MCKNIGHT BRAIN RESEARCH FOUNDATION (MBRF)
Meeting of the Research Committee
of the Board of Trustees

Tuesday, January 28, 2025
6:00 pm ET – 7:00 pm ET

Members Attending:	Dr. Madhav Thambisetty, Committee Chair; Dr. Sue Pekarske, Trustee; Dr. Patricia Boyle, Trustee; Dr. Roy Hamilton, Trustee
Also Attending:	Ms. Melanie Cianciotto, Corporate Trustee; Dr. Lee Dockery, Chair Emeritus; Amy Porter, Interim Executive Director
Unable to Attend:	Dr. Mike Dockery, MBRF Chair

AGENDA

5:00pm ET	1.	Call to Order/Roll Call	Dr. Madhav Thambisetty
ACTION	2.	Approval of Minutes, September 24, 2024	Dr. Madhav Thambisetty
	3.	Updated Activity Timeline	Dr. Madhav Thambisetty
5:25pm **ACTION**	4.	Current Grants/Programs a. 2025 CAMI-Core Pilot Grant Applications b. 2024 Research Partnership Report with FNIH/NIA *(This report is not available at this time but will be submitted for review at the Feb. 24 Trustees' Meeting.)* c. 2024 MBRF Innovator Awards in Cognitive Aging and Memory Loss (with AFAR) Press Release d. 2025 MBRF Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss (with ABF) Acceptance Letters (confidential until April)	Dr. Madhav Thambisetty
5:55pm	5.	Other Business	Dr. Madhav Thambisetty
6:00pm ET **ACTION**	6.	Adjourn	Dr. Madhav Thambisetty

MINUTES
MCKNIGHT BRAIN RESEARCH FOUNDATION (MBRF)
RESEARCH COMMITTEE
CONFERENCE CALL
September 24, 2024

The Research Committee of the MBRF was called to order at 5:05 pm EDT on September 24, 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
Dr. Sue Pekarske, Trustee

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

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

1. Call to Order

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

2. Minutes of the April 25, 2024 Meeting

The minutes of the April 25, 2024, Research Committee Meeting (Attachment 1) were approved as presented.

Action Item 1: The minutes of the April 25, 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.

4. Cognitive Aging and Memory Core (CAMI) – RFA

Dr. Thambisetty expressed his excitement about the revamp of the program. This year 10 Letters of Intent were received, 8 were invited to submit full proposals. Proposals are from 30 investigators across all four of the MBIs.

The Committee was asked to consider the $200 honorarium Dr. Sara Burke requested for the outside reviewers. The $200 was approved previously, but Dr. Burke wanted to confirm the amount is approved for eight reviewers. As part of the program revamp, the MBRF requested reviewers from outside the MBIs review the CAMI Core Pilot proposals. Dr. Mike Dockery proposed a motion to approve an honorarium up to $200 for external reviewers and the motion was approved.

Action Item 2: The $200 honorarium for eight external reviewers was approved.

5. Cognitive Aging Summit IV Summary

Dr. Thambisetty offered his thoughts on the Cognitive Aging Summit IV Executive Summary (Attachment 3) sharing that he felt the summary was very high level and it would be helpful to have a summary from the NIH in addition to the FNIH. He thought the program and content of the Summit overall was very strong with a high level of engagement and discussion and noted the limited opportunities for networking as an area for improvement. He also noted that the Executive Summary didn't focus on the science aspects of the meeting or how the meeting could potentially drive new RFAs. Dr. Lee Dockery noted that the CAS IV contract includes that a science writer would draft summaries of the science presented during the Summit and he and Ms. Porter agreed to follow up with Dr. Molly Wagster and her team about the summaries.

Action Item 3 : Dr. Lee Dockery and Ms. Porter will follow up with Dr. Molly Wagster and her team to find out the status of the summaries of the science presented during the Summit.

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

Dr. Thambisetty directed the committee's attention to the September 2024 AFAR Progress Report (Attachment 4). It is a very detailed report submitted by AFAR that includes background information on all of the awardees named to date, links to their research summaries and updates on where their research has been published and featured in media coverage.

11 applications were received this cycle up from five received in 2023. He and Dr. Hamilton agreed the basic applications received are all excellent and meet the award criteria of focusing on cognitive aging. It was noted that one clinical application was submitted by an MD and one basic application was submitted by an MD/PhD. Ms. Patmintra was asked to reach out to AFAR for additional details on the media coverage secured to make sure it is reaching the correct target audience. Drs. Thambisetty, Hamilton and Boyle will participate in the application review meeting on September 30, 2024.

Action Item 4: Ms. Patmintra will reach out to AFAR to additional details on the media coverage secured to make sure it is reaching the correct target audience.

