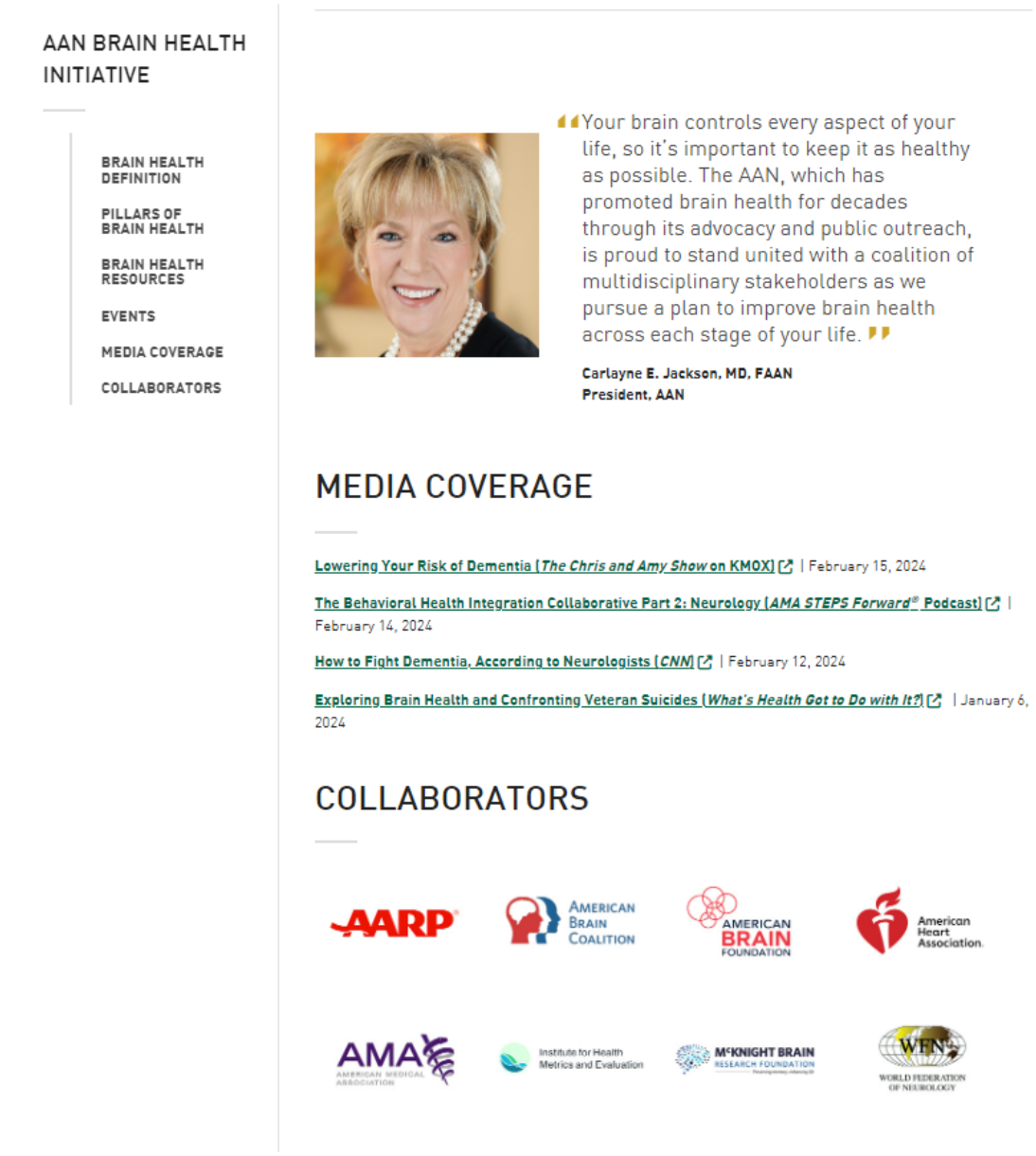
Concluding Remarks by Director Bizon

MBRF Partner Updates

1. **MBRF is now a featured Collaborator on the AAN Brain Health Initiative Website**

https://www.aan.com/tools-and-resources/brain-health

(Collaborators section, below, is on the bottom of the page)



2. **MBRF has accepted AARP's invitation to join as a Founding Advisor of their Brain Health Action initiative.**

"**Brain Health Action** is a multi-year, multi-faceted AARP initiative to energize all of us to choose brain healthy lifestyles throughout our lifespans. We want to create a movement toward better brain health across sectors. We hope to transform the current narrative around dementia and cognitive decline from one of fatalism to one of action. In particular, we are focused on engaging people and communities who

have struggled against systemic inequities and racism and that currently have disproportionate rates of cognitive decline. (See the information sheet here.)

As we continue to build Brain Health Action, we anticipate a variety of activities, including:

- Thinking about how your existing priorities and planned activities can be integrated as part of Brain Health Action so your efforts show up in the movement;
- Sharing collaborative members' brain health resources within the group and with the public through Brain Health Action Collaborative website and other communications vehicles.
- Co-Creating and sharing Brain Health Action resources and toolkits for groups, individuals & communities;
- Convening networking and knowledge-building gatherings, both in-person and virtually; and
- Providing a platform from which all of us can help people support brain health."

The Kick-off Meeting took place on March 8th and the formal, public launch of the initiative will take place at the ASA (American Society on Aging) Conference on March 25-28 in San Francisco.

Current List of Founding Advisors includes:

Rajiv Ahuja, Milken Institute
Anne Basting, PhD, TimeSlips
Leanne Clark-Shirley, PhD, American Society on Aging (ASA)
Peggye Dilworth-Anderson, PhD, University of North Carolina at Chapel Hill
Fayron Epps, PhD, RN, FGSA, FAAN, UT Health San Antonio School of Nursing and Alter Program
Terry Fulmer, PhD, RN, FAAN, The John A. Hartford Foundation
Kate Gillespie, PhD, MPH, Institute for Health Metrics and Evaluation (IHME)
Lindsay Goldman, LMSW, Grantmakers In Aging (GIA)
Julene Johnson, PhD, UCSF and Sound Health Network
Nancy Lynn, BrightFocus Foundation
Susan Magsamen, International Arts + Mind Lab, Johns Hopkins School of Medicine
Karen Moseley, Health Enhancement Research Organization (HERO)
Upali Nanda, PhD, HKS
Kelly O'Brien, UsAgainstAlzheimer's
Angelika Schlanger, PhD, McKnight Brain Research Foundation
Vicki Shepard, MPA, ACSW, Tivity Health
Stephani Shivers, MEd, OTR/L, CaringKind
Rani E. Snyder, MPA, The John A. Hartford Foundation
Diane Ty, Milken Institute
Jennie Ward-Robinson, PhD, Society to Improve Diagnosis in Medicine (SIDM)
Bonnie Wattles, Hilarity for Charity (HFC)

3. **The American Brain Foundation has a new Executive Director, following the retirement of Jane Ransom: Michelle Heritage**

You can find the official announcement here:
https://www.americanbrainfoundation.org/visionary-leader-joins-american-brain-foundation-as-executive-director/

McKnight Brain Research Foundation 25th Anniversary -
Proposed Ideas and Strategies to Commemorate and Celebrate this Milestone

I. Celebrating the 25th Anniversary at 2024 events:

Cognitive Aging Summit IV

Budget Estimate: The items below are not expected to incur a cost

- Digital Signage (monitors in foyer and at reception) featuring content ("slides") provided by the MBRF, including celebratory messaging.
- Cake at reception (one for MBRF and one for NIA's 50th anniversary)
- Remarks from Mike – opening/closing remarks; remarks at reception

Inter-Institutional Meeting

Budget Estimate: $3,150 (or less, if certain items are not included)

- Champagne Toast ($775)
- MBRF 25th Anniversary Cake for photo opportunity ($100)
- MBRF Step and Repeat Backdrop for Photos with MBRF logo, which can be reused at future events ($675)
- Standing Banners: one for MBRF and one for each MBI, which can be reused at future events ($875 for banners, $200 stand)
- MBRF Vases as Centerpieces (UF will reuse ones from their anniversary event and will develop additional ones for the MBRF's 25th anniversary) ($225)
- Decorative Balloon Arch ($300)
- Remarks from Trustees and MBI Directors during reception and dinner

**Note: the 25th Anniversary of the UF MBI and the 15th Anniversary of the IIM meeting will also be commemorated*
**Note: MBRF signage can be used at future events, e.g. the SfN Poster Reception and AAN Scholars Dinner, etc.*

II. Funding a Research Award, Prize, Lecture, or Initiative in Honor of the 25th Anniversary

Budget Estimate: The cost of each will depend on the chosen level of investment and administrative fees.

These opportunities can present a meaningful way to commemorate the MBRF's anniversary in a long-lasting, impactful way that advances the mission.

- The Trustees will review a proposal and budget by the FNIH to establish an annual cash award or prize for the most outstanding Clinical Translational Research in Cognitive Aging at the March 19th, 2024 meeting.
- Additional ideas include:
  - developing a new scholarship or research award;
  - funding a lecture or series of lectures;
  - funding a post-doctoral fellowship;
  - naming the MBRF Pilot Grant Program or renaming another existing funded award;
  - offering the MBIs a grant/gift to donate to a local relevant charity or organizations or to implement/expand a community outreach/education initiative

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III. Proposed Communications Budget Additions (Reviewed by Finance and Communications Committees)

Proposed Additional Budget Ranges (BRG) – Three levels:

- **Total estimated budget for Anniversary Video, Logo, and Vignettes: $12,500 to $14,500**
- **Total estimated budget for Anniversary Video and Logo only: $9,500 to $11,000**
- **Total estimated budget for Anniversary Video only: $7,000-8,000**

- 25th Anniversary Video
  - Sizzle reel style using existing video footage and graphics
  - Will be posted on MBRF web site and social media platforms
  - Depending on approval timeline, may be ready to debut at the IIM

  Budget Estimate: $7,000.00 - $8,000.00

  Includes:
  - Video treatment (outlining video structure)
  - Graphics development
  - Potential new soundbites from leadership (newly taped or lifted from existing footage)
  - Two rounds of edits

- 25th Anniversary Logo Development

  Budget Estimate: $2,500.00 - $3,000.00
  - 2-3 social media posts with the anniversary logo will be woven into the campaign
  - Logo will be posted on MBRF website
  - Logo can be used on celebratory signage, swag, and/or (cup)cakes at 2024 events (CAS IV, IIM)
  - Trustees, MBIs and other partners will be asked to share anniversary posts on their social media platforms

  Note: We may be able to identify an online program, service, or student who can add an anniversary treatment to our existing logo for a relatively low cost.

- Video Vignettes with Trustees, Chair Emeritus, MBI Directors and Partners reflecting on the MBRF's 25- year history

  Budget: $3,000.00 - $3,500.00

  Includes:
  - Outlining/scripting soundbite as needed
  - Securing footage from videographer and correct format
  - Editing up to 3-4 videos into vignettes

IV. Initiatives within the Current Communications Budget (No additional funds needed)

- 25th Anniversary language woven in campaign messages

- Dedicated outreach leveraging the 25th anniversary in May-June. Leverage any approved anniversary initiatives (community program and/or new scholarship). Example: "as part of the BrainWorks campaign and McKnight's 25th anniversary, McKnight is announcing new grant…")

- MBRF existing brochure updated to reflect campaign and 25th anniversary and incorporated into campaign microsite content
  - Updated layout
  - New Graphics / look and feel
  - Incorporate updated photo(s) of the Leadership Council, MBIs, Trustees, etc. (*Note: new copy to be provided by MBRF)

Pre-meeting for 15th Annual McKnight Brain Research Foundation Inter-Institutional Meeting

Wednesday, May 15, 2023

8:30- 10:15 AM **Session A: Intervention Strategies**

Intervention: Neuromodulation

Adam Woods (UF) and Keith McGregor – Chairs

Eric Porges (UF)
John Williamson (UF)
Gordon Mitchell (UF)
Matt Burns (UF)
Eleanora Rossi (UF)

Victor Del Bene (UAB)
Kristina Visscher (UAB)
Elizabeth Lucas (UAB)

Stephen Cowen (UA)
Meredith Hay (UA)
Jessica Andrews-Hanna (UA)
Mariam Hovhannisyan (UA)

Ihtsham Haq (UM)
Christian Agudelo (UM)
Sonya Kaur (UM)

Intervention: Precision Aging

C. Barnes (UA) and T. Rundek –Chairs

Aprinda Idahlastari (UF)
Rougu Fang (UF)
Joseph Gullett (UF)

Virenda Mishra (UAB)
Daniel Tyrrell (UAB)
Ron Lazar (UAB)

Matt Huentelman (UA)
Matt Grilli (UA)
Arne Ekstrom 3 (UA)
Lee Ryan (UA)

Stacy Merritt (UM)
Susan Fox-Rosellini (UM)
Nicole Sur (UM)
Bonnie Levin (UM)

10:30AM- 12:15 PM **Session B: Risk Factors for Cognitive Aging**

Metabolism and Cardiac Function

Sara Burke (UF) and Lee Ryan (UA) – Chairs

Ramon Sun (UF)
Matt Gentry (UF)
Ron Cohen (UF)
Russ Hepple (UF)

Kristina Visscher (UAB)
Caesar Hernandez (UAB)
Briana De Miranda (UAB)
Daniel Tyrrell (UAB)
Ron Lazar (UAB)

Neuroinflammation

Tom Foster (UF) and M. Hay (UA**)-** Chairs

Adam Woods (UF)
Yenisel Cruz-Almeida (UF)
Eric Porges (UF)
Steve Weisberg (UF)
Aprinda Idahlastari (UF)
Rougu Fang (UF)
Joseph Gullett (UF)

Farah Lubin (UAB)
Keith McGregor (UAB)
Virendra Mishra (UAB)
Victor Del Bene (UAB)

Asta Haberg (UA)
Betty Glisky (UA)
Ashley Huggins (UA)

Carol Barnes (UA)
Matt Huentelman (UA)
Leigh Nicholson (UA)

Tatjana Rundek (UM)
Nicole Sur (UM)
Ihtsham Haq (UM)

Ami Raval (UM)
Kunjan Dave (UM)
Susan Fox-Rosellini (UM)

12:30-1:45 Lunch – Special Topic Community Outreach (Susan Fox-Rosellini and Ron Lazar, Lead)

2:00- 3:45 PM Session C: New Approaches and Insights into Cognitive Aging

AI and Neuroimaging

K. Visscher (UAB) & Arne Ekstrom (UA) -Chairs

Adam Woods (UF)
Aprinda Idahlastari (UF)
Rougu Fang (UF)
Joseph Gullett (UF)
Steve Weisburg (UF)

Victor Del Bene (UAB)
Viendra Mishra (UAB)
Keith McGregor (UAB)

Sabina Srokova (UA)
Li Zheng (UA)
Paul Hill (UA)
Bob Wilson (UA)
Caroline Phelps (UA)
Alana Muller (UA)

Ihtsham Haq (UM)
Taylor Ariko (UM)
Christian Agudelo (UM)

Neuromodulatory and Psychiatric Influences

B Setlow (UF) and B Levin (UM)- Chairs

Sara Burke (UF)
Barry Setlow (U
John Williamson (UF)
Eric Porges (UF)

Farah Lubin (UAB)
Caesar Hernandez (UAB)
Elizabeth Lucus (UAB)
Abbi Hernandez (UAB)

Ashley Huggins (UA)
Jessica Andrews-Hanna (UA)
Carol Barnes (UA)
Betty Glisky (UA)

Sonya Kaur (UM)
Stacy Merritt (UM)
Bonnie Levin (UM)

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15th Annual McKnight Brain Research Foundation Inter-Institutional Meeting

Defining Therapeutic Avenues: Bridging Animal and Human Insights on Cognitive Aging

May 15-17, 2024
University of Florida

Wednesday, May 15, 2023

12:00 – 5:00 PM	MBRF Board Meeting Location TBD
1:00 – 6:00 PM	Registration Eleo Hotel - Lobby
6:00 PM	Load Buses and Transport to Stadium
6:30– 8:30 PM	Opening Reception with Trainee Posters Bull Gator Zone, UF Football Stadium

7:15 PM **Welcome Remarks**

Jennifer L Bizon, PhD
Director, Evelyn F. McKnight Brain Institute
Professor and Chair, Department of Neuroscience
University of Florida

UF Leadership

Michael L. Dockery, MD
Chair, McKnight Brain Research Foundation

Thursday, May 16, 2023

7:00 – 8:00 AM **Breakfast**
Eleo Hotel, Rm TBD

8:00 – 8:30 AM **Bus or Walk to Harrell Medical Education Building**
Studio TBD

8:30 – 8:50 AM **Opening Remarks and Welcome**

Jen Bizon, PhD
Director, Evelyn F. McKnight Brain Institute
Professor and Chair, Department of Neuroscience, UF

	UF Leadership
	Michael L. Dockery, MD Chair, McKnight Brain Research Foundation
8:50– 8:55 AM	**Introduction for Dr. Resnick, Adam Woods, PhD** co-Director, Center for Cognitive Aging and Memory
8:55– 9:25 AM	**Title TBD** Sue Resnick, PhD, Chief, Laboratory of Behavioral Neuroscience National Institute on Aging
9:25- 9:30 AM	**Introduction for Dr. Rapp, Sara Burke, PhD** co-Director, Center for Cognitive Aging and Memory
9:30–10:00 AM	**Title TBD** Peter Rapp, PhD, Senior Investigator, Laboratory of Behavioral Neuroscience National Institute on Aging
10:00 - 10:15 AM	Discussion (co-moderated by Drs Burke and Woods)
10:15 - 10:30 AM	**Break**

Session 1: Risk Factors for Cognitive Aging: Metabolic and Cardiovascular Function

Moderators: Sara Burke, PhD (UF) and Lee Ryan, PhD (UA)

10:30 –10:45 AM	Matt Gentry, PhD, Metabolism (UF)
10:45 – 11:00 AM	Abbi Hernandez, PhD, Metabolism (UAB)
11:00 – 11:15 AM	Merideth Hay, PhD, Cardiovascular function (UA)
11:15 – 11:30 PM	Tatjana Rundek, MD, Cardiovascular function (UM)
11:30 – 11: 35 AM	*Farah Lubin- 2023 Pilot Awardee Highlight*
11:35 – 11:45 PM	Summary of Recommendations from Pre-meeting and Discussion
11:45 AM - 1:15 PM	**Lunch – Highlights of Training Programs in Cognitive Aging Across Institutes, Harrell Medical Education Building, Studio TBD**

Session 2: Risk Factors for Cognitive Aging: Neuroinflammation

Moderators: Tom Foster (UF) and Merideth Hay (UA)

1:15 – 1:30 PM	Yenisel Cruz-Almeida, Ph.D., Pain (UF)
1:30 – 1:45 PM	Roger McIntosh, PhD – HIV (UM)
1:45 – 2:00 PM	Bonnie Levin, PhD- Heat stress (UM)
2:00 – 2:15 PM	David Vance, PhD- HIV (UAB)
2:15 – 2:25 PM	Summary of Recommendations from Pre-meeting and Discussion

Session 3: New approaches to advance hypotheses of cognitive aging

Moderators: Kristina Visscher, Ph.D. (UAB) and Arne Ekstrom (UA)

2:25 – 2:40 PM	Stephen Cowen, PhD, Electrophysiological approaches (UA)
2:40– 2:55 PM	Ramon Sun, PhD, Spatial Proteomics (UF)
2:55 – 3:10 PM	Virendra Mishra or Richard Kennedy, Imaging/AI (UAB)
3:10 - 3:25 PM	Ihtsham Haq (UM)
3:25 – 3:35 PM	Summary of Recommendations from Pre-meeting and Discussion
3:35 – 3:50 PM	**Break**

Session 4: Neuromodulatory and Psychiatric Influences on Cognitive Aging

Moderators: Bonnie Levin, Ph.D (UM) and Barry Setlow, Ph.D. (UF)

3:50 - 4:05 PM	Caesar Hernandez, PhD, (UAB)
4:05 - 4:20 PM	Carol Barnes, PhD, LC in non-human primates (UA)
4:20 – 4 :35 PM	Natalie Ebner, PhD (UF), Oxytocin
4:35 – 4:40 PM	*Joseph Signorile, PhD (UM)- 2023 Pilot Awardee Highlight*
4:40 PM– 4:50 PM	Summary of Recommendations from Pre-meeting and Discussion
4:50-5:00 PM	Bus or Walk to Hotel Eleo
6:00-6:30 PM	Load Buses and Transportation to Thomas Center
6:30 -7:30 PM	Cocktail Hour
7:30 PM	**Dinner Celebration, "Looking Back and Looking Forward: Celebration of 15 years of Inter-institutional Collaboration" Remarks by Leadership and Members of MBIs, Trustees?**
9:30 PM	Transportation back to Eleo Hotel

Friday, May 17, 2023

7:00 AM – 8:30 AM	Breakfast and Checkout (check-out time is 12pm) Hotel Eleo, Rm TBD
7:30 AM – 8:30 AM	Board Meeting, Trustees and Leadership Council, Room TBD
8:30AM – 8:45 AM	Walk or Bus to Evelyn F and William L McKnight Brain Institute DeWeese Auditorium

Session 5: Interventions for cognitive resilience I- Neuromodulation

Moderator: Adam Woods (UF) and Keith McGregor (UAB)

9:00 AM – 9:15 AM	Eric Porges, PhD, Vagus Nerve Stimulation (UF)
9:15 AM– 9:30 AM	Keith McGregor, PhD, Biofeedback (UAB)
9:30 AM– 9:45 AM	Jessica Andrews-Hanna (UA)
9:45 AM – 10:00 AM	Gordon Mitchell, PhD, Intermittent Hypoxia (UF)
10:00 AM- 10:15 AM	Summary of Recommendations from Pre-meeting and Discussion

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Session 6: Interventions for cognitive resilience II- Precision Aging

Moderators: Carol Barnes, Ph.D. (UA) and Tatjana Rundek (UM)

10:15 AM- 10:30 AM	Ron Lazar, PhD, FANA, Brain Care score (UAB)
10:30 AM- 10:45 AM	Matt Huentelman, PhD, Precision Aging (UA)
10:45 AM -11:00 AM	Alberto Ramos/Sonya Kaur, Sleep (UM)
11:00 AM – 11:15 AM	Aprinda Indahlastari, Ph.D., AI (UF)
11:15 AM- 11:30 AM	Summary of Recommendations from Pre-meeting and Discussion

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11:30 – 12:00 PM	**Closing Remarks** Jen Bizon, PhD Director, Evelyn F. McKnight Brain Institute Professor and Chair, Department of Neuroscience University of Florida Molly V. Wagster, PhD Chief, Behavioral & Systems Neuroscience Branch Division of Neuroscience National Institute of Aging Michael L. Dockery, MD Chair, McKnight Brain Research Foundation
12:00 PM	Pick-up Boxed Lunches
12:15 PM	Buses depart for Hotel Eleo

Optional Museum or Butterfly Garden Visit.

Buses to Airport from Museums or Hotel Eleo

McKnight Brain Research Foundation

Projected Minimum Investment Return Calculations

(As of 9/30/2023 for fiscal year ending 6/30/2024)

Average Fair Market Value	$58,421,845.77
Less:	
Cash held for charitable purposes (1 1/2 %)	($876,327.69)
Net value of non-charitable use assets	$57,545,518.09
Minimum Investment Return (5%)	$2,877,275.90

Net Minimum Investment Return Calculation:

Minimum investment return		$2,877,275.90
Less:		
sub total	Qualifying Distributions	($3,162,856.81)
		($285,580.91)
	Excess distribution carryover (actual for '19, '20, '21, '22)	$63,874.58
	(estimate for '23)	$285,580.91
		$349,455.49

McKnight Brain Research Foundation

Minimum Distribution Calculation

Fiscal years 2000 - 2023

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**	**$2,806,006 (estimate)**	**$2,741,695 (estimate)**	**$0**	**$64,311**
$60,787,370	**7/1/2023 - 6/30/2024**	**$2,877,275 (estimate)**	**$3,162,856 (estimate)**	**$285,581**	
			$75,538,701.13	**$349,455.58**	**(estimated total excess carryover)**

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 Costs	Evelyn F. McKnight Neurocognitive Clinical Scholar in Brain Health and Aging (UM)	*FNIH - CAS IV*	Reserve and Resiliency Workshop IV	2024 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)	$115,000 (4/2021 - 4/2025)	$250,000 payable over 5 years	*$313,573.28 (6/2023 - 5/2024)*	$30,000	$26,800
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	$5,750	$50,000	$49,847.00	$30,000	$24,450.97
7/1/24-6/30/25	$1,000,000	$330,000	$1,000,000	$5,750				
7/1/25-6/30/26		$330,000	$500,000					
7/1/26-6/30/27		$330,000						
7/1/27-6/30/28		$330,000						
7/1/28-6/30/29		$165,000						
7/1/29-6/30/30								
Total	$15,000,000	$3,300,000	$4,500,000	$115,000	$250,000	$313,573.28	$30,000	$26,800
Balance	$2,000,000	$1,661,750	$1,500,000	$11,500	$150,000	$108,496.08	$0	$2,349.03

Total Active Grants
$23,165,000

Active Grants Remaining Balance
$5,434,095

as of 2.29.2024

McKnight Brain Research Foundation Pilot Grants

	A Novel Invention Tool (Levin) $60,000 (5/1/2018) $60,000 (5/1/2019) *completed - remaining balance will not be used*	**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*	**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*	**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*
7/1/18 - 6/30/19	$11,256.57 UF $6,895.45 UA	$6,799.94 UF		
7/1/19 - 6/30/20	$33,845.70 UF $40,000 UM	$14,581.29 UF	$9,881.16 UF	
7/1/20 - 6/30/21	$830.52 UF $21,604.96 UA	$1,694.96 UF $18,363.11 UA	$12,500.21 UF	
7/1/21 - 6/30/22	$3,583.98 UF	$19,326.94 UF	$19,472.95 UF $1,231.60 UA	
7/1/22 - 6/30/23		$5,593.54 UA	$10,391.27 UF $8,276.60 UA	$39,734.56 UAB
7/1/23 - 6/30/24		$1,951.26 UF	$7,154.71 UF $19,833.63 UA	$41,638.89 UAB
7/1/24 - 6/30/25				
Total Award	$120,000.00	$120,000.00	$120,000.00	$112,288.00
Unpaid Balance	$1,982.82	$51,688.96	$33,411.80	$30,914.55

	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*	**Feasibility of a Timed Bright Light Exposure Therapy to Improve Circadian Function (Kaur) $60,000 (5/1/2023) $60,000 (5/1/2024)**	**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)**	**Cue High-Speed Multidirectional Yoga: Impact on Retinal Microvascular and Cognitive Measures (Signorile) $59,997 (5/1/2023) $59,742 (5/1/2024)**
7/1/18 - 6/30/19				
7/1/19 - 6/30/20				
7/1/20 - 6/30/21				
7/1/21 - 6/30/22	$6,801.70 UAB			
7/1/22 - 6/30/23	$14,028.50 UAB			
7/1/23 - 6/30/24	$135,530.06 UAB			$21,531.66 UM
7/1/24 - 6/30/25				
Total Award	$60,400.00	$120,000.00	$121,532.00	$119,739.00
Unpaid Balance	$4,039.74	$120,000.00	$121,532.00	$98,207.34

balances as of 2/29/2024

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
Remaining Balance			**$15,058.05**

MBRF Operating & Communications Budget
7/1/2023 - 6/30/2024

Operating Expenses

	Budget	Actual
Board of Trustee Fees	$320,000.00	$160,000.00
Legal Fees	$24,000.00	$21,161.90
CPA Fees	$20,000.00	$3,099.00
Consulting Fees*	$228,000.00	$146,249.95
Truist Bank Fees	$170,000.00	$98,508.82
Taxes	$107,000.00	$50,000.00
Meetings	$30,000.00	$22,767.43
Website Fees	$840.00	$840.00
Memberships	$4,815.00	$4,830.00
Conferences/Travel - Executive Director	$3,000.00	$2,452.78
Strategic Planning **	$10,000.00	$10,158.56
Insurance	$1,667.00	$1,652.63
Total Operating Expenses	**$919,322.00**	**$521,721.07**

Communications Expenses

	Budget	Actual	
Whereoware		$6,666.00	
BRG Communications			
Phase One Activities (July - November)	$125,000.00	$164,200.00	
Phase Two Activities (November - February)	$65,000.00	$47,500.00	
Phase Three Activities (February - June)	$310,000.00	$68,210.74	
Website Support and Social Media Advertisir	$1,500.00		
Out of pocket expenses for social media promotion, web hosting and support functions		$201.00	MailChimp
		$1,895.10	Facebook
		$936.00	Google
		$150.00	Zoom
		$850.00	Pantheon
		$36.00	At Net Domain Renewal
		$696.00	Paperturn Brochure Hosting Service
		$15.00	Canva Trial Subscription
		$60.00	Punchbowl Holiday card subscription
Senior Communications Advisor Consulting F	$81,000.00	$53,250.00	
Travel	$2,500.00	$1,169.79	
Total Communications Expenses	**$585,000.00**	**$345,835.63**	

Budget approved at May 3, 2023 Board of Trustees' Meeting

** represents payment to Executive Director*

*** Strategic Planning Budget was approved via email and added to budget* , fee is $10,000 plus expense reimbursements

Membership & Governance Committee Activity Timeline
For the Period June 1, 2021, to June 30, 2024

Updated March 8, 2024

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	Size of 7 Trustees, plus 1 Corporate Trustee and 1 Chair Emeritus was established as goal (Maximum 11 Trustees)	June 27, 2019	DONE
	Update/Revise Orientation Packet for New Trustees	The orientation packet required the addition of new material and updated information	October 5, 2020 June 2023	Completed and presented to new Trustees and posted on the secure site
	Provide Ongoing Updates to the Orientation Packet as needed	Appointments of New Trustees and the new Executive Director necessitated updating the orientation material	January 2022 August 2022 June 2023	DONE DONE DONE
	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	DONE (2) DONE (1)	New Appointments to the Board of Trustees: Dr. Patricia Boyle September 2020 Dr. Allison Brashear September 2020 Dr. John Brady

				December 2021
		Any in 2024/2025?	DONE (2) At its March 4, 2024 committee meeting, the committee decided not to add a public member at this time.	Dr. Sharon Brangman July 2023 Dr. Roy Hamilton July 2023
	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 Ongoing Oct 11,2022 October 27, 2022 January/February 2023 At its March 4, 2024 committee meeting, the committee decided not to add a public member at this time	DONE DONE DONE DONE DONE DONE

"identify, recruit, and recommend…" Continued	Develop Process for Recruiting, Vetting, and Recommending Candidates **(The following is a summary of the process document and a reminder of steps in the process)**	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
	Names Submitted to and Reviewed by Committee			
	Selected Names Forwarded to Board with vetting information and Committee recommendation			
	Board selects Candidates to contact			
	Nominator and/or MBRF Chair (or Executive Director, if assigned) contact candidate(s) to assess interest and request CV			
	Committee conducts further vetting, reviews CVs, ranks candidate(s), and makes final recommendation to Board			
	Board selects finalist(s), invites to interview, can invite to attend events or trustees meeting. Trustees vote on appointment. Vote must be unanimous			
	New Trustee(s) notified. Executive Director requests time for orientation call. Orientation provided by Executive Director and current Trustee as approved by MBRF Chair.			
"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.	September 2019 October 2019 January 2020	The Committee developed new self-assessment form and process.

		New form was distributed for January 2021 Review of Input on Forms and conversations with the Chair	Self-Assessment January 2021 Conversations took place with Chair Feb. 2021	No new changes to form were suggested
	Identify needed questions and revisions to the current Trustee Self-Assessment Form			DONE ONGOING
	Decide to send either current form or revised form in January with responses due to corporate trustee in one – two weeks		December 2019 January 2020 January 2021	MBRF proceeded as has been done in the past in 2019/2020 New Form used in 2021 and 2022
	Discuss whether to develop Board Self-Assessment to review progress toward Board goals (this would be an assessment of the impact of the full Board of Trustees)		March 2020 Considered in 2021	Request for Suggestions to improve Board were added to individual Self-Assessment as a way to assess the full Board's impact DONE
		Self-Assessment form distributed to Trustees and Returned to Corporate Trustee	Dec. 2021 January 2022 Dec. 2022 Dec. 2023	There were no changes to the form from 2021
"…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 Committee approved an amendment to trustee term of service at its March 4, 2024 meting	March 4, 2024	DONE The Board will discuss the proposed amendment at its March 19, 2024 meeting.

"…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

	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	

MINUTES
MCKNIGHT BRAIN RESEARCH FOUNDATION
Membership and Governance Committee
TEAMS Conference Call
March 4, 2024

The Membership and Governance Committee of the MBRF TEAMS conference call was called to order at 5:00 p.m. ET on March 4, 2024.

The following members were present:

Dr. Susan L. Pekarske, Chair of the Membership & Governance Committee
Dr. Michael Dockery, MBRF Chair
Dr. J. Lee Dockery, Chair Emeritus, MBRF
Dr. Madhav Thambisetty, MBRF Vice Chair
Ms. Melanie Cianciotto, Corporate Trustee,
Truist Bank Foundations and Endowments Specialty Practice

Others attending:
Dr. Angelika Schlanger, Executive Director

1. Call to Order/Welcome/Roll Call

Dr. Sue Pekarske, Chair, welcomed the committee members and thanked them for their review of the materials in preparation for the meeting.

2. Approval of Minutes from August 29, 2023 Meeting

The minutes from the August 29, 2023, meeting (Attachment 1) were reviewed and approved as amended. The changes are:

Change EST to ET after 5:00 p.m. and 5:55 p.m.

Action Item 1: The minutes from the August 29, 2023, meeting (Attachment 1) were approved as amended.

3. Review of Updated Committee Activity Timeline

The updated Committee Activity Timeline was shared with the committee for information (Attachment 2).

