

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

**Friday, January 10, 2020
11:00 am – 12:00 Noon EST**

Conference Call Number 877-934-2901 Passcode 8630398

Members: Dr. Madhav Thambisetty, Committee Chair; Dr. Robert Krikorian; Dr. Richard Isaacson; and Dr. Mike Dockery, MBRF Chair
Unable to Attend: Dr. Sue Pekarske
Also Attending: Ms. Amy Porter, Ms. Melanie Cianciotto

AGENDA

- | | | | |
|----------------------------------|-----|--|-----------------------------------|
| 11:00 AM EST | 1. | Call to Order/Roll Call | Dr. Thambisetty |
| | a. | Welcome to Dr. Robert Krikorian | |
| | 2. | Review of Minutes from June 13, 2019 | Dr. Thambisetty |
| | 3. | Review of Updated Committee Activity Timeline | Dr. Thambisetty
Ms. Porter |
| ACTION | 4. | Request by the University of Arizona for Support of the University of Miami's participation in the Precision Aging Demonstration Pilot | Dr. Thambisetty |
| ACTION | 5. | Request for MBRF support for the McKnight Poster Reception at the Society for Neuroscience 2020 Meeting | Dr. Thambisetty
Ms. Cianciotto |
| ACTION | 6. | Review Report and Request for a No-Cost Extension of the McKnight Brain Aging Registry (MBAR) | Dr. Thambisetty |
| | 7. | McKnight Clinical Translational Scholarship Awards | Dr. Thambisetty |
| | a. | Confidential until AAN Announcement in late April | Dr. Isaacson |
| | b. | 2020 Scholars will not be invited to the inter-institutional meeting April 1 – 3, 2020 as hoped | |
| | c. | Changes to the 2021 McKnight Scholarship RFA | |
| | 8. | Foundation for NIH Report (Resubmission) | Dr. Thambisetty |
| | 9. | Next Steps/Other Business | Dr. Thambisetty |
| | | <u>Dates for Dr. Krikorian's Calendar:</u> | |
| | | • April 1 – 3, 2020 University of Miami, FL (UM) | |
| 12:00 Noon EST
ACTION | 10. | Adjourn | Dr. Thambisetty
All |

MINUTES
MCKNIGHT BRAIN RESEARCH FOUNDATION
Research Committee
Conference Call
June 13, 2019

The Research Committee of the MBRF conference call was called to order at 4:30 p.m. on June 13, 2019 (See Agenda – Attachment 1)

The following members were present:

Dr. Madhav Thambisetty, Chair

Dr. Richard Isaacscon

Dr. Sue Pekarske

Unable to attend:

Dr. Michael Dockery, Chair, MBRF

Others attending:

Ms. Amy Porter, Executive Director

1. Call to Order/Welcome/Roll Call

Roll was called. Dr. Thambisetty, Chair, welcomed the committee members to the first meeting of the Research Committee.

a. Committee Charter

The committee received the Charter of the Research Committee for information (Attachment 2).

2. McKnight Clinical Translational Research Scholarship Awards

a. Review of Marketing Proposal

The committee reviewed the marketing proposal provided by the American Brain Foundation. It was noted that the plan covered all 19 of the AAN/ABF's scholarships of which the McKnight Scholarship is one. Discussion ensued on how to increase the number of applications. Dr. Thambisetty suggested NPR attributions and ads in the publications, Nature and Science. The Green Journal of Neurology was also mentioned. Ms. Porter to research rates.

Dr. Isaacson mentioned that he includes a slide in his presentations promoting the McKnight Scholarship opportunity. He suggested encouraging the leaders at the MBIs to do the same. Ms. Porter to forward the RFA to the MBI Leadership Council and the members of the Communications Working Group. Dr. Isaacson

also suggested writing emails to the fellows of the United Council of Neurological Subspecialties (UCNS) and forwarding the RFA. Ms. Porter to draft an email to share with Dr. Isaacson before sending.

b. Selection of/Invitation to Reviewers

The committee discussed reviewers for the McKnight Scholarship applications. Dr. Isaacson and Dr. Thambisetty will be reviewers once again. Dr. Richard O'Brien will be invited again. Dr. Pekarske could be back up if needed. Dr. Isaacson mentioned the individual from the AAN who was the 4th reviewer on last year's applications. Ms. Porter will research his/her name and share with the committee members.