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

Dr. Thambisetty noted the CTRS program is also on an upward trajectory with 10 applications submitted this year compared to only two submitted in 2023. The applications haven't been sent to MBRF for review yet and Dr. Thambisetty thanked Drs. Boyle and Hamilton for serving as reviewers.

Dr. Lee Dockery and Ms. Amy Porter attended the Meet the Researchers webinar and noted that it was a very formal presentation with limited time for audience questions or discussion. In response to Dr. Yang not mentioning the MBRF as his scholarship funder, the committee noted the need to make sure the MBRF branding is included as part of the scholarship award. Ms. Porter agreed to discuss that point when she meets with Ms. Julia Miglets-Nelson later in October.

Ms. Porter asked if there was support for ABF's inquiry about awarding a third scholarship this year since only one was awarded last year. This would keep the program on track towards 10 researchers over 5 years. Dr. Thambisetty is open to the idea, but hesitant to commit before seeing the quality of the applications received. Dr. Lee Dockery encouraged the committee to consider awarding scholarship funds to all worthy applicants. The review committee meeting is scheduled for November 7, 2024. The slate will be presented to the MBRF Trustees in mid-November via email and scholarship recipients will be announced in April at the AAN's annual meeting.

Action Item 5: Ms. Porter will discuss the need to make sure the MBRF branding is included as part of the scholarship award when she meets with Ms. Julia Miglets-Nelson in October.

8. Society for Neuroscience Poster Session

Dr. Thambisetty noted 48 abstracts will be presented to the SfN poster session, including Dr. Carol Barnes presenting a poster as first author. Dr. Boyle is attending the event on October 6, 2024, representing the MBRF. Dr. Mike Dockery asked for confirmation that Dr. Molly Wagster and Dr. Jonathan King have been asked to attend the event as judges as in past years. Ms. Porter will make sure they both receive invitations to attend the event and serve as judges.

Dr. Lee Dockery offered to check in with Ms. Vicki Hixon to request a draft of the formal event invitation for review by the MBRF to ensure the MBRF Trustees are listed as hosts of the event. He also asked if it would be appropriate to ask Dr. Carol Barnes to represent the MBRF in the event Dr. Boyle is unable to attend. Ms. Porter will reach out to confirm Dr. Boyle's attendance and Dr. Barnes will be asked to represent the MBRF only in the event Dr. Boyle is unable to attend.

Action Item 6: Ms. Porter will confirm Dr. Molly Wagster and Dr. Jonathan King have been asked to attend the event as judges.

Action Item 7: Ms. Porter will reach out to confirm Dr. Boyle's attendance at the Poster Session.

Action Item 8: Ms. Porter will reach out to Ms. Hixon to request a draft of the formal event invitation.

9. Adjourn

Dr. Thambisetty asked if there was any further discussion. Hearing none, he called for adjournment of the meeting at 5:56 p.m. EDT.

Summary of Action Items:

Respectfully Submitted,

Melanie A. Cianciotto
Corporate Trustee

Research Committee Activity Timeline

2022 - 2026

Updated January 15, 2025

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

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
		UM submitted a request for $250,000 to co-fund a fellowship over 5 years – The Evelyn F. McKnight Neurocognitive Clinical Scholar in Brain Health and Aging"	A memorandum notifying UM of the approval for funding the Evelyn F. McKnight Neurocognitive Clinical Scholar in Brain Health and Aging for a total of $250,000 ($50,000 over 5 years) to be matched by UM was signed on Nov 10, 2021.	There is a balance of $150,000 on this grant commitment.
	Review of Travel Award Fund: Originally established to fund research scholars and faculty to visit other McKnight institutions.	Few applications for travel. The funds allocated for travel have been used to fund the activities of focus groups: Epigenetics, MRI standardization and cognitive test battery working group	Reviewed as needed	Travel funds have been approved to fund travel and lodging for Innovator Award winner(s) to attend the 2024 IIM meeting at UF – Dr. Denise Cai attended.
	Inter-Institutional Block Grants	Cognitive Assessment and McKnight Brain Aging Registry (MBAR) Core	The Leadership Council, by way of Dr. Kristina Visscher, submitted a proposal to support MBAR with remaining dollars. The proposal was approved with minor amendments by the research committee on April 25, 2024 and by the Full Board at its May 15, 2024 Meeting. The Board also approved an	