Action Item 2: The committee received the updated Committee Activity Timeline for information (Attachment 2).

4. Trustee Self-Assessment Update

a. Report on Number Completed/Received

Dr. Pekarske shared that Trustee Self-Assessment Forms were received from all of the Trustees with the exception of Dr. Brangman and Dr. Hamilton. They did not have to complete the assessment form, since both started their first terms on July 1, 2023 (and, therefore were not with the foundation for the entire year).

b. Follow-up Conversations with Trustees

Dr. Mike Dockery shared that he spoke with each of the trustees separately to review their Self-Assessment form. Suggestions to improve communication, particularly with more succinct communication in emails, seemed to be a common theme.

c. Summary Report to the Board of Trustees

Dr. Dockery will share a summary of his discussions at the March 19, 2024, Trustees' Meeting.

5. Membership of the Board of Trustees

a. Proposed Amendment to Trustee Term of Service

Dr. Pekarske shared the Proposed Amendment to Trustee Term of Service (Attachment 3). The proposed amendment was reviewed at the October 22, 2023, Trustees' Meeting. At that time, it was decided to table the discussion and have the Membership and Governance Committee review and revise the proposed language based on the feedback from the board.

The committee reviewed the proposed amendment and made the following suggested revisions:

Item 6 – reworded to read the following "*Under special circumstances, additional terms of service as Trustee in excess of nine (9) years can be requested and approved by the Board of Trustees under the following conditions:"*

Item 6 a – add "unique" before qualifications

The committee recommends approval of the Trustee Term of Service section of the MBRF Qualifications for New Trustee document as amended to the full board. The committee authorized the Executive Director to review the proposed language with the Foundation's legal counsel in advance of the full board review.

b. Review, Monitor and Build Board Membership to Optimize Diversity and Skillsets

The committee feels that the board has reached a nice number of Trustees at the current time, with a well-rounded mix of expertise and skillsets, and has strived to improve diversity.

c. Discussion/Consideration of Adding Public Member(s)

The committee discussed adding a Public Member to the Board. The committee feels the current board works well together and has been very productive. In addition to the onboarding of two new Board members, there is a lot going on right now and onboarding an additional new member at this time may be disruptive. After discussion, the committee decided now is not the best time to consider adding a public member.

d. Succession Plan for Trustees

The committee feels this is addressed in part through the use of the Trustee Appointment History and Terms document, as well as through the job descriptions that have been created for the various positions, including Chair, Vice Chair, Chair Emeritus, Executive Director and Corporate Trustee, and the Trustees Responsibilities and Duties Document.

There being no further business, the meeting was adjourned at 5:55 p.m. ET.

Summary of Action Items:

Respectfully Submitted,

Melanie A. Cianciotto
Truist Bank, Corporate Trustee

McKnight Brain Research Foundation
Qualifications for New Trustee

1. The Board of Trustees must be composed of at least three (3) and not more than eleven (11) individual Trustees and one (1) Corporate Trustee.

2. A Trustee must have either a Medical Degree or a Ph.D. Degree in one of the Basic Sciences or an equivalent degree in fields thought to be of benefit in advancing the Mission and Purpose of the MBRF.

3. It is desirable for a Trustee to have been an active practitioner, an active research scientist, a medical educator, have experience in administrative medicine or to be active, or have past experience, in a field or profession thought to be of value in advancing the Mission and Purpose of the MBRF.

4. An additional Trustee or replacement Trustee must be elected by a unanimous vote of the current Trustees.

5. The length of term is three (3) years, which may be renewed for additional terms, pending approval of the Board of Trustees, for a maximum of nine (9) years.

6. *Under special circumstances, additional terms of service as Trustee in excess of nine (9) years can be requested and approved by the Board of Trustees under the following conditions:*

    a. *The Trustee possesses unique qualifications and experience beneficial and desired by the McKnight Brain Research Foundation.*

    b. *The specific Trustee has declared an interest in and is agreeable to serving additional terms.*

    c. *The appointment of a Trustee for an additional three (3) year term of service must be approved by a unanimous vote of the current Trustees.*

7. A Trustee must be committed to the Values, Vision, Mission and Code of Ethics of the McKnight Brain Research Foundation.

Approved April 19-20, 2005 Trustees Meeting
Reviewed and reaffirmed, April 16-18, 2008 Trustees' Meeting
Reviewed and reaffirmed, March 14, 2012, Trustees' Meeting
Approved October 14, 2014
Reviewed and reaffirmed, July 25, 2017
Reviewed and amended, May 8, 2018
Reviewed and amended July 31, 2019
Approved Length of Term added to document (#5) July 22, 2020
Reviewed and amended March 19, 2024

MBRF Trustee Appointment History and Terms

August 2023

	First Appointment	Renewal Second Term	Renewal Third Term	Conclusion of Board Service if Extended For 3rd Term
Trustees				
Michael L. Dockery, MD MBRF Chair	May 26, 1999	n/a	n/a	Founding Trustee Permanent Appointment
Madhav Thambisetty, MD, PhD MBRF Vice Chair	August 12, 2015	July 16, 2018	August 12, 2021	August 12, 2024
Susan L. Pekarske, MD	July 1, 2018	July 1, 2021	July 1, 2024	July 1, 2027
Patricia Boyle, PhD	Oct. 1, 2020	Oct. 1, 2023	Oct. 1, 2026	Oct. 1, 2029
Allison Brashear, MD, MBA	Oct. 1, 2020	Oct. 1, 2023	Oct. 1, 2026	Oct. 1, 2029
John E. Brady, MD	January 1, 2022	January 1, 2025	January 1, 2028	January 1, 2031
Sharon A. Brangman, MD	July 1, 2023	July 1, 2026	July 1, 2029	July 1, 2032
Roy H. Hamilton, MD	July 1, 2023	July 1, 2026	July 1, 2029	July 1, 2032
J. Lee Dockery, MD, Chair Emeritus	May 26, 1999	n/a	n/a	Founding Trustee, Chair Emeritus Permanent Appointment
Melanie Cianciotto, Corporate Trustee	May 26, 1999	n/a	n/a	Duration of Tenure Truist

Nina Ellenbogen Raim, MD, JD,
Founding Trustee,
Was Named Trustee Emerita
April 10, 2019

Finance Committee Activity Timeline
For the One-Year Period July 1, 2023, to June 30, 2024

Updated February 22, 2024

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) Efficient Frontier Analysis (Shelly Simpson) Monte Carlo Simulation Investment Performance Review	July 24, 2023 July 24, 2023 July 24, 2023	***completed*** ***completed*** upon recommendation by Truist or request of the MBRF ***completed***
		Investment Performance & Asset Allocation Review (Mike Hill)	October 22, 2023	***completed***
		Investment Performance & Asset Allocation Review (Mike Hill)	March 19,2024	
		Investment Performance & Asset Allocation Review (Mike Hill)	May 17, 2024	

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	July 24, 2023 October 22, 2023 March 19, 2024 May 17, 2024	***completed*** ***completed***
	Compensation Review	Examples Presented for Comparison	July 24, 2023	***completed***
	Tax Filing	Legal Counsel for the MBRF reviews the completed tax form before filing		
	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	July 24, 2023 October 22, 2023 March 19, 2024 May 17, 2024	***completed*** ***completed***
		Travel Award Program Report	July 24, 2023 October 22, 2023 March 19, 2024 May 17, 2024	***completed*** ***completed***
	Review MBRF Operating Expenses	Year to Date Operating Expenses Report	July 24, 2023 October 22, 2023 March 19, 2024 May 17, 2024	***completed*** ***completed***
		Review & Approve Annual Operating Budget	May 17, 2024	

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 22, 2024	***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	September 22, 2022	***Completed*** *Signers are good for 5 years unless there is a change in the signers for the account*
	Conflict of Interest	Conflict of Interest Policy signed by all new and re-elected Trustees and by all Advisory Members of MBRF Committees	ONGOING	

MINUTES
MCKNIGHT BRAIN RESEARCH FOUNDATION
Finance Committee
Via TEAMS
January 22, 2024

The Finance Committee of the MBRF TEAMS conference call was called to order at 5:05 p.m. EST on January 24, 2024 (See Agenda – Attachment 1)

The following members were present:

Dr. Michael Dockery, MBRF Chair
Dr. Sue Pekarske, Trustee
Ms. Melanie Cianciotto, Corporate Trustee,
Truist Foundations and Endowments Specialty Practice

The following members were absent:
Dr. Allison Brashear, Chairman

Others attending:
Dr. Angelika Schlanger, Executive Director

1. **Approval of Minutes**
   The minutes of the MBRF August 22, 2023, TEAMS Committee conference call (Attachment 2) were reviewed and approved as presented.

   Action Item 1: The Finance Committee members approved the minutes of the August 22 2023, Finance Committee TEAMS conference call as amended (Attachment 2).

2. **Review of the Updated Finance Committee Activity Timeline**
   The Finance Committee reviewed the updated Finance Committee Activity Timeline (Attachment 3) for information.

   Action Item 2: The Finance Committee members received the updated Finance Committee Activity Timeline (Attachment 3) for information.

3. **Review Financial Information in the MBI Annual Reports**
   The Finance Committee reviewed the financial information provided in the MBI Annual Reports (Attachment 4).

a. University of Alabama at Birmingham

The committee had the following questions/comments regarding the financial information:

Please fill in the "institute" line on each report.

The general starting balance for all Endowments is listed at $18,299744.91, but the ending balance from last year's report was $18,010,730. These should be the same. Which is correct, or please provide an explanation for the difference.

All the reports list the distributions as additive to the ending balance, but these amounts should be subtracted. Please correct and resubmit.

All the reports list the investments as a negative return. Is this correct?

The general summary report lists "additional contributions" as $28,379.22. In looking through the various items, these come out of individual Endowments as:

+ $35K into the Lowder Professor

+ $250K into the Rebecca Gale Professorship

- $256,260.78 OUT OF the Protective Life Chair. How can there be a negative contribution, and if so, why and where did it go, and under whose authority?

Under the Protective Life Chair in Healthy Aging, it states that the starting amount for this FY as $1,610,040.24, but the ending amount on last year's report was $1,321,025. Which is correct and why?

Under the Matching Funds sheet, what are you defining as "corpus"? Some monies are different from last year. The total at the bottom of this page is off by $1.

Prior correspondence (from 2021) indicated that successive $250K contributions are planned for 2022 and 2023 to bring the Gale Professorship up to $1.5M by the end of the year (2023). Please provide an update.

Please provide an update on the status of the 2023 Annual Report which has not yet been received.

b. University of Arizona

The committee had the following questions/comments regarding the financial information:

The second page of the report states that the UA Foundation provided a financial report to the MBRF with an end date of 6/30/2023. Please provide a copy of that report.

The 2022 Annual Report lists the unmatched balance as $417,568. The 2023 Annual Report notes that $161,587.81 was given towards that unmatched balance. The difference between these two numbers is $255,980.19 (not $207,954.85 as listed in the 2023 Annual Report). Were additional funds received between 11/20/2022 and 6/30/2023? If so, how much and how can this be reported?

Provide an update on the status of the 2023 Annual Report which has not yet been received.

c. University of Florida

The committee did not have any questions/comments regarding the financial information.

d. University of Miami

The committee had the following questions/comments regarding the financial information:

The committee requests clarification of the following statement found at the bottom of the report:

**Half remaining FY23 funding used this year and half will be used in FY 25

4. <u>Proposal for Funding the Evelyn F. McKnight Clinical Translational Research Scholars Dinner at the 2024 AAN Meeting</u>

The Finance Committee reviewed the proposal for funding the Evelyn F. McKnight Clinical Translational Research Scholars Dinner at the 2024 AAN Annual Meeting (Attachment 5). The Finance Committee recommends approval of the $4,400 budget for the McKnight Clinical Translational Research Scholars Dinner at the 2024 AAN Annual Meeting to be paid from the MBRF Travel Award Fund.

Action Item 3: The Finance Committee recommends approval of the $4,400 budget for the McKnight Clinical Translational Research Scholars Dinner at the 2024 AAN Annual Meeting to be paid from the MBRF Travel Award Fund.

5. **Next Steps/New/Old Business**

Ms. Cianciotto shared the feedback and final costs from the 2023 MBRF SfN Poster Session (Attachment 6). The final cost of the Poster Session was $24,450.97 versus an approved budget of $26,800. The committee recommends asking Ms. Hixon to submit a proposal for the 2024 MBRF SfN Poster Session.

Dr. Schlanger discussed ideas of how to commemorate and celebrate the MBRF's 25th anniversary, this would include having BRG develop a 25th Anniversary video to showcase at the Cognitive Aging Summit IV and 2024 Inter-Institutional Meeting, and other promotional activities. She asked the committee if they would consider reviewing an estimated budget for these items. The committee recommends that Dr. Schlanger present a budget to the committee by email.

There being no further business, the meeting was adjourned at 6:00 p.m. EST.

Summary of Action Items:

Respectfully Submitted,

Melanie A. Cianciotto
Truist Bank, Corporate Trustee

Proposal
McKnight Brain Research Foundation Poster Reception
In conjunction with the
Society for Neuroscience (SfN)
Chicago, IL
October 6, 2024

Background

Scientists from around the world gather annually at the Society for Neuroscience (SfN). SfN gives investigators an avenue to share their research. Beginning in 1971, the meeting has grown and now has an annual attendance of thousands. It consists of poster sessions, symposia, and lectures presenting the latest findings on numerous topics. In the evening hours, the Society sponsors themed social events. These socials provide a casual atmosphere in which researchers interested in a particular topic can network.

In 2008, the McKnight Brain Research Foundation began sponsoring a poster reception in conjunction with SfN. This gives investigators from the four McKnight Brain Institutes located at the University of Arizona, the University of Florida, the University of Miami and the University of Alabama at Birmingham (UAB), an opportunity to display their research and share their findings. SfN normally rotates between the cities of San Diego, California, Chicago, Illinois and Washington DC.

2023 Progress Report Washington, DC

The 13th Annual McKnight Brain Research Foundation Poster Reception was held at the Embassy Suites DC Convention Center on Sunday, November 12th from 5:00 to 7:00 p.m. There were approximately 150 guests, along with 67 registered posters and 3 additional posters which were added the night of the event. Abstracts received prior to the deadline were included in a poster competition. As space allowed, those submitting after the deadline were allowed to present their posters at the reception but were not included in the judging.

A QR code (Quick Response code) was used for the first time which allowed guests to view the posters via the QR code. The code was distributed prior to the event and prominently displayed on signage at the event. Using a cell phone or electronic device, the QR code allowed guests to view the posters at their leisure prior to the event, during the event, and after the event.

Registered posters included representation from all four McKnight Brain Institutes. The McKnight Brain Institute from the University of Florida received high marks as the awards went to Johleen Seedansingh (1st Place), Sabrina Zequerra (2nd Place), Katherine Gobnzalez (3rd Place), Zachary Simon (Honorable Mention), and Samantha Smith (Honorable Mention). Zoe Bassett from the Evelyn F. McKnight Brain Institute at the University of Miami Miller School of Medicine received an Honorable Mention.

Attendees included scientists, researchers, clinicians, postdoctoral fellows, graduate, and undergraduate students. Prominent scientists from the National Institutes of Aging as well as

neuroscientists at different stages of their careers interested in investigating age-related memory loss were in attendance. Posters were displayed and research was discussed throughout the evening.

A variety of hor d'oeuvres and drinks were provided. The event fulfilled its goal of showcasing McKnight research being conducted at all levels and provided a venue where neuroscientists were able to network and discuss ideas centered on normative aging. Establishing new collaborations is always a possibility when researchers gather to discuss their projects.

Proposal

The 2024 McKnight Brain Research Foundation Poster Reception will be held in Chicago, IL on Sunday, October 6, 2024. Pending budget approval, an event will be planned at one of the local venues. While viewing abstracts from each of the McKnight Brain Research Institutes, a selection of beverages and hor d'oeuvres will be available for guests to enjoy.

Records

Attendees will be required to sign-in and note the institute/organization they represent. Upon signing-in, attendees will receive two tickets for two free drinks. Using the ticket method, will encourage everyone to sign-in and will ultimately provide documentation needed to verify attendance. The tickets will also allow the event planner to monitor expenses associated with beverage purchases, thus ensuring the bar tab does not exceed the budget.

Budget

Poster boards will be rented from an outside vendor. Food and beverage costs have been broken down into three options. Caterer will be consulted and the best menu will be selected at a cost that is within the approved budget. As noted above, each attendee will receive 2 tickets for beverages thus providing a system to monitor beverage expenses. Using the approved budget, the catering expenses will be closely monitored to ensure no overages are incurred. The Appendix provides a 3-tiered budget proposal for consideration.

Appendix

	Tier 1	Tier 2	Tier 3
Standing podium and microphone set-up	$ 800	$ 800	$ 800
Rental of Poster Boards 35 Double sided boards Size 4'x6' Price includes delivery, set-up and removal	6,000	6,000	6,000
Printing	500	500	500
Photographer	400	400	400
Office supplies	200	200	200
Event Planner (Hourly rate) $50 x 46 estimated hours	2,300	2,300	2,300
Event Planner Expenses (Receipts to be provided for air, hotel 2 nights, meals, Uber to/from airport/hotel, airport parking)	1,200	1,200	1,200
Subtotal Miscellaneous Costs	11,400	11,400	11,400
Food Catering	Hot and cold appetizers	Hot and cold appetizers	Hot and cold appetizers
Beverage Catering	Small selection of beer and wine	Large selection of beer and wine	Open bar with wine, beer, and liquor
Subtotal Catering fees including service and tax	14,000	16,000	18,000
Estimated Grand Total	$25,400	$27,400	$29,400

Education Committee Activity Timeline
For the Years 2019 – 2024

Updated March 2024

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 Review of Topics and Content for Primary Care Physician (PCP) pages on website February 2021	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 drafting content for the PCP area of the website based on the approved outline navigation of the section	DONE June 30, 2020 DONE September/ October/November	

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
		The committee reviewed proposed navigation and drafted content for the Primary Care Physician (PCP) pages of the website Content will be revised and edited to include feedback from the committee and used to build out a mock-up of the PCP section An Update to the Trustees will be provided The PCP section will be shared with suggested primary care physicians for feedback and suggestions. Dr. John Brady, Chair of the Education Committee will be instrumental in helping to develop strategy and content	DONE February 2021 DONE February – March 2021 DONE April 30, 2021 Winter/Spring 2022 ONGOING	
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 but development of content is on hold until PCP content is identified and developed.	Winter/Spring 2022	
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

"shall review all educational materials…:	Brochure copy in development to raise awareness and promote the MBIs and MBRF to individuals, partners, donors	Review of Brochure was conducted and committee concurs with suggestions by Communications Committee	DONE Posted on website January 2021	
"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 14th Annual Inter-Institutional Meeting, UAB McKnight Scholars Will be invited to next Inter-institutional Meeting	2020 Meeting was canceled 2021 Meeting will be virtual Meeting was in-person Meeting was in-person Develop Feature on McKnight Scholars on McKnightBrain.org	April 28 & 29 2021 Mar 23-25, 2022 May 3-5, 2023	DONE Will help promote scholarship and engage scholars
	McKnight Scholars Dinner at AAN	2020 Toronto, AAN Meeting was canceled 2021 Virtual AAN Meeting Took place at the April 2023 AAN Meeting Finance C	April 17 – 22, 2021	Held over - MBRF approved funding of $4,000 to cover travel, hotel for the night, dinner, UM staff travel Approved by full board at February 2023 meeting
	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. 7th lectureship was by Dr. George Koop March 11, 2019 2020 Lecture was canceled.	Annual Lectureship established honoring the Founding Director of the Evelyn F. and William L. McKnight Brain Institute at the University of Florida Events as part of the William G. Luttge Lecture

			2021 Lecture to be held in Fall 2021 2022 Virtual Lectures January 13 - Dr. Alexis Stranahan, PhD, UF Feb 24 – Dr. Perla Moreno Castilla, PhD, "Rising Star" Luttge Lecturer, NIA March 3 – Dr. Dan Nicholson, PhD, Rush March 31 – Dr. Kirk Erickson, PhD, University of Pittsburgh 2023 Lecture: February 23rd – Dr. Joshua A. Gordon, MD, PhD, Director, National Institute of Mental Health (NIMH) 2024 Lecture: February 2, 2024 – Dr. Adam Gazzaley, M.D. Ph.D.	Series were expanded in 2021 to become a Lecture Series. DONE DONE Taking place during UF MBI 25th anniversary event
"work to elevate the importance of age-related cognitive decline and memory loss on the national agenda…(work toward) greater investment in research	IOM Study	"Public Health Dimensions of Cognitive Health" was released by the IOM (see attached document)	DONE April 14, 2015	Study funded by MBRF and federal agencies (NIA, CDC, NINDS, HHS), AARP, Retirement Research Foundation

and education by federal health agencies…."		Working Group formed under the lead of Dr. Molly Wagster	CURRENTLY NOT MEETING	
		MBRF has initiated and implemented several of the IOM recommendations.	ONGOING	
		Dr. Lee Dockery was in contact with IOM (now Academy of Medicine) about issuing a report on progress	October 23, 2019 NOT TO BE PURSUED	This would be unusual for the Academy of Medicine to do per Dr. Molly Wagster.
"work to elevate the importance of age-related cognitive decline and memory loss on the national agenda…" continued		Dr. Ralph Sacco, former President of AAN, recommended to AAN that they support adding age-related cognitive decline and memory loss to curricula for requirements	July 11, 2019	Letters were sent from AAN to MBRF, American Board of Psychiatry and Neurology, and ACGME
		Dr. Robert Wah and Dr. Lee Dockery spoke by phone with Dr. Gordon Smith, Chair, AAN Education Committee, and Dr. Jaffar Khan, Chair, AAN Graduate Education Subcommittee, to discuss collaborative steps	August 8, 2019	

		Follow-up communication with Drs. Smith and Kahn and Kathy Malloy re: schedule for review of special requirements by ACGME	DONE September 16, 2019 June 2020 NOT TO BE PURSUED	On distribution list for ACGME e-Communication with schedule for review of special requirements Committee feels they've done all they can do at this time.
	Discuss strategy to achieve MBRF Education goals to reach Primary Care Physicians and the Public. Discuss benefits of additional staffing and advisory groups working with the MBRF Identify and hire consultant for feasibility assessment and scoping document assessing the educational needs and opportunities with PCPs regarding cognitive decline.	Consultant (SCP) was selected by the Trustees on September 20, 2022 after a thorough vetting process, and the project kicked off on Oct 10, 2022 with a meeting with a group of Trustees. The study and final report will be completed February, 2023. SCP gave a progress update to Trustees at their Board Meeting. Another update to Trustees took place on Dec 21, 2022. SCP presented the draft scoping document to the Education Committee. The committee provided feedback to SCP. SCP is working to revise the document with a final version presented	Done March 13, 2022 October 10, 2022 October 27, 2022 Dec 21, 2022. Jan 25th, 2023	

		before the Feb 16, 2023 BoT meeting. SCP presented the final report at the February 16, 2023 Board of Trustees meeting. A consultant may be needed to implement the Education Initiative. If so, the Education Committee will make a recommendation to the Trustees on seeking and engaging a firm to implement the initiative	 February 16, 2023 TBD	
	Education Outreach Initiative to Primary Care Providers and Consumers	Key Messages document was completed for both PCPs and consumers, with input from Trustees Outreach to national organizations has taken place to aligned organizations to explore potential synergies and partnerships; outreach began in March 2023. Updates will be provided to the education committee and board on an ongoing basis. SMRC and UW submitted proposals to advance the MRBF's Brain health initiative. GSA submitted a concept paper.	March 2023 Ongoing July 11, 2023	

		The Committee discussed the proposals and did not advance a recommendation for approval to the board. Committee goals and strategies for 2023 - 2027 were identified as part of the Strategic Planning Process. It was decided that the comprehensive campaign objectives will drive the goals and strategies of both the communications and education committees. Committee deliverables for the campaign were completed. Committee reviewed resource hub categories, sources, and materials; also reviewed wireframe for the microsite for the communications campaign. Microsite is oriented toward consumers with a section for healthcare providers.	Completed in Oct, 2023 January 29, 2024	

MINUTES
MCKNIGHT BRAIN RESEARCH FOUNDATION (MBRF)
EDUCATION COMMITTEE
CONFERENCE CALL
January 29, 2024

The Education Committee of the MBRF was called to order at 4:00 pm EST on January 29, 2024, by Dr. John Brady.

The following members were present:

Dr. John Brady, Education Committee Chair
Dr. Michael Dockery, MBRF Chair
Dr. Sharon Brangman
Dr. Allison Brashear
Dr. Roy Hamilton

The following member was absent:

Dr. Patricia Boyle

Others attending:

Dr. Lee Dockery, Chair Emeritus
Dr. Angelika Schlanger, Executive Director
Ms. Valerie Patmintra, Senior Communications Advisor
BRG Team – Mr. Shannon McDaniel, Ms. Nicole Grady, Ms. Kate Worthy

1. Call to Order

Dr. Brady welcomed the members of the committee and Dr. Lee Dockery to the call.

2. Minutes of the November 27th, 2023, Meeting

The minutes of the November 27, 2023, joint Education and Communications Committee Meeting (Attachment 1) were approved as amended to reflect edits submitted via email.

Action Item 1: The minutes of the November 27, 2023, joint Education and Communications Committee Meeting were approved as amended to reflect edits submitted via email. (Attachment 1).

3. Updated Activity Timeline

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

4. Communications Campaign Update and Discussion

Ms. Worthy reviewed a draft of the Brain Works microsite landing page, which will feature (from top to bottom): a section summarizing the campaign purpose and call to action; a section featuring the MBRF's resources; the Brain Works resource hub; and a "Hot Topics" section, which would rotate the latest news on cognitive aging and brain health. The Trustees discussed the benefits of having a "Hot Topics" section and recommended that parameters be developed to determine the appropriate items that would be rotated into this section. The Trustees agreed that scientific studies or medical content would need to be vetted by the Trustees. BRG will develop a protocol to share with the Trustees that will describe the vetting process. Dr. Brady suggested that the Education Committee could vet the scientific items.

Dr. Lee Dockery asked whether a question-and-answer section could be added to the site. Mr. McDaniel confirmed that this is possible, but that a vetting process would need to be developed for posting the answers. Dr. Michael Dockery suggested that this is a feature that could be explored and possibly added after the hub goes live.

Ms. Worthy reviewed, in depth, an outline of the partner resources suggested for inclusion on the Brain Works resource hub, which will be a carefully curated listed of resources on brain health. The hub will include the MBRF's own resources, as well as those developed by trusted and well-regarded organizations and government agencies that complement the Foundation's own resources. Dr. Michael Dockery shared that the original version of the hub included a category related to brain health disease-related conditions to be inclusive of providing answers to all questions that may come up related to brain aging, but these were removed based on Dr. Michael Dockery's guidance to avoid diluting the MBRF's messaging related to cognitive aging.

The committee discussed the proposed resources and organizations to be included in the hub (Attachment 3). Ms. Grady addressed questions as to why certain organizations were included and clarified that research from all four McKnight Brain Institutes will be represented in the "Research Highlights" section and updated regularly. Dr. Brangman raised questions about whether the site will be able to reach diverse audiences and if the site is best oriented for those who have a higher level of education and own a smartphone. Ms. Grady suggested that one way to reach out to those facing digital barriers is to share the Brain Works resources with community health centers and community-based organizations based in under-served communities.

Dr. Hamilton advised that the cognitive self-assessments listed in the hub should be tested for validity. He also suggested adding a disclaimer clearly stating that MindCrowd is a research study. Ms. Grady affirmed that the goals of including cognitive self-assessments is so that visitors could use these as tools at home and discuss their results with their doctors.

Dr. Michael Dockery suggested that each link be reviewed by members of the committee and that the links be divided up and assigned to the members. He also pointed out that, at times, the resource hub may include organizations that are more disease-focused in nature for the strategic purposes of expanding the MBRF's reach to new audiences.

Action Item 2: Dr. Schlanger will divide up the links from the resource hub and assign them to committee members for their scientific/medical review.

5. **Adjourn**

Dr. Brady asked if there was any further discussion. Hearing none, he called for adjournment of the meeting at 5:00 p.m. EST.

Summary of Action Items:

Action Item 1: The minutes of the November 27, 2023, Education Committee Meeting were approved as amended to reflect edits submitted via email. (Attachment 1).

Action Item 2: Dr. Schlanger will divide up the links from the resource hub and assign them to committee members for their scientific/medical review.

Respectfully Submitted,

Dr. Angelika Schlanger
Executive Director

Research Committee Activity Timeline

2022-2024

Updated March 8, 2024

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	DONE February 5, 2020 DONE June 15, 2020 DONE Feb. 26, 2021 Annual Reports were reviewed by the Trustees on Feb. 9, 2022	Reviewers presented at Feb. 2021 Trustees Meeting. Follow up letters were written and sent to each of the MBIs. All Requests of MBIs have been addressed by MBIs. MBRF/MBI Task Force was established April 2021 to streamline Annual Report Recommendations. Recommendations were reviewed Oct 28, 2021 by Trustees. New Template was used for 2021 Annual Reports
	Review of all New Funding Requests from MBIs. Most Funding Requests should be reviewed by the Interventional Core Committee of the MBIs first.	UM submitted a request for $200,000 for Neurocognitive Post-Doctoral Fellowship over the next two years Christian Agudelo, MD, was selected	October 23, 2019 Trustees voted to fund -- payable over two years. Position Start Date – July 2020	The notification letter mentioned that future funding should come from other sources (See "The Evelyn F. McKnight Neurocognitive Clinical Scholar in Brain Health and Aging" on page two)

		UA submitted a request for $244,400 for UM's participation in the Precision Aging Demonstration Pilot	The proposal was reviewed and approved by the Trustees on Feb 5, 2020. The budget was revised and approved June 2020	Dr. Mike Dockery notified UA of the Trustees' approval Trustees were notified of the revised budget and approved no-cost revisions
		A Funding Request "Centralized, telephone-based, computer-assisted…Spanish" for $129,000 was submitted in April 2021 by Dr. Ron Lazar	Reviewed by Cmte in July and not recommended	This request was reviewed by the Trustees in July 2021 and was denied. Suggestion was provided to Dr. Lazar to work though MBI Core Committee if he chooses to resubmit.
		UM submitted a request for $ 3 million to endow a Neurocognitive Training Fund in Brain Health and Aging. 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"	July 1, 2021 October 2021 Research Cmte reviewed on October 21, 2021; Recommended funding; Trustees reviewed and approved funding October 28, 2021 Grant Notification Memorandum was dated Nov. 10, 2021	This request was denied by Trustees on July 28, 2021, but Dr. Lee Dockery was asked to pursue conversations with UM about how they might proceed. Dr. Dockery had several conversations and exchanges with UM with ideas for strengthening the program infrastructure. 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 sent by Dr. Mike Dockery to UM and agreed to and signed by Drs. Sacco and Rundek.