Action Item One:

Dr. Thambisetty suggested NPR attributions and ads in the publications, Nature and Science. The Green Journal of Neurology was also mentioned. Ms. Porter to research the cost for these.

Action Item Two:

Ms. Porter will forward the RFA to the MBI Leadership Council and the members of the Communications Working Group to ask that they post, distribute, and include in their presentations.

Action Item Three:

Dr. Isaacson suggested writing emails to the fellows of the United Council of Neurological Subspecialties (UCNS) and forwarding the RFA with the email. Ms. Porter to prepare a draft email and share with Dr. Isaacson before sending.

Action Item Four:

Dr. Richard O'Brien will be invited again. Either Dr. Thambisetty or Ms. Porter will extend this invitation.

Action Item Five:

Dr. Isaacson mentioned the individual from the AAN who served as the 4th reviewer on last year's applications. Ms. Porter will research his/her name and share with the committee members.

3. Society for Neuroscience McKnight Poster Session, October 20, 2019, Loews Hotel, Chicago

a. Selection of/Invitation to Reviewers

Dr. Molly Wagster and Dr. Jon King will be invited to review the poster session abstracts. Ms. Porter will draft an invitation for Dr. Mike Dockery's review.

b. Invite McKnight Scholars to Poster Session

Discussion ensued about inviting any of the McKnight Scholars who might be in attendance at the SfN to attend the Poster Session to meet the MBRF representatives.

Action Item One:

Dr. Molly Wagster and Dr. Jon King will be invited to review the poster session abstracts. Ms. Porter will draft an email invitation for Dr. Mike Dockery's review.

Action Item Two:

Ms. Porter to contact the McKnight Scholars individually to ask if they might be attending the SfN meeting. If so, to invite them to the Poster Session and possibly coffee with the MBRF Leadership.

4. Proposal – McKnight Scholars to Attend/Present at 12th Inter-Institutional Meeting in Miami

The committee discussed the UM proposal to invite the McKnight Scholars to attend the 12th Inter-Institutional Meeting in Miami April 1 – 3. This idea was perceived to be a good one and it has the committee's support. Because the meeting schedule is a crowded one, it was suggested that the two "graduating" McKnight Scholars be asked to present each year at the Inter-institutional Meeting. This proposal will be reviewed by the Finance Committee and the Education Committee.

5. ~~Proposal – Pre Meeting Sessions 12th Inter Institutional Meeting in Miami~~

This item was struck from the agenda. The proposal was not submitted from the University of Miami in time for the Research Committee meeting.

6. Cognitive Aging and Memory Interventional Core Report

This subject line for this item was inaccurate. Dr. Thambisetty clarified that the two progress reports submitted by Dr. Rundek are not core grants but are pilot grants to encourage development of inter-institutional clinical translational projects relevant to age-related cognitive impairment.

The consensus of Drs. Isaacson and Thambisetty was that both pilot projects are doing okay. This was the consensus of the Interventional Core Committee as well when they forwarded these reports for Trustee review. Dr. Isaacson remarked that the exciting part is that both of these pilots have led to proposals for NIH funding. Dr. Thambisetty agreed. The committee voted to recommend to the Board of Trustees that these funded studies have made adequate progress and unanticipated challenges during their course appear to have been addressed satisfactorily.

Action Item: Recommend approval of the pilot grant progress reports.

7. Cognitive Reserve & Resilience Symposium Update

The Committee reviewed the information about the Reserve & Resilience workshop on September 9 – 10 in Bethesda, MD. The committee reviewed the email from Dr. Yaakov Stern with the link <https://reserveandresilience.com> and his invitation for any MBRF representatives to attend. Ms. Porter to ask Trustees if any would like to attend. The conditions of the sponsorship will be reviewed by Ms. Porter to ensure they are fulfilled.

Action Item One:

Ms. Porter to ask Trustees if any would like to attend.

Action Item Two:

Ms. Porter to review conditions of sponsorship to ensure they are fulfilled.

8. Cognitive Aging Conference Spring 2020

Dr. Thambisetty shared his conversation with his contact at Georgia Tech and will reach out to him again to ask the conference organizers to submit a proposal to the MBRF.

Action item:

Dr. Thambisetty to reach out to his contact.