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
			additional $88,000 to cover the proposed budget for the MBAR over the next two years, based on a recommendation from the Finance Committee.	
	Inter-institutional Block Grants	Cognitive Aging Core Working Groups	No Updates	5 Areas: Brain and Cognitive Health Cognitive Aging & Memory Cognitive Testing Battery Epigenetics MRI standardization
	Inter-institutional Block Grants	Bio-Informatics Core (Epigenetics)	No Updates	
	Inter-institutional Block Grants	Neuroimaging Core	No Updates	
"Identify opportunities…to foster greater interest in cognitive aging and age-related memory loss (in the scientific community)"	Research Partnership with the Foundation for NIH and the NIA.	1st cycle-2009, 2nd cycle-2014, 3rd cycle-2019	2023 annual progress report was submitted in January and reviewed by the board on March 19, 2024 2024 annual progress report is due Jan/Feb 2025.	History: Established 2009 $5 M over 5 years from MBRF; match from NIA and partners was $23 M for total of $28 M (17 five-year grants funded). The 2014 Partnership renewal funded one 5-year project for $15 million with $5 M from MBRF and $10 M from NIA

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
			Final payment is due March 2025 Final report will be due Jan/Feb 2026	Current Cycle: NIA committed to provide $15M to be pooled with MBRF's $5M. Two grants were provided from the Research Partnership, led by to Dr. Thomas Perls and Dr. Emily Rogalski.
		Cognitive Aging Summit (CAS) IV	CAS IV, with a theme of "Precision Aging and Brain Health" took place on March 20-21, 2024. There were 170 in-person attendees and up to 449 virtual attendees. Session Chairs, NIA leaders, FNIH and the MBRF met for an Executive Session following the summit.	The FNIH/NIA developed the meeting summaries and the recordings have been posted online (here). Follow-up reflections and takeaways from the Summit and the Executive Session will be shared by NIA, by way of Dr. Molly Wagster and Dr. Jonathan King, later this year. In August, FNIH provided a report on the Cognitive Aging Summit IV. It is included in the material for the September 24, 2024, Research Committee meeting.

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
	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. AFAR was invited to submit a renewal proposal for three additional years with updated program guidelines to broaden the applicant pool and able greater access to applicants from institutions with fewer resources	AFAR award cycles under the current grant were implemented (2021, 2022, 2023) AFAR presented a renewal proposal to provide two 3-year awards each year for the next three years. It was approved by the MBRF board on March 19, 2024. The MBRF committed to $4,626,500 over the next 5 years.	The research committee reviewed the draft RFA and Institutional Commitment Form at its meeting on April 25, 2024. The committee suggested several edits to the documents. The RFA and application were finalized and posted by AFAR at the end of May, following input from the Board at its meeting on May 15, 2024. 2024 grant cycle deadlines include: *July 1: application period opens *August 12: application submission deadline *September 30: review committee meets *Oct 1: Award start date November 2024	AFAR Review Committee: Chair: Dr. Anna Maria Cuervo Members: Dr. Rafa de Cabo Dr. Thambisetty Dr. Boyle and Dr. Roz Anderson Dr. Hamilton (joined in 2023) The Review Committee met on September 30 to review 9 applications (11 were submitted). Awards were made to Janine Kwapis, PhD of Pennsylvania State University and Sanaz Sedaghat, PhD, University of Minnesota as 2024 recipients after MBRF Trustee review and support. Having met all institutional requirements, Dr. Christopher Thaiss' 2023 Innovators Award was transferred from Penn to the ARC Institute and Stanford

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
"Encourage young investigators in this area of research"	McKnight Brain Research Foundation Clinical Translational Research Scholarship with American Academy of Neurology (AAN) and American Brain Foundation (ABF)	Seven award cycles have been completed. Two awardees have received the CTRS every year since 2018, with the exception of 2023, when one award was made. Members of the 2022-23 Review Committee include Dr. Madhav Thambisetty and Dr. Patricia Boyle. Dr Hamilton joined in 2023-24.	The Research Committee approved the draft RFA for 2024 with minor amendments at the April 25, 2024 meeting. Upcoming 2024 grant cycle deadlines include: *May: application period opens *September 10: application submission deadline *November 7: review committee met *January: notification of awardees *July: Award start date	<u>2023-24: Seventh Scholarships</u> Two applications were submitted to the MBRF Award mechanism, and one was awarded to Haopei Yang, PhD. The Trustees determined that the other project did not align with the scope or spirit of the award guidelines. 10 applications were received by the deadline of September 10 and they appear to all be focused on cognitive aging. Last year only 2 applications were received; in 2023, 8 were received; and in 2022 there were 5 received. 2025 Recipients (2) were notified by letter on January 5, 2025. An announcement will be made at the AAN meeting in April. Names are kept confidential until then.
	Poster Reception at Society for Neuroscience annual meeting	Poster sessions were held in 2008 - 2019, and began again in 2023.		Vicki Hixon submitted a proposal to organize the poster session to take place on October 6, 2024 in Chicago. The trustees approved the proposal

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
		A question has been raised – Several posters presented at the 2024 poster reception were not related to cognitive decline or memory loss. The call for abstracts does not specifically require alignment with the MBRF mission. What is the committee's position on whether		at their March 19, 2024 meeting. On June 23rd, Vicki sent a Save-the-Date to MBI leadership and communications teams to announce the event will take place on October 6, 2024 at the Chicago Hilton. Dr. Patricia Boyle will attend as a representative of the MBRF. Ms. Vicki Hixon reported that 48 abstracts have been received with a few more expected before the event. Included in the Sept 24 meeting material are a list of those abstracts, a report and information about the event. There were 64 registered posters and 3 additional posters were added the night of the event. Vicki Hixon has submitted a proposal for the 2025 SfN Poster Session which will be reviewed by the Finance Committee on January 21, 2025.