"Encourage and assess research at the McKnight Brain Institutes (MBIs)" continued	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 at each Trustees' Meeting ON HOLD DUE TO UNIVERSITY TRAVEL RESTRICTIONS	Approved in 2009 In the amount of $100,000 Approximately $30,000 remains in the fund
	Inter-institutional Block Grants	Cognitive Aging Core Working Groups	N/A	5 Areas: Brain and Cognitive Health Cognitive Aging & Memory Cognitive Testing Battery Epigenetics MRI standardization
	Inter-institutional Block Grants	Bio-Informatics Core (Epigenetics)	Funding period: 9/1/2013-8/31/2015	Tom Foster, UF still lead scientist.
	Inter-institutional Block Grants	Neuroimaging Core	Funding period: 1/1/2015 to 12/31/2017 $931,759.00	
	Inter-institutional Block Grants	Cognitive Assessment and Brain Registry Core	Funding period: 9/1/2015-8/31/2017 Request for another extension was approved at the Feb 5, 2020, Trustees' meeting.	No-cost Extension Request submitted for April 30, 2021. Trustees approved the extension.
	Review of Pilot Grants (Funding Requests and Progress Reports)	1)A Novel Invention Tool – Levin 2)Revitalizing Cognition in Older Adults – Bowers	1)Funding Period: 5/1/2018-4/30/2020 2)Funding period: 5/1/2018-4/30/2020	1)Funding for 2-years for total of $120,000 2)Funding for 2-years for total of $120,000

				No-cost Extension Request submitted and approved for April 30, 2021.
		3)Transcutaneous Vagal Nerve Stimulation and Cognition Training – Williamson/Alexander	3)Approved July 2019 Funding period: 10/1/2019-9/30/2021 Deadline was extended	3)Funding for 2-years for total of $120,000
			Request for no-cost Extension	Trustees approved at their August 29, 2022 meeting
	Applications for 2021 Pilot Grants	5 Letters of Intent were Submitted	Research Cmte Reviewed LOIs for 2020 Jan. 29, 2021.	Trustees approved 3 grants
		3 Grants were approved	Feb. 26, 2021	
		With Dr. Gomes-Osman's subsequent departure from UM, the Core Committee recommended the next application in line to replace Dr. Gomes-Osman's. This was submitted by Dr. Sonya Kaur "Sleep Intervention…"	The Research Cmte did not recommend funding the next-in-line proposal in its July 2021 meeting "Reuniting the Brain and Body to Understand Cognitive Aging: The Nexus of Geroscience and Neuroscience" pilot grant August 2022	The Trustees denied funding and setting this precedent in its July 2021 meeting. Dr. Rundek was notified. Interim Report submitted. Trustees reviewed and approved on August 29, 2022
	Checked RFA for 2022 before it was posted to be sure it stresses Junior Faculty. It does.	Drs. Lazar and Levin shared that only 1 LOI was received for 2022 funding cycle.	January 31, 2022 Leadership Council Meeting attended by Drs. Thambisetty and Mike Dockery and A. Porter	Several reasons for only 1 LOI were cited. The Leadership Council drafted a new RFA to address these reasons and broaden the scope of the research for Trustee review at their February meeting

			February 23, 2022 September 12, 2022	Dr. Mike Dockery, on behalf of the Trustees, responded to the LC and the members of the Core Committee that they did not wish to change the focus of the pilot grant program by changing the RFA Dr. Mike Dockery, on behalf of the Trustees, and Angelika Schlanger attended the Leadership Council meeting and asked the Council to follow up with the MBRF on the status of the Cognitive Aging and Memory Intervention Core Workgroup, in terms of its membership and plans to respond to the Memo from February 23, 2022.
	2023 Pilot Grants	5 Applications Submitted on February 7, 2023 via Ron Lazar and Bonnie Levin. The research Committee approved three of the pilot grant applications.	March 28, 2023	Dr. Sonya Kaur (PI): "Feasibility of a Timed Bright Light Exposure Therapy to Improve Circadian Function" Dr. Farah Lubin (PI): "Ketogenic Diet Improvement of Age-Related Memory Impairments, Nominates Cell-type Specific O-GicNAc Deficiencies in the Aged Hippocampus" Dr. Joseph Signorile (PI): "Cued High-Speed Multidirectional Yoga: Impact on Retinal Microvascular

				and Cognitive Measures"
"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 approved 2019 to begin Spring of 2020	Fund balance of $1 million from 2nd five-year partnership returned to MBRF Report received on all FNIH/MBRF activities RFA posted: "Network for Identification, Evaluation, and Tracking of Older Persons with Superior Cognitive Performance for Age" FNIH Report submitted For information only	DONE August 2019 FNIH Report in October 2019 had an error. A corrected report resubmitted on Feb. 5, 2020. Posted Feb 2020; Deadline LOI Sept. 1; Application October 1, 2020 First payment was made to FNIH by March 31, 2021. Will continue until 2025 Dr. Molly Wagster will be attending the March 23-25 Inter-institutional Meeting at UA. The Trustees have invited her to present at their	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) 2014 Partnership renewal funded one 5-year project for $15 million with $5 M from MBRF and $10 M from NIA Valerie connected with Julie Wolf-Rodda and Molly Wagster on promoting STARRS study. NIA will provide $14M to be pooled with MBRF $5 M. A 2.8 Match. RFA was shared with Communications Working Group for posting and with Leadership Council. Two grants were provided from the Research Partnership ""Network for Identification, Evaluation and Tracking of Older Persons with Superior Cognitive Performance for their Chronological Age" to Dr. Thomas

			meeting on March 23, and to the idea of inviting the grantees for a video presentation. Dr. Julie Gerberding, Julie Wolf-Rodda, FNIH, and Dr. Molly Wagster, NIA, attended MBRF Trustees Meeting on October 27, 2022, in DC Planning for CAS IV is underway. The date and location will be March 20-21, 2024 in Bethesda, MD	Perls, Boston University, and Dr. Emily Rogalski.
"Identify opportunities…to foster greater interest in cognitive aging and age-related memory loss (in the scientific community)"	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 underlying cognitive aging and memory loss.	Program was Approved by the Trustees Potential administrative and/or funding partners were approached American Federation of Aging Research (AFAR) was identified as an excellent partner organization. AFAR presented a proposal and draft contract for review Revised Agreement signed between AFAR and the MBRF	October 14, 2020 December 2020 January 2021 February 2021 2021 July 15, 2021 August 2021 Mid Oct. 2021 Dec. 15, 2021 March 2022 2022	AFAR Review Committee: Chair: Dr. Anna Maria Cuervo Members: Dr. Rafa de Cabo Dr. Thambisetty Dr. Boyle and Dr. Roz Anderson LOI Deadline – 9 LOIs Received LOI Review – 7 applicants asked to submit full application Application Deadline Award Announcement

			August 2, 2022 September 19, 2022 December 7, 2022 July 31, 2023 Sept 7, 2023	*LOI Submission and review was eliminated due to the small number of applicants in 2021* Application Deadline Application Review – 4 applied. Award Announcement 2023 5 Applications Received Dr. Roy Hamilton joined the review committee Application Review
	Reserve & Resilience Workshop 2019 Reserve & Resilience Workshop Pilot Grants 2020 Reserve & Resilience Workshop 2021 Reserve & Resilience Workshop 2023	Over 300 Attendees (8 MBI researchers) Organizers requested $30,000 to support (1 – 3) pilot grants	September 9 and 10th, 2019 Bethesda In-Person Meeting CHANGED TO VIRTUAL MTG September 14 and 15, 2020; Report Submitted Jan. 2021 Oct 31/Nov 1 Bethesda Meeting will be a hybrid – part virtual and part person. The program is posted on reserveandresilience.com. Of note, Jen Bizon and Tom Foster are panelists.	This is an outcome from Cog. Aging Summit III held in 2017. Research Committee approved support in first and second years. Dr. Stern requested support for the Final R & R Workshop (#4) to take place Oct. 31/Nov. 1 in Bethesda. He did not request a specific amount but support MBRF provided last year was $30,000. Committee supports recommendation to fund at no more than $30,000, and full board approved the grant on July 24, 2023.

			In-person meeting took place on September 21 – 22, 2023 in Bethesda, MD on "Data Sharing." Panelists include Carol Barnes, Matt Huntelman, Thomas Foster, PhD, and Sara Burke.	Final Report was submitted by Dr. Stern and reviewed by the Research Committee on January 29, 2024
"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)	2021-2022 MBRF Reviewers are Dr. Boyle, Dr. Thambisetty, and Dr. Isaacson	Reviewers meet in Dec. Two Scholars are selected and alternates were identified. Awardees are notified in January. Funding starts July 1 of each cycle Edits to 2021 RFA were made and approved by Research Cmte. RFA was posted as of July 4, 2020, on AAN site. Advertising followed 2019 Plan for 2020 Award and begin in August, 2020. 8 applications for 2021 were received. October 14, 2020, Renewal for next five years was approved by the Trustees 2022-23 Deadlines	First Scholarships Awarded January 2018 (McConnell, Albert) Second Scholarships Awarded January 2019 (Camargo, Sedaghat) Third Scholarships Awarded January 2020 (Baxter, Getz) Fourth Scholarships were Awarded in January 2021 to Dr. Wendy Yau Wai-Ying (Brigham and Women's) and ~~Dr. Matthew Burns (UF)~~ Dr. Reem Waziry (Publicly announced in April 2021 (Dr. Matthew Burns [UF] received a K-Award from NIA and had to decline the McKnight Scholarship.) Fifth Scholarships Advertising was conducted in August and September 5 Applications received Oct. 1. Review was in Dec. 2021 Sixth Scholarships

		Members of the 2022-23 Review Committee include Dr. Madhav Thambisetty and Dr. Patricia Boyle Members of the 2023-24 Review Committee include Dr. Madhav Thambisetty, Dr. Patricia Boyle, and Dr. Roy Hamilton	September 1, 2022 Application Deadline Spring 2023 Announcement of Recipients The review committee met In November, 2023.	New 2022-23 RFA Draft was reviewed and has been posted and advertised - 9 applications were reviewed 2023 Scholars Announced (Drs. Eva Klinman, MD, PhD and Sheena Baratano, MD, PhD) <u>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.
"Encourage young investigators…" Continued	Poster Reception at 2019 Society for Neuroscience annual meeting (Chicago) MBRF/MBI Poster Reception 2020 Society for Neuroscience (SfN) annual meeting in DC October 24 – 28, 2020 canceled due to DC pandemic closing guidelines Society for Neuroscience will meet in San Diego Nov 12 - 16		October 20, 2019 August 29, 2022 September 5, 2022	First Poster Reception held in 2008. (50 submissions received) Sponsored by MBRF. Hosted by Directors of MBIs. Submissions open to researchers at MBIs and invited guests only MBRF Trustees Decided not to host the MBRF/MBI Poster session at the 2022 meeting. Dr. Mike Dockery updated the Leadership Council on Sept. 12, 2022 by Zoom. Dr. Mike Dockery wrote to the Leadership Council to ensure it will take place in 2023.

	Society for Neuroscience will meet in DC, Nov 11 - 15 Society for Neuroscience will meet in Chicago, October 5 - 9		September 1, 2022	Ms. Porter wrote to Dr. Molly Wagster to alert her that the poster reception will not take place this year. The poster session took place on Nov 12, 2023, planned by Vicki Hixon. Dr. Thambisetty represented the MBRF. Sixty-seven abstracts were submitted. Vicky Hixon has submitted a proposal to organize the poster session to take place on October 6th. The trustees will review the proposal at their March 19, 2024 meeting.

MINUTES
MCKNIGHT BRAIN RESEARCH FOUNDATION (MBRF)
RESEARCH COMMITTEE
CONFERENCE CALL
January 29, 2024

The Research Committee of the MBRF was called to order at 5:30 pm EST on January 29, 2024, by Dr. Madhav Thambisetty.

The following members were present:

Dr. Madhav Thambisetty, Chair of the Research Committee, Trustee
Dr. Mike Dockery, MBRF Chair
Dr. Roy Hamilton, Trustee

The following members were absent:
Dr. Patricia Boyle, Trustee
Dr. Sue Pekarske, Trustee

Others attending:

Dr. Lee Dockery, Chair Emeritus
Ms. Melanie Cianciotto, Corporate Trustee
Dr. Angelika Schlanger, Executive Director

1. Call to Order

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

2. Minutes of the September 20, 2023 Meeting

The minutes of the September 20, 2023, Research Committee Meeting (Attachment 1) were approved as amended.

The changes were:

5 a. third paragraph – add "of" before "high quality"

5 b. first sentence – add a space before (Attachment 6)

Action Item 1: The minutes of the September 20, 2023, 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. MBI Leadership Council's Proposal

The committee reviewed the Cognitive Aging and Memory Intervention (CAMI) Core Pilot Grant Program proposal (Attachment 3). The proposal was submitted by Dr. Sara Burke on behalf of the Leadership Council and represents a consensus plan to revitalize and organize a robust, sustainable CAMI Core Pilot Program.

The committee discussed the proposal at length and appreciates the significant progress that has been made toward developing a sustainable infrastructure and strategy that would revitalize the Pilot Grant program and reconstitute the CAMI Core. The committee's main concerns revolved around strong and continuous leadership for the program, as well as having champions at each MBI to ensure that the program is being promoted to increase the number and quality of applications.

The committee requested the proposal be revised and resubmitted to address the following questions/comments:

- Since the Cognitive Aging and Memory Intervention (CAMI) Core proposal was approved in 2016, the trustees request a reaffirmation or suggested modification to the vision statement and core objectives of the CAMI Core Pilot Grant program.

- A shared priority for the Pilot Grant Program is to increase the number and quality of proposals submitted. Please describe, in greater detail, the communications plan to accomplish this goal. Please outline the specific strategies that will be used to ensure that potential applicants are aware of the opportunity and encouraged/motivated to apply.

- The MBRF recommends that members of the CAMI Core be senior faculty. We hope that this criterion can be included in the updated proposal and that the proposed membership of the Core aligns with this direction.

- Concerns were raised that previous recipients of the pilot grant awards may not be experienced enough to evaluate the proposals. Can the composition of the review committee be revised to ensure that all members are senior investigators?

- Due to conflict-of-interest issues, a member of the MBRF board or staff may not serve as the Scientific Review Officer (SRO). Please propose an alternative profile of an individual who can serve in this role.

The committee also deliberated adjusting the budget for the program, citing rising costs of equipment and staffing, and whether basic science applications should be funded at a different level than clinical or translational projects. Finally, it was suggested that the pilot grant program should be focused on a particular set of focus area(s) each year, as recommended by the CAMI Core.

Dr. Schlanger will draft a response to the Leadership Council sharing the concerns/comments of the committee and request that the proposal be revised and resubmitted.

Action Item 2: Dr. Schlanger will draft a response to the Leadership Council sharing the concerns/comments of the committee and request that the proposal be revised and resubmitted.

5. Current Grants/Programs

a. McKnight Brain Aging Registry (MBAR) Proposal Update

Dr. Schlanger provided an update on the McKnight Brain Aging Registry (MBAR) Proposal. Dr. Kristina Visscher is taking the lead on drafting the proposal for submission to the MBRF in February. However, Dr. Visscher did clarify that her intent is to provide the best infrastructure possible for the resource for others to use in their development of proposals to NIH but does not feel she is the best person to lead those future proposals.

b. MBRF Innovator Awards in Cognitive Aging and Memory Loss (AFAR)

AFAR is in the process of fielding a survey to identify non-financial forms of institutional commitment. They will gather these findings and share them with their recommendations, alongside their draft renewal proposal, hopefully in time to be reviewed at the March meeting of the MBRF Trustees.

c. MBRF Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss (ABF)

Dr. Schlanger spoke with ABF to get their thoughts on why the applications fell this year, and to explore strategies for increasing engagement in future years, which yielded the ABF NGRG Marketing and Applications Trends Memo (Attachment 4). The memo contains suggestions for increasing engagement and aligned applications.

One recommendation for the 2025 grant cycle is to host an informal webinar for prospective applicants. The webinar could offer an opportunity to educate and excite prospective applicants about the McKnight scholarship opportunities. ABF recommends that this webinar be led by an MBRF Trustee who has reviewed applications in the past, and can speak to the components of a successful application.

The committee approves this recommendation and Dr. Hamilton is willing to participate in the webinar.

Dr. Schlanger also shared that she introduced the MBRF's main contacts at ABF and AFAR. The meeting went well, and the teams will collaborate to cross-promote each other's McKnight funded award mechanisms.

d. Reserve and Resiliency Collaboratory (Workshop #4) Final Report

The committee reviewed the Reserve and Resiliency Collaboratory Workshop # 4 Final Report (Attachment 5) for information. During the workshop, there were separate breakout sessions for human and non-human investigators. These were designed to generate, discuss and define specific research projects that groups of attendees would be interested in working on together. These were then reported back to the entire group in plenary format. This process resulted in eight separate groups of investigators with interests in specific research questions that could be addressed using shared data.

Dr. Stern shared that they are seeking ways to help fund the continuation of these collaborations.

Dr. Thambisetty shared that given the high level of engagement, attendance and the results of the collaboration, the return was well worth the MBRF's financial investment.

6. Adjourn

Dr. Thambisetty asked if there was any further discussion. Hearing none, he called for adjournment of the meeting at 6:30 p.m. EST.

Summary of Action Items:

Respectfully Submitted,

Melanie A. Cianciotto
Corporate Trustee

**Pending committee chair review*

MINUTES
MCKNIGHT BRAIN RESEARCH FOUNDATION (MBRF)
RESEARCH COMMITTEE
CONFERENCE CALL
March 4, 2024

The Research Committee of the MBRF was called to order at 6:15 pm ET on March 4, 2024, by Dr. Madhav Thambisetty.

The following members were present:

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

The following members were absent:
Dr. Roy Hamilton, Trustee

Others attending:
Dr. Lee Dockery, Chair Emeritus
Ms. Melanie Cianciotto, Corporate Trustee
Dr. Angelika Schlanger, Executive Director

1. Call to Order

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

2. Minutes of the January 29, 2024 Meeting

The minutes of the January 29, 2024, Research Committee Meeting (Attachment 1) were approved as presented.
The changes were:

Action Item 1: The minutes of the January 29, 2024, Research Committee Meeting were approved as presented (Attachment 1).

3. Updated Activity Timeline

The committee reviewed the updated Activity Timeline (Attachment 2) for information. Dr. Thambisetty noted the items that have taken place recently include planning for the Cognitive Aging Summit IV, which is well underway, and the final report that was submitted for the Reserve and Resiliency Collaboratory, which the committee previously reviewed.

4. FNIH/NIA Annual Report on the Research Partnership in Cognitive Aging

The committee received the 2023 Research Partnership in Cognitive Aging report prepared by the FNIH/NIA (Attachment 3) for information. 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 report also includes updates on the Mindfulness, EDucation, and EXercise for Age-Related Cognitive Decline (MEDEX) trial (now complete) continuation study, as well as two additional initiatives that stemmed from the Cognitive Aging Summit III, including the STARRS study, led by Dr. Peter Rapp of the NIA.

The committee felt the report was well put together. Dr. Thambisetty shared that these clinical trials of mindfulness, meditation and physical activity are important, but there has not been a clinical trial that has shown a real benefit of these types of interventions on cognition. Have we reached a threshold where the trials are demonstrating an actual impact - or are we going to keep tweaking the studies trying to attain a better result, in which case we may be redirecting resources? If these interventions are repeatedly failing, at what point does the research community and the MBRF decide to focus on pursuing the study of other interventions?

5. American Federation for Aging Research (AFAR) Renewal Proposal for the Innovator Awards

The committee received the American Federation for Aging Research (AFAR) proposal (Attachment 4). The proposal is to renew the current Innovator Awards grant for another three years in the amount of $4,626,500 for three additional cohorts of investigators (6 total). The proposed budget represents an increase of $11,500 in administrative costs. The proposal includes survey results based on a questionnaire that AFAR fielded to identify the most commonly recognized forms of non-monetary institutional commitment.

The committee discussed the proposal and agreed that the program has identified and supported an outstanding group of six scientists. The committee reached consensus that the proposal is worthy of renewal. The committee discussed the existing match requirement and alternative non-monetary forms of institutional commitment that could be accepted instead. The committee agreed that revising the monetary match requirement should be pursued to make the program more inclusive and open the eligibility to more talented researchers. Additionally, the committee recommended that eligibility requirements be expanded to include researchers who have had extenuating circumstances that led to pauses in their career and may not meet the time-specific career requirements currently listed in the RFA. The committee asked about the process to revise the RFA. Dr. Schlanger will work with AFAR to revise the current RFA and Institutional Commitment form, taking into account the survey responses related to accepted forms of institutional commitment that are non-monetary in nature.

The committee recommended approval to continue with the Innovator Awards grant and to revise the RFA and Institutional Commitment form as appropriate.

Action Item 2: **The committee recommended approval to continue with the Innovator Awards grant and to revise the RFA and Institutional Commitment form as appropriate.**

6. Proposal for MBRF Research Award/Prize in Collaboration with the Foundation for the National Institutes of Health

Dr. Lee Dockery presented a proposal for a research award/prize in collaboration with the Foundation for the National Institutes of Health (FNIH) intended to advance the research mission of the MBRF and to recognize and celebrate the foundation's 25th anniversary (Attachment 5). This is intended to keep advancing the MBRF's focus on research, which has not been a focus of the communications outreach campaign.

The committee discussed the proposal and approved the concept at an award level of $25,000, recognizing that additional administration expenses will be added. The committee also empowered Dr. Lee Dockery to carry out any necessary negotiations with Mr. David Carmel, Chief Growth and Innovation Officer, FNIH related to the administrative fee, which is currently quite significant. Dr. Schlanger will invite Mr. Carmel to attend the March 19, 2024, Trustees' Meeting to make a formal presentation on the proposed research prize and related budget.

The committee proposed the research award/prize be named in honor of Dr. Lee Dockery. Dr. Dockery appreciated the gesture but feels the MBRF needs to be kept in the forefront.

Action Item 3: The committee approvals the concept of creating a research award/prize in the amount of $25,000 in collaboration with the FNIH to recognize and celebrate the foundation's 25th anniversary and empowers Dr. Lee Dockery to carry out any necessary negations with Mr. David Carmel, Chief Growth and Innovation Officer, FNIH.

Action Item 4: Dr. Schlanger will invite Mr. Carmel to attend the March 19, 2024, Trustees' Meeting to make a formal proposal.

7. American Brain Foundation 2025 RFP – Questions for Consideration

The committee reviewed the 2025 McKnight CTRS in Cognitive Aging and Age-Related Memory Loss Award RFP: Questions for Consideration (Attachment 6). The ABF will be producing the draft of the 2025 RFP in the coming weeks and had some recommendations for the Trustees to consider related to the eligibility requirements and the name of the award. The committee discussed proposed revisions to the RFP which included removing "progress" and replacing it with "advance" in the last bullet of the evaluation criteria, and adding additional disciplines to

the eligibility requirements, with suggested language, "MD, PhD, and other related degrees" to reflect that cognitive aging researchers can represent a broad range of disciplines. The Trustees recommended keeping the name of the award as is.

Action Item 5: Dr. Schlanger will share the proposed revisions to the RFA with the ABF team.

8. Adjourn

Dr. Thambisetty asked if there was any further discussion. Hearing none, he called for adjournment of the meeting at 7:30 p.m. ET.

Summary of Action Items:

Respectfully Submitted,

Melanie A. Cianciotto
Corporate Trustee

McKnight Brain Research Foundation Proposal for Research Prize/Award

Date: March 1, 2024

TO: Madhav Thambisetty, MD, PhD
Vice Chair, McKnight Brain Research Foundation
Chair, Research Committee

From: J. Lee Dockery, MD
Chair Emeritus, McKnight Brain Research Foundation

Subject: Research Award/Prize for Clinical Translational in Cognitive Aging

Proposal: The McKnight Brain Research Foundation (MBRF) in collaboration with the Foundation for the National Institutes of Health (FNIH) to establish an Award or Prize for the most outstanding research contributing to the knowledge and understanding of age-related cognitive decline and memory loss.

Concept: The MBRF has inaugurated a public communications campaign aimed at educating the public and scientists about cognitive again and brain health. This initiative although important, reduces the visibility and the importance of the support for research in cognitive aging intended for clinical application. The research support for each of the McKnight Brain Institutes (MBI), the American Brain Foundation (ABF) and the American Federation of Aging Research (AFAR) has not met MBRF's expectations.

The FNIH and the MBRF have been partners since 2007 when the Research Partnership in Cognitive Aging was formed between the National Institute on Aging (NIA) and the MBRF. The FNIH has managed the three cycles of funding the research proposals totaling approximately $60 million. In addition, the MBRF has been pleased with the management by the FNIH and the outcome of the three Cognitive Aging Summits and anticipates the successful outcome for the Cognitive Aging Summit IV scheduled for March 20-21, 2024.

The FNIH has also collaborated with other individuals and organizations to institute programs and in research with funding from donors to create scholarships, research awards, and prizes named for individuals, organizations, or sponsors. Under such arrangements with the FNIH, the donor supplies the funds for the award as well as the management fees to the FNIH. (See Attachment).

Recommendation:

a. The MBRF in collaboration with the FNIH and in recognition and celebration of the 25th Anniversary of the MBRF approve in concept the establishment of an **annual** cash award or prize in the minimum amount of $10,000 to be awarded for the most outstanding Clinical Translational Research in Cognitive Aging.

b. Invite a representative for the FNIH (David Carmel, Senior Vice President, Chief Growth and Innovation Officer) to attend the Trustees' meeting March 19, 2024, to discuss the arrangements for future collaboration in establishing the award/prize.

Donate

FNIH
Foundation for the National Institutes of Health

Trailblazer Prize For Clinician-Scientists

The Trailblazer Prize for Clinician-Scientists (Trailblazer Prize) recognizes the outstanding contributions of early career clinician-scientists whose work has the potential to or has led to innovations in patient care. This $10,000 honorarium and prize is made possible by a generous donation from John I. Gallin, MD, and Elaine Gallin, PhD, to the FNIH.

Nominations for the 2024 Trailblazer Prize may be submitted via our **online portal**. Nominations will be accepted through Friday, March 15th at 5 pm ET. Please review these **frequently asked questions** prior to submitting your nomination. For questions, contact us at **trailblazerprize@fnih.org**.

Nomination Portal

Frequently Asked Questions

Donate

FNIH

All Programs

Home > Our Programs > **All Programs**

Search Program NEUROSCIENCE

Displaying 1 - 16 of 16

The Biomedical Research Community Responds to the Opioids Crisis

Overview Opioid addiction, misuse and overdose is an ongoing and rapidly evolving public health crisis. According to the Centers for Diseas...

The Pew Scholars and Fellows Program in the Biomedical Sciences

Donate

FNIH

Pre-competitive Analytical Validation of SV2A PET as a Biomarker of Synaptic Density (SV2A PET Project)

The Problem Although researchers have established biomarkers to diagnose Alzheimer's disease, no biomarker can track cognitive decline ...

Research Partnership in Cognitive Aging

The Problem With a rapidly growing aged population, maintaining cognitive function is critical for the health and well-being of U.S. citize...

Robert Whitney Newcomb Memorial Lecture and Internships

Overview Since 2001, the Robert Whitney Newcomb Memorial Fund has endowed the annual Robert Whitney Newcomb Memorial Lecture in neuroscienc...

Sayer Vision Research Lecture & Award

Overview In 2006, Dr. Jane Sayer, an NIH Research scientist in National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), es...

National Institute of Neurological Disorders and Stroke – Congress of Neurological Surgeons Foundation K12 Scholar Awards

Overview In 2015, the Congress of Neurological Surgeons (CNS) and the National Institute of Neurological Disorders and Stroke (NINDS) estab...

NINDS Health Disparities in Tribal Communities Summer Internship Program

Overview The NINDS Health Disparities in Tribal Communities Summer Internship Program addresses the critical need for a robust and diverse ...

Biomarkers Consortium – Neurofilament as a Blood-Based Biomarker of Neurodegeneration in Familial Frontotemporal Degeneration (FTD)

FNIH

Biomarkers Consortium – Inflammatory Markers for Early Detection and Subtyping of Neurodegenerative and Mood Disorders

The Problem Neurodegenerative and psychiatric conditions such as Alzheimer's disease and Major Depressive Disorder present very differentl...

Biomarkers Consortium – Plasma Aβ and Phosphorylated Tau as Predictors of Amyloid and Tau Positivity in Alzheimer's Disease

The Problem Early treatment of Alzheimer's disease requires early diagnosis. Yet available methods to diagnose early AD are expensive or ...

Alzheimer's Disease Neuroimaging Initiative 3 (ADNI 3)

The Problem Individuals with Alzheimer's disease often do not show symptoms during the early stages of disease, limiting clinicians' ab...

AMP Alzheimer's Disease 1.0

Fusce volutpat nunc non lectus interdum, vitae sollicitudin lacus condimentum. Pellentesque vel nisl. Fusce volutpat nunc non lectus interdu...

AMP Schizophrenia

The Accelerating Medicines Partnership® (AMP®) Program Schizophrenia (AMP SCZ) is the first neuropsychiatric project of the landmark AMP p...

AMP Parkinson's Disease

The Accelerating Medicines Partnership® (AMP®) Program Parkinson's disease (AMP PD) is a public-private partnership among NIH and privat...

AMP Alzheimer's Disease 2.0

The Accelerating Medicines Partnership® (AMP®) Program Alzheimer's disease (AMP AD 2.0) is a precompetitive public-private partnership t...

Research Partnership in Cognitive Aging

The Problem

With a rapidly growing aged population, maintaining cognitive function is critical for the health and well-being of U.S. citizens. Roughly 87% of people age 65 and older may experience cognitive changes due to the normal aging process.

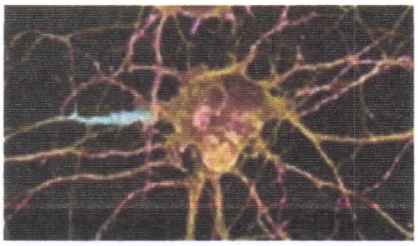
The Solution

Improving our understanding of age-related cognitive decline can lead to interventions and treatments that may delay or prevent brain aging, contributing to better quality of life for older adults.

Overview

Focused on better understanding and, eventually, moderating age-related memory loss, the Research Partnership in Cognitive Aging, a 15-year long collaboration between **the McKnight Brain Research Foundation (MBRF)** and the National Institute on Aging (NIA), is coordinated by the Foundation for the National Institutes of Health (FNIH).

Donate



In 2021, NIA awarded two major Research grants, funded jointly by NIA and the MBRF, to establish a network to identify, evaluate, track and conduct Research across multiple sites on older adults with superior cognitive performance for their age. Although these "cognitive super agers" are believed to constitute a very small minority of older individuals, they represent an unparalleled resource in which to study the behavioral, environmental, health, neural and genetic profiles that lead to sustained cognitive and brain function in advanced age. Conducted over a five-year period, this Research is expected to reveal important information about the factors that are critical for maintenance of cognitive function, as well as the factors that do not figure prominently.

Other initiatives made possible by the Research Partnership in Cognitive Aging include:

- Plasticity and Mechanisms of Cognitive Remediation in Older Adults, a five-year NIH grant awarded in 2014 that supported a multicenter clinical Research trial on remediating age-related cognitive decline through **mindfulness-based stress reduction and exercise**.
- 17 awards made in 2009 to support Research on neural and behavioral profiles of cognitive function in aging and interventions to remediate age-related cognitive decline.
- Three **Cognitive Aging Summits**, the most recent of which brought together a multidisciplinary group of investigators to consider age-related cognitive decline, as well as cognitive reserve and resilience.

Cognitive Aging

This partnership helps accelerate discovery of the causes and risk factors associated with disease and disability among older adults, and opens new paths for discoveries and improved brain health for our aging population.

Partners

Research Partnership in Cognitive Aging

A report to the McKnight Brain Research Foundation

January 31, 2024

Foundation for the National Institutes of Health
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 2023 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 report also includes updates on the Mindfulness, EDucation, and EXercise for Age-Related Cognitive Decline (MEDEX) trial (now complete) continuation study, as well as two additional initiatives that stemmed from the Cognitive Aging Summit III.

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 third year of award. The NIA is supporting a multi-year administrative supplement to enhance diversity and data capture, 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 enhanced the diversity of the RADCO cohort. The goal is to enroll 234 Black participants, thus increasing the Black participant proportion of the RADCO sample from 7.2% to 22.2%.

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 its third year of award. This year has seen a change in the locus of the primary award. Dr. Rogalski has transferred from Northwestern University to the University of Chicago. Dr. Mesulam has stepped down as one of the Multi-Principal Investigators (MPI) and remains active on the project as a co-investigator. Dr. Geula remains as an MPI. Both Drs. Geula and Mesulam are still on faculty at Northwestern. The team published findings in the Journal of the American Geriatrics Society in 2023 regarding the medication usage profiles of cognitive SuperAgers compared to age-peers. They reported that the medication profiles of cognitive SuperAgers showed no significant difference compared to cognitively average-for-age older controls in total medications, prescription medications, OTC medications, or in 10 medications/medication categories of interest. In another 2023 publication in Journal of the International Neuropsychological Society, they demonstrated that the episodic memory measure from the NIH Toolbox® is useful for differentiating cognitive SuperAgers from those with average-for-age cognition. These publications are 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.

Follow-on Study of the MEDEX Clinical Trial

Participants in the MEDEX ("Remediating Age-related Cognitive Decline: Mindfulness-based Stress Reduction and Exercise") clinical trial are being followed through a new award (R01AG072694, "Resilience and Brain Health of Older Adults During the COVID-19 Pandemic") to Dr. Eric Lenze (PI of MEDEX; Washington University St. Louis), Dr. Breno Diniz (University of Connecticut School of Medicine), and Dr. Julie Wetherell (University of California San Diego).

The project goals are to elucidate whether exercise and mindfulness can mitigate the effects of stressors from the COVID-19 pandemic on cognitive function and emotional health in later life, including neurobiological measures of risk for Alzheimer's disease. By following the MEDEX participants, repeated sets of clinical, cognitive, molecular, and neuroimaging measures spanning 7.5 years and covering the pre-, during-, and post-pandemic period are being generated.

The abstract for R01AG072694:

DESCRIPTION (provided by applicant): Exercise and mindfulness are believed to be effective stress reduction interventions, but research to date has not been able to assess their benefits while individuals are coping with a major stressor in real time. The COVID-19 pandemic is an unwanted natural experiment in the deleterious effects of stress – especially social isolation (social disconnectedness and loneliness), a stressor particularly strongly associated with the pandemic – on older Americans' cognitive and emotional health and risk for Alzheimer's disease (AD). This project will elucidate whether exercise and mindfulness can mitigate the effects of pandemic stress on cognitive function and emotional health in later life, including neurobiological measures of risk for AD. We will leverage a unique resource: the NIH-funded trial, MEDEX. By leveraging MEDEX and following these participants, who continue to attend monthly booster sessions of their randomized condition remotely during the pandemic, we will have repeated sets of clinical, cognitive, molecular, and neuroimaging measures covering 7.5 years during the pre-, during-, and post-pandemic period. We can examine intervention effects, as well as individual factors such as resilience, on long-term outcomes. Among other innovative aspects of the project, we will analyze effects on two novel peripheral biomarkers: Senescence Associated Secretory Phenotype (SASP), which measures mechanisms of biological aging, and plasma amyloid Aβ42 and Aβ40, which measure AD risk. In the proposed project, (1) during the pandemic, we will use novel methods such as Ecological Momentary Assessment (EMA) to characterize social isolation both objectively (e.g., number of social contacts) and subjectively (e.g., loneliness), and its biological mechanisms on aging (such as elevations in SASP and plasma amyloid); (2) post-pandemic, we will assess downstream effects on cognitive function, emotional well-being, and brain health, including AD risk, using neuropsychological assessments, EMA, and neuroimaging. Outcomes include (Aim 1) changes in cognitive performance and emotional well-being and decline in emotional well-being measured by positive

and negative effect and sleep quality; increases in biological aging and decreasing AB42/40 ratio in the post-pandemic phase, indicating higher risk of AD; and atrophy in hippocampal and prefrontal volume (structural MRI) and reduced global functional connectivity (resting state fMRI). Modifiers of these effects (Aim 2) include exercise and mindfulness; psychological resilience; COVID-19 exposure; medical morbidities; and APOE genotype. Mechanisms of cognitive, emotional, and brain health changes (Aim 3) include amyloid (Aβ40 and Aβ42), SASP, DNA methylation, and cortisol during the pandemic. This project will advance our knowledge of the impact of social isolation and other stressors on older adults, including mechanisms by which these stressors produce deleterious cognitive, emotional, and brain health changes over time, and whether exercise and mindfulness have durable protective effects.