9. Other Business/Adjourn

The committee discussed possible new members. Dr. Isaacson expressed his regard for Dr. Robert Krikorian. The Research Committee conference call was adjourned at 5:45 pm.

Action Item:

Ms. Porter to contact Dr. Krikorian to ascertain interest. Dr. Thambisetty to follow up with phone call.

Respectfully Submitted,

Amy Porter
Executive Director

Research Committee Activity Timeline
For the One-Year Period July 1, 2019, to June 30, 2020
Updated January 2020

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	February 5, 2020	Reports are submitted annually by mid-January. Reviewers have been assigned and will present at Feb 5 Trustees Meeting
	Review of all New Funding Requests from MBIs	UM has submitted an adjusted request for \$200,000 for pilot funding for a Neurocognitive Post-Doctoral Fellowship over the next two years	October 23, 2019 Trustees voted to fund -- payable over two years. Drs. Sacco and Rundek received a notification letter from Dr. Mike Dockery. The notification letter indicated that future funding should come from other sources.	The request for a gift to establish a fund to support the fellowship in perpetuity was a component of the "Investing in the Future" considered at the July 2019 Trustees' Meeting
		UA submitted a request for \$244,400 for UM's participation in the Precision Aging Demonstration Pilot	The proposal is on the agenda for Trustee review on Feb 5, 2020	Research Cmte ACTION Required

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
	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	Approved in 2009 In the amount of \$100,000 Approximately \$30,000 remains in the fund
<i>"Encourage and assess research at the McKnight Brain Institutes (MBIs)" continued</i>	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. \$76,276.49 still unexpended funds
	Inter-institutional Block Grants	Neuroimaging Core	Funding period: 1/1/2015 to 12/31/2017 \$931,759.00	Remaining balance: \$514,229.21
	Inter-institutional Block Grants	Cognitive Assessment and Brain Registry Core	Funding period: 9/1/2015-8/31/2017 Report due 2/2020 Review request for another extension at Feb 5 Trustees meeting.	No-cost extension was provided until December 2019 Research Cmte ACTION Required Remaining Balance: \$101,275.15

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
	Review of Pilot Grants (Funding Requests and Progress Reports)	A Novel Invention Tool – Levin	Funding Period: 5/1/2018-4/30/2020	Funding for 2-years for total of \$120,000 Progress Report --on Target
		Revitalizing Cognition in Older Adults – Bowers	Funding period: 5/1/2018-4/30/2020	Funding for 2-years for total of \$120,000 Progress Report --on Target
		Transcutaneous Vagal Nerve Stimulation and Cognition Training – Williamson/Alexander	Approved July 2019 Funding period: 10/1/2019-9/30/2021	Funding for 2-years for total of \$120,000
<i>"Identify opportunities...to foster greater interest in cognitive aging and age- related memory loss (in the scientific community)"</i>	Research Partnership with the Foundation for NIH and the National Institute of Aging. 1 st cycle-2009, 2 nd cycle 2014, 3 rd cycle approved 2019 to begin Spring of 2020	Fund balance of \$1 million from 2 nd five- year partnership returned to MBRF	August 2019	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).
		Report requested on plans for 3 rd cycle. Share Report with Trustees	FNIH Report in October 2019 had error. A corrected report was resubmitted. Trustees will review on Feb. 5, 2020.	2014 Partnership renewal funded one 5-year project for \$15 million with \$5 M from MBRF and \$10 M from NIA Renewal in 2020 will be same match balance. RFA not decided

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
		Expected Status of Research Partnership: RFA NIA Council Review Through Dr. Thambisetty, MBRF requested information about sponsoring a panel and/or poster session reception Proposal Expected from CAC	Fall 2019 May 2020	MBRF Payment delayed until FY 2020/2021
	Cognitive Aging Conference (CAC) 2020		April & July 2019 Waiting	MBRF sponsored a successful panel at Cognitive Aging Conference May 2018
	Reserve & Resilience Workshop 2019	Over 300 Attendees (8 MBI researchers) Report requested from organizers; List of attendees to be provided Next Reserve & Resilience Workshop	September 9 and 10 th , 2019 Bethesda September 14 and 15, 2020, Bethesda	Outcome from Cognitive Aging Summit III held in 2017 Alert Leadership Council and CWG Members of dates
"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)	12 applications were received – great improvement over 4 applications last year Applications were reviewed	Reviewers met in Dec. Two Scholars were selected and alternates were identified. Awardee to be notified in January. Public Notice in late April 2020.	First Scholarships Awarded January 2018 (McConnell, Albert) Second Scholarships Awarded January 2019 (Camargo, Sedaghat)