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
		alignment with the MBRF's focus should be a requirement?		

Dear Amy,

I was excited about how the CAMI Core panel review went, so I have already compiled the scores and summaries of each discussion for all 6 proposals. The table below contains the scores for each grant in the order discussed and the panel's consensus recommendation on funding. I have also attached the detailed summaries with each grant in rank order by the committee's recommended funding priority.

One thing to note, the grant from Arne Ekstrom (UA) was among the 2 strongest proposals. However, there was concern about funding overlap with Steve Weisberg's K-award. Steve is also the junior faculty member on this award, and he is leaving UF at the end of this semester to take a position in Texas. Thus, the committee felt that the Salan (UMiami) and Porges (UF) proposal should be prioritized over the Ekstrom grant even though the score was not as good.

Also, if funding is awarded to Huggins (UA)/Hernandez (UAB) and Salan (UMiami)/Porges (UF), faculty from each of the 4 institutes will be awarded. We did not take this into consideration during review, but it is nice that it could work out that way.

Grant	Reviewer 1 Score	Reviewer 2 Score	Reviewer 3 Score	Summary Consensus Score Average	Funding Recommendation
1) Role of Glymphatic Clearance as a Mediator in Sleep and Age-Related Cognitive Decline	7	4	8	6.6	**Do not Fund**
2) Development of an eye tracker application for identifying risk factors and providing interventions to ameliorate cognitive	5	7	6	6	**Do not Fund**

decline in aging adults					
3) Targeting metabolism as a strategy to mitigate cognitive decline in aging	5	5	5	5	**Do not Fund**
4) Reduction in alcohol consumption on cognition in normal aging	2	5	3	3.5	**Fund, minor weaknesses noted**
5) Effects of age on fear generalization and its underlying neurobiological substrates in female adults: a cross-species investigation	2	4	2	3	**Fund**
6) Rival approaches to cognitive interventions that target navigation skills in healthy older adults.	4	3	2	3	**Fund, but concerns about overlap with already funded projects**

I will be sharing the reviews with applicants to help them get future funding. I am really keen on how the CAMI Core could have an impact in helping faculty get other grants even if they do not get funded here. That is really cool.

Finally, would you like me to email you all the proposals and reviews for the MBRF records?

Kind regards,
Sara

Book time to meet with me

Sara N. Burke, Ph.D.
Professor and Vice Chair for Faculty Development, Department of Neuroscience
Director of the Center for Cognitive Aging and Memory
McKnight Brain Institute, University of Florida
Florida Consortium on the Neurobiology of Cognition (FCNC)
http://fcneurocog.org/

Cognitive Aging and Memory Intervention Core Pilot Grant Scientific Review Panel
Summary 2025 Review January 17, 2025

Summary of format: Eight reviewers (4 internal to the Evelyn F. McKnight Brain Institutes and 4 external reviewers) met over zoom to discuss the six proposals that were submitted to this funding mechanism. Each grant received 3 written reviews and preliminary impact scores, consistent with the NIH scoring system (from 1 to 9, with lower numbers indicating a more impactful proposal). All grants were evaluated on the following criteria: 1) Significance and likelihood of leading to a larger successful grant application, 2) Candidates and rationale for multi-site collaboration, and 3) Rigor and innovation of research plan.

During the review panel, Reviewer 1 introduced and summarized the grant and then the three designated reviewers discussed the score driving strengths and weaknesses of the proposal. After which, discussion was opened to the full panel. After the general discussion, those panel members not in conflict with the proposal (for example, current collaborators could not score) provided a final score. The final scores were averaged to calculate the overall impact score. Below is a summary of the evaluation of each grant, ordered by impact. Of the six proposals the committee recommends two for funding. One is from early career/junior investigators (Huggins, UA and Hernandez UAB), and the other is from a collaborative team with an early-stage investigator (Salan, UMiami) and an established investigator (Porges, UF). A third proposal was strong (Ekstrom, Weisberg, and Ebner), but the committee was concerned that there was overlap with other funded projects.