PUBLIC HEALTH RELEVANCE: As referenced above, the COVID-19 pandemic provides an undesired natural measure of the detrimental effects of stress and social isolation on older Americans' cognitive and emotional health and risk for Alzheimer's disease. This project will advance our knowledge of the impact of social isolation and loneliness on older adults, including mechanisms by which these stressors produce negative cognitive, emotional, and brain health changes and how we can prevent those negative effects.

Additional Initiatives Stemming from the Cognitive Aging Summit III

In addition to RFA-AG-21-015 providing support for the two network grants to identify, evaluate, and track cognitive SuperAgers, which was jointly sponsored by the MBRF and the NIA, the NIA launched two additional research initiatives based on knowledge gaps and research opportunities identified 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 NIA hopes will yield insight 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 2023, 440 animals have been enrolled into the project, including animals that now have completed or are nearing completion of the longitudinal study. Brain MRI scans have been collected on almost 100 animals at two time points, along with data from motor activity, memory, attention, olfaction, frailty, and anxiety assessments.

An additional recommendation from the 2017 Summit was to develop operational definitions of constructs such as cognitive reserve, resilience, compensation, etc., that could be used uniformly by researchers. The Summit brought together a multidisciplinary group of investigators with shared interest in research on age-related cognitive decline as well as cognitive reserve and resilience. There was unanimous agreement that a significant barrier to progress in the field was the lack of clear and universally accepted definitions of important concepts related to cognitive reserve and resilience, and that it was imperative to address this deficit. An RFA (RFA-AG-18-024) was released by NIA, and one award was made to Dr. Yaakov Stern and Columbia University Health Sciences for a network grant titled "Collaboratory on Research Definitions for Cognitive Reserve and Resilience" (R24 AG061421).

Through a no-cost extension this past year, Dr. Stern and his co-investigators (Drs. Marilyn Albert, Carol Barnes, Roberto Cabeza, Alvaro Pascual-Leone, and Peter Rapp) were able to continue work on this effort and to hold a fourth workshop. The website for the effort, https://reserveandresilience.com/, contains information for these four workshops, the latest being in early December 2023. The framework for operational definitions of reserve and resilience concepts was published in 2023 in Neurobiology of Aging, along with a Commentary by Dr. Wagster and Dr. King. Both publications are attached to this report. Besides conducting workshops and developing and publishing the framework, this grant allowed for the award of pilot grants to explore and expand the constructs of resilience and reserve in the service of the framework development as well as to establish resources for future exploration. A publication was generated in 2023, resulting in part from one of the pilot awards (see Appendices for full publication): Gray, D. T., et al., Extracellular matrix proteoglycans support aged hippocampus networks: a potential cellular-level mechanism of brain reserve, Neurobiology of Aging, 2023.

The abstract for R24AG061421:

DESCRIPTION (provided by applicant): Research indicates that specific life exposures and genetic factors contribute to some people being more resilient than others, with lower rates of cognitive decline with aging, and reduced risk of developing Alzheimer's disease and related dementias (ADRD). There are likely several complex and highly interactive mechanisms that lead to these individual differences in vulnerability to decline, probably reliant on both structural and functional brain mechanisms. Key concepts often used in research in this area are cognitive reserve, brain reserve and brain maintenance. However, the definitions of these concepts differ across researchers, and the translation from human to animal research is not well developed. Also, their relationship to other invoked concepts such as efficiency, capacity, and compensation are not well explicated. The goal of this project is to work towards achieving state-of-the-art definitions for these concepts to allow researchers to use common nomenclature. In addition, the goal is to validate approaches to help advance research on these approaches that will lead to better maintenance of brain and cognitive health and treatment and/or prevention of ADRD. To that end, we will hold three cross-discipline workshops that will bring together investigators to discuss and come to consensus on these concepts,

create focused workgroups that will examine each of these issues, fund pilot grants designed to further the understanding and research applicability of these concepts, and develop data sharing and information exchange platforms to help guide and promote research in this area.

PUBLIC HEALTH RELEVANCE: To achieve state-of-the-art definitions and research guidelines for key concepts associated with resilience against cognitive aging and Alzheimer's disease related dementias, this project will hold three multidisciplinary workshops, establish focused work groups, create a data sharing and information platform, and support pilot grants designed to further the understanding of these concepts.

APPENDIX

- Journal of the American Geriatrics Society: Medical characterization of cognitive SuperAgers: Investigating the medication profile of SuperAgers
- Journal of the International Neuropsychological Society: NIH Toolbox® Episodic Memory Measure Differentiates Older Adults with Exceptional Memory Capacity from those with Average-for-Age Cognition
- Neurobiology of Aging: A framework for concepts of reserve and resilience in aging
- Neurobiology of Aging: Lost – and Found – in Translation
- Neurobiology of Aging: Extracellular matrix proteoglycans support aged hippocampus networks: a potential cellular-level mechanism of brain reserve

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Medical characterization of cognitive SuperAgers: Investigating the medication profile of SuperAgers

INTRODUCTION

Aging is associated with decline in cognition, with episodic memory changes representing the most common complaint of older adults.[1] SuperAgers are 80+ years with episodic memory capacity at least equal to persons in their 50s to 60s.[2] Their youthful memory phenotype offers a unique model for identifying factors for optimizing healthspan. Initial investigations have identified biologic, genetic, and psychosocial features that distinguish SuperAgers from their average episodic memory peers.[2–4] However, medications have not been characterized.

Medications, both as therapies supporting cognition and as indicators of overall health may contribute to the youthful SuperAging phenotype. Polypharmacy (i.e., use of >5 medications), affects ~40% of US older adults and is associated with increased risk of adverse drug events, falls, and mortality. When considering medication type, opiates, benzodiazepines, and non-benzodiazepine hypnotics are on The American Geriatrics Society (AGS) Beers Criteria list of potentially inappropriate medications (PIMs) for older adults, in part due to their detrimental effects on cognition. Conversely, common medications from antihypertensives to statins to vitamin D have been investigated for possible memory benefits.[5,6]

This study examined whether medication profiles differed between SuperAgers and controls.

METHODS

Community-dwelling participants age 80+ were prospectively enrolled as SuperAgers or cognitively average older controls. Detailed inclusion criteria have been previously reported.[2] Briefly, SuperAgers must perform at or above average normative values for 50–65-year-olds in episodic memory and at least average-for-age normative values in other cognitive domains. Controls were required to perform average-for-age across cognitive domains. The study received institutional review board approval and informed consent was obtained.

Participants reported current medications and supplements, dosage, and duration for each medication/supplement. Staff verified responses. Two physicians independently categorized medications as prescription or OTC; discrepancies were adjudicated by consensus.

Secondary analysis further classified participants as users/non-users of 10 medications/medications classes. Aspirin, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, and statins were highlighted given their roles in cardiovascular health. Using the updated AGS Beers Criteria, diuretics, opiates, benzodiazepines, and non-benzodiazepines hypnotics were examined as PIMs. Vitamin D, metformin, and thyroid hormones were included for their potential role in supporting cognition.

Linear regression models were used to analyze differences in the number of medications (prescription, OTC, total medications) used, and logistic regression was used to model binary variables (use versus non-use) for 10 specific medications or medication classes. Race, gender, and age were included as covariates. Uncontrolled *t*-test and Fisher's exact tests were performed for continuous and binary variables respectively. Significance was set at $p = 0.05$.

RESULTS

Table 1 provides demographics and neuropsychological performance for 96 SuperAgers and 46 controls. No significant difference was detected in total, mean prescription, or OTC medication use between SuperAgers and controls in the uncontrolled *t*-test or the linear regression controlling for age, gender, and race (Figure 1). The specified medications/medication use categories also showed no significant difference between groups (Figure 1).

DISCUSSION

The medication profiles of SuperAgers, older adults with exceptional episodic memory, showed no significant difference compared to cognitively average-for-age older controls in total medications, prescription medications, OTC medications, or in 10 medications/medication categories of interest. On average, prescription medications were higher in the current study (SuperAgers: 3.48, controls 3.20) than in larger epidemiologic studies like the Bronx Aging Study (BAS: 2.3) and the Monongahela Valley Independent Elders Survey (MoVIES: 2.0).[7,8] Notably,

Janessa R. Engelmeyer and Alice Kerr contributed equally to the work.

TABLE 1 Demographics and neuropsychological performance.

Demographics	SuperAgers ($n = 96$) [range]	Cognitively normal controls ($n = 46$) [range]
Age (years)	82.3 ± 3.4 [80–101]	84.2 ± 4.7 [79–102]
Education (years)	16.3 ± 2.4 [12–20]	16.7 ± 2.9 [6–20]
Sex, men:women	26:70	17:29
Race, Caucasian:African American	85:11	42:4
Handedness, right:left:ambidextrous	90:4:2	44:2:0
Neuropsychological test performance		
RAVLT delay recall raw score	11.0 ± 1.9	5.7 ± 1.3
Trail making test B raw score	87.9 ± 3.4	106.6 ± 43.3
Category fluency: Animals raw score	21.4 ± 5.2	19.0 ± 5.0
Boston naming test (BNT) 30 item raw score	28.1 ± 2.3	26.9 ± 2.9
Weschler test of adult reading (WTAR) estimated FSIQ (80+)	115.5 ± 8.0	114.4 ± 9.1

Note: Data are shown as means ± standard deviations and [ranges] RAVLT delay: measure of episodic memory with possible scores ranging from 0 to 15. Trail making test B: timed measure of executive function, testing discontinued at 300 s. Category fluency: measure of semantic fluency in which participants list as many items as possible (animals) in 60 s. BNT: measure of object naming with possible scores ranging from 0 to 30. WTAR FSIQ: measure of premorbid intelligence.

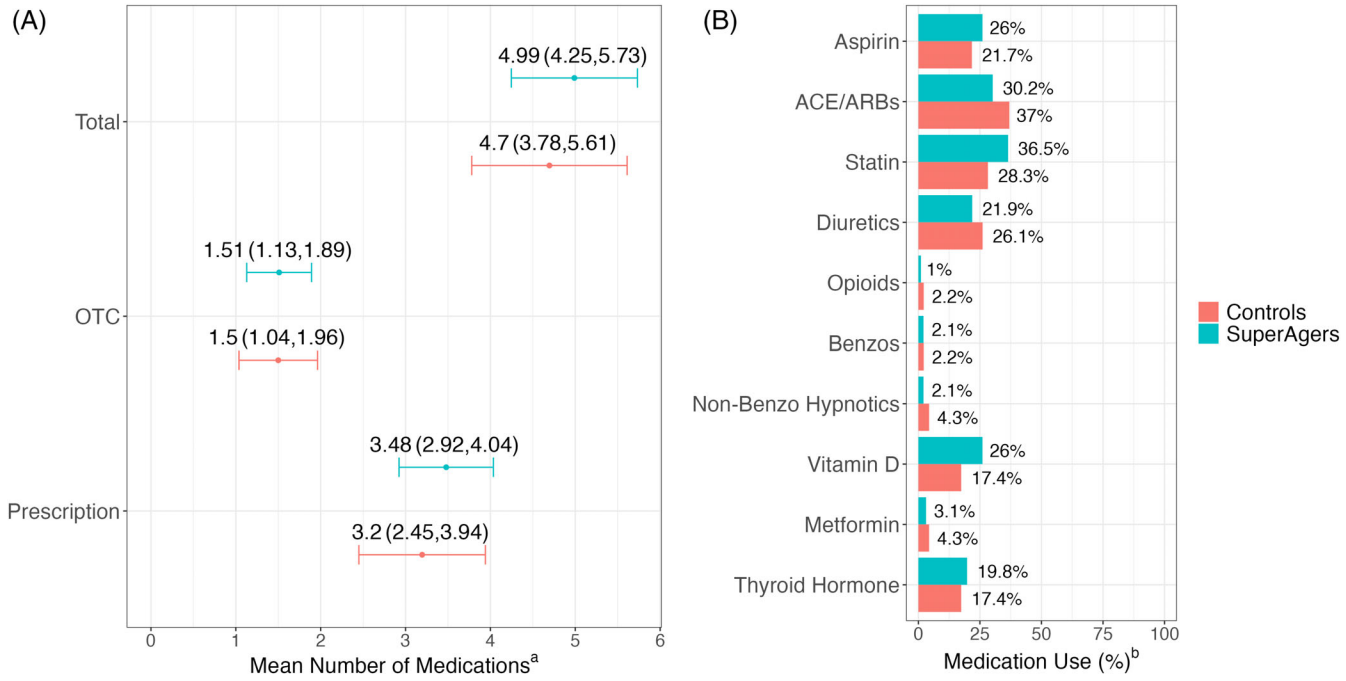

FIGURE 1 Medication use does not differ between SuperAgers and controls. (A) Mean number of medications did not differ between SuperAgers and controls (p values, total: 0.63, OTC: 0.97, prescription: 0.55; or controlled p-values, total: 0.37, OTC: 0.85, prescription: 0.37). (B) Percent of individuals taking a medication did not differ between SuperAgers and controls for p-values range: 0.29–0.82; controlled p-values range: 0.16–97). [a]p-value from a t-test for difference of means. Controlled p-value takes race, gender, and age into consideration using a linear regression analysis. [b]p-value from a Fisher's exact test. Controlled p-value takes race, gender, and age into consideration using a logistic regression analysis. ACE/ARBs, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers; benzos, benzodiazepines; OTC, over the counter.

these studies were completed over 20 years prior with younger participants (average age: 79.2, 73.1 years, respectively). Higher use in the current study likely reflects temporal changes rather than intrinsic medical differences, given that prescription use increases over the life span and in recent decades.[9]

Use of potentially inappropriate medications tended to be lower in this study than National Social Life, Health, and Aging Project (NSHAP) cohort, a representative sample of adults aged 57–85 at enrollment.[10] Statins were the most commonly used medications for both SuperAgers (36.5%) and controls (28.3%), while the NSHAP was 46.2%. Similarly, the NSHAP participants reported higher aspirin use (40.2%) compared to SuperAgers (26.0%) and controls (21.7%). Definitive conclusions cannot be drawn without statistical comparison; however, higher use of these medications in larger, representative samples of older adults relative to this study raises the possibility our controls may not represent typical older adult medication use.

In summary, while SuperAgers differ in memory performance from controls, their medication use—total, prescription, and pre-specified subclasses of medication use—did not differ. Thus, distinctive medication profiles cannot fully account for memory performance differences between SuperAgers and cognitively average older adults. However, our previous findings point to slower brain atrophy and psychosocial factors, as potential contributors to youthful memory performance.[2–4]

AUTHOR CONTRIBUTIONS

Janessa R. Engelmeyer contributed to data acquisition, analysis, and drafted the manuscript. Alice Kerr contributed to data analysis, interpretation and drafted the manuscript. Beth A. Makowski-Woidan contributed to data acquisition and critical revision of the manuscript. Nathan P. Gill and Hui Zhang contributed to data analysis, interpretation, and critical revision of the manuscript. Lee Lindquist contributed to analysis, interpretation, and critical revision of the manuscript. M.-Marsel Mesulam, Sandra Weintraub, and Emily J. Rogalski contributed to the study conception and design, data acquisition, and critical revision. All authors gave final approval and agreed to be accountable for all aspects of the work.

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CONFLICT OF INTEREST STATEMENT

Emily J. Rogalski, M.-Marsel Mesulam, Hui Zhang, Nathan P. Gill, Lee Lindquist, and Sandra Weintraub report NIH funding. Emily J. Rogalski, M.-Marsel Mesulam, and Sandra Weintraub report receiving honoraria.

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The sponsor was not involved in the design, methods, subject recruitment, data collection, analysis, or preparation of the manuscript.

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Janessa R. Engelmeyer BA[1]
Alice Kerr MD[2]
Beth A. Makowski-Woidan BA[1]
Nathan P. Gill PhD[3]
M.-Marsel Mesulam MD[1,4]
Sandra Weintraub PhD[1,5]
Hui Zhang PhD[3]
Lee Lindquist MD, MPH, MBA[6]
Emily J. Rogalski PhD[1,5]

[1]*Mesualm Center for Cognitive Neurology and Alzheimer's Disease, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA*
[2]*Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA*
[3]*Division of Biostatistics, Department of Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA*
[4]*Department of Neurology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA*
[5]*Department of Psychiatry and Behavioral Sciences, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA*
[6]*Division of General Internal Medicine and Geriatrics, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA*

Correspondence
Janessa R. Engelmeyer, Mesulam Center for Cognitive Neurology and Alzhiemer's Disease, Northwestern University Feinberg School of Medicine, 300 East Superior Street, Tarry 8, Chicago, IL 60611, USA.
Email: jrengelmeyer@gmail.com

ORCID

Janessa R. Engelmeyer https://orcid.org/0000-0002-3973-6256
Lee Lindquist https://orcid.org/0000-0002-4290-5081

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BRIEF COMMUNICATION

NIH Toolbox® Episodic Memory Measure Differentiates Older Adults with Exceptional Memory Capacity from those with Average-for-Age Cognition

Tatiana Karpouzian-Rogers[1,2,*], Beth Makowski-Woidan[2], Alan Kuang[3], Hui Zhang[3], Angela Fought[4], Janessa Engelmeyer[2], M.-Marsel Mesulam[1,5], Sandra Weintraub[1,2] and Emily Rogalski[1,2]

[1]Mesulam Center for Cognitive Neurology and Alzheimer's Disease, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA
[2]Department of Psychiatry and Behavioral Sciences, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA
[3]Division of Biostatistics, Department of Preventative Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA
[4]Department of Biostatistics and Informatic, Colorado School of Public Health, University of Colorado-Denver Anschutz Medical Campus, Aurora, CO
[5]Department of Neurology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

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Abstract

Objective: Older adults with exceptional memory function, designated "SuperAgers," include individuals over age 80, with episodic memory at least as good as individuals ages 50s–60s. The Northwestern University SuperAging cohort is defined by performance on an established test of verbal memory. The purpose of this study was to determine if superior verbal memory extends to nonverbal memory in SuperAgers by examining differences in the National Institutes of Health Toolbox® (NIHTB) between older adults with exceptional memory and those with average-for-age cognition. **Method:** SuperAgers ($n = 46$) and cognitively average-for-age older adults ($n = 31$) completed a comprehensive neuropsychological battery and the NIHTB Cognition module. Multiple linear regressions were used to examine differences on subtests between groups. **Results:** There was a significant effect of group on the Picture Sequence Memory score, ($p = .007$), such that SuperAgers had higher scores than cognitively average-for-age older adults. There were no other group effects across other non-episodic memory NIHTB Cognition measures. **Conclusions:** Findings from this study demonstrated stronger performance on the memory measure of the NIHTB in SuperAgers compared to cognitively average-for-age older adults demonstrating superior memory in not only verbal but also nonverbal episodic memory in this group. Additionally, this study adds to the literature validating the NIHTB in older adults, particularly in a novel population of adults over age 80 with exceptional memory.

Keywords: "SuperAgers", normal aging, NIH Toolbox, memory, cognition, dementia

INTRODUCTION

Decline in memory functions is often accepted as part of "normal" aging, with mild changes beginning in mid-life and more accelerated changes occurring over the age of 60 (Nyberg et al., 2012). However, at the Northwestern Mesulam Center for Cognitive Neurology and Alzheimer's disease, we have identified a group of individuals that we designated "SuperAgers," who are over age 80 and able to maintain superior memory performance compared to their same age peers and at a level that is at least "average" for 50- and 60-year-olds (Rogalski et al., 2013). Longitudinal follow-up of these individuals suggests that superior memory performance can be maintained over time, providing additional support for their resistance to the typical age-related decline (Gefen et al, 2014; Rogalski et al., 2019). With respect to psychological factors, SuperAgers report greater levels of social relationships compared to cognitively average-for-age peers (Cook Maher et al., 2017). Neuroimaging studies have demonstrated greater cortical integrity and slowed rates of atrophy compared to cognitively average age-matched peers and thicker anterior cingulate cortex compared to

*Correspondence and reprint requests to: Tatiana Karpouzian-Rogers, PhD, 320 E. Superior St., Chicago, IL 60611, USA. E-mail: t-karpouzian@northwestern.edu

50-–65-year-olds (Harrison et al., 2012; Cook et al., 2017). Further, post-mortem studies suggest a lower frequency of Alzheimer neuropathology and higher density of von Economo neurons in the anterior cingulate compared to cognitively average older adults and individuals with amnestic mild cognitive impairment (Gefen et al., 2015).

The operationalization of memory capacity in SuperAgers was defined on the basis of scores on the Rey Auditory Verbal Learning Test (RAVLT), a difficult 15-item list-learning test of verbal episodic memory, which is widely used and has good psychometric properties. However, performance on tests of other episodic memory measures, including memory tests that place less emphasis on verbal abilities, has not been systematically investigated in this population. A recent research tool that was designed to measure cognitive functions in adults is the National Institutes of Health Toolbox® for Assessment of Neurological and Behavioral Function (NIHTB; Gershon et al., 2013; Weintraub et al., 2014). Traditionally, the evaluation of cognitive abilities in older adults has included either brief cognitive screening measures or lengthy neuropsychological batteries that often require clinical expertise and these batteries frequently differ across studies, making direct comparisons difficult to conduct. The NIHTB is a computerized suite of tests that measure cognitive, emotional, motor and sensory domains in individuals aged 3–85, and was designed to be used across a variety of settings, particularly in longitudinal research studies so that findings across studies could be conveniently compared. The Cognition Module includes a test of episodic memory, the Picture Sequence Memory test, that relies less heavily on verbal abilities, requiring participants to recall sequences of pictured actors and actions in the order they were originally learned over several trials.

The present study examined differences across all subtests of the Cognition module of the NIHTB between older adults with exceptional memory and those who are cognitively average-for-age. Our particular focus was to determine if the NIHTB episodic memory test specifically, which is less reliant on verbal abilities in comparison to our gold-standard of memory capacity, would be sensitive to differences between SuperAgers and "normal" agers. This is important as it would extend the contexts in which SuperAgers display superior episodic memory performance and opens the possibility of using the NIHTB as an efficient tool for future identification of SuperAgers. This study is also the first characterization of NIHTB Cognition module in an established cohort of older adults with exceptional memory. Given that SuperAgers display superior memory capacity, we hypothesized that the SuperAger group would demonstrate greater performance on the episodic memory test of the NIHTB.

METHODS

Participants

Participants 80 years or older were recruited through the Mesulam Center and Northwestern's Alzheimer's Disease Research Center Clinical Core, community lectures, and/or word of mouth. SuperAgers were referred on the basis of high memory scores and the absence of impairment in any other cognitive domain but were not necessarily superior in non-memory domains. Inclusion criteria for SuperAgers included: (1) score at or above the average level for 50–65-year-olds (equivalent to the Superior range for their own age) on the delayed recall condition of the (RAVLT; Schmidt, 1996), a 15-word list-learning memory test; and (2) performance within one standard deviation of the average range for their age on nonmemory measures including the Trail Making Test Part-B, Category Fluency Test, and 30-item Boston Naming Test according to published normative data (Heaton, 2004, Randolph, 1998, Mack et al., 1992). Inclusion criteria for Cognitively Average-for-Age Older Adults included: performance within the average-for-age normative range on the RAVLT and on all non-memory tests administered in the study. Full scale IQ was measured using the Wechsler Adult Intelligence Scale, Third Edition (WAIS-III). Additional inclusion criteria for both groups were that all participants maintained their cognitive status (as measured by neuropsychological battery described above) from their visit to the time the NIH Toolbox® was administered to maintain the integrity of our SuperAger sample. The administration of the NIHTB and collection of the neuropsychological battery occurred no more than three months apart. Additionally, all participants were required to have preserved activities of daily living. Participants with significant neurologic or psychiatric illnesses were excluded. All participants provided written informed consent. The Institutional Review Board at Northwestern University approved all study procedures. Research was completed in accordance with the Helsinki Declaration.

Study Measures

As described in previous studies (Gefen et al., 2014), all participants underwent a neuropsychological battery, including measures of attention, executive functions, language, and episodic memory. Participants completed the Cognition module of the NIH Toolbox® as part of the biyearly standardized battery. The Cognition Battery consists of tests assessing Executive Function and Attention (Dimensional Change Card Sort Test and Flanker Inhibitory Control and Attention Test), Episodic Memory (Picture Sequence Memory Test), Language (Oral Reading Recognition Test and Picture Vocabulary Test), Processing Speed (Pattern Comparison Processing Speed Test), and Working Memory (List Sorting Working Memory Test) (Weintraub et al., 2014). In addition to individual test scores, Cognitive Function, Fluid Cognition, and Crystallized Cognition composite scores are computed. In the Picture Sequence Memory Test, participants are shown a series of pictures depicting a sequence of events, for example, playing in the park. Then, the pictures are assembled in the center of the screen and participants are asked to reproduce the spatial placement of the previously demonstrated sequence of pictures. For additional details on these modules, refer to the original publications (Weintraub et al., 2013; Gershon et al., 2010; Gershon et al., 2013) and the NIHTB website (nihtoolbox.org).

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Table 1. *Study sample characteristics and NIHTB subtest scores*

	SuperAgers ($n = 46$)	Cognitively average-for-age 80+ year-olds ($n = 31$)	Test statistic (t or χ^2)
Demographics and estimated IQ			
Age, mean (SD)	84.2 (3.3)	84.0 (3.9)	.3
Sex, M:F	10:21	16:30	.1
Race, CA:AA	43:3	24:7	.3
Years of education, mean (SD)	17.2 (2.1)	16.5 (2.0)	1.3
WAIS-FSIQ, mean (SD)	133.0 (12.2)	118.7 (15.2)	4.5***
Performance on Standardized Neuropsychological Measures used for Study Inclusion			
RAVLT Delay Raw, mean (SD)	11.0 (1.8)	5.2 (1.4)	1.3***
BNT-30 Raw, mean (SD)[a]	28.2 (1.6)	26.3 (2.8)	3.5**
Animal Fluency Raw, mean (SD)[b]	22.7 (4.4)	19.8 (5.3)	2.6**
Trails B Raw (s), mean (SD)	78.9 (28.3)	104.0 (42.9)	2.9**
NIH toolbox performance			
Oral reading recognition (Language), mean (SD)	7.4 (1.3)	6.2 (2.1)	.03
Picture vocabulary (Language), Mean (SD)	7.8 (1.7)	6.9 (2.0)	.1
Flanker inhibitory control (Executive Attention), mean (SD)	7.4 (.6)	7.2 (.9)	.5
Dimensional Card Sort, (Executive Switching), mean (SD)	7.5 (.7)	7.4 (.8)	.5
Pattern comparison (Processing Speed), mean (SD)	35.5 (9.4)	33.5 (8.0)	.0
List sorting (Working Memory), mean (SD)	15.5 (2.4)	14.6 (3.1)	.1
Picture sequence memory (Episodic Memory), mean (SD)	441.2 (65.8)	388.0 (58.9)	7.7**

*$p < .05$, **$p < .01$, ***$p < .001$
SD = standard deviation; M = male; F = female; CA = Caucasian; AA = African American.
*Note two participants (1 control, 1 SuperAger) had low Boston Naming Test (BNT) scores at the time of NITB but met qualifying criteria at their initial visit. Four participants (3 Controls, 1 SuperAger) had consistently low BNT scores, for one English was a second language and may have contributed to lower scores. These participants were retained in all analysis as there were no other objective or subjective reports of difficulty with language.

Statistical Analyses

Differences in participant demographics were assessed using two-sample *t*-tests. NIH Toolbox® scores were summarized using frequencies and percentages for categorical variables or mean and standard deviation for continuous variables. Histograms and scattered plots of each NIH Toolbox® measure were examined to explore the shape of distributions and identify potential outliers. For the Cognition Module, computed scores were calculated for Flanker, Dimensional Change Card Sort, Pattern Comparison, and Picture Sequence Memory subtests, theta scores were calculated for Reading and Vocabulary, and raw scores were used for List Sorting. For details regarding computation of theta and computed scores, refer to NIHTB Scoring and Interpretation Guide (http://www.healthmeasures.net/images/nihtoolbox/Training-Admin-Scoring_Manuals/NIH_Toolbox_Scoring_and_Interpretation_Manual_9-27-12.pdf). Composite scores were calculated by averaging the normalized scores of each measure, and then deriving scale scores based on this new distribution. For each NIH Toolbox® measure, multiple linear regressions were used to examine differences between groups. Covariate adjustments included Wechsler Adult Intelligence Scale -Full Scale Intelligence Quotient (WAIS-FSIQ), sex, age, and education. Linear regression model fit was assessed using measures of collinearity and non-linearity, including residuals *versus* fits plots, histograms, Q-Q plots of residuals, and Dfbeta statistics. Adjusted R2 values were used to summarize variability explained in the linear models. All analyses were conducted in R 3.5.3 software.

RESULTS

Groups did not differ with respect to age, race, years of education, or sex (*ps* > .05) (Table 1). SuperAgers had a higher WAIS-FSIQ than cognitively average-for-age older adults ($p < .001$). Across all linear models, r-squared values ranged from .03–.34. Collinearity was not a concern, with pairwise correlations ranging from 0 to .56 for model covariates. Multicollinearity was not a concern, with variance inflation factor ranging from 1.03 to 1.79. Dfbeta statistics indicated there are some observations of influences. In order to improve linearity for measures that were positively skewed, scores were log-transformed, which included scores on the Picture Sequence Memory test.

Within the Cognition Module, there was an effect of group on Picture Sequence Memory scores (F (1,63) = 7.7, $p = .007$, $\beta = .10$), such that the SuperAger group had higher scores than the Cognitively Average-for-Age Older Adults (Figure 1). The effects of sex, age, education level, and FSIQ were not significant in this model. There were no other

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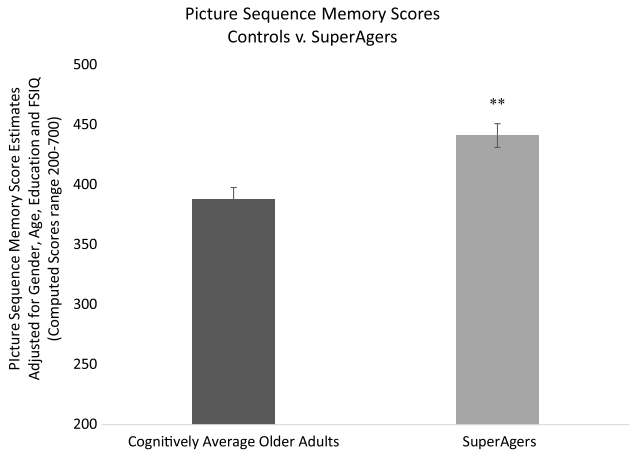

Fig.1. SuperAgers perform significantly better than cognitively average-for-age 80+ year-olds on the NIH Toolbox® Picture Sequence Memory. $^{**}p < .01$

effects of group across all other NIHTB Cognition tests of non-memory domains or on Composite Scores (all *p*s > .05).

DISCUSSION

This study sought to extend the superiority of episodic memory compared with other cognitive domains in the Northwestern University SuperAging cohort by comparing SuperAgers with cognitively average-for-age older adults on the tests of the NIHTB Cognition Battery. Findings of this study demonstrated greater performance on a test reliant on nonverbal episodic memory, the Picture Sequence Memory Test, in the SuperAging group compared to cognitively average-for-age older adults. Performance across all other measures of cognition on the NIHTB were comparable between groups. These findings confirm the exceptional episodic memory in SuperAgers.

The criteria for inclusion in the Northwestern University SuperAging research program involve completion of neuropsychological measures examining multiple aspects of cognition, with particular emphasis on memory abilities. SuperAging status requires performance at or above the average level of 50–65-year-olds on the RAVLT, a well-established measure of verbal episodic memory shown to be sensitive to early changes in memory and structural brain changes in Alzheimer's disease (e.g., Estévez-González et al., 2003). Longitudinal studies of SuperAgers have demonstrated that superior memory performance tends to be stable, suggesting that exceptional memory capacity is not necessarily a function of superior premorbid cognitive abilities, but rather a resistance to age-related cognitive changes (Gefen et al., 2014; Rogalski et al., 2019). The finding that performance on the NIHTB Picture Sequence Memory, a measure of episodic memory that places less emphasis on verbal memory abilities, also differentiates the SuperAging group and cognitively average-for-age older adults is further confirmation of the memory superiority in SuperAgers. This suggests that superior memory capacity in SuperAgers may not be specific to the list learning of the RAVLT, but is more general to episodic memory. Additionally, scores on all other NIHTB measures were similar between groups, which mirrors our criteria that SuperAgers may score in at least the average range on all other measures of cognition, including object naming, semantic fluency, and executive attention. Although it is unclear why there were no differences at the group level across other NIHTB subtests, it is possible there may be nuanced profiles at the individual level; this is similar to what was observed in recent work from the SuperAging Research Program, which demonstrated significant intragroup variability on multiple cognitive domains (Maher et al., 2021). Additional explanations include differences in the specific domains assessed by our neuropsychological measures *versus* the NIHTB (i.e. verbal fluency), as well as differences in tests used in this study compared to the neuropsychological tests used to validate the NIHTB (Weintraub et al., 2013).

The NIHTB has been validated in older adults without cognitive impairment and has also been investigated in older adults with varying degrees of cognitive impairment. In particular, one study examined the psychometric properties of the NIHTB cognition module in cognitively intact older adults and found acceptable test-retest reliability over a one-year period, as well as a relationship between NIHTB Fluid Composite and cerebral volumes, and a strong correlation between Fluid and Crystallized Composites with their respective gold standard composites (Scott et al., 2019). In a study of older adults with subjective decline, mild cognitive impairment, or mild dementia, performance on the NIHTB Cognition module was consistent with performance on traditional neuropsychological tests and had greater discriminative ability when supplemented with RAVLT delayed recall performance (Hackett et al., 2018). Further, neuroimaging studies have demonstrated relationships between NIHTB performance and hippocampal volume and tau deposition in older adults (O'Shea et al. 2016; Snitz et al., 2020). One important limitation is that the sample was a predominantly white, well-educated group, and therefore replication with a more diverse sample is needed. The present study is one of the first, to our knowledge, to examine performance in the NIHTB in an established cohort of adults over age 80 with exceptional memory and adds to the utility of using the NIHTB to measure cognitive functioning in the oldest of old age groups.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose.