		Announcement – keep secret until Awardees have accepted, then keep confidential until late April when AAN issues press release. New Scholars will not be invited to Inter-institutional meeting in April at UM. Discuss changes to RFA for 2021	Funding starts July 1 of each cycle	Third Scholarships to be Awarded January 2020 Fourth Scholarships will be Awarded in January 2021 Fifth Scholarship will be awarded in January 2022 Research Cmte ACTION Required
		Dr. Robert Krikorian will be a 4th Reviewer with Drs. Thambisetty, Isaacson, O'Brien in 2020.		
		Dinner with the McKnight Scholars will be held at next AAN meeting in Toronto (Also see Education committee Timeline)		
		72nd Annual AAN Meeting April 25 – May 1, 2020 Toronto		The MBRF approved \$4,000 in funding to support hosting of McKnight Scholars, MBI and MBRF Leadership for reception/dinner/orientation

Duty (from Committee Charter)	Activity/Action	Outcome	Date	Comments
<i>"Encourage young investigators..."</i> <i>continued</i>	Poster Reception at 2019 Society for Neuroscience annual meeting Poster Reception at 2020 Society for Neuroscience annual meeting	Was held on October 20th, 5 to 7 pm, Loews Hotel in Chicago 70 submissions were received Dr. Mike Dockery, Dr. Robert Wah, Dr. Gene Ryerson and Amy Porter attended. Dinner followed with Molly Wagster and Jon King of NIH. Proposal has been submitted	October 20, 2019 Trustees will review at Feb 5 2020 Trustees meeting	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 Note: Government regulations require that Dr. Wagster and Dr. King pay for their own dinner. Research Cmte ACTION Required

November 25, 2019

Dr. Michael Dockery
Trustee and Chair, McKnight Brain Research Foundation

Dear Mike,

There are several opportunities that have arisen over the past few months, and as recently as last Thursday that I would like to share with you. Lee Ryan and I were able to have coffee this morning with Sue Pekarske, to catch her up on the latest news, and to get her input on our ideas of how to move forward. As I believe you and the other Trustees know, the U19 Precision Aging grant was reviewed, and it was reasonably close to the pay line for the National Institute on Aging, although not within the current funding range. I would like to summarize the critiques raised by the reviewers and how we intend to respond to each, and then to describe how the University of Arizona is supporting the Precision Aging resubmission process, how the University of Miami is trying to do the same, and finally I would like to describe the outcome of a meeting several of us from Arizona had last Thursday with three National Institute on Aging Program Officers (Molly Wagster, Jonathan King and Dallas Anderson).

There were four main concerns raised by the reviewers with respect to the U19 Precision Aging grant:

- **recruitment feasibility** for the face-to-face testing at our 4 sites – which includes Tucson, Miami, Atlanta and Baltimore
- **power** – what hypotheses can we test with good power, and what must be considered more exploratory
- **data science core** was not well enough developed
- **better overall integration** across the proposal to emphasize how all the Cores and Projects are integrated.

Since receiving the reviews, we have developed strong approaches to solve questions about power, we have restructured and expanded our Data Science Core in exciting ways, and have a strategy to be clearer on how the Cores serve the Projects, and how the Projects rely on the Cores. The one thing we cannot 'fix' without pilot experiments is the demonstration that we can recruit people from minority groups into the lab to participate in additional cognitive testing, MRI, neurological exams and biospecimen collection across multiple sites. The University of Arizona President has chosen Healthy Aging to support from his strategic plan as one of the Pillars of Excellence. Furthermore, he identified the Precision Aging Group in Arizona as eligible for funding from this mechanism.

We will use part of the Strategic Initiative funds (~\$250,000) to support the infrastructure and experimental costs for demonstration of the recruitment feasibility here in Tucson. Lee Ryan is the Lead for this Project for all 4 sites (Tucson, Miami, Atlanta and Baltimore) that will recruit individuals identified and selected from the MindCrowd web-based tests in those geographic areas. The funding from the President's fund will allow us to collect the feasibility data needed – namely, that we can recruit Hispanic and other individuals into our full battery of laboratory tests. These data can then be used for our target resubmission date of September 2020. Additionally, the Senior Vice President for Research has committed to create a unique clinical testing space that can be used by the U19 Precision Aging group, which is adjacent to the MRI imaging facility. This will include neuropsychological testing rooms, biospecimen collection and neurological exam rooms. This space will be a model facility for advancing clinical and translational research.