Consensus Ranking and Summary

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

Principal Investigator(s):
Ashley Huggins PhD (University of Arizona)
Caesar Hernandez PhD (UAB)
Early-stage/New Investigator: Yes for both

IMPACT: 3, consensus of recommend for funding

SUMMARY: The grant proposal put forward by two early career investigators from the University of Arizona (UA; Huggins) and the University of Alabama at Birmingham (UAB; Hernandez) aims to address critical gaps in our understanding of how aging impacts fear learning and memory, specifically focusing on fear generalization in older women and female rats. Utilizing a comprehensive, multi-species approach, the research posits that age-related cognitive changes may lead to increased post-traumatic stress disorder (PTSD) susceptibility due to impaired fear cue discrimination influenced by hormonal fluctuations, particularly estrogen depletion post-menopause. Key strengths of the proposal include its innovative cross-species design that runs parallel experiments in both human subjects and rat models across all 3 aims, effectively integrating behavioral

assessments, neuroimaging techniques, optogenetic circuit manipulation, and pharmacological interventions to elucidate age-related neural mechanisms. The collaboration between UA and UAB is well-justified, showcasing a structured plan for disseminating findings. However, minor weaknesses arise from the lack of justification regarding discrepancies in estrogen administration strategies between human and rat subjects and the absence of elaboration on the mentorship structure that the PIs will receive from senior faculty, which limits the scope for guidance. Additionally, while the timeline for obtaining extramural funding is reasonable, concerns remain about the feasibility of subgroup analyses given the small sample sizes and the ambitious nature of the aims, particularly in relation to the complexity of Aim 3 focused on estrogen administration. Despite these concerns, the proposal is well-positioned to generate pilot data that could lead to larger funding opportunities and promising advancements in the field of cognitive aging and PTSD research.

2) GRANT: Effect of Alcohol Reduction and Probiotic Interventions on Cognition and Brain Glucose Metabolism in Normal Aging Adults who are High-Risk Alcohol Drinkers

Principal Investigator(s):
Teddy Salan, PhD (UMiami)
Eric Porges, PhD (UF)
Early-stage/New Investigator: Yes for Salan

IMPACT: 3.5, consensus of recommend for funding, with weaknesses noted

SUMMARY: This pilot grant proposal aims to explore the potential effects of probiotics in conjunction with alcohol cessation behavioral training among older adults who are classified as high-risk drinkers. The study plans to enroll 20 participants who do not have diabetes and will be randomized into either a probiotic group or a placebo group. At baseline and after 30 days, participants will undergo brain imaging using deuterium metabolic spectroscopy (DMT) to assess glucose metabolism in specific brain regions, notably the medial frontal area, as well as cognitive performance evaluations focusing on fluid cognition. The proposal stands out for its innovative use of state-of-the-art imaging techniques and its significant focus on a pressing public health issue: the impact of excessive alcohol consumption on cognitive function in an aging population. The collaboration between researchers from the University of Florida (UF) and the University of Miami (UM) brings together a multidisciplinary team with expertise in neuroimaging, biochemistry, neuropsychology, and neurology, which strengthens the overall approach. The methodology includes both quantitative measures of cognitive performance and metabolic analysis, generating a rich dataset capable of revealing insights about the gut-brain axis and the role of probiotics in enhancing cognitive health. The use of magnetic resonance spectroscopy (MRS) techniques to quantify changes in glucose metabolism provides a valuable, non-invasive method for tracking metabolic changes related to cognitive performance. The straightforward nature of the probiotic intervention may increase participant adherence, which is often a challenge in clinical trials involving older

adults. Additionally, the careful consideration of demographic factors and the inclusion of both biological sex and language preferences in the study design enhance its relevance and applicability to diverse populations.

However, the proposal also presents certain weaknesses. The brief 30-day duration of the intervention may be inadequate to observe significant changes in cognitive function, especially given the known variability in cognition among older adults. Additionally, the lack of discussion about how insulin resistance and prediabetes among the population could impact results further complicates the study's design. Another limitation that was noted was the inability to differentiate between the efficacy of the behavioral intervention versus the probiotic on cognitive function. Overall, while the innovative design and methodical approach hold promise for generating significant pilot data, the concerns regarding intervention duration, and variability in participant response may hinder the study's ability to provide robust findings that can support future, larger-scale investigations into probiotic interventions for cognitive enhancement in older adults at risk for alcohol abuse. Despite these weaknesses the committee felt that a CAMI Core pilot award could facilitate this work getting completed and benefit the career and future funding opportunities for Dr. Salan.

3) GRANT: A novel intervention to address orientation and navigation declines with aging

Principal Investigator(s):
Contact PI: Arne Ekstrom, University of Arizona, Professor
Co-PI – Steven Weisberg PhD, University of Florida, Assistant Professor
Co-I – Paul Hill PhD, University of Arizona, Research Scientist
Co-I – Natalie Ebner PhD, University of Florida, Professor (Psychology)
Co-I – Kristina Visscher PhD, UAB, Associate Professor (Neurobiology)Early-

Early-stage/New Investigator: Yes for Weisberg, however, Dr. Weisberg is leaving UF this spring. After which, Dr. Ebner would step in as site PI for UF.