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Commentary

A framework for concepts of reserve and resilience in aging

Yaakov Stern[a,*], Marilyn Albert[b], Carol A Barnes[c], Roberto Cabeza[d], Alvaro Pascual-Leone[e], Peter R. Rapp[f]

[a] Cognitive Neuroscience Division, Department of Neurology, Columbia University Vagelos College of Physicians and Surgeons, New York, NY, USA
[b] Departments of Psychiatry and Neurology, John Hopkins University, Baltimore, MD, USA
[c] Departments of Psychology, Neurology and Neuroscience, and Evelyn F. McKnight Brain Institute, University of Arizona, Tucson, AZ, USA
[d] Center for Cognitive Neuroscience, Department of Psychology and Neuroscience, Duke University, Durham, NC, USA
[e] Department of Neurology, Harvard Medical School, Boston, MA, USA
[f] Laboratory of Behavioral Neuroscience, Neurocognitive Aging Section, National Institute on Aging, Baltimore, MD, USA

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ABSTRACT

The study of factors, across species, that allow some individuals to age more successfully than others has important implications for individual wellbeing as well as health education, policy and intervention. Design of studies and communication across investigators in this area has been hampered by a diversity of terminology. The Collaboratory on Research Definitions for Reserve and Resilience in Cognitive Aging and Dementia was funded by the National Institute on Aging and established in 2019 as a 3-year process of developing consensus definitions and research guidelines. The proposed Framework is based on an iterative process including 3 annual Workshops, focused workgroups, and input from numerous international investigators. It suggests the overarching term: resilience, and presents operational definitions for 3 concepts: cognitive reserve, brain maintenance, and brain reserve. Twelve pilot studies that integrate these definitions are presented. The use of a common vocabulary and operational definitions will facilitate even greater progress in understanding the factors that are associated with successful aging.

1. Introduction

The study of factors that allow some individuals to age more successfully than others, including for example genetics and life exposures, has important implications for individual wellbeing as well as health education, policy and intervention. Moreover, identifying factors that are relevant across species (i.e., humans and nonhumans) is fundamentally necessary to facilitate studies of the neurobiological underpinnings of such factors.

In this context, overarching concepts like reserve and resilience are often invoked for capturing differential susceptibility to brain aging and disease. However, design of studies and communication across investigators in this area has been hampered by a diversity of terminology. Several groups have published proposed nomenclature and operational definitions for concepts including resilience, cognitive reserve (CR), brain reserve (BR), brain maintenance (BM), compensation, scaffolding, resistance, and resilience. Across these papers there are often disparate definitions for the same term. In addition, most of these papers focus on human studies, so the definitions and nomenclature are not optimally suitable for nonhuman studies.

The Collaboratory on Research Definitions for Reserve and Resilience in Cognitive Aging and Dementia was funded by the National Institute on Aging of the National Institutes of Health in the USA and established in 2019 as a 3-year process of developing consensus definitions and research guidelines for CR and related concepts. The present document is the result of an iterative process including 3 large annual Workshops, input from focused workgroups, and the extensive participation and consultation of over 40 selected, international expert investigators who utilize multiple research approaches and study both humans and nonhumans. Here we present a framework that includes definitions for 3 concepts, CR, BM, and BR, along with suggested operational definitions to help guide the design of research investigating these concepts. We also include resilience as an overarching term that subsumes all of the concepts presented.

Our aim is to present a well-defined set of operational definitions in order to encourage, advance, and develop research on

Abbreviations: CR, Cognitive reserve; BM, Brain maintenance; BR, Brain reserve.

* Corresponding author at: Columbia University Vagelos College of Physicians and Surgeons, 630 W 168th St, P&S Box 16, New York, NY 10032, USA, Phone: 212-342-1350.
E-mail address: ys11@columbia.edu (Y. Stern).

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these concepts. At the same time, we want to encourage investigators who have different views or use a given concept differently to note how their definitions relate or differ with one of those described here. Similarly, this framework provides a basis for describing how the operational definition of another concept differs from those suggested here.

Our intention is not to limit the creativity or ingenuity of investigators, or to claim that the framework presents the only way to investigate these important concepts. We hope to encourage research that provides either evidence-based support for these concepts or that presents data that cannot be accommodated by the proposed operational definitions of these concepts. We also hope that referring to this framework will facilitate collaboration and comparison of findings across studies and species.

The Collaboratory also sponsored 12 studies that were intended to implement the suggested research guidelines and thus provide experimental examples of their operational utility. This disparate set of studies incorporates humans and nonhumans, as well as multiple approaches including epidemiologic, neuroimaging, and interventions. We include in the supplementary material descriptions of the pilot projects as wells as a table that summarizes the projects and how they incorporate the framework presented here. These provide useful real-world examples that illustrate how study designs can incorporate the suggested framework.

Our hope for this framework is that the use of a common vocabulary and operational definitions will facilitate even greater progress in understanding the factors that are associated with successful aging.

2. Resilience

The term resilience has been used in many contexts. Here we consider it a general term that subsumes any concept that relates to the capacity of the brain to maintain cognition and function with aging and disease. There can be substantial variability in the mechanisms underlying resilience. Here, we present 3, CR, BM, and BR.

3. CR

3.1. Definition

CR is a property of the brain that allows for cognitive performance that is better than expected given the degree of life-course related brain changes and brain injury or disease:

- Property of the brain refers to multiple potential mechanisms including molecular, cellular and network levels. The working hypothesis is that these mechanisms help cope with or compensate for brain changes and the consequences of brain injury or disease.
- These mechanisms can be characterized via biological or cognitive-experimental approaches.
- Better than expected cognitive performance refers to differences ideally measured longitudinally.

CR can be influenced by multiple genetic and environmental factors, operating at various points or continuously across the lifespan.

3.2. Operational definition: general considerations

Research aimed at further elucidating CR requires the inclusion of 3 components:

1. Measures of life course-related brain changes, insults, disease, or risk factors that theoretically impact cognitive outcomes,
2. Measures of associated change in cognition, and
3. A variable that influences the relationship between 1 and 2.

Ideally, the aim is to demonstrate that any proposed CR measure (e.g., a sociocultural or functional brain measure) moderates the relationship between 1 and 2. For example, in an analysis where change in brain atrophy/pathology measures (component 1) predict change in cognition (component 2), and includes education as a hypothesized CR proxy (component 3), there is a statistical interaction between brain measures and education, such that level of education significantly moderates the association of brain measures with cognitive change.

Even without evidence for moderation, it can also be sufficient to demonstrate that a hypothesized CR proxy or measure is associated with cognitive performance over and above (e.g., after adjusting for) the effects of brain change, pathology, or insult. For example, in a multiple regression analysis of change in cognition that includes brain atrophy/pathology measures and a hypothesized CR proxy, the proxy should account for variance in cognitive performance. In this analysis, the CR proxy simply adds predictive information (a protective factor), a weaker form of CR evidence than moderation.

All 3 components are needed when investigating CR. For example:

Demonstrating that expression of higher connectivity within a specific resting BOLD network is associated with slower cognitive decline is not sufficient to conclude that expression of this network reflects CR. To make a claim about CR it must also include measures of age-related brain change, insult or disease that theoretically impact cognitive outcomes.

Similarly, a relationship between a particular genotype and rate of cognitive decline would not be sufficient to conclude that this genotype is associated with CR. It would be important to demonstrate that the genotype's relationship to reduced rates of cognitive decline is expressed through moderation of age-related brain change or reduction of the expected impact on cognitive performance of a given brain insult or disease.

3.3. Specification of the 3 components needed to elucidate CR

3.3.1. Measures of life course-related brain developmental changes, injury, or disease that theoretically impact cognitive outcomes

This could consist, for example, of measures of anatomic changes such as loss of brain volume or white matter tract integrity, or onset and progression of disease pathology such as biomarkers of neurodegenerative disease.

These changes could be more extensively specified. Measures/mechanisms underlying aging that impact cognitive outcomes could include change in structure or function of synapses, oxidative damage/stress, impaired stress response signaling, Ca2+ dyshomeostasis and/or dysregulation, mitochondrial function, impaired waste disposal, inflammation, epigenetics, stem cell depletion, and altered neuronal activity/connectivity.

It is likely that unmeasured or unknown brain or pathologic changes contribute to inter-individual variance in the cognitive outcomes. Their eventual inclusion would increase the precision of elucidating CR.

3.3.2. Measures of cognition

This term encompasses measures of cognition and day-to-day function that change with aging and disease. When possible, it would be useful to adopt cognitive tests that show changes with age or brain disease, and that can be used across species. In this case, it is important to be mindful that formal operational similarity between human and nonhuman tasks is not sufficient, or even necessary; the tasks need to tap similar underlying neural systems.

3.3.3. CR proxy/mechanism:*a hypothesized variable that influences the relationship between 1 and 2*

As the definition of CR states, these mechanisms can be characterized via biological or cognitive experimental approaches.

Proxies for CR in human studies have included features associated with both endowment and experience, including early age IQ, cognitively stimulating exposures across the age span, education, occupational exposures, leisure activity, social networks, or other exposures, hypothesized or to be discovered, that might impart CR. Similar proxies such as behavioral training, physical exercise, environmental enrichment, social housing, or diet are applicable to nonhuman studies.

In addition, the nature of the CR proxy or mechanism that influences the relationship between component 1 and 2 can be explored. For example, investigators might explore whether differential expression of a specific functional network is associated the degree of sustained cognitive function in the face of age-related brain changes that impact cognition. More generally, mechanisms underlying CR could be specified at the molecular, cellular or network levels.

3.4. Example of studies of CR

In studies of CR, longitudinal designs optimally address the 3 features underlying the concept of CR. However, rich information can be gained from cross-sectional studies including discovering variables that appear to be critical for CR, establishing preliminary observations, providing insight into neurobiological mechanisms and developing research or conceptual approaches.

3.4.1. Longitudinal study incorporating measures of brain and cognitive change

In a longitudinal study, one could explore whether some life exposure conceptually linked to CR moderates the relationship between change in brain status (e.g., volume, white matter tract integrity, white matter hyperintensity burden) and change in cognition. For example, one could establish a relationship between age-related changes in cortical thickness/surface area, brain volume, and white matter tract integrity with changes in cognition. The potential moderation by education of this relationship could then be explored. Such moderation would provide support for the idea that higher education is associated with CR.

Some longitudinal studies may have no direct measures of brain change. Analyses that assume parity across all followed individuals or incorporate risk factors for brain changes could suggest hypotheses and guide subsequent studies.

3.4.2. Neural implementation of CR

Although variables such as IQ, education, occupational attainment etc. can be associated with CR as described in 4.1, that is, moderating between measures that theoretically impact cognitive outcomes (component 1) and measures of associated change in cognition (component 2), more insight into the mechanisms underlying CR might be obtained from studies that directly examine neural mechanisms. In both human and nonhuman studies, imaging techniques including functional MRI (fMRI), spectroscopy, and EEG are uniquely suited for longitudinal measurements, providing in-depth assessments of brain structure, neural activity, and the chemistry in the aging brain. CSF, plasma/serum, and extracellular vesicle biology in blood are advancing rapidly and may provide a translatable fluid biopsy for relevant brain changes in this context.

Thus, one goal might be to identify functional networks or circuits, whose differential expression moderates the relationship between age-related brain changes that impact cognitive outcomes and the associated change in cognition. For example, longitudinal studies of aging or neurodegenerative disease can investigate how the relationship between changes in structure/function and cognition/clinical status can be moderated by proposed reserve-related networks. It would be of interest to determine whether differential expression of this network is related to life exposures such as education or occupational experience. This would create a relationship between a proxy for CR and a potential brain mechanism underlying that proxy.

3.4.3. Intervention studies and natural experiments

Intervention studies can most directly test whether some exposure or mechanism underlies CR by examining whether the intervention moderates the effect of age-related brain changes on cognitive outcomes. These studies can help explore mechanisms underlying CR.

Similarly, controlled perturbations such as transcranial magnetic or direct current stimulation could model brain insult, stressor or disease. Alternately, they could be used to modulate activity in networks/circuits associated with CR, and by suppressing it or facilitating it, gain causal and mechanistic insights, and even potentially explore therapeutic interventions.

Sometimes, environmental changes can be used as natural experiments. A natural experiment is a situation when some change occurs in the environment that is not under experimental control and approximates random assignment. An example of such a natural experiment is changes to compulsory schooling laws. Conversely, animal models that feature increased individual differences in cognitive aging, under conditions of tightly controlled life-course exposures, can test for inherent genetic and biological moderators or mediators of CR. Quasi-experimental twin design is closest to this experimental design in humans. This design can utilize cotwins with different levels of exposures such as educational or occupational attainment.

4. BM

4.1. Definition

BM refers to the relative absence of changes in neural resources or neuropathologic change over time as a determinant of preserved cognition in older age.

BM can be influenced by multiple genetic and environmental factors, operating at various points across the lifespan.

4.2. Operational definition

BM is influenced by factors (genes, sex, early life influence or differential experiences) that slow or prevent brain changes associated with aging and disease. The emphasis centers on change over time. Thus, BM may be operationalized as minimal changes in brain markers of aging or disease associated with preservation of cognitive function.

Research aimed at further elucidating BM requires the inclusion of 3 components.

1. Measures of age-related brain changes, injury or disease that theoretically impact cognitive outcomes,
2. Measures of change in cognition.

Demonstrating a link between less change in 1 and less change in 2 would be evidence of BM.

To investigate potential mechanisms of individual differences in BM one could examine:

1. A hypothetical variable that influences 1.

This variable can encompass many of the same exposures potentially associated with CR. However, their impact on BM in this context would be specific to maintaining the structural and functional integrity of the brain.

4.3. Example studies of BM

BM is optimally ascertained in longitudinal designs. A single time point measurement cannot definitively differentiate people who have maintained their brain from those who did not but started at a higher baseline level. In both human and nonhuman studies this issue can be addressed to some degree by determining what level of brain status is expected for a particular age, or considering a given brain measure relative to the distribution seen in younger subjects. However, longitudinal designs are preferable to examine factors underlying interindividual differences in the change in neural resources that are in turn associated with differences in cognitive outcomes.

4.3.1. Longitudinal study of BM

A general approach to studying BM would be to examine longitudinally whether individual differences in the rate of age- or disease-related brain anomalies accumulated over time are related to individual differences in the rate of cognitive change.

4.3.2. Exposures related to BM

An extension of study 3.1 would be to assess potential proxies or mechanisms (e.g., genetic, lifestyle, neural) that are associated with these different trajectories of BM/change.

In summary, BM and CR are complementary concepts. BM accounts for individual differences in cognitive trajectories that are associated with differences in rate of brain change. In contrast, CR addresses individual differences in cognitive trajectories controlling for changes in neural resources or neuropathology.

5. BR

5.1. Definition

BR has been used to reflect the neurobiological status of the brain (numbers of neurons, synapses, etc.) at any point in time. BR does not involve active adaptation of functional cognitive processes in the presence of injury or disease as does CR.

5.2. Operational definition and example studies

Research aimed at further elucidating BR requires the inclusion of 2 components:

1. Measures of brain features that theoretically are associated with cognition.
2. Associated measures of cognition.

5.3. Example studies of BR

Longitudinally, differences in BR at a point in time could account for the observation that individuals starting at a different level of cognition may show the same rate of age- or disease-related cognitive decline. This could reflect different initial levels (intercepts) due to variation in BR, but similar rates of change (slopes) due to similar depletion of BR. This is distinguished from BM, where slopes would differ as a function of the degree of BM.

BR has also been associated with individual differences in level of cognition given a specific amount of brain change, injury or disease, such as amyloid plaques and neurofibrillary tangles. This association could rely on a threshold model, where a specific amount of depletion of neurobiological capital results disease-related changes. Those who initially have a higher BR can tolerate more depletion before they show symptoms.

6. Conclusion

Here we present a framework that includes well defined operational definitions for 3 concepts: CR, BM and BR. We also propose the term resilience to subsume all of the concepts presented. The operational definitions were carefully designed to be applicable to both human and nonhuman studies.

We believe that the use of a common vocabulary and operational definitions will facilitate research design and communication. The framework also provides a basis for describing how the operational definition of another concept differs from those suggested here.

Our hope for this framework is that a common vocabulary and operational definitions will facilitate even greater progress in understanding the factors that are associated with successful aging and lifelong brain health.

Disclosure statement

None of the authors have actual or potential conflicts of interest to disclose.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.neurobiolaging.2022.10.015. This includes: 1. Aknowledgment list 2. descriptions of funded pilot projects and 3,a table that summarizes the projects and how they incorporate the framework presented here.

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Commentary

Lost – and Found – in Translation

Molly V. Wagster[a,*], Jonathan W. King[b]

[a] Division of Neuroscience, National Institute on Aging, Bethesda, MD, USA
[b] Division of Behavioral and Social Research, National Institute on Aging, Bethesda, MD, USA

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In 2017, the National Institute on Aging (NIA) with the support of the Foundation for the National Institutes of Health on behalf of the McKnight Brain Research Foundation, held the Cognitive Aging Summit III. This third Summit was focused on cognitive reserve and resilience, highlighting the increasing importance of these concepts towards understanding age- and pathology-related cognitive change. At the same time, the Summit also highlighted important gaps in our shared understanding of how to characterize terms such as *reserve, resilience*, and *maintenance*; moreover, these gaps appeared to result from a lack of clear and consistent definitions of these and related terms. Disagreements over nomenclature and terminology are hardly new in psychology and neuroscience; indeed, the recognition of Jingle/Jangle fallacies in the measurement literature (Kelley, 1927) has long exposed the obstacles to knowledge advancement that these create. Especially clear at the Summit was that differences in usage of key terms had become serious enough to be more than just a nuisance, impeding (among other things) the ability of researchers using human vs. animal models, cross-sectional vs. longitudinal designs, or neuroimaging vs. neuropsychological approaches to appreciate each other's scientific contributions, much less potentially collaborate. In order to know whether and how a lifestyle, a gene or genes, a personality trait, other factors, or all of the aforementioned confer cognitive reserve, brain maintenance, or resilience to neurodegenerative disease, we need common definitions and a universal language.

When we use the same term to refer to different things (the Jingle Fallacy) or different terms to refer to the same thing (the Jangle Fallacy), fundamental knowledge accumulation and progress predictably grind to a halt. Given the gravity of the inconsistencies in the field, the NIA published a funding opportunity announcement (RFA-AG-18-024, "Collaboratory on Research Definitions for Cognitive Reserve and Resilience to Alzheimer's Disease") to drive the development of operational definitions for the constructs of resilience and reserve, as well as related and often used terms such as compensation, brain maintenance, and even resistance.

In 2018, an award was made to support a unique structure to develop uniform, research-based definitions. Designated as the Collaboratory, the award allowed the investigators to use multiple routes to build definitions and consensus by forming working groups and holding workshops, and to enable the cross-validation of proposed definitions and concepts by supporting small pilot projects.

Besides fostering a common language and thus understanding among researchers for these constructs, the framework developed by the team and presented in this issue of *Neurobiology of Aging* will have far-reaching impact. Understanding, treating, and preventing Alzheimer's disease and Alzheimer's disease related dementias is a national priority for the U.S. If we can harness the knowledge of what confers reserve and resilience, treatments could be targeted to mimic these factors and hopefully prevent or slow disease progression.

The paper in this issue describes the thought processes in which the blue-ribbon Executive Committee for the Collaboratory, aided by many experts around the globe, engaged to reach consensus and provide distilled guidance for the scores of researchers hoping to crack the code on how to gain or maintain successful cognitive performance and brain function with age. As the authors note, these definitions may be subject to revision as we gain more knowledge, but it is the generation of operational definitions like

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* Corresponding author at: Molly V. Wagster, Division of Neuroscience, National Institute on Aging, Gateway Building, Suite 3E400, 7201 Wisconsin Avenue, Bethesda, MD, 20892, USA. Tel.: 301-496-9350; fax: 301-496-1494.
E-mail address: wagsterm@nia.nih.gov (M.V. Wagster).

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these in this framework that will help us more clearly communicate.

Uniformity has its benefits - a common language, operational definitions, and a platform from which to propose alternatives. If we aren't speaking the same language, we will be lost in the translation. This effort insures we can find a path forward.

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Regular article

Extracellular matrix proteoglycans support aged hippocampus networks: a potential cellular-level mechanism of brain reserve

Daniel T. Gray [a], Marc Zempare [b], Natalie Carey [b], Salma Khattab [b], Irina Sinakevitch [b], Lindsay M. De Biase [a], Carol A. Barnes [b,c,*]

[a] Department of Physiology, David Geffen School of Medicine, UCLA, Los Angeles, CA, USA
[b] Evelyn F. McKnight Brain Institute, University of Arizona, Tucson, AZ, USA
[c] Departments of Psychology, Neurology and Neuroscience, University of Arizona, Tucson, AZ, USA

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ABSTRACT

One hallmark of normative brain aging is vast heterogeneity in whether older people succumb to or resist cognitive decline. Resilience describes a brain's capacity to maintain cognition in the face of aging and disease. One factor influencing resilience is brain reserve—the status of neurobiological resources available to support neuronal circuits as dysfunction accumulates. This study uses a cohort of behaviorally characterized adult, middle-aged, and aged rats to test whether neurobiological factors that protect inhibitory neurotransmission and synapse function represent key components of brain reserve. Histochemical analysis of extracellular matrix proteoglycans, which play critical roles in stabilizing synapses and modulating inhibitory neuron excitability, was conducted alongside analyses of lipofuscin-associated autofluorescence. The findings indicate that aging results in lower proteoglycan density and more lipofuscin in CA3. Aged rats with higher proteoglycan density exhibited better performance on the Morris watermaze, whereas lipofuscin abundance was not related to spatial memory. These data suggest that the local environment around neurons may protect against synapse dysfunction or hyperexcitability and could contribute to brain reserve mechanisms.

1. Introduction

One often held misconception of brain aging is that neurodegenerative disease is inevitable; however, only 10%–14% of individuals over 65–70 years of age in the United States are demented (Manly et al., 2022; Plassman et al., 2007). This is not to imply that there are no cognitive changes that occur in normative aging. Rather, the extent of the decline and the domains impacted vary widely across healthy older individuals (e.g., Nyberg et al., 2012; Ryan et al., 2019). These individual differences may be a result of resilience or the capacity of the brain to maintain cognition and function across the lifespan (Stern et al., 2022). While there is still considerable debate regarding the exact nature of resilience, it can be achieved both through active adaptation and by tapping into existing neuronal resources (e.g., Cabeza et al., 2018; Stern et al., 2019, 2022). The factors that facilitate the engagement of brain reserve mechanisms can be either intrinsic to the brain or result from life exposure and can arise through a variety of mechanisms that range from molecular to cellular to network levels.

It has proven relatively challenging to identify robust intrinsic neurobiological features associated with resilience, particularly at cellular and molecular levels of analysis. One major reason for this challenge is that it is difficult to study mechanisms of resilience in animal models. This is because resilience is optimally assessed either through longitudinal study designs that can assess whether life exposure moderates the relationship between brain status and cognition or through cross-sectional studies that require very large sample sizes to appropriately sample the variability in cognitive outcomes necessary to study resilience (Stern et al., 2019, 2022). Despite these challenges, the much wider array of tools available to study the brain at multiple levels of analysis in nonhuman animals compared to humans highlights the importance of developing research aimed at understanding variability in cognitive function in these models of human aging. In rodents and nonhuman primates, one of the neurobiological features that most closely predicts cognitive performance is the number or function of synapses (e.g., Burke and Barnes, 2006; Dumitriu et al., 2010; Hara et al., 2012; Morrison

Abbreviations: CA3, cornu Ammonis 3; CIPL, Corrected Integrated Path Length; NDS, Normal Donkey Serum; OCT, Optimal Cutting Temperature; PBS, Phosphate Buffered Saline; WFA, *wisteria floribunda agglutinin*

* Corresponding author at: Evelyn F. McKnight Brain Institute, University of Arizona, Life Science North, Room 355, Tucson, AZ 85724-5115, USA.
E-mail address: carol@nsma.arizona.edu (C.A. Barnes).

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and Baxter, 2012; Smith et al., 2000). Thus, understanding the details of the variables that impact synapse health is critical to elucidating the biological mechanisms of cognitive resilience in aging. To this end, the present study combines histochemical and image-based analyses of tissue from a relatively large cohort of young adult, middle-aged, and aged rats to investigate potential neurobiological correlates of brain reserve, which is one mechanism by which resilience is thought to be accomplished.

Brain reserve refers to a neurobiological status that allows certain older individuals to evade robust declines in cognition. For a neurobiological factor to be considered brain reserve, it must be associated with some aspect of cognitive function independently of age (Stern et al., 2019, 2022). For example, it has been demonstrated that, regardless of age, rodents with more durable long-term potentiation (LTP) also have more durable memory (Bach et al., 1999; Barnes, 1979; Dieguez and Barea-Rodriguez, 2004). Furthermore, work from rodents, monkeys, and humans has shown that neuronal hyperexcitability of the CA3-dentate gyrus region of the hippocampus emerges with advanced age, most prominently in individuals that exhibit the greatest degree of memory impairment (Spiegel et al., 2013; Thomé et al., 2016; Wilson et al., 2005; Yassa et al., 2011). Immunohistochemical labeling and slice physiology of CA3 neurons indicate that age-associated deficits in inhibitory neurotransmission likely play central roles in this hyperexcitability (Spiegel et al., 2013; Thomé et al., 2016; Tran et al., 2018). These observations predict that neurobiological factors that work to maintain neuronal plasticity and excitatory-inhibitory balances in the hippocampus may represent a form of brain reserve for hippocampus-dependent aspects of cognition.

In this study, we provide evidence that the status of the brain extracellular matrix may represent a form of brain reserve, and we suggest that this is likely accomplished by mediating the relationship between altered inhibitory signaling, CA3/dentate gyrus hyperexcitability (e.g., Small et al., 2002; Thomé et al., 2016; Wilson et al., 2005; Yassa et al., 2011), and memory abilities later in life. The extracellular matrix is a network of proteins and sugars that are secreted from multiple cell types and play critical roles in regulating tissue hydration, ionic balances, and neuronal plasticity (Dityatev et al., 2010). Specialized insoluble aggregations of extracellular matrix proteoglycans called perineuronal nets have garnered significant attention due to their roles in regulating inhibitory neuron function (Sorg et al., 2016). Age-associated reductions in perineuronal nets around inhibitory neurons have been observed in the retrosplenial cortex (Gray et al., 2022; Ueno et al., 2019), which is a region that is critically involved in mnemonic processing and exhibits increased cFos expression (Haberman et al., 2017) and reduced functional connectivity (Ash et al., 2016) in memory-impaired aged rats. While perineuronal net structures in the cortex preferentially aggregate around inhibitory neurons (Brückner et al., 1993; Härtig et al., 1992), the proteoglycans in the hippocampus preferentially accumulate around the somas of CaMKII-expressing excitatory neurons in the pyramidal cell layers of CA2 and CA3 (Lensjø et al., 2017). Whether age impacts hippocampal perineuronal net structures distinctly from those in the cortex has not been assessed. Here, we examine the impact of age on extracellular matrix proteoglycans, specifically in CA3, of behaviorally assessed rats at different points of the lifespan.

2. Materials and methods

2.1. Subjects

A total of 29 adult (6–8 months), 33 middle-aged (15–17 months), and 34 aged (23–25 months) male F344 rats (Harlan Sprague-Dawley, Indianapolis, IN, USA) participated in the study. Rats were housed individually in Plexiglas guinea pig tubs on a reverse 12-hour light-dark cycle and were given free access to food and water. Rats were handled between 5 and 10 minutes per day following their arrival prior to behavioral testing. All protocols described adhered to NIH guidelines and guidelines set by the Animal Care and Use Committee at the University of Arizona (Tucson, AZ).

2.2. Behavioral testing

Rats were tested on the spatial and visually cued versions of the Morris watermaze (Morris, 1984). Rats that were not able to perform the visually cued version of the Morris watermaze were excluded from participation in the study due to the visual demands of this paradigm. The watermaze apparatus consisted of a circular pool with an approximate diameter of 120 cm and a depth of 36 cm. An escape platform was hidden beneath the surface of the water for the spatial version and just above the surface of the water for the cued version (Fig. 1A). Water was made opaque using nontoxic white Crayola paint and maintained at a temperature range between 26°C and 28°C. The apparatus sat in the center of a 2.3 × 2.73 × 2.5 m room that contained several visual stimuli on the walls as distal cues. A chair and a metal board were placed adjacent to the pool as proximal cues.

The full protocol for the Morris watermaze procedure used in this study has been published previously (Barnes et al., 1996). Briefly, the spatial version of the watermaze consisted of 4 sequential days of testing with each rat performing 6 trials per day. For each trial, the rats were given 1 minute to locate the escape platform. If the rat failed to locate the platform after 1 minute, it was guided and placed on the platform for 30 seconds. The procedure for the cued version of the watermaze was identical to the spatial version with the exception that testing was conducted over 2 consecutive days instead of 4. A corrected integrated path length (CIPL) measure was calculated as described in detail elsewhere (Gallagher et al., 1993; Shen and Barnes, 1996; Vorhees and Williams, 2014). Briefly, this measure is derived by calculating an average swimming speed for each animal on each trial as well as the amount of time required to swim to the escape platform in a straight line at that speed. This speed-corrected optimal pathlength is then removed from the record to get the CIPL score. This procedure corrects for the locations of the different start location entry points (some being closer to the platform than others). To evaluate improvement in task performance, a within-subject measure was derived by subtracting the average session 4 CIPL from the average session 1 CIPL (Day 1 – Day 4).

2.3. Histological preparations

Following behavioral testing, all rats were anesthetized with 5% isoflurane and decapitated using a rodent guillotine. The brains were rapidly extracted, flash-frozen in isopentane, cooled over an ethanol bath containing dry ice, and stored at −80°C until cryosectioning. For sectioning, brains were blocked in optical cutting temperature (OCT) compound such that an adult, middle-aged, and aged brain were included on the same slide to reduce technical variability. Sections of 20 µm in thickness were then cut and mounted using a cryostat. Slides were stored at −80°C.

The day before staining, the slides were moved into a −20°C freezer. On the first day of the histological protocol, slides were first removed from the freezer and allowed to thaw for approximately 20 minutes. The tissue was then fixed by submerging slides in 4% paraformaldehyde in phosphate buffer saline (PBS; Sigma-Aldrich, P-5368, 0.01 M, pH 7.4) for 30 minutes. Slides were rinsed in PBS buffer containing 0.01% Triton-X (PBS-TX) and then incubated for 1 hour in a blocking solution consisting of 1% normal donkey serum (NDS; Sigma-Aldrich, D9663) in PBS-TX. A hydrophobic pen was used to

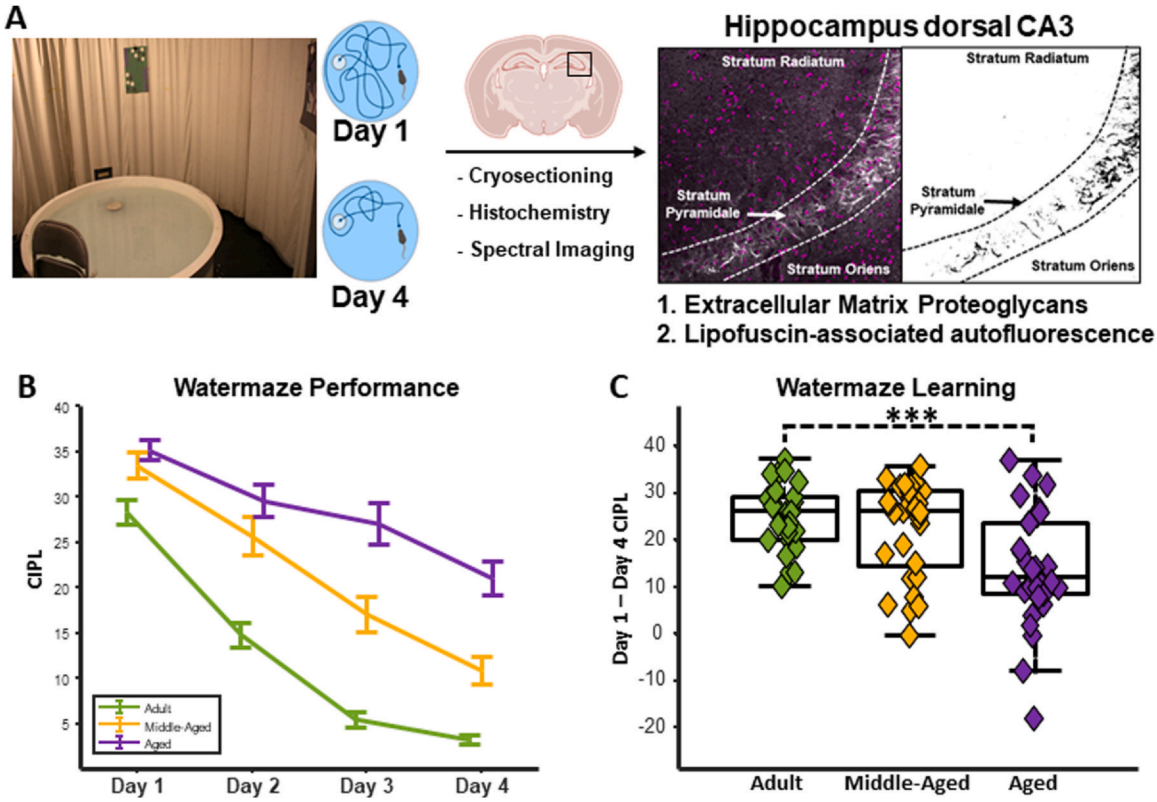

Fig. 1. Experimental design and age comparisons of spatial memory on the Morris watermaze. (A) Image of the Morris watermaze testing environment. The watermaze apparatus consisted of a circular pool with an approximate diameter of 120 cm and a depth of 36 cm and an escape platform hidden beneath the surface of the water for the spatial version and just above the surface of the water for the cued version. Rats underwent 4 sequential days of testing with each rat performing 4 trials per day, and a corrected integrated path length (CIPL) to the escape platform was calculated (see "Methods"). Brains from all animals underwent histological and image-based analyses of extracellular matrix proteoglycan abundance (*wisteria floribunda agglutinin*) and lipofuscin-associated autofluorescence. (B) Average CIPL scores across the 4 days of testing for the adult, middle-aged, and aged rats used in the histochemical analyses. Green represents adult rats, yellow represents middle-aged rats, and purple represents aged rats. Both aged and middle-aged rats exhibited higher CIPL scores than did young across all sessions, and aged rats exhibited higher CIPL scores on the third and fourth days of testing compared to middle-aged rats. (C) The difference measured between day 1 and day 4 of testing. Boxplots denote the middle 50% of the data, and horizontal lines indicate the median of each distribution. Aged rats exhibited a smaller difference, indicating poorer spatial learning. **, $p < 0.01$.

draw a perimeter around all the tissue on the slide, and the blocking solution was pipetted onto the slide. Following incubation in the block solution, the sections were incubated overnight in a solution containing 1% NDS, 0.01% PBS-TX, and biotinylated wisteria floribunda agglutinin (WFA; 1:50; Vector Laboratories, B-1355), which selectively labels N-acetylgalactosamines beta 1 (GalNAc beta 1–3 Gal) residues of glycoproteins within the extracellular matrix (Hilbig et al., 2001). The slides were then washed in PBS-TX (3 × 5 minutes) and incubated in a solution consisting of 1% NDS, PBS-TX, and streptavidin-conjugated Cy5 (peak emission: 670 nm, 1:50; Vector Laboratories, Burlingame, CA, United States; SA-1500). Slides were washed again in PBS (3 × 5 minutes) and coverslipped using 80% glycerol (Vector Laboratories, Burlingame, CA, United States, H-1200-10).

2.4. Confocal imaging and image processing

Brain sections were first imaged with a 40x/1.3 oil objective using a Zeiss LSM 880 inverted confocal microscope to obtain images of native tissue autofluorescence. Image acquisition was performed using a 405-nm laser (Diode 405-30), a 488-nm laser (Argon), and a 633-nm laser (Helium-Neon). All 3 laser lines were used simultaneously in Lambda collection mode using ZEN Black 2.1 imaging software. Lambda collection mode imaging enables the collection of pixel intensity data along the full emission spectrum (410–695 nm) in 32 distinct bins (8.9 nm/bin). For each tissue section, a Z-stack was collected centered on the pyramidal cell layer of the CA3 region of the dorsal hippocampus (Fig. 1A), and these images were fed into a linear unmixing analysis to classify and separate the native tissue autofluorescence from fluorophore fluorescence. The linear unmixing analysis was conducted using ZEN Blue software. The analysis uses a least-squares fit-based algorithm to classify individual pixels into different channels based on their relative contribution to each channel's reference spectrum (Mansfield et al., 2005; Zimmermann, 2005). Unlabeled brain sections were imaged in Lambda mode using the 405-, 488-, and 633-nm lasers to obtain autofluorescence reference spectra, and the reference spectra for each fluorophore were obtained by imaging brain sections with just a single fluorophore. A full description of the linear unmixing procedure was previously published (Pyon et al., 2019). All brain sections were imaged a second time using a 20x objective on a Zeiss Apotome microscope to obtain images of WFA. Again, Z-stacks centered on the CA3 region of the dorsal hippocampus were obtained.

2.5. Image analysis

Image analysis was performed using custom-written macros in Fiji (ImageJ; Schneider et al., 2012) image analysis software. Images of the native tissue autofluorescence and WFA were imported into Fiji, and their contrast was enhanced using the "Enhance Contrast" command. The images were then thresholded using the

"setAutoThreshold" command with the "RenyiEntropy dark" setting with a lower pixel intensity cutoff of 145. The thresholded images were binarized, and the proportion of pixels above the threshold was extracted as an estimate of native autofluorescence abundance and WFA deposition.

2.6. Statistical analyses

Analysis of Morris watermaze performance between age groups was performed using a 2-way analysis of variance (ANOVA) with age as a factor and an α-level of 0.05. *P* values underwent a Bonferroni-Holm correction for post-hoc comparisons. An analysis of WFA deposition and the abundance of autofluorescence were also assessed using a 2-way ANOVA with age as a factor. Individual relationships between anatomical variables and Morris watermaze performance were assessed using a robust regression analysis, also with an α-level of 0.05. All analyses were performed using R Studio statistical analysis software (Boston, MA) or MATLAB (Natick, MA).

3. Results

3.1. Spatial memory deficits increase as a function of age

All rats underwent testing on the spatial version of the Morris watermaze across 4 consecutive sessions. There was a significant effect of the session on the average CIPL scores across sessions, indicating that the animals learned the location of the escape platform (repeated measures AVOVA; $F(3255) = 92.03$; $p < 0.0001$; Fig. 1B). A significant age-by-session interaction was also observed, indicating that older rats exhibit poorer spatial learning across sessions (repeated measures AVOVA; $F(3255) = 11.73$; $p < 0.0001$; Fig. 1B). Post-hoc analyses indicate that middle-aged rats exhibited higher CIPL scores than did young adults across all sessions (*t*-test, Bonferroni-Holm correction; Day 1: $t(53) = -2.65$, $p = 0.01$; Day 2: $t(53) = -4.15$, $p < 0.0001$; Day 3: $t(53) = -5.34$, $p < 0.0001$; Day 4: $t(53) = -3.11$, $p < 0.0001$), as did the aged rats (*t*-test, Bonferroni-Holm correction; Day 1: $t(56) = -4.13$, $p < 0.0001$; Day 2: $t(56) = -6.19$, $p < 0.0001$; Day 3: $t(56) = -8.00$, $p < 0.0001$; Day 4: $t(56) = -8.28$, $p < 0.0001$). Post-hoc comparison also indicates that aged rats exhibited a higher CIPL than did the middle-aged rats on the third and fourth sessions (*t*-test, Bonferroni-Holm correction; Day 1: $t(59) = -0.98$, $p = 0.33$; Day 2: $t(59) = -1.39$, $p = 0.16$; Day 3: $t(59) = -3.29$, $p < 0.01$; Day 4: $t(59) = -4.10$, $p < 0.001$). The difference between day 1 and day 4 CIPL scores was calculated as an estimate of spatial learning, with the older animals showing lower scores (ANOVA; $F(2, 95) = 6.34$, $p = 0.003$; Fig. 1C). Post-hoc tests confirm that aged rats exhibited a smaller difference in performance between day 1 and day 4 compared to young adults (*t*-test; $t(61) = 4.01$, $p = 0.00037$). Although not statistically significant, the same trend was observed when directly comparing middle-aged and aged rats (*t*-test; $t(65) = 2.04$; $p = 0.09$). On the cued version of the watermaze, there was an effect of day of training in all age groups (ANOVA, $F(1, 95) = 72.4$, $p < 0.0001$), indicating that the animals improved performance over days. There was no overall statistically significant difference between age groups (ANOVA, $F(2, 95) = 3.07$, $p = 0.0512$), nor was there an age-by-day interaction (ANOVA, $F(2, 95) = 0.84$, $p = 0.43$).

3.2. Reduced proteoglycan density is associated with spatial memory only in aged rats

An age-associated decrease in WFA deposition was observed (2-way ANOVA; age: $F(1, 84) = 10.187$, $p = 0.002$; Fig. 2B). Post-hoc tests confirm that WFA deposition was lower in aged rats compared to young adults (*t*-test; $t(56) = 3.77$; $p = 0.00079$) but was not different between middle-aged and aged rats (*t*-test; $t(60) = 1.25$; $p = 0.42$), nor between adult and middle-aged rats (*t*-test; $t(54) = 1.73$; $p = 0.17$), although middle-aged rats appeared to show WFA coverage that was intermediate between the young adult and aged rats. When WFA deposition was analyzed with respect to watermaze learning scores, no relationship was observed in the young-adult or middle-aged groups (robust regression; adult: $t(24) = -1.11$, $p = 0.27$; middle-aged: $t(28) = -0.59$, $p = 0.56$; Fig. 2C). Among the aged rats, however, the animals with more WFA in CA3 exhibited better watermaze learning (robust regression; *t*

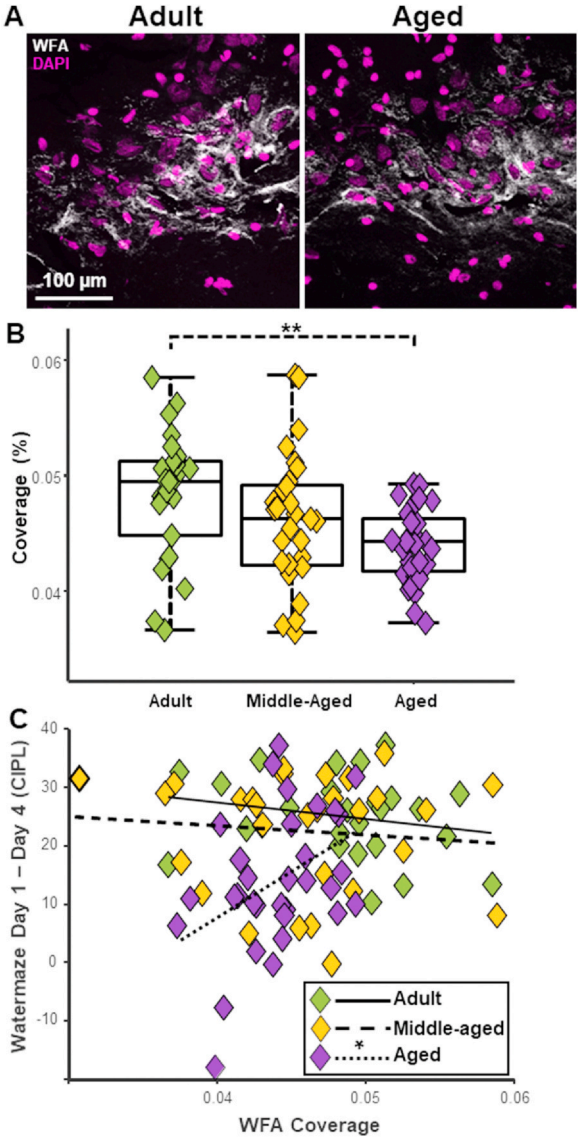

Fig. 2. Aged rats with more extracellular matrix in CA3 exhibited better spatial memory. (A) Representative photomicrograph of *wisteria floribunda agglutinin* (WFA) labeling in the CA3 region of the dorsal hippocampus from a young-adult and aged rat. (B) WFA coverage of dorsal CA3 separated by age. Aged rats exhibited lower WFA coverage than young-adult rats. Boxplots denote the middle 50% of the data, and horizontal lines indicate the median of each distribution. (C) Scatter plot of WFA coverage and Morris watermaze learning scores (Day 1 – Day 4 CIPL difference). There was no significant relationship observed between WFA coverage and CIPL difference scores for the adult and middle-aged rats. Amongst the aged rats, however, the animals with the most WFA coverage showed the best learning on the Morris watermaze. ***, $p < 0.001$.

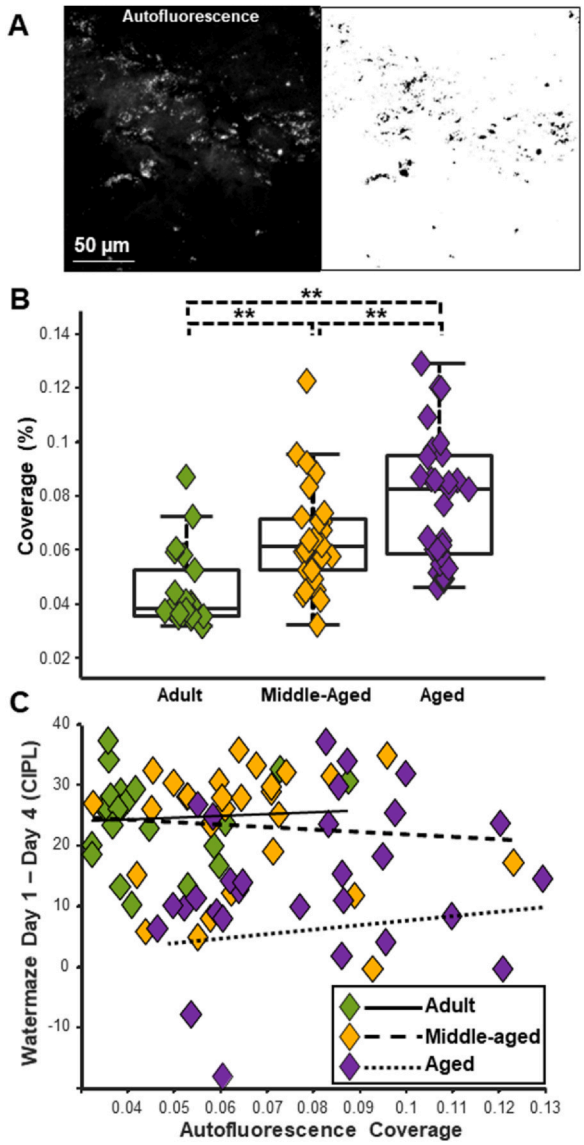

Fig. 3. Lipofuscin increases with age but is not associated with spatial memory. (A) (Left) Representative photomicrograph of lipofuscin-associated autofluorescence in the CA3 region of the dorsal hippocampus. (Right) A threshold image of the same micrograph to show the lipofuscin-associated autofluorescence. (B) Lipofuscin-associated autofluorescent coverage of dorsal CA3 separated by age. Boxplots denote the middle 50% of the data, and horizontal lines indicate the median of each distribution. The older animals exhibited more lipofuscin than did middle-aged or young-adult animals. Middle-aged animals showed more lipofuscin than did young adults. (C) Scatter plot of lipofuscin coverage and Morris watermaze learning scores (Day 1 – Day 4 CIPL difference). There was no significant relationship observed between lipofuscin coverage and CIPL difference scores for any age group. *, $p < 0.05$; ***, $p < 0.001$.

(30) = 2.06; $p = 0.04$; Fig. 2C). These data suggest that extracellular matrix proteoglycans in CA3 represent a biological variable that both changes with advanced age and has an impact on cognitive outcomes.

3.3. Age-associated increases in lipofuscin-associated autofluorescence are not associated with memory

The proportion of a field of view that was covered by lipofuscin-associated autofluorescence (Fig. 3A) was greater in the aged rats compared to young-adult and middle-aged rats (2-way ANOVA; age: $F(1, 75)$: 36.51, $p < 0.0001$; Fig. 3B). Post-hoc tests indicate that tissue from the middle-aged rats contained more lipofuscin compared to young adults (*t*-test; $F(48) = -4.04$, $p = 0.00038$; Fig. 3B), and aged tissue had more lipofuscin than both adult tissue (*t*-test; $F(48) = -5.95$, $p < 0.0001$) and middle-aged tissue (*t*-test; $F(55) = -2.44$, $p = 0.036$). No significant relationships were observed for any age group when lipofuscin coverage was analyzed with respect to watermaze learning scores (robust regression; adult: $t(20) = 0.29$, $p = 0.77$; middle-aged: $t(26) = -0.30$, $p = 0.76$; aged: $t(27) = 0.99$, $p = 0.33$; Fig. 3C). These data indicate that lipofuscin-associated autofluorescence represents a biological variable that changes with advanced age but has no impact on cognitive outcomes.

4. Discussion

The primary finding in this experiment is that aged rats with greater extracellular matrix proteoglycan deposition across the CA3 region of the hippocampus exhibited better spatial memory abilities compared to aged rats with less extracellular matrix protein. Conversely, age-related increases in lipofuscin-associated autofluorescence showed no relationship with spatial memory abilities in any of the age groups. Importantly, the relationship between greater proteoglycan deposition and spatial memory was only observed in aged rats and not in adult or middle-aged rats. This constellation of results fulfills the requirements of the operational definition of brain reserve that was proposed by Stern et al. (2022), which requires measures of aging brain features to be significantly related to cognitive phenotypes expressed in aged animals. In addition, the case for the extracellular matrix being an important component of brain reserve is made stronger by demonstrating the selectivity of this relationship, as age-associated increases in lipofuscin were not related to behavior.

4.1. The extracellular matrix regulates neuronal excitability

Age-associated hyperexcitability in the CA3-dentate gyrus region is thought to arise from a combination of factors, including decreases in inhibitory neuron drive onto excitatory neurons (Spiegel et al., 2013). Proteoglycans in the extracellular matrix play important roles in regulating processes that impact neural network excitability through a variety of different mechanisms. For example, enzymatic degradation of the extracellular matrix results in a significant reduction in inhibitory neuron firing (Balmer, 2016). Proteoglycans likely modulate firing properties due to their strong negative charge, which impacts the local electric field around neurons (Morawski et al., 2015). With age, as proteoglycan deposition decreases, it is possible that the voltage dependence of ion channels is impacted. One hypothesis that emerges from the present data is that, as deficits in inhibitory signaling begin to accumulate in aged brains, the proteoglycans of the extracellular matrix act as a buffer to maintain the network in a healthy physiological state. By extension, aged animals that maintain higher proteoglycan levels may avoid spatial memory impairments. This would be consistent with the idea that the preservation of the extracellular environment may represent a critical aspect of brain reserve.

Enzymatic degradation of extracellular matrix proteoglycans also results in the diffusion of AMPA receptors away from postsynaptic sites, which could alter postsynaptic sensitivity to glutamate release (Frischknecht et al., 2009). At glutamatergic synapses onto inhibitory neurons, the extracellular matrix stabilizes interactions between AMPA receptors and secreted scaffolding proteins such as neuronal pentraxins (Chang et al., 2010). Thus, another hypothesis that emerges from these data is that a breakdown of the hippocampus extracellular matrix and neuronal pentraxins decreases the stability of the glutamatergic drive onto inhibitory neurons. In humans, neuronal pentraxin 2 has been shown to decline in healthy aging and

to be substantially reduced in individuals with Alzheimer's disease. Importantly, in those cases where cognition is within a normal range but the brains show histopathological markers of Alzheimer's disease, neuronal pentraxin 2 is at age-matched control levels (Soldan et al., 2019; Xiao et al., 2017). These authors suggest that this protein protects cognitive function by maintaining a normal excitatory-inhibitory balance in these neural circuits.

4.2. The extracellular matrix regulates synapse function

With age, hippocampal neurons become susceptible to alterations in plasticity by becoming less able to maintain LTP (Bach et al., 1999; Barnes, 1979), more prone to long-term depression (Norris et al., 1996), and LTP reversal (Burke and Barnes, 2006; Norris et al., 1996). In addition to its role in regulating network excitability patterns that impact thresholds for the induction of different forms of plasticity, the extracellular matrix is also positioned to regulate mechanisms of structural synapse plasticity (Dityatev et al., 2010; Nguyen et al., 2020; Sorg et al., 2016). In the adult brain, extracellular matrix structures are thought to inhibit structural plasticity because they emerge toward the end of developmental critical periods and because genetic depletion of critical proteoglycans reinstates these critical periods (Lensjø et al., 2017; Pizzorusso et al., 2002, 2006). Furthermore, it has been shown that the release of matrix metalloproteinases and other degradative enzymes that target the extracellular matrix is necessary for experience-dependent plasticity (Nguyen et al., 2020; Wlodarczyk et al., 2011). Thus, in the adult brain, one function of the extracellular matrix might be to maintain a plasticity threshold that allows neuronal circuits to separate relevant from interfering stimuli. This would fit with the idea that one feature of brain reserve is the ability to preserve homeostatic balance within cells, which serves to optimize circuit function, thereby facilitating higher levels of cognition.

4.3. Extracellular matrix integrity may represent a form of brain reserve

The present findings indicate that it is the relative lack of change in the aged hippocampus extracellular matrix that provides some of the support necessary to maintain spatial memory in aged rats, consistent with a brain reserve mechanism. It is not possible to determine from the present data, however, whether contributions from cognitive reserve or brain maintenance as operationally defined by Stern et al. (2022) also contribute to our findings. A longitudinal design would be necessary to determine whether these other mechanisms of resilience were at play. For example, if the preserved extracellular matrix structure was a result of active adaptation to life-course exposures resulting in better-than-expected cognitive performance given the degree of brain insults sustained, then this would be consistent with a cognitive reserve mechanism. On the other hand, an absence of age-associated changes in the extracellular matrix over time would be consistent with a brain maintenance mechanism. Future longitudinal study designs in nonhuman models of aging will be necessary for determining which mechanisms beyond brain reserve may be playing a role. This would require extremely large initial cohorts to be examined at different time points across the lifespan. Such a study design should be able to capture the true impact that the extracellular matrix, or any other relevant neurobiological variable, has on cognitive outcomes across time.

Authors contributions

DTG conceptualized the experiment, oversaw imaging data collection, performed statistical analyses, and wrote the manuscript. MZ collected and analyzed behavioral data and revised the manuscript. NC collected and analyzed behavioral data. SK collected imaging and behavioral data. IS performed histochemistry, collected imaging data, and revised the manuscript. LMDB provided imaging resources and revised the manuscript. CAB conceptualized the experiment, oversaw behavioral data collection, and wrote the manuscript.

Verification

This manuscript is original, has not been published, and is not under consideration for publication elsewhere. We have no conflicts of interest to disclose.

Disclosure statement

The authors do not have any conflicts of interest.

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afar american federation for aging research

Proposal to The McKnight Brain Research Foundation Continue the MBRF Innovator Awards in Cognitive Aging and Memory Loss

Submitted by
the American Federation for Aging Research (AFAR)

February 15, 2024

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Executive Summary

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 provides up to two 3-year awards of $750,000 (USD) each. One award is to 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 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. The award provides 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.

To date, 6 talented investigators have been supported by the program. This proposal outlines AFAR's request to the McKnight Brain Research Foundation (MBRF) to provide support in the amount of $4,626,500 for three additional cohorts of investigators (6 total) and to develop efforts to capitalize on and put to new uses the considerable human capital investments made to date through past awardees.

Introduction and Rationale

By 2050, the number of people aged 60 and above is projected to reach 2 billion**.** While longevity brings numerous benefits, not all adults experience good health as they age and this has broad implications for our economies, healthcare systems and quality of life of both older adults and their families.

As we age, our brains undergo natural changes. Some cognitive decline is expected after middle age. However, the older we get, the more likely we are to experience signs of cognitive changes. For instance, mild cognitive impairment affects approximately 6.7% of individuals aged 60 to 64, but this percentage increases to over 25% among those aged 80 to 84[1]. These cognitive changes can impact abilities like processing speed and decision-making and can contribute to certain types of memory loss.

At this point in time, when the older population is rapidly growing in the United States and across the globe, it is important that we build a network of investigators and support their research on cognitive aging and memory loss. The MBRF Innovator Awards were designed to

[1] https://www.alz.org/media/Documents/alzheimers-facts-and-figures-special-report-2022.pdf

address this need. The Awards target independent investigators who are at a critical phase in their careers when they face challenges such as securing tenure, maintaining productivity, and balancing administrative responsibilities. The current research environment is forcing some investigators to take alternative career options. The rationales for supporting such individuals are that: 1) they are proven scientists, with a demonstrated commitment to research on cognitive aging and memory loss; 2) they bridge the gap between early-career investigators and seasoned experts and supporting them ensures continuity in scientific progress and knowledge transfer; 3) with very rare exceptions, they would already have gained peer-review support and have active laboratories; 4) given the above, they are deemed to be particularly receptive to embarking on research that offers significant promise of yielding transforming discoveries.

By providing research funding to these promising investigators as they continue to grow their careers and research portfolios, the MBRF aims to build a cadre of outstanding research scientists across the United States with the potential to lead transformative research in the field of cognitive aging.

Since its inception, AFAR's vision has been to fund and nurture talented scientists and physicians and encourage them to pursue lifelong careers in research focused on aging processes and age-related diseases. The partnership between the American Federation for Aging Research (AFAR) and MBRF over the past few years has proven to be a productive and positive collaboration, allowing both organizations to achieve their mutual goals.

AFAR proposes to continue and build on the partnership with MBRF by managing the grant review and administration for the MBRF Innovator Awards program.

Progress to date

The program was successfully launched in 2021. AFAR, in partnership with MBRF, designed, announced and broadly disseminated the RFA, identified a Selection Committee (Attachment 1) and established review procedures. After each Selection Committee, funding recommendations were presented to the MBRF board, and awards issued upon final approval. AFAR has also worked with MBRF to issue joint press releases after each awards cycle.

During the past three years, we identified two areas that needed further examination:

1. **Number of applications received:**

Although this is a substantial award, the number of applications has been relatively low compared to other programs AFAR manages. There may be barriers for investigators to apply to

this program reflecting on difficult academic environments. These barriers may include 1. Very targeted eligibility criteria; 2. Matching funds requirement, which may be especially difficult for investigators who are at institutions with limited resources.

Year	LOIs/Applications	Funded
2021	9	2
2022	5	2
2023	5	2

AFAR recently conducted a survey among academic leadership and other funding agencies to try and identify alternative markers of institutional commitment to help make recommendations for updated program guidelines. More details are outlined in the proposal below.

2. **Greater balance between basic science and clinical science applications**

During each grants cycle, we received more applications in basic science. As a result, we broadened the eligibility criteria for MD investigators in 2022. And for the 2023 program we instituted two review tracks (basic and clinical/translational).

However, for each grant cycle we received applications from high caliber candidates with strong research proposals, and the committee was confident recommending awardees for funding. The list of awardees can be found in Attachment 2. Although too soon to track progress on the most recently selected cohort, the first two cohorts have been very productive, publishing papers, making presentations at national and international meetings, and have secured additional grant support.

Proposal

AFAR proposes to manage the MBRF Innovator Awards in Cognitive Aging and Memory Loss, and that MBRF funds this effort in the amount of $4,626,500 over a period of five years, in support of 6 investigators. There will be three grant cycles, in which each year, the goal is to fund one award to support studies focusing on clinical translational research and another award toward understanding basic biological mechanisms underlying cognitive aging and age-related memory loss.

During the last three grant cycles we required the institutions to identify 50% in matching funds. However, this may be limiting the applicant pool and we have explored ways to grow the pool and enable applicants from less-resourced institutions to apply, creating a more equitable

funding opportunity. AFAR developed a brief survey to get input from the scientific community on adjusting the matching requirement to include **non-monetary indicators of institutional commitment.**

The survey was sent to 53 individuals in various leadership roles, including:

- Current McKnight Committee members
- AFAR scientific leadership
- Deans
- Chairs of Neurology/Neuroscience Programs
- Directors of Alzheimer's Disease Research Centers
- Leaders at other Funding Agencies/Foundations

32 people (~60%) completed the survey. The entire survey can be found in Attachment 3 but a summary can be found below:

- Protected Time: 97% indicated important
- Overhead: 56% indicated important
- Administrative Support: 75% indicated important
- Start-up Funds: 87% indicated important (but highly variable depending on the type of research performed by the lab and the wealth of the institution)
- Tenure or tenure-equivalent position: 56% indicated important
- Dedicated Lab Space/Equipment: 77% indicated important (though less relevant for clinicians)
- In-kind matching: 60% indicated important (but not always possible)
- Leadership positions given to candidate: 59% not important
- Considerations for less-resourced institutions: 76% important to consider
- Other suggestions for institutional commitment include mentor support, support for grant writing, career development support, support for travel/sabbaticals, release from teaching, etc.

In summary, there are several ways to determine non-monetary institutional commitment, but this will be different for each applicant, depending on the type of research and the institutional resources (wealth) available.

Program Implementation

- **Develop and issue guidelines and application materials**

The application materials will be developed with input from AFAR's and MBRF scientific leadership and the Selection Committee. Based on the survey results, we propose eliminating the 50% matching requirement but instead, require that institutions provide a more detailed description of their institutional commitment to the investigator, providing details on several non-monetary indicators of commitment. The Selection Committee will be asked to evaluate and determine the institutional commitment for each investigator taking the applicant's type of research and institutional resources/wealth into consideration.

Once finalized, the materials will be posted on the AFAR website https://www.afar.org/grants/mcknight-award.

- **Program Announcement Activities**

The program will be promoted through a variety of mailings and e-mail announcements. AFAR manages a range of programs in aging research, providing unique opportunities to raise the visibility of the MBRF Innovator Awards program. For example, through dissemination channels of our NIA-supported programs, which include websites, twitter feeds and direct communications to more than 100 NIA-supported Centers, we can make opportunities widely known across the NIA aging community. In addition, AFAR has a distribution list that includes more than 8,000 individuals in the aging research community, and beyond. We will also reach out to several other organizations such as the Health Research Alliance, GSA and AGS to help promote these programs. In addition, we will reach out to other organizations and research groups that support research on brain health. For example, MBRF recently introduced AFAR to the American Brain Foundation, which is another MBRF partner, and we agreed that we would coordinate efforts to help each other with program announcements to our respective audiences.

- **Review and Selection Process**

AFAR's nationally respected and scientifically rigorous grant review ensures that the highest-quality research is supported. For the Innovator Awards, AFAR will solicit Letters of Intent (LOI), and a small group of key AFAR Scientific Board members and if needed, members of AFAR's National Scientific Advisory Committee (NSAC) will review the LOIs for program relevance and eligibility. The NSAC consists of a large network of expert reviewers (about 300 members) with

aging-related expertise, and it currently includes about 40 members with specific expertise in cognition and brain aging. A subset of applicants is then invited to submit full applications which are reviewed by a Selection Committee comprised of leading investigators with expertise in brain aging and cognition. The MBRF may designate up to three representatives to serve on the selection committee, provided they do not represent/have a majority vote on the committee. All applications for MBRF-funded Innovator Awards will be made available to all members of the selection committee. The committee's recommendations will be presented to MBRF and AFAR for final funding decisions.

The most current (2023) eligibility criteria and selection criteria are outlined below however, these would be updated if the requirements for institutional commitment are changed.

To be eligible, the applicant must:

- Have completed research training prior to the beginning of this award (October 1, 2023):
  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.
- Be an independent investigator at the rank of Assistant Professor or Associate Professor (appointed no earlier than October 1, 2020), 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 matching funds as described in a form completed by the Dean or 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, 2020.
- 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.

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 provide matching funds.

Example Timeline:
Includes Letter of Intent (LOI) review stage.

April (pending approval):	Prepare Program Guidelines & Letter of Intent (LOI) and Program Announcement
June 1:	LOI Deadline
June 1-7:	Administrative review.
June 7 – July 1:	Scientific review – program relevance
July 1:	Subset of applicants are invited to submit a full application
August 15:	Full Application deadline
August 15-17:	Applications sent to the Selection Committee
September 15:	Selection Committee to review and recommend applications for funding. Final approval made by MBRF.
September 23:	AFAR notifies awardees
October 1:	Award Start Date
December 1:	Press release and public announcement of awards

- **Annual Meeting**

Recipients of the MBRF Innovator Awards program are invited to the AFAR Annual Grantee Conference, which is one the highlights and key components of our programs. Encouraging scientific exchange and networking among grantees and leadership in aging research is an important aspect of programs that not only supports research, but nurtures career development and provides opportunities for collaborations. Grant recipients participate in this Grantee Conference, which for almost 35 years has provided valuable opportunities to learn from each other and to engage in informative and enriching discussions with peers and senior investigators. Grantees become part of a community, and we support their continued participation in aging research. The meeting is held in Santa Barbara and one day is held jointly with the Glenn Workshop in the Biology of Aging, which provides additional opportunities to interact with leaders in aging research. We propose that the MBRF grantees participate in all the annual grantee conference activities.

- **Dissemination**

AFAR has centralized information on one website, www.afar.org. The grantees are listed on the Grantee page https://www.afar.org/2023-grant-recipients#H. Individual profiles will be posted for the MBRF/AFAR grantees. AFAR will also include special announcements in the AFAR newsletter and annual report, on its website, in all press kits, and through other regular AFAR communications vehicles, including social media. As in previous years, we have worked with MBRF to issue press releases to announce each cohort https://t.e2ma.net/click/6h01tv/i38bobff/ekz8q7b.

We further disseminate information through the Nathan Shock Centers Coordinating Center which serves the biology of aging community, Clin-STAR Coordinating Center, which provides resources for clinician-investigators in aging research, and the Research Centers Collaborative Network , which aims to stimulate cross-disciplinary research networks and serves more than 100 aging research programs across the United States.

AFAR also shares research findings and other lessons learned through social media and holds webinars, scientific panel discussions and workshops around specific topics. We also provide travel sponsorships for grantees who want to present their AFAR-supported research findings at national and international scientific meetings.

- **Grants Management**

AFAR will issue the award materials and grant payments to the grantees who are required to submit annual reports describing accomplishments, updates on research activities and findings, and the impact the program has had on their career development. The reports allow AFAR to monitor progress and provide feedback, as well as educate us about new research developments, their potential impact on the aging field and whether results can be disseminated to a larger audience. Relevant grantee data will also be uploaded to the Health Research Alliance's HRA Analyzer, which is a grant database for, with functional similarity to NIH Reporter.

- **Evaluation**

AFAR monitors and tracks the progress of its grantees to measure the impact and success of the programs. Grantees with active grants are required to complete a narrative interim report as well as a final narrative report to inform us about their progress and research findings. We also require financial reporting on the grant. AFAR also surveys past and current grantees to measure the impact of these awards on expanding the aging field, grantees' research accomplishments and career trajectory. Reliable statistics on the research and career paths help determine whether investments are yielding desired outcomes or whether the programs need to be fine-tuned.

The expected outcomes of the program are:

- Build a core group of outstanding investigators who pursue research and academic careers in cognitive aging and memory loss research.
- Research that yields findings to better understand and alleviate age-related cognitive decline and memory loss, which ultimately will enhance the health and quality of life of older adults.