IMPACT: 3, consensus of recommend for funding, however, concerns were raised that this project has overlap with Dr. Weisberg's K award

SUMMARY: This grant proposal aims to investigate the impacts of two distinct interventions—navigation training and useful field of view (UFOV) training—on spatial navigation and orientation declines in cognitively normal older adults. The study intends to enroll 36 participants and examine the potential benefits of these interventions over a planned 80-hour training period. With a strong emphasis on addressing a critical gap in cognitive interventions for older adults related to navigation skills that significantly affect autonomy and quality of life. The proposal is well-grounded in preliminary data demonstrating feasibility in younger adults. The research team, comprised of established experts from three McKnight Brain Institute sites, brings together diverse expertise in virtual reality, aging, and cognitive training, further enhancing the rationale for developing and implementing these interventions. Strengths include the innovative use of advanced methodologies like multi-modal measurements of cognitive and neural reserve, the

incorporation of an active control condition, and a strong collaborative framework anticipated to deepen both data collection and dissemination. However, the small sample size raises concerns about detecting meaningful effects, and the rationale for the comparative efficacy of the interventions remains underexplained. Additionally, the proposal does not establish whether the findings will significantly advance the field, given that the investigators have previously worked on similar interventions. Further weaknesses include a potentially insufficient justification for the chosen measures of cognitive reserve and inadequate details on the recruitment strategy and participant variability. Overall, while the proposal has strong foundational elements and addresses relevant health issues in aging, there are concerns that may hinder its potential impact and effectiveness in securing further funding for larger-scale investigations. Moreover, there was an impression from the committee that this work might be done regardless of obtaining CAMI Core pilot grant funding.

4) GRANT: Targeting metabolism as a strategy to mitigate cognitive decline in aging
Principal Investigator(s):
Zhang UAB McKnight (contact PI)
Darley-Usmar and Ballinger (UAB), Li biostatistician in UAB.
Sun U of F McKnight.

Early-stage/New Investigator: No

IMPACT: 5, consensus of potential funding but with notable weaknesses

Summary: This grant proposal aims to explore the effects of glutamine supplementation on mitochondrial function and cognitive performance in 21-month-old male and female mice, with a secondary focus on assessing plasma markers related to mitochondrial health in cognitively healthy adults over 85 years old, obtained from the McKnight Brain Aging Registry (MBAR). The investigators hypothesize that a 3-month period of 4% glutamine mixed in drinking water will enhance mitochondrial bioenergetic activity, improve membrane integrity, reduce indicators of mitochondrial stress, and subsequently enhance working memory function as evaluated through Y-maze tests. Strengths of the project include the expertise of the research team in mitochondrial biology, a rigorous research plan that leverages pre-collected data from successful agers, and a comprehensive analysis of mitochondrial variables using innovative techniques. However, significant weaknesses raise doubts about the necessity and translational value of the animal studies, as the effects of glutamine supplementation can be observed directly in humans without the intermediate rodent phase. Concerns also exist regarding the clarity of the statistical analysis plan, the lack of adequate control groups for which to compare the MBAR data, and insufficient background information to justify expectations of positive outcomes in healthy aging mice. Additionally, the rationale for exploring anxiety and depressive behaviors is not clearly defined, and ambiguities surrounding dosage, sample size, and cross-sectional analysis methods further undermine the proposal. Overall, while the project has the potential to yield valuable insights into mitochondrial health and cognitive aging, its effectiveness may be significantly limited by the concerns over experimental design and the necessity of employing animal models when human

studies could provide immediate insights. Notably, the reviewers all appreciated the proposed use of the MBAR data and believe that this project could be refocused and successfully obtain funding at a later date or through a different mechanism.

5) GRANT: Development of an eye tracker application for identifying risk factors and providing interventions to ameliorate cognitive decline in aging adults
Principal Investigator(s):
Matthew Feldman (University of Miami)
Victor Del Bene (University of Alabama at Birmingham)

Early-stage/New Investigator: Yes, for both PIs

IMPACT: 6, consensus of not recommended for funding

Summary: This grant proposal aims to develop a non-invasive eye-tracking application for identifying digital biomarkers of cognitive risk, with an emphasis on improving cognitive health and managing vascular risk factors in aging adults. The project is supported by a well-rounded team of junior and senior clinician scientists and highlights a collaborative effort between two EMBIs that is justified. Strengths of the proposal include its timely focus on novel digital biomarkers and personalized interventions to mitigate cognitive decline, as well as a robust mentorship plan and strong industry partnerships that could enhance funding opportunities. However, several weaknesses diminish the overall impact of the research plan. The rationale for utilizing eye-tracking outcomes alongside traditional neuropsychological assessments is unclear, and the proposal lacks sufficient background on the effectiveness of personalized text-based interventions, creating uncertainty regarding its implementation. Additionally, the absence of a control group for the intervention significantly undermines the potential for robust data collection and reduces the likelihood of obtaining extramural funding. Concerns also arise from the lack of established recruitment pipelines, unclear statistical plans, and limited data supporting the feasibility of the eye-tracking software in primary care settings. Without comprehensive evidence and a clearer plan, the project risks limited external validity and generalizability, ultimately reducing the enthusiasm for the potential contributions of this pilot study to the field of cognitive aging research. Overall, while the proposal shows promise, it requires further refinement in its approach and the clarification of its aims to realize its potential impact.

6) GRANT: Role of Glymphatic Clearance as a Mediator in Sleep and Age-Related Cognitive Decline
Principal Investigator(s):
Virendra R Mishra (UAB)
Jerzy P Szaflarski (UAB)
Alberto Ramos (UMiami)

Early-stage/New Investigator: None of the PIs, but co-Is are junior investigators

IMPACT: 6.6, consensus of not recommended for funding

Summary: This grant proposal seeks to investigate the relationship between sleep, the glymphatic system, and cognitive function, specifically focusing on individuals with medial temporal lobe tumors and control participants. The research aims to uncover the role of sleep in glymphatic clearance and its impact on executive functioning, employing advanced imaging techniques such as Magnetic Resonance Encephalogram (MREG) and Diffusion Tensor Imaging Along the Perivascular Spaces (DTI-ALPS). Strengths of the proposal include the timely relevance of investigating glymphatic clearance as a mechanism underlying cognitive decline, and the involvement of a highly qualified multi-disciplinary team with expertise in MRI and EEG methodologies. Furthermore, the comparative analysis between imaging techniques and correlating sleep quality with cognitive performance merits significant interest from the research community. However, notable weaknesses include the lack of focus on healthy aging, as the study primarily targets young to middle-aged adults with a specific clinical population, limiting its relevance to broader aging studies. Additionally, the proposal does not present a clear intervention aiming to improve sleep quality, which diminishes its alignment with the goals of the funding mechanism. Other concerns include insufficient justification for the chosen focus on executive functioning, the absence of a diverse participant demographic, and potential overstatements regarding the novelty of the proposed research despite existing studies linking sleep with glymphatic clearance. Overall, while the study holds potential for enhancing understanding in this critical area, the current approach may not adequately address the broader implications of cognitive aging or provide actionable insights into therapeutic strategies without clear interventions.

December 17, 2024

Contact: John Chaich
john@afar.org

ANNOUNCING THE 2024 MCKNIGHT BRAIN RESEARCH FOUNDATION INNOVATOR AWARDS IN COGNITIVE AGING AND MEMORY LOSS:

Janine Kwapis, PhD (Pennsylvania State University) and
Sanaz Sedaghat, PhD (University of Minnesota)
will each receive $750,000 to lead transformative research in the field of cognitive aging

NEW YORK CITY and ORLANDO— The American Federation for Aging Research (AFAR) and the McKnight Brain Research Foundation (MBRF) are pleased to announce the 2024 recipients of **The McKnight Brain Research Foundation Innovator Awards in Cognitive Aging and Memory Loss: Janine Kwapis, PhD**, of Pennsylvania State University, and **Sanaz Sedaghat, PhD,** of the University of Minnesota.

Now in its fourth year, the Innovator Awards provide funding to research scientists pursuing groundbreaking studies in the field of cognitive aging.

Janine Kwapis, PhD, is an Assistant Professor and Paul Berg Early Career Professor in Biology at Pennsylvania State University. Dr. Kwapis' project, "Improving Cognitive Flexibility in Old Age by Fixing the Transcriptome within Memory Cells", aims to better understand the molecular and cellular mechanisms that support the memory updating process. Most human memories are updates, changes to things we have already learned. Although there is evidence that aging individuals across species have difficulty updating memories, we know very little about the mechanisms that underlie this decline.

Sanaz Sedaghat, PhD, is an Assistant Professor at the University of Minnesota. Dr. Sedaghat's project, "Biological Aging Clock: A Tool to Differentiate Cognitive Aging Trajectories", aims to study whether biological aging can predict different paths of cognitive decline. Dr. Sedaghat's lab is developing "protein-based aging clocks" that use protein data to measure a person's biological age, which can differ from their actual age. By studying these clocks, Dr. Sedaghat hopes to identify who might be at risk for faster cognitive decline, which could help develop ways to slow down the process and improve quality of life.