We collect information on so-called "markers of success", including indicators that demonstrate career development (promotions, appointments, honors, awards, etc.) and research progress (subsequent research support, publications, collaborations, patents, new hypotheses, changes in protocol, changes in standard practice, etc.)

As mentioned above, the first two cohorts have been very productive, publishing papers, making presentations at national and international meetings, and have secured additional grant

support. However, all grants are still active and full evaluation will have to be conducted once the grants are completed.

Organizational Capacity

- **Capacity to conduct the proposed project**

The American Federation for Aging Research (AFAR) is a leading national non-profit organization whose mission is to support and advance healthy aging through biomedical research. AFAR's grant programs and scientific convenings have provided essential support to groundbreaking research that has defined the biology of aging and established the scientific research pipeline. AFAR is ideally suited to administer this grant program and its staff, advisors and volunteers have the expertise to implement and execute this program. Since its founding in 1981, AFAR has granted approximately $193 million to more than 4,350 talented researchers and students to help them begin and further careers in aging research and geriatric medicine.

AFAR's Board of Directors consists of over 30 individuals from both the scientific and business sectors. AFAR's staff, currently consisting of 12 members, focus activities on funding aging-related research through a portfolio of grant programs, as well as organizing an array of annual scientific meetings to encourage scientific exchange, career development, networking, and collaborations. Additionally, AFAR is leading several strategic initiatives, including a biomarker study and the SuperAgers Initiative, which seeks to understand the correlation between age-related diseases and living an exceptionally long, healthy life. We also provide educational resources to the general public about the state-of-the-art research and lifestyle interventions, primarily through webinars and symposia.

AFAR's partners gain visibility as key contributors to a research area that is crucial to the health of our nation. There is growing media attention and public awareness around the importance of biomedical research on aging and prominent publications such as *Time*, *Newsweek*, *The Wall Street Journal*, and *The New York Times* regularly feature stories on aging research highlighting many AFAR-supported scientists and leaders. AFAR also provides its grant sponsors with a communications conduit to professional and public audiences via AFAR's national scientific conferences, media briefings, websites, webcasts, and more. For example, in 2022, AFAR and MBRF were featured in the November 29, 2022 issue of *"Inside Philanthrophy"* on advancing research on cognitive aging: *"As Americans Grow Older, These Funders are Advancing the Field of Cognitive Aging Research."*

- **Past and current relevant experience**

AFAR's major activities are well-aligned with the goals of the MBRF Innovator Research Awards and offers a range of grant programs, providing grant support to graduate students, postdoctoral fellows, junior faculty and senior faculty in aging and aging-related topics.

AFAR focuses its activities on these major initiatives:

- Identifying and funding a broad range of cutting-edge research most likely to increase knowledge about healthy aging.
- Attracting more physicians to specialize in geriatric medicine to meet the demands of an aging population with expert health care.
- Creating opportunities for scientists and clinicians to share knowledge and exchange ideas to drive innovation in aging research.
- Providing information to the public on new medical findings that can help people live longer lives that are less susceptible to disease and disability.

AFAR has an established national network with most research institutions in the U.S., and we continue to build our networks internationally.

In addition to our grant programs, AFAR provides infrastructure support and leadership for three initiatives funded by the National Institute on Aging (NIA): the Nathan Shock Centers Coordinating Center, the Research Centers Collaborative Network, and the Clinician-Scientists in Transdisciplinary Aging Research (CLIN-STAR) Coordinating Center.

We have longstanding partnerships with the National Institute on Aging, The Glenn Foundation for Medical Research, and the Rosalinde and Arthur Gilbert Foundation. More recently we established a partnership with The Hevolution Foundation. These partnerships continue to strengthen our ties to and networks within the aging research community. AFAR is also supported by a large network of leaders in aging who volunteer their time and expertise to advance the field.

- **Key Staff members**

Stephanie Lederman, AFAR's Executive Director, has served in leadership positions in the not- for-profit sector for more than 35 years and has been the Executive Director of AFAR since 1992. Under her leadership AFAR has grown into an organization that has been able to support thousands of new investigators and students conducting biomedical research on the aging process and age-related diseases. Odette van der Willik is the Deputy Executive Director and Director of Grant Programs and has been with AFAR since 1994. She develops

and oversees the organizations' series of grant programs and NIA Initiatives, supporting early and mid-career scientists, physicians, and medical students in the fields of aging research and geriatric medicine. Hattie Herman has been Program Officer at AFAR since 1994 and oversees the day-to-day grant management activities, including the development of RFAs, organizing the grant reviews, inviting committee members and scheduling committee reviews, and organizing annual grantee meetings.

The budget can be found in Attachment 4 and the proposed payment schedule in Attachment 5.

2023 MBRF Innovator Awards Committee

Ana Maria Cuervo, MD, PhD, *Chair*
Albert Einstein College of Medicine

Rozalyn Anderson, PhD
University of Wisconsin, Madison

Patricia Boyle, PhD
Rush University/
The McKnight Brain Research Foundation

Rafael de Cabo, PhD
National Institute on Aging

Roy H. Hamilton, MD, MS
University of Pennsylvania Perelman School of Medicine/
The McKnight Brain Research Foundation

Madhav Thambisetty, MD, PhD
The McKnight Brain Research Foundation

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

2021 Awardees

Lindsay De Biase, PhD, Assistant Professor, University of California, Los Angeles: Synapse health in cognitive aging: central roles for microglial regulation of extracellular matrix (ECM)

Cognitive decline during aging is tightly linked to changes in the status of synapses, the connections between neurons where information is stored. Yet, the factors that regulate synapse health during aging are not well understood. Microglia are immune-like cells in the brain that respond to infection, disease, and injury. Surprisingly, these cells can also regulate the function and integrity of neuronal synapses. Dr. Biase will investigate the possibility that microglia shape synapse health during aging via modification of the extracellular matrix (ECM). The ECM is a meshwork of proteins and sugars woven tightly around neurons that potently regulates synapse stability. Recent studies and Dr. Biase's preliminary data show that microglia express numerous genes involved in building up and breaking down the ECM and that they can engulf ECM components. Dr. Biase will use multiple technical approaches to elucidate links between microglial-ECM interactions, synapse stability, and cognitive performance in aging mice and rats. The overarching goal is to identify molecular pathways for therapeutic modulation of microglial-ECM interactions to preserve cognition.

Saul Villeda, PhD, Assistant Professor, University of California, San Francisco: Caloric-restriction Induced Mechanisms of Cognitive Rejuvenation

Identifying novel therapies to delay, and potentially reverse, age-related cognitive decline is critical given the projected increase of dementia-related disorders in an aging population. Caloric restriction counters age-related impairments in cognitive function in the aged brain. Dr. Villeda’s lab and others have shown that systemic interventions, including administration of blood plasma derived from young or exercised aged animals rejuvenates cognition at old age. The rejuvenating effects of caloric restriction mirror those observed with a youthful circulation, raising the possibility that caloric restriction similarly functions through blood factors to exert its beneficial effects. The goal of the proposed research is to investigate the rejuvenating potential of caloric restriction-induced blood factors on the aged brain at the cellular, molecular and cognitive level. The proposed studies aim to identify molecular mechanisms that can be targeted to promote cognitive rejuvenation at old age, with clear therapeutic implications for dementia-related neurodegenerative disorders.

2022 Awardees

Emilie Reas, PhD, Professor, University of California, San Diego: The mediating role of bloodbrain barrier dysfunction in effects of systemic inflammation on brain microstructure and memory

Dr. Reas' lab uses advanced brain imaging methods to develop biomarkers of early Alzheimer's disease and to characterize the neurobiological changes leading to brain aging and dementia. Although inflammation and vascular dysfunction are risk factors for dementia, it remains unclear how they promote cognitive decline. Given the brain's privileged protection from the periphery by the "blood-brain barrier," the ways by which systemic inflammation affects the brain remains a critical unanswered question. Her project aims to examine relationships of blood-borne inflammatory factors with microstructural brain injury and memory, and to determine if a leaky blood-brain barrier mediates these associations. She will also evaluate whether individuals with high genetic risk for Alzheimer's disease show stronger connections between inflammation and brain microstructure, vascular leakage, and memory impairment. Findings are expected to clarify how inflammation and vascular dysfunction accelerate brain aging, and to guide development of therapeutic approaches to optimize cognitive health with age.

Tara Tracy, PhD, Assistant Professor, Buck Institute for Research on Aging: Role of KIBRA in Age-Related Memory Loss

The dynamic modulation of the synaptic connections between neurons in the brain is critical for memory. Decline in synapse function underlies memory loss in aging, but little is known about what factors make synapses more vulnerable to dysfunction with age. KIBRA (KIdney/BRAin) is a postsynaptic protein required for synaptic plasticity and memory. Genetic variation in KIBRA is associated with age-related memory deficits in older adults. Given the critical role of KIBRA protein at synapses, the amount of KIBRA expressed in the brain may modulate susceptibility to memory decline in aging. In this proposal, Dr. Tracy's lab will investigate how KIBRA levels impact synapse dysfunction and memory loss in aging. The goal of this research is to uncover mechanistic insight into the susceptibility of synapses to dysregulation in aging which could guide development of a therapeutic approach to repair synapse function as a treatment for age-related memory loss.

2023 Awardees

Denise Cai, PhD, Associate Professor, Icahn School of Medicine at Mount Sinai: Memory stability and flexibility across a lifetime

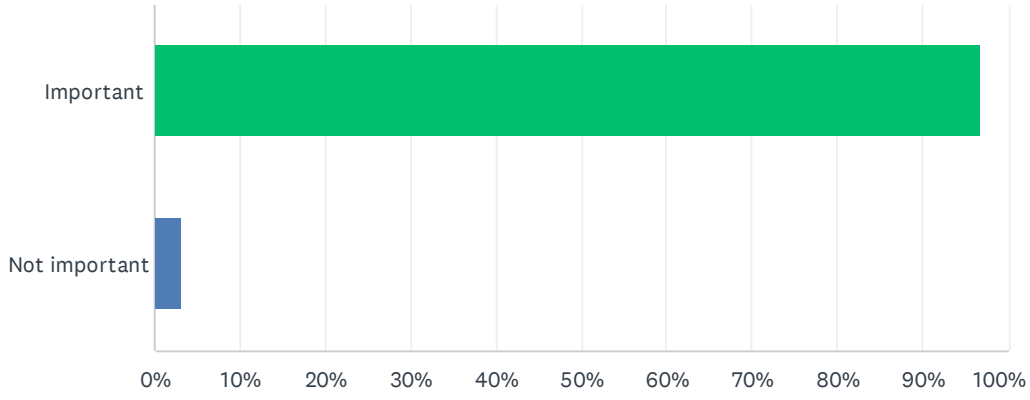
Aging is inevitable, but cognitive deficits may not have to be. By tracking the neural activity of hundreds of neurons in freely behaving mice as they form multiple spatial maps during young adulthood and middle age, Dr. Cai's McKnight Innovator award will unveil how the brain stably stores and flexibly integrates memories across a lifetime. This work will help identify biomarkers and behavioral markers that can predict age-related cognitive deficits and provide early intervention to prevent or slow age-related cognitive decline. Dr. Cai's lab combines cellular, circuit, and behavioral techniques to study how memories are stably stored and flexibly updated across time and experience. By studying memory-linking, or how events are connected when they occur closely in the time, she hopes to understand memory disorders such as post-traumatic stress disorder and memory declines in aging.

Christoph Thaiss, PhD, Assistant Professor, University of Pennsylvania: Counteracting age-associated cognitive decline via gut-brain signaling

Aging is associated with a decline in memory function, which greatly affects the quality of life of a large proportion of older individuals. The rate of cognitive decline is highly heterogeneous, with some individuals retaining fully intact memories at old age, while others lose the ability to participate in public life due to a dramatic inability to form and recall memories. New strategies to understand and counteract the age-associated decline in memory function are thus urgently needed. This study will explore the hypothesis that age-associated cognitive decline is not solely brain-autonomous but regulated by body-brain pathways originating in the gastrointestinal tract. This approach provides a framework for how age-related diseases of the brain may be treated by means of peripheral intervention from the gastrointestinal tract.

Q1 Do you consider protected time to be an important or not important indicator of institutional commitment?

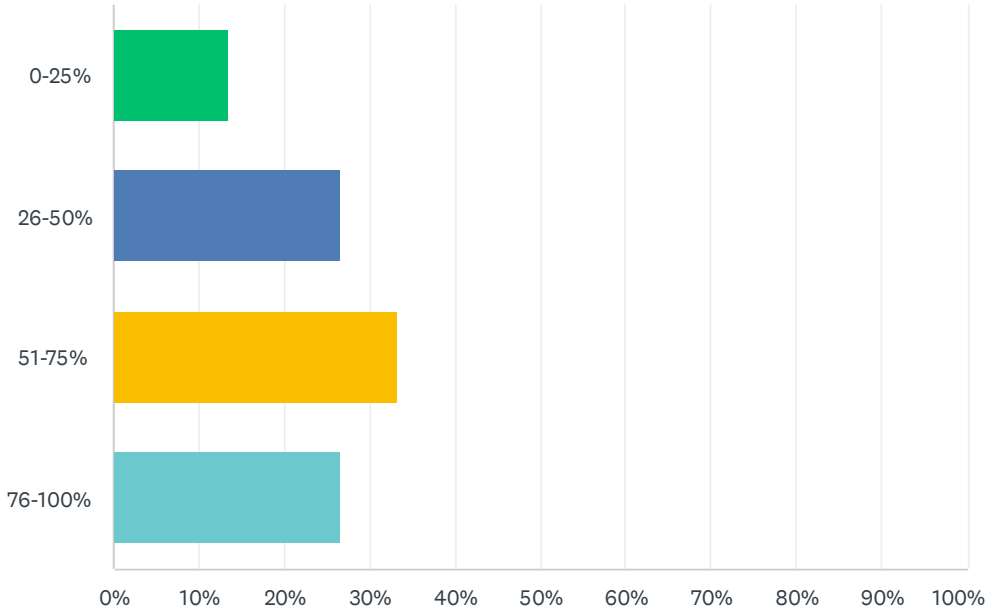
Answered: 32 Skipped: 0



ANSWER CHOICES	RESPONSES	
Important	96.88%	31
Not important	3.13%	1
TOTAL		32

Q2 If you responded that protected time is important, what is a reasonable % of protected time for research for an investigator doing non-clinical work?

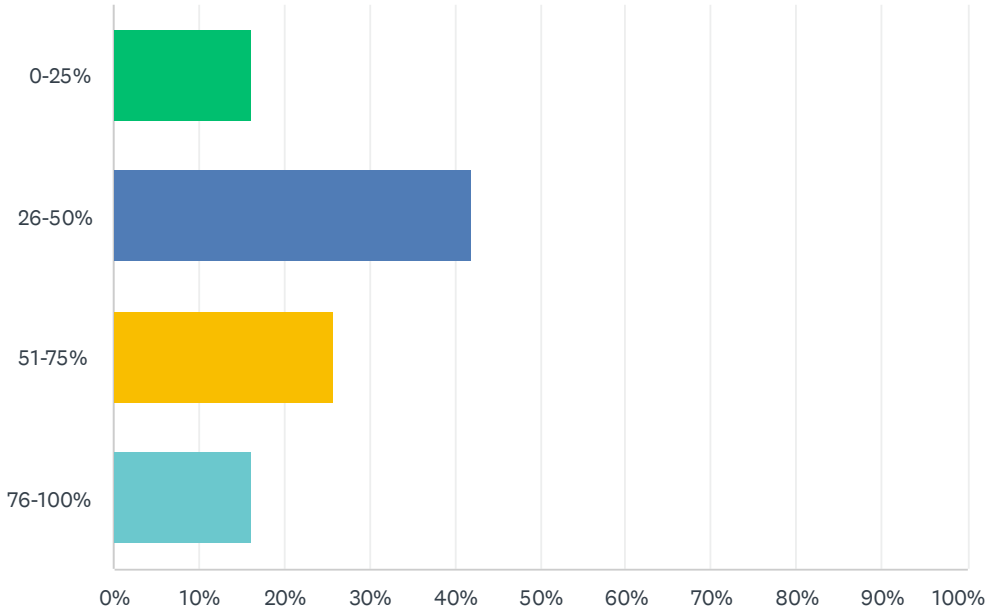
Answered: 30 Skipped: 2



ANSWER CHOICES	RESPONSES	
0-25%	13.33%	4
26-50%	26.67%	8
51-75%	33.33%	10
76-100%	26.67%	8
TOTAL		30

Q3 If you responded that protected time is important, what is a reasonable % of protected time for research for an investigator doing clinical work?

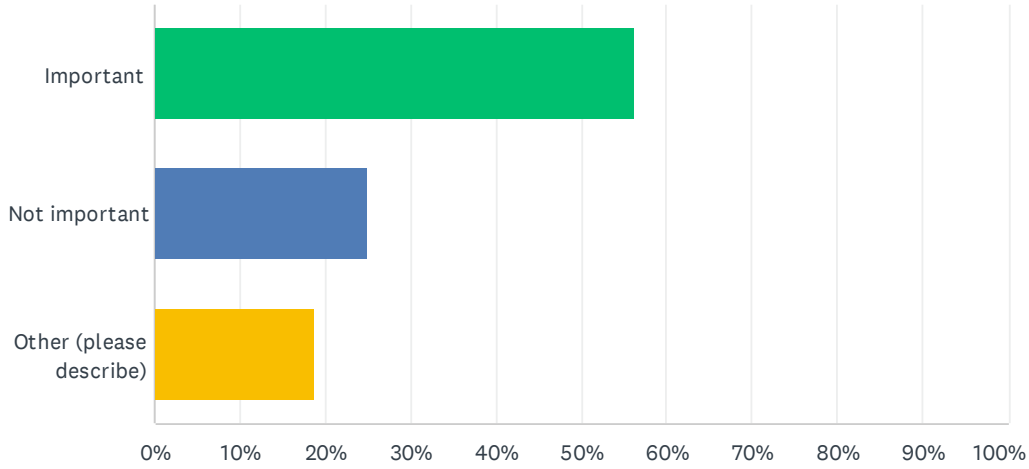
Answered: 31 Skipped: 1



ANSWER CHOICES	RESPONSES	
0-25%	16.13%	5
26-50%	41.94%	13
51-75%	25.81%	8
76-100%	16.13%	5
TOTAL		31

Q4 Do you consider overhead to be an important or not important indicator of institutional commitment? (The program currently allows 10% maximum overhead.)

Answered: 32 Skipped: 0

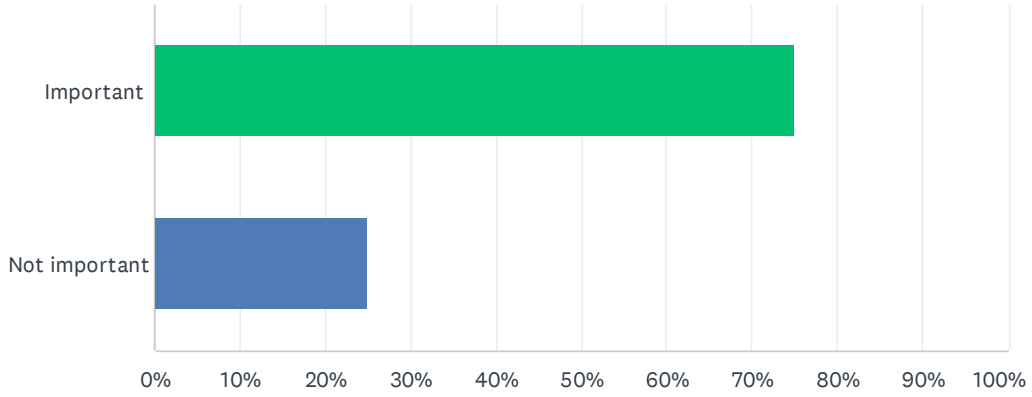


ANSWER CHOICES	RESPONSES	
Important	56.25%	18
Not important	25.00%	8
Other (please describe)	18.75%	6
TOTAL		32

#	OTHER (PLEASE DESCRIBE)	DATE
1	I had not thought of overhead as an indicator of commitment but can see the possibility that agreeing to accept a grant that pays less overhead than a governement grant could be a form of institutional commitment.	1/31/2024 1:25 PM
2	institutions consider overhead, or indirects, to be critical to supporting the research at their instituition mission	1/23/2024 10:13 PM
3	Sorry, are you asking if the institution will waive the overhead/indirect totally?	1/23/2024 5:23 PM
4	I do not understand the question.	1/23/2024 5:17 PM
5	Look at support more broadly for not overhead per se but research project support costs that may or may not be overhead but are project dependent (computer time, TTO time, etc.)	1/23/2024 4:54 PM
6	It could be an indicator of commitment among others.	1/23/2024 4:37 PM

Q5 Do you consider the level of administrative support provided to investigators to be an important or not important indicator of institutional commitment? (For example, paying for an administrative assistant)

Answered: 32 Skipped: 0



ANSWER CHOICES	RESPONSES	
Important	75.00%	24
Not important	25.00%	8
TOTAL		32

Q6 If you responded that level of administrative support is important, describe forms of support.

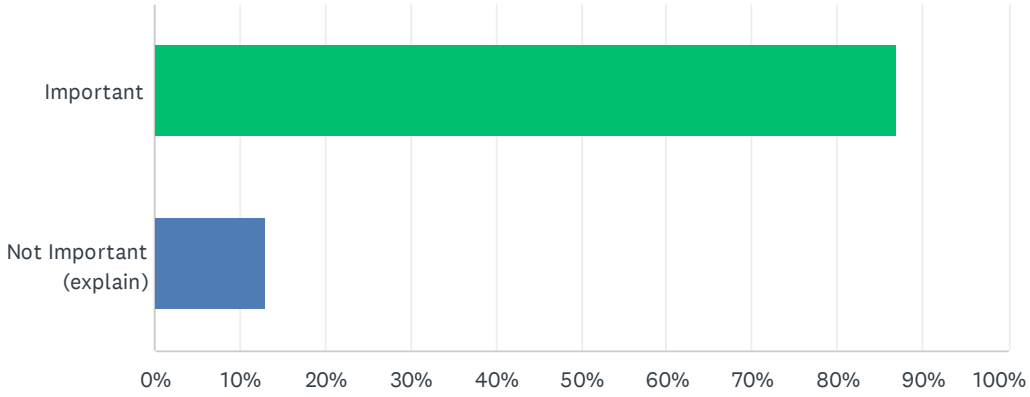
Answered: 23 Skipped: 9

#	RESPONSES	DATE
1	Dedicated time for an administrative assistant to work with the candidate (25%, possibly)	2/1/2024 11:48 AM
2	Managing calendars/appointments, travel request processing (including conference registration, travel, hotel, per diem), communications support, IRB oversight (administrative monetary support for this)	2/1/2024 10:58 AM
3	Administrative personnel time for regulatory affairs, HR, data management, IT, environmental management etc	1/31/2024 5:30 PM
4	adminsitrative support can also include pre- and post-award management of the grant, and personnel hiring	1/31/2024 4:28 PM
5	Support with grant preparation and submission.	1/31/2024 3:58 PM
6	helping with pre-awards admin part of application including budget, resources, bio sketches, LOS, data sharing, MPI plans, IRB and other regulator and required documents, and post-award grant management	1/31/2024 3:28 PM
7	Scheduling, reimbursements, clinical issues, supply purchasing, travel accommodations/booking	1/31/2024 2:59 PM
8	Pre- and post-award grant management, budgeting, secretarial support, informatics and data management support, biostatistical support	1/31/2024 1:36 PM
9	% of effort covered by institution for administrative assistance (administrator) as well as % effort covered by institution for adminstrative time and committees.	1/31/2024 1:35 PM
10	Administrative tasks take time, for example an assistant. Some institutions have a shared assistant resource for faculty and some have their own.	1/31/2024 1:27 PM
11	Grant administration and support for activities outline in a proposal	1/31/2024 1:22 PM
12	calendar management, IT/computing support, faxing and copying, reliable and skillful grants administrative support	1/29/2024 10:26 PM
13	pre-, and post-award administration, discounted access to institutional core facilities, dedicated space	1/24/2024 6:25 PM
14	many things weigh on faculty, reducing time for resaerch. Admin support helps with numerous smaller tasks that can seriously impede the PI's focus on work (death by a thousand cuts)	1/23/2024 10:15 PM
15	Laboratory space or an office in a convenient place for clinicians. Nursing support for clinicians.	1/23/2024 10:07 PM
16	Admin assistance	1/23/2024 9:06 PM
17	Helping with financial lab issues, RPPRs, the daily 'grind', that takes away from thought and actual experiment time.	1/23/2024 6:31 PM
18	Grant submission, financial, computer time	1/23/2024 5:36 PM
19	Project administrators, pre/post-award budget support, research coordinators, regulatory/compliance personnel, research assistants, are all important roles that an institution can provide, particularly for fractional share effort.	1/23/2024 5:32 PM
20	For an early career investigator, not a full time admin, but it can be anything from a lab tech to someone to help put together a grant applications, scheduling, etc.	1/23/2024 5:24 PM
21	This is David Allison from IU (Allison@IU.EDU). I will be glad to discuss on phone if you wish,	1/23/2024 5:19 PM

	but am finding these survey questions difficult to answer.	
22	Assitant, grant submission personnel, finance	1/23/2024 4:42 PM
23	Clerical work, budget assistance, assisting in subject recruitment, scheduling.	1/23/2024 4:38 PM

Q7 Do you consider start-up funds provided by the institution to be an important or not important indicator of institutional commitment? (Excluding grants from outside funding sources).

Answered: 31 Skipped: 1



ANSWER CHOICES	RESPONSES	
Important	87.10%	27
Not Important (explain)	12.90%	4
TOTAL		31

#	NOT IMPORTANT (EXPLAIN)	DATE
1	It is important but whether they are available are dependent on the departmental resources. For this reason, lack of start up funds may not be an indicator of lack of commitment.	1/31/2024 1:27 PM
2	It depends - some schools just don't have the money - insistence on substantial support would exclude investigators from smaller institutions	1/24/2024 10:08 AM
3	Start up funds are not necessarily part of a hiring package.	1/23/2024 10:08 PM
4	These are an indicator, but so dependent on the wealth of an institution and the situation of the early investigator (are they just hired, toward the end of their first couple of years, etc.)	1/23/2024 6:32 PM

Q8 If you responded that start-up funds are important, describe minimum amount and how amount is determined.

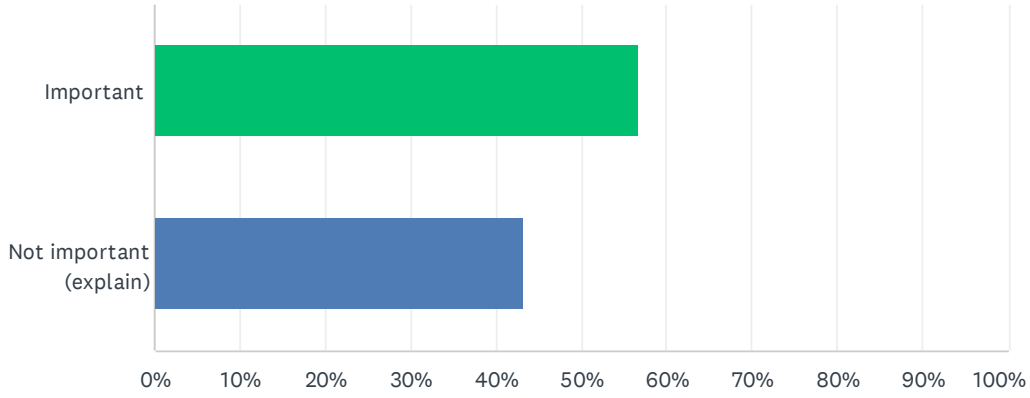
Answered: 24 Skipped: 8

#	RESPONSES	DATE
1	Really depends on whether a wet-bench versus dry-lab scientist. The former often requires commitments of $750K or larger over 3 years while the latter may be more like $300K. The bottom line is that there is space, equipment, and some technician support for the investigator to develop their research program	2/1/2024 11:49 AM
2	Varies, often up to $30-50,000/year; can be much higher, too.	2/1/2024 10:59 AM
3	Determined by line of research and cost of goods and services necessary to establish a lab.	1/31/2024 5:31 PM
4	Amounts are based on the realistic needs of the candidate. Typically, assistant professors are now getting set up funds approaching a million dollars or more.	1/31/2024 4:29 PM
5	Ideally some monetary packages with min of $100K would be great for first eve assistant prof to start their work and have some start up funds to have post-doc or some equipment	1/31/2024 3:30 PM
6	Highly variable. Depends on the type of researcher (e.g., computational vs wet lab) and whether many resources needed already exist on campus.	1/31/2024 3:00 PM
7	Minimum would be around $250-300K. The amount should support equipment, supplies, technician or postdoc salary, remodeling expenses, etc.	1/31/2024 1:40 PM
8	This is so variable but a minimum of $250,000 might be a good starting point as a minimum for biomedical research.	1/31/2024 1:36 PM
9	The amount depends on the investigator and the area of investigation. Funds should provide for pilot work, not for a fully developed study. These should provide evidence for when investigator is pursuing grants outside intuition	1/31/2024 1:24 PM
10	Totally depends on discipline. These are not necessary to demonstrate support, but it is one way that an institution can show its support. Can be $50K for new faculty in some fields or $2M for new faculty in basic science	1/29/2024 10:27 PM
11	That totally depends on the nature of the research.	1/28/2024 1:44 PM
12	salary support ($50,000/yr), funds for equipment ($100,000), unrestricted funds (>$50,000)	1/24/2024 6:26 PM
13	That is going to be school-specific. Not all schools can offer same size start-up funds but they should be comparable to those they have offered to any new recruitment in the last 5 years.	1/24/2024 7:48 AM
14	this depends. a basic scinetist with wet lab will need $1M minimum to laucnh a new indepdnent career. A clinician-scientist, or computational scientist, might need fewer funds.	1/23/2024 10:16 PM
15	1 mil	1/23/2024 9:06 PM
16	50,000	1/23/2024 5:40 PM
17	Really hard to answer this. A biomarker study could require hundreds of thousands to get off the ground where as a study looking at archival data, or adding elements to an established project in an ancillary study, could take substantially less.	1/23/2024 5:34 PM
18	$1.5M for 3 years for junior faculty	1/23/2024 5:30 PM
19	protection of 50-75% time with salary support for 2-3 years	1/23/2024 5:28 PM
20	So I would say $400k is a generous number, but that can also be negotiated based on the presence of an admin, lab tech, presence of equipment on campus and use of that equipment, whether there is a partner hire, I hate to put an exact number on it.	1/23/2024 5:26 PM
21	varies tremendously based on the nature of the research (i.e. wet lab vs dry lab; vertebrate	1/23/2024 5:21 PM

	animals; need for expensive microscopy; IPSC and other supply cost-intensive experiments)	
22	This is really research-area dependent. Need to be a scale for animal work, in situ work, etc.	1/23/2024 4:56 PM
23	depends on the level and the institution/location.	1/23/2024 4:43 PM
24	Start up funds could be an important part of a package of support.	1/23/2024 4:39 PM

Q9 Do you consider tenure or tenure-equivalent requirements an important or not important indicator of institutional commitment?

Answered: 30 Skipped: 2

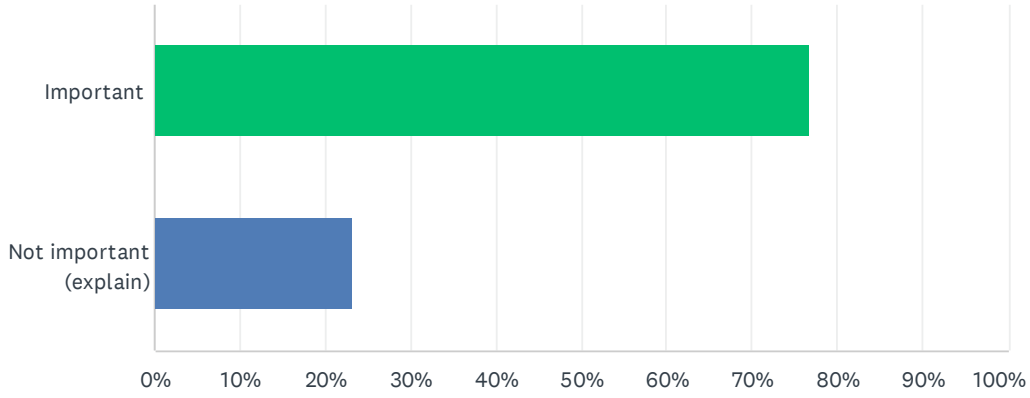


ANSWER CHOICES	RESPONSES	
Important	56.67%	17
Not important (explain)	43.33%	13
TOTAL		30

#	NOT IMPORTANT (EXPLAIN)	DATE
1	In medical schools, this distinction has less meaning	2/1/2024 11:50 AM
2	Great research can also be conducted by individuals who are in a soft money position.	1/31/2024 4:30 PM
3	From experience, a large number, if not the majority, of clinicians are not in tenure tracks.	1/31/2024 1:31 PM
4	Some schools of medicine don't offer tenure, or don't offer to any non-clinical faculty	1/29/2024 10:29 PM
5	Non-tenure trach faculty (must be assistant professors (NOT research scientists) should be eligable	1/24/2024 6:27 PM
6	Unfortunately some schools have very different criteria for tenure (some give it as Associate, others as Professor) so it is difficult to generalize, but at least the investigator should be in the "tenure track" path.	1/24/2024 7:50 AM
7	not sure what you are after here.	1/23/2024 10:17 PM
8	What Jurrasic period are you living in :-) In 2019, just 10.5 percent of faculty positions in the U.S. were tenure-track and 26.5 percent were tenured, according to the AAUP	1/23/2024 6:36 PM
9	not an indication of committment	1/23/2024 5:41 PM
10	I am not on tenure track and know that many of me peers have opted out of tenure track. I just don't think it carries the same weight it once did	1/23/2024 5:35 PM
11	Depends on the instuitute	1/23/2024 5:32 PM
12	our institution defers tenure decision	1/23/2024 5:30 PM
13	Although tenure can be one indicator of support, there are many other employment arrangemetns.	1/23/2024 4:40 PM

Q10 Do you consider dedicated lab space/equipment an important or not important indicator of institutional commitment?