Dr. Kwapis and Dr. Sedaghat each will receive a three-year award totaling $750,000. The successful program has already supported six investigators in previous years. This year, MBRF renewed its commitment with a $4,626,500 award to AFAR to expand the network of investigators who focus their research on cognitive aging and memory loss.

“The Innovator Awards underscore the McKnight Brain Research Foundation’s commitment to identifying and rewarding the outstanding scientists leading groundbreaking cognitive aging research,” said Michael L. Dockery, MD, Chair of the McKnight Brain Research Foundation. "With Dr. Kwapis and Dr. Sedaghat already demonstrating a strong commitment to the field, we are excited to support their work to better understand and prevent the effects of age-related cognitive decline and memory loss and hope their findings move us closer to our ultimate goal of helping people maintain their brain and cognitive health throughout their lifespan.”

“In their first four years, the McKnight Brain Research Foundation Innovator Awards have supported an impressive roster of talent who are making great advances in the field of cognitive aging,” notes Stephanie Lederman, EdM, Executive Director, AFAR. “AFAR is pleased to continue our partnership with the McKnight Brain Research Foundation and is proud to support these inspiring investigators, continuing our long support of promising research on cognitive health and healthy aging.”

Learn more about **The McKnight Brain Research Foundation Innovator Awards in Cognitive Aging and Memory Loss here.**

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About AFAR

The American Federation for Aging Research (AFAR) is a national non-profit organization that supports and advances pioneering biomedical research that is revolutionizing how we live healthier and longer. For more than four decades, AFAR has served as the field’s talent incubator, providing $212,500,000 to 4,460 investigators at premier research institutions to date—and growing. In 2024, AFAR expects to provide approximately $12,270,00 to 60 investigators. A trusted leader and strategist, AFAR also works with public and private funders to steer high quality grant programs and inter-disciplinary research networks. AFAR-funded researchers are finding that modifying basic cellular processes can delay—or even prevent—many chronic diseases, often at the same time. They are discovering that it is never too late—or too early—to improve health. This groundbreaking science is paving the way for innovative new therapies that promise to improve and extend our quality of life—at any age. Learn more at www.afar.org

About the McKnight Brain Research Foundation

Founded in 1999, the McKnight Brain Research Foundation is the nation’s only private foundation devoted exclusively to discovering the mysteries of the aging brain and helping people achieve a lifetime of cognitive health. Over the past 25 years, the Foundation has funded more than $200 million in research specifically targeting cognitive aging and age-related cognitive decline and memory loss through direct contributions and strategic initiatives in partnership with the four McKnight Brain Institutes and the National Institute on Aging through the Foundation for the National Institutes of Health. Learn more about the Foundation at: www.mcknightbrain.org.

January 5, 2025

Giovanna Pilonieta, PhD
1720 University Blvd
EFH 500 J
Birmingham, AL 35295

Dear Dr. Pilonieta,

Congratulations! The McKnight Brain Research Foundation and American Brain Foundation are pleased to announce that you have been awarded a 2025 McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss for your proposed project "Role of Modifiable Health Behaviors in the Associations between Depression, Anxiety and Cognitive Function in a National Database". This is a two-year, $150,000 award. Your project dates are July 1, 2025 – June 30, 2027.

You are invited to attend several events that will be held by the McKnight Brain Research Foundation, American Brain Foundation, and American Academy of Neurology during the duration of your award. More details will be provided as they become available.

Ashley Nielsen, the Research Grants Administrator from the American Academy of Neurology Institute will be in contact with you shortly with more details and instructions to move forward with your grant agreement. In the meantime, please feel free to contact Julia Miglets-Nelson, PhD, Senior Manager, Research Programs and Partnership at the American Brain Foundation at jmiglets-nelson@americanbrainfoundation.org or 612-928-6315 with any questions.

Again, congratulations on being selected for this award. We look forward to seeing the results of your research.

Sincerely,

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

Michelle Heritage
Executive Director
American Brain Foundation

January 5, 2025

Deborah Rose, MD
4610 Mews Drive
Owings Mills, MD 21117

Dear Dr. Rose,

Congratulations! The McKnight Brain Research Foundation and American Brain Foundation are pleased to announce that you have been awarded a 2025 McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss for your proposed project "The associations between adverse childhood experiences (ACEs) and age-related cognitive decline in racially and ethnically diverse population studies using a proteome-wide approach". This is a two-year, $150,000 award. Your project dates are July 1, 2025 – June 30, 2027.

You are invited to attend several events that will be held by the McKnight Brain Research Foundation, American Brain Foundation, and American Academy of Neurology during the duration of your award. More details will be provided as they become available.

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Again, congratulations on being selected for this award. We look forward to seeing the results of your research.

Sincerely,

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

Michelle Heritage
Executive Director
American Brain Foundation