Answered: 30 Skipped: 2

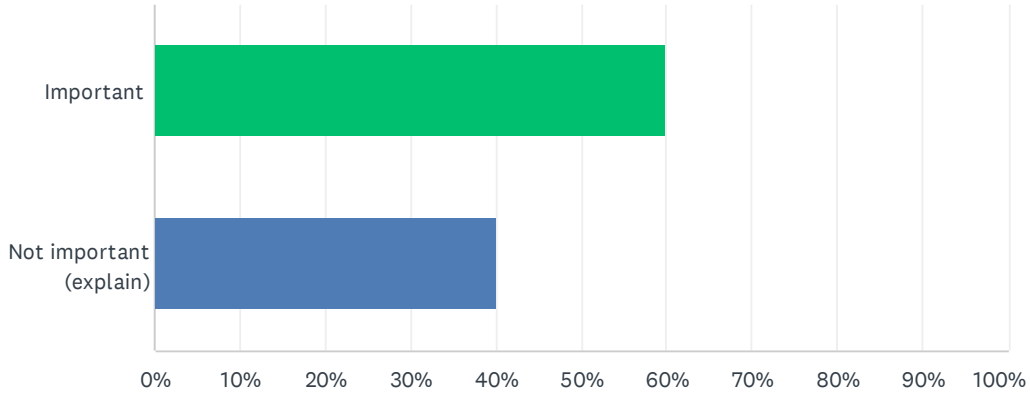


ANSWER CHOICES	RESPONSES	
Important	76.67%	23
Not important (explain)	23.33%	7
TOTAL		30

#	NOT IMPORTANT (EXPLAIN)	DATE
1	Some researchers space may be located in a more senior faculty space. The research can be conducted, it is just that universities will only indicate that tenured or tenure-track faculty are assigned the space.	1/31/2024 4:30 PM
2	If the campus has a shared equipment model, then dedicated is not important. If there is no shared equipment, then dedicated is important.	1/31/2024 3:27 PM
3	Dedicated lab space/equipment is an important indicator of commitment. However, this is not easy to assess if one is supporting clinicians, for whom dedicated lab space may not be applicable if they work in a clinical research setting that does not require a laboratory.	1/31/2024 1:31 PM
4	for a basic scientist, absolutely	1/23/2024 10:17 PM
5	not generally needed	1/23/2024 5:41 PM
6	it depends. more important there is a great training and intellectual environment, and these usually have equipment. Sometime one's own lab immediately encourages less mentorship than is ideal rather than a commitment to provide the necessary equpmenet and space as the faculty member grows	1/23/2024 5:30 PM
7	If the research requires equipment/lab space.	1/23/2024 4:40 PM

Q11 Do you consider in-kind matching by institution an important or not important indicator of institutional commitment?

Answered: 30 Skipped: 2



ANSWER CHOICES	RESPONSES	
Important	60.00%	18
Not important (explain)	40.00%	12
TOTAL		30

#	NOT IMPORTANT (EXPLAIN)	DATE
1	In-kind matching can be challenging for public institutions	2/1/2024 11:00 AM
2	Not sure what type of in kind matching is meant here	1/31/2024 5:32 PM
3	Most institutions are not going to engage in in-kind matching on all new investigator or career development type grants. If someone is already at the Associate Professor level, typically they have built a program that is self sufficient and matching funds would not be an option	1/31/2024 3:27 PM
4	The institution for a tenure track faculty member has typically already invested 1 million of more dollars into a new faculty member. It's hard to then ask the institution/dept to then invest more matching funds for an outside grant.	1/31/2024 1:38 PM
5	This is likely not sustainable for many institutions after start up funds are given	1/31/2024 1:25 PM
6	Institutions may show their commitment in other ways	1/29/2024 10:29 PM
7	other than salary support	1/24/2024 6:27 PM
8	I consider it important but not always possible. I fear that by forcing matching that some schools may not be able to offer we will end selecting elites. Maybe we could define the matching better and if they offer discounts for use of facilities or something like that it can count.	1/24/2024 7:50 AM
9	It depends on the resources the institution has,	1/23/2024 10:09 PM
10	difficult to do	1/23/2024 5:41 PM
11	Its an independent policy universities wants and need their money	1/23/2024 5:32 PM
12	can be important, but easy to finagle with fungible dollars	1/23/2024 5:23 PM

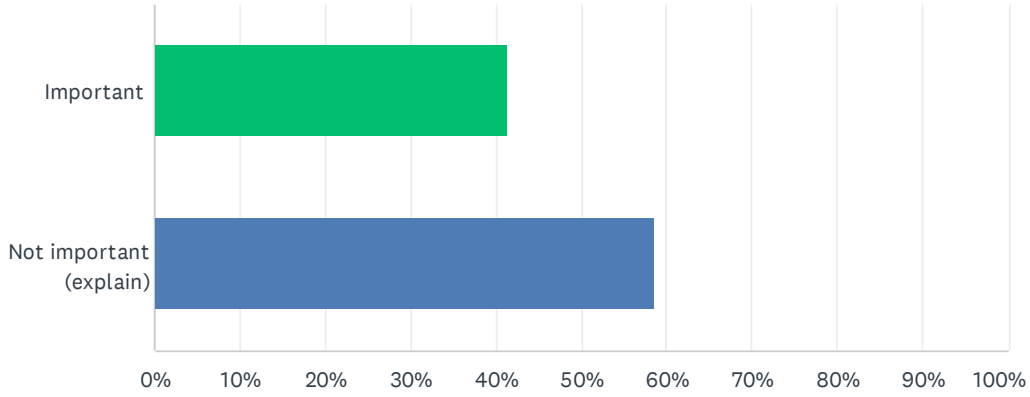
Q12 If you responded that in-kind matching is important, please describe types of in-kind matching that can be provided

Answered: 13 Skipped: 19

#	RESPONSES	DATE
1	Depends on size of award, but some percentage of the award matching would be evidence of significant investment in the candidate. However, some universities simply will not give so may limit candidates.	2/1/2024 11:51 AM
2	Salary support from the university should be counted as in-kind matching, especially since less of the grant dollars that are awarded will need to cover the salary of the PI and can be used for research, which is their intended purpose.	1/31/2024 4:32 PM
3	for instance covering some %effort of salary that is not funded by grants or clinical work; e.g., PIs on T32 grants do not get any %effort supported by NIH but institutions can provide some in-kind support (5-10% effort); or provide some in-kind support for mentoring.	1/31/2024 3:32 PM
4	Mentorship support is one example of support that is often provided in-kind but not quantified. That said, compensating for this effort can help the applicant have leverage to attain high quality mentorship and time commitment from the mentor.	1/31/2024 1:31 PM
5	It varies from institution to institution. Some might be able to match by reducing or waiving fees for important goods or services associated with a project. Some might be able to offer the labor and time of valuable teammates who would otherwise not be engaged.	1/28/2024 1:48 PM
6	Some awards ask for half which is pretty steep, especially for smaller schools that just don't have a strong research portfolio	1/24/2024 10:09 AM
7	funds to support research, funds to support a fellow	1/23/2024 10:18 PM
8	Financial	1/23/2024 9:07 PM
9	You might consider if the applicant can demonstrate support (in-kind – offers to defray assay costs, access to unique equipment, expertise) not only locally, but from collaborators at institutions outside their home-base. In fact, demonstrating being embedded in a team or network of outside expert collaborators even if the applicant was at a "poor" institution might be a positive sign for future success. And of course consider people move to other institutions all the time so support is a dynamic or moving target.	1/23/2024 6:38 PM
10	Dollar-for-dollar matching of direct costs	1/23/2024 5:35 PM
11	salary support/protected time	1/23/2024 5:30 PM
12	Waiving indirect fees, presence of start up funding, protected teaching time (that is restricted commitment to teaching if that's important), admin, lab space, and also, perhaps a share of indirects that come back from the big federal grants. Like if it's 60%, 10% goes directly back to the lab.	1/23/2024 5:27 PM
13	Administrative costs, supply costs, other traditional "overhead" costs.	1/23/2024 4:57 PM

Q13 Do you consider leadership positions given to investigators within the institution an important or not important indicator of institutional commitment?

Answered: 29 Skipped: 3



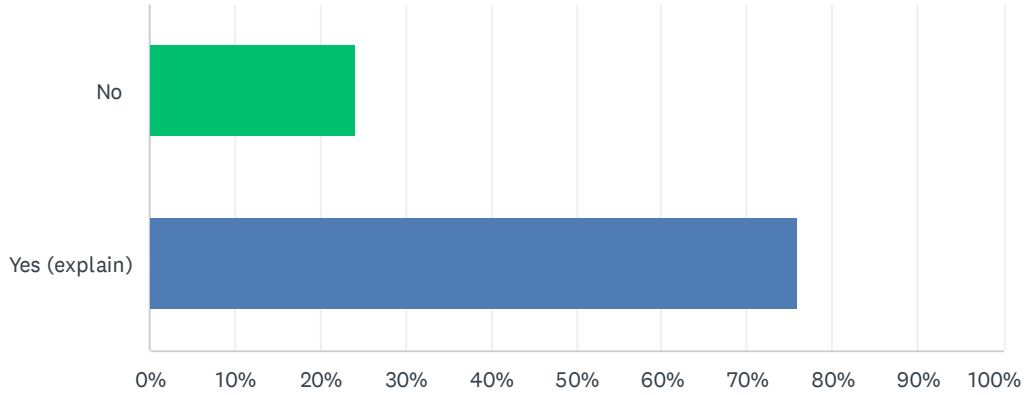
ANSWER CHOICES	RESPONSES	
Important	41.38%	12
Not important (explain)	58.62%	17
TOTAL		29

#	NOT IMPORTANT (EXPLAIN)	DATE
1	Not always meaningful	2/1/2024 11:52 AM
2	Not necessarily	1/31/2024 6:01 PM
3	It depends. Not all investigators are good leaders. Sometimes they are excellent scientists but not appropriate for leadership roles within the institution.	1/31/2024 3:28 PM
4	Appointment to leadership positions may be subject to factors other than institutional commitment and disadvantage some. I am not sure that I would consider leadership positions as a sign of institutional commitment.	1/31/2024 1:36 PM
5	The focus for an investigator should be their science	1/31/2024 1:27 PM
6	Junior faculty should not be burdened	1/24/2024 6:28 PM
7	many of this leadership positions can be by default or be more onerous than rewarding so I would not put much value on them.	1/24/2024 7:53 AM
8	this is indepd=endent of instituitional commitment	1/23/2024 10:20 PM
9	Leadership positions in early stages of a career are not beneficial.	1/23/2024 10:10 PM
10	This is a relative NI - it is easy to give people titles. If they come with support or concrete authorities and roles that makes them more important	1/23/2024 6:42 PM
11	not relevant	1/23/2024 5:42 PM
12	In my opinion, leadership opportunities bring administrative burden that take away from time, energy, and focus that could be dedicated to building a research program	1/23/2024 5:37 PM

13	not important for a new investigator; rather he/she focus on getting their research going	1/23/2024 5:31 PM
14	sometimes for early career investigators this is just a pain in the ass	1/23/2024 5:29 PM
15	often these detract from, rather than support, time for research	1/23/2024 5:23 PM
16	If it will give opportunities to have a diversity leadership it is important, otherwise not.	1/23/2024 4:46 PM
17	This can be an indicator of support, but can also distract from research.	1/23/2024 4:43 PM

Q14 Are there considerations we need to take into account for less-resourced institutions (receiving less than $50,000,000 annually from NIH)?

Answered: 29 Skipped: 3



ANSWER CHOICES	RESPONSES	
No	24.14%	7
Yes (explain)	75.86%	22
TOTAL		29

#	YES (EXPLAIN)	DATE
1	Matching and start-up may be much less achievable at smaller institutions which could reduce the diversity of applicants.	2/1/2024 11:52 AM
2	Unsure	2/1/2024 11:00 AM
3	But I have worked in such settings	1/31/2024 6:01 PM
4	They would have far less institutional resources, shared resources, well oiled systems for animal and human subjects research, admin staff used to dealing with contracts and pre/post award activities	1/31/2024 3:28 PM
5	potential collaborators, existing expertise and resources, protected time	1/31/2024 1:44 PM
6	Much less likely to have institutional resources to committ.	1/31/2024 1:39 PM
7	As shared in previous responses, some expressions of institutional commitment may be subject to institutional resources so using them as an across the board marker could exclude less resourced institutions.	1/31/2024 1:36 PM
8	Lack of infrastructure may be an issue for supporting pre and post awards	1/31/2024 1:27 PM
9	Some institutions may have less ability to provide tangible investment (discretionary $) to faculty	1/29/2024 10:30 PM
10	Smaller schools are unlikely to have the resources to match funds for awards.	1/28/2024 7:19 PM
11	They cannot provide the match and generally have lower overheads to provide admin support etc	1/24/2024 10:12 AM
12	Unless we want to end just selecting always from elite schools, this is important and maybe	1/24/2024 7:53 AM

	the matching funds should be proportional to the NIH grant amount the institution receives?	
13	maybe dont have quite the high level of required matching funds.	1/23/2024 10:20 PM
14	It would seem obvious that these institutions usually also don't have wealthy foundations or private philanthropy operations, so they just don't have that discretionary "stretch" funding to help investigators trying to get things off the ground (or even sustain mid-career folks).	1/23/2024 6:42 PM
15	favoritism andbias	1/23/2024 6:22 PM
16	they can't support as much	1/23/2024 5:42 PM
17	Space, time	1/23/2024 5:37 PM
18	a less research intensive university may not have resources to support protected time	1/23/2024 5:31 PM
19	I say all these things about in kind, many universities may not have $400k in startup, and many universities are known to be places where people sit for a few years before going on to a better place.	1/23/2024 5:29 PM
20	I'm sure there are but am not that familiar with the environment at these places	1/23/2024 5:23 PM
21	Support in general to the researcher, protected time, lab space, support to participate as reviewer, mentorship	1/23/2024 4:46 PM
22	It may be more difficult for such institutions to identify inkind match.	1/23/2024 4:43 PM

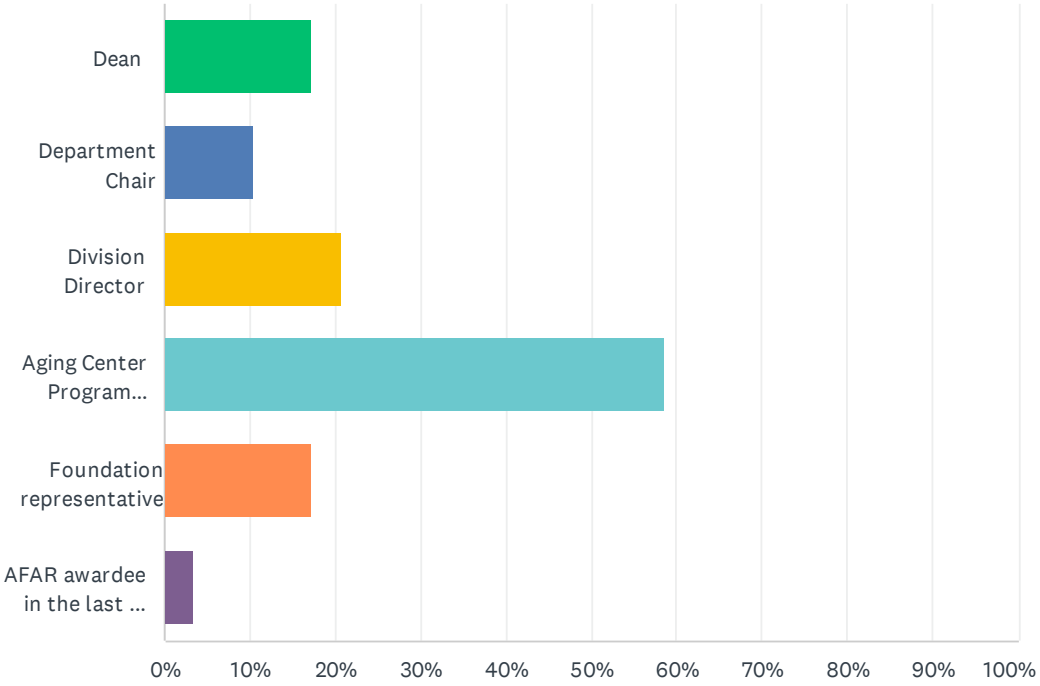
Q15 If there other non-monetary indicators of commitment we should consider, please describe:

Answered: 8 Skipped: 24

#	RESPONSES	DATE
1	Mentor time, shared resources like scanner time, advanced lab equipment etc.	1/31/2024 6:01 PM
2	Free lab space, return of indirect funds to the investigator,	1/31/2024 1:44 PM
3	Support for grant writing, coaching, research support for those with extra professional caregiving responsibilities, support to enable participation of researchers with disabilities, practical approaches by mentors and institutional officials to address bias and cultural competency.	1/31/2024 1:36 PM
4	Staff time Space Access to equipment Reduced cost to access otherwise costly services (e.g. statistical consultation and analysis, lab services, MRIs, etc.)	1/28/2024 7:19 PM
5	institutional letters	1/24/2024 6:28 PM
6	Institutional letter should show knowledge of the applicant along with plans for career track progression	1/24/2024 10:12 AM
7	Teaching responsibilities, paid time off, mentorship responsibilities, opportunities for training in general, support for travel to conferences and other meetings, maybe these are monetary, sabbaticals	1/23/2024 5:29 PM
8	the opportunity for sabbatical, release from teaching, mentoring, career development.	1/23/2024 4:43 PM

Q16 What is your role? (Check all that apply)

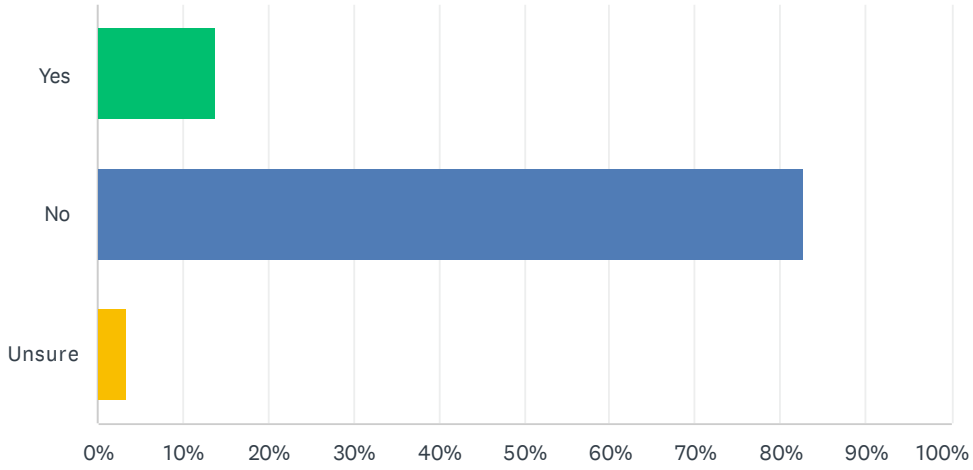
Answered: 29 Skipped: 3



ANSWER CHOICES	RESPONSES	
Dean	17.24%	5
Department Chair	10.34%	3
Division Director	20.69%	6
Aging Center Program Director	58.62%	17
Foundation representative	17.24%	5
AFAR awardee in the last 3 years	3.45%	1
Total Respondents: 29		

Q17 Can your institution be defined as a limited-resourced institution (receiving less than $50,000,000 annually in NIH support)?

Answered: 29 Skipped: 3



ANSWER CHOICES	RESPONSES	
Yes	13.79%	4
No	82.76%	24
Unsure	3.45%	1
TOTAL		29

Q18 Your name and Institution (optional)

Answered: 14 Skipped: 18

#	RESPONSES	DATE
1	University of Pennsylvania	2/1/2024 11:53 AM
2	Frank LaFerla, UCI	1/31/2024 4:33 PM
3	Sindy Escobar Alvarez, Doris Duke Foundation	1/31/2024 1:37 PM
4	Heather Whitson	1/29/2024 10:30 PM
5	University of Pennsylvania	1/28/2024 7:20 PM
6	Hassy Cohen, USC Gerontology	1/24/2024 6:29 PM
7	Rozalyn Anderson University of Wisconsin Madison	1/24/2024 10:13 AM
8	Ana Maria Cuervo (Albert Einstein)	1/24/2024 7:54 AM
9	Henry Paulson, Univ MIchigan	1/23/2024 10:20 PM
10	Gary Rosenberg. University of New Mexico	1/23/2024 10:11 PM
11	Jeff Kaye - OHSU	1/23/2024 6:43 PM
12	Allan Levey MD, PhD Emory University	1/23/2024 5:32 PM
13	Alycia Halladay, Autism Science Foundation	1/23/2024 5:29 PM
14	Brown Unviversity	1/23/2024 4:43 PM

Attachment 4
McKnight Brain Research Foundation - AFAR Budget
McKnight Brain Research Foundation Innovator Awards in Cognitive Aging and Memory Loss

Budget	**2024**	**2025**	**2026**	**2027**	**2028**	**Total**
Innovator Awards						
Two three-year grants at $750,000	$500,000	$500,000	$500,000			$1,500,000
Two three-year grants at $750,000		$500,000	$500,000	$500,000		$1,500,000
Two three-year grants at $750,000			$500,000	$500,000	$500,000	$1,500,000
Grant Administration AFAR	$33,000	$33,000	$33,000	$5,500	$5,500	$110,000
Indirect Cost @15% (on admin only)	$4,950	$4,950	$4,950	$825	$825	$16,500
Total	$537,950	$1,037,950	$1,537,950	$1,006,325	$506,325	$4,626,500

Attachment 5
McKnight Brain Research Foundation - Payment Schedule

2024	
Due April 1 (or execution of contract)	$37,950
Due November 1	$500,000
2025	
Due April 1	$37,950
Due November 1	$1,000,000
2026	
Due April 1	$37,950
Due November 1	$1,500,000
2027	
Due April 1	$6,325
Due November 1	$1,000,000
2028	
Due April 1	$6,325
Due November 1	$500,000
Total	$4,626,500

Communications Activity Timeline
Updated March 7, 2024

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 posted to the website and are now included on the new Helpful Resources page: https://mcknightbrain.org/brain-health-cognitive-aging/helpful-resources/. The brochures will be featured prominently on the Brain Works resource hub and promoted throughout the campaign. 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, along with the Foundation's tip sheet on healthy aging.
McKnight Brain Website	**September 2022 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. With the launch of the campaign, a new section of the website will be built out to include the Brain Works microsite and resource hub. The microsite will be featured as the primary visual on the McKnightBrain

				homepage to launch the campaign and will be integrated into the existing site navigation and architecture.
	May 2021 – COMPLETE **March 2022 – ON HOLD**	Develop content to build a dedicated area of the website for PCP education	V. Patmintra	Created web content to educate PCPs on the differences between Alzheimer's disease and cognitive decline/age-related memory loss. Content emphasizes the need for appropriate patient screening and offers vetted screening tools/resources PCPs can use with patients. PCP section of the website was added in early May 2021. Efforts to further build out the PCP web content and promote it to relevant audiences will be developed with BRG's engagement.
	Spring 2021 ONGOING	Expert Interview Blog Series	V. Patmintra	Interviewing McKnight Trustees and experts from the MBIs to post the bi-monthly "Three Questions with…" Expert Interview blog series. Coordinating with CWG members to interview an expert from one of the MBIs each month as outlined in the calendar presented to the CWG during their October meeting. A blog post featuring Dr. Tatjana Rundek (UM) was posted to the website in late January.
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. Q4 Web and Social Media metrics will be included for review with materials for the March 19 Trustees meeting.

Tracking and Quarterly Reports	**Began in 2019 ONGOING**	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. Q4 2023 Media Tracking report will be included for review with materials for the March 19 Trustees meeting package.
Communications Working Group	**Began in 2019 ONGOING**	Zoom meetings with members of the Communications Working Group	A. Schlanger/V. Patmintra Last Meeting: February 27, 2024 Upcoming Meeting: April 2024	Every other month meetings with members of the Communications Working Group to discuss and engage in ongoing activities, including: • 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
Precision Aging Network Collaboration	**ONGOING**	Meeting with members of the Precision Aging Network team to engage on sharing news, events and information about the initiative via the MBRF's website and social media channels		Meeting with members of the Precision Aging Network team to engage on sharing news, events and information about the PAN initiative via the MBRF's website and social media channels. • First meeting held in December 2022 at the suggestion of Dr. Carol Barnes to introduce the MBRF and PAN marketing and communications contacts • Follow up meeting held in September 2023 to discuss featuring PAN on the MBRF website and in upcoming newsletters and Ask the Experts blog posts • PAN featured resources and a link to a blog post featuring Dr. Carol Barnes in their September newsletter

FY2023-2024 Communications Planning	**ONGOING**		A. Schlanger/V. Patmintra	After approval during the February Trustees' meeting, an RFP was drafted requesting proposals for a three-year visibility campaign at three different budget levels. RFPs were sent to 5 agencies in early April. Proposals were reviewed by the Communications Committee during the committee's April 19 meeting. BRG previewed ideas for creative campaign concepts with the Communications Committee in early October and presented their recommended Campaign Concepts for the Trustees to review and provide feedback on during the October 23 Trustees meeting. Based on the Trustees' input and results from a creative testing survey, the campaign concept being implemented is ***Brain Works: Optimize Your Brain Span***. BRG is working with the MBRF team on all elements of the campaign to launch on Friday, March 22, immediately following the Cognitive Aging Summit IV.

MINUTES
MCKNIGHT BRAIN RESEARCH FOUNDATION (MBRF)
COMMUNICATIONS COMMITTEE MEETING
February 15, 2024

The Meeting of the Communications Committees of the MBRF was called to order at 6:00 pm EST on February 15, 2024, by Dr. Patricia Boyle.

The following members were present:

Dr. Patricia Boyle, Communications Committee Chair
Dr. Mike Dockery, MBRF Chair
Dr. John Brady, Trustee
Dr. Sue Pekarske, Trustee

Others attending:

Dr. Lee Dockery, Chair Emeritus
Ms. Melanie Cianciotto, Corporate Trustee
Dr. Angelika Schlanger, Executive Director
Ms. Valerie Patmintra, Senior Communications Advisor
Mr. Shannon McDaniel, BRG Communications
Ms. Kate Worthy, BRG Communications
Ms. Nicole Grady, BRG Communications

1. Call to Order

Dr. Boyle welcomed the members the committee to the call and noted that Dr. Brangman is unable to attend the meeting.

2. Minutes of the November 27, 2023 Joint Communications and Education Committee Meeting

The minutes of the November 27, 2023, Joint Communications and Education Committee Meeting (Attachment 1) were reviewed and approved as presented.

3. Communications Activity Timeline

The committee members reviewed the updated Activity Timeline (Attachment 2). Dr. Boyle shared that the majority of the communications work has focused on planning and developing materials to support launching the Brain Works campaign in mid-March. She noted that the Communications Working Group continues meeting every other month and will meet later in February to discuss updating the MBI content that's included in the MBRF organizational brochure and that a new version of the brochure will be posted to the website to tie in with the Foundation's 25th anniversary celebration later in the spring.

4. Q4 2023 Website and Media Tracking Report

Ms. Patmintra reviewed highlights from the Q4 2023 Website and Media Tracking report, noting that the top five visited pages to the website in 2023 were the home page, Innovator Award Recipients page, For Researchers page, About Us page, Blog and Innovator Awards page. She noted that this indicates the majority of site visitors have likely been researchers or those interested in

award/scholarship opportunities. Ms. Patmintra also noted that with the launch of the Brain Works campaign, this trend should shift significantly with an increase in traffic from visitors seeking information on cognitive aging and brain health.

5. Roon.com Review and Discussion

Dr. Boyle noted that the Roon Overview document was shared with the meeting materials to help give everyone a sense of how the Foundation's content is featured and presented on the Roon website and app. She mentioned that since Roon's dementia module launched in December concerns have been raised about whether the Foundation should be included on a website focused on dementia and that the committee members are being asked to resolve this question.

After discussing the process that was followed to vet and pursue the Roon opportunity and the updates that have been made to better position the Foundation within the site, the committee members decided that being featured on Roon was not in the Foundation's best interest at the time. Dr. Schlanger agreed to ask the contacts at Roon to remove the Foundation's content from the website.

6. Communications Campaign Update

a. Discussion and Review of Influencers

Kate Worthy, BRG Communications, reviewed a presentation outlining the process of working with influencers and shared examples from BRG's past client work. The BRG team responded to questions about the benefits of working with influencers and asked the committee members if they would be comfortable with BRG reaching out to Drs. Ben Rein and Sanjay Gupta as potential influences to engage to support the campaign's launch in March. The committee members agreed that both Dr. Rein and Dr. Gupta align with the Foundation's mission and would be good fits to activate for the campaign launch. BRG agreed to continue outreach to both and to keep the committee updated on progress and interest.

B . Campaign Materials and Next Steps

Nicole Grady, BRG Communications, noted that in the coming weeks, the committee will receive drafts of the campaign launch press release, frequently asked questions and infographic for review. Once approved, these materials will be released on March 22 to kick off the Brain Works campaign.

7. 25th Anniversary Budget Discussion

Dr. Schlanger reviewed highlights from the 25th Anniversary Outline related to communications initiatives, noting that the Finance Committee has reviewed the outline and budget and requested feedback from the Communications Committee. She noted that additional ideas to acknowledge the foundation's anniversary milestone through more impactful investments -- such as funding an award, scholarship, or lectureship -- will be presented to the Trustees in March, with the committee meeting's focus being on the items related to communications. The three main communications items presented were a 25th anniversary video, anniversary logo, and recording of brief videos of the Trustees and partners discussing the Foundation's outstanding impact over 25 years.

Dr. Mike Dockery noted that the Finance Committee supports a new MBRF video as a priority, but had questions around the benefit of developing an anniversary logo or pursuing the other suggested ideas.

Dr. Lee Dockery suggested that a new scholarship or award in honor of the 25th anniversary could be a more meaningful way to commemorate the milestone with outside audiences. He also mentioned that the goal to request budget approval at the Trustees' February 20th virtual should be moved to the March 19th Trustees meeting to enable more time for review of the various strategies.

The committee agreed with Dr. Lee Dockery's suggestion and decided to table any decision on the 25th Anniversary ideas and budget until the Trustees meeting on March 19th.

8. Adjourn

Dr. Boyle asked if there was any further discussion. Hearing none, she called for adjournment of the meeting at 7:15 p.m. EST.

Respectfully Submitted,

Valerie Patmintra
Senior Communications Advisor

2023 Q4 McKnightBrain.org Traffic Report

Quarterly web traffic and social media reach for 2023 is summarized below. With support from consistent Google ads and the Mental Health Awareness Campaign, all four quarters of 2023 outperformed the 2022 quarterly average.

With the Mental Health Awareness Campaign concluding at the end of May, we enjoyed spill-over effects from the additional paid Google and social advertising in June, boosting our second quarter numbers to an all time high. Google Analytics switched to a new platform in October of 2023, which caused a temporary drop in web traffic numbers in October and losing access to web traffic prior to November 2023 in the platform. A new graph will be used to track 2024 web traffic.

Quarterly Breakdown of 2023 Traffic

	2022 Quarterly Average	Q1 Totals	Q2 Totals	Q3 Totals	Q4 Totals
Users	2,415	5,245	41,878	3,631	2,568
Sessions	2,888	6,285	53,361	4,506	3,200
Page Views	5,610	10,856	71,654	8,241	6,215
Session Duration	1:15	1:10	:59	1:16	:47
Bounce Rate	-	76.67%	83.40%	70.10%	N/A

Top Visited Pages

1. Home Page: 795 views
2. Announcing Recipients of the 2023 Innovator Awards: 278 views
3. For Researchers: 106 views
4. About Us: 101 views
5. Blog: 95 views
6. Innovator Awards in Cognitive Aging: 84 views

Q3 2023 Social Media Reach

Facebook **Page Likes: 123 Page Followers: 202** ***13 new page likes and 42 new followers since the Q3 2023 report***					
	Total Reach	**New Page Likes**	**Engagements**	**Comments & Shares**	**Link Clicks**
October	27,079	3	1,865	56	102
November	28,577	2	1,678	42	112
December	15,228	8	2,156	48	124

Twitter

435 followers (139 new followers since the end of Q3)

Linked In

223 followers (47 new followers since the end of Q3)

Q4 2023 Media Highlights

Why Healthspan May be More Important than Lifespan, November 30, 2023, Time: https://time.com/6341027/what-is-healthspan-vs-lifespan/?utm_medium=email&utm_source=sfmc&utm_campaign=newsletter+health+default+ac&utm_content=+++20231130+++body&et_rid=207289625&lctg=207289625

Now What Was I Looking For? Why Your Short Term Memory Falters and Tips to Make it Better, November 28, 2023, New York Times: https://www.nytimes.com/2023/11/28/well/mind/short-term-memory-forgetfulness.html?unlocked_article_code=1.DU0.Vxaw.6SAsURVA0Cys&smid=url-share&fbclid=IwAR3ZWdoWrD3nj-WfZt7cqd6-waMBC6WmikCvrKY0iCblZRVkeWJNe1SaYek

Definition of Key Terms

User: Any person who has visited the website. The moment a person lands on any page of the site, they are identified as a User.

Page Views: Total number of pages loaded by Users on the website, including when Users load the same page of the website.

Sessions: A group of user interactions within the website that take place within a given time frame. A single session may include multiple page views, events and social interactions. Sessions track the number of times a user interacts with the website.

Session Duration: How long a visitor remains on the website. Average session duration for direct traffic is 44 seconds.