Tanja Rundek and Bonnie Levin are co-Leads of the Miami site for the U19, and they will coordinate identical testing protocols in the Miami area as we will implement in Tucson. They would very much like to be able to mount a similar pilot effort in Miami, and Ralph Sacco has been investigating ways in which he can help defray some of the costs (such as for MRIs). If we had two of the 4 sites collecting "feasibility data" for the U19 – it would be even stronger evidence that we could be successful - not only in one city, but in two – and would provide evidence that 2 of the 4 sites could work seamlessly together. I will come back to this shortly.

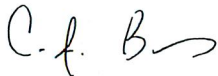
The final news is that myself, Lee Ryan, Matt Huentelman, Meredith Hay and Paul Worley visited NIH last Thursday to meet with three NIA Program Officers about our progress in preparing for a resubmission for September 2020. We presented our ideas, they gave us input and feedback, and at the very end, suggested that we should provide them with a detailed letter of reply to the reviewers concerns for all aspects of the grant. They would then consider making our case to the NIA Council that meets in the first week of December. If it is favorably reviewed, funding would be awarded this round, without having to resubmit. Our case for the 'urgency for this particular grant' is that with the President and Vice President for Research's support for our project at UA, we would be able to start these studies immediately. This, combined with the U19 funding in this grant cycle would allow us to have data in hand and outcomes to report to NIA within 18 months. If we resubmit in September, there would be a gap between UA funding and U19 grant funding, which would delay data read outs to 30 months or more. There is a strong case to be made for a public health urgency – the sooner the data from the Precision Aging grant can begin to be collected, the sooner we will begin to optimize brain and cognitive health for older adults.

We believe that our case for Council would be made even stronger if it was possible to match what the UA administration has done for Tucson at our Miami site. We hope the Board of the McKnight Brain Research Foundation would entertain reviewing a request to fund a pilot project at the Miami site. With your permission, we would include in our letter to the Program Officers that the MBRF is considering our request. This would strengthen the Program Officer's case to the NIA Council.

The budget for the Miami request is outlined below. I know this is an impossible timeline – we were not expecting to receive the opportunity to send in a rebuttal for Council – sorry to ask this of you now, during the holidays – but we are excited by the possibility.

I am grateful for your appreciation of our Precision Aging 'cause' – we know that this is well aligned with the goals of the McKnight Brain Research Foundation and are grateful for any assistance you may be able to provide in support of this effort.

Sincerely,



C. A. Barnes, Ph.D.
Regents' Professor, Psychology and Neurology
Evelyn F. McKnight Chair for Learning and Memory in Aging
Director, Evelyn F. McKnight Brain Institute
Director, Division of Neural Systems, Memory and Aging



Evelyn F. McKnight
Brain Institute

Budget

The goal of the project is to recruit 30 Hispanic individuals, and 30 matched non-Hispanic white older adults (50-79 years) over a one year period. The protocol will include in depth neuropsychological testing, neurological exam, MRI and blood draw. Participants who consent, will also provide a CSF sample.

Salaries	
Project Coordinator (1.0 FTE) = \$60,000 plus benefits	\$79,200
Neurophysiology Testing Technician (0.5 FTE) = \$20,000 plus benefits	\$26,400
Research Nurse (0.3 FTE) = \$40,000 + benefits	\$52,800
Subtotal	\$158,400
Operations	
Participant remuneration for testing, blood draw, MRI (60 x \$200)	\$12,000
Two blood draws (60 x \$225)	\$13,500
Blood tubes	\$1,000
Shipping	\$1,000
Participant transportation, parking, incidentals (60X \$100)	\$6,000
Patient remuneration for lumbar puncture (est. 30 x \$250)	\$7,500
Lumbar puncture (est. 60 x \$1,500)	\$45,000
Subtotal	\$86,000
Total Request - McKnight Brain Research Foundation	\$244,400
University of Miami Commitment	
MRI (60 x \$565) will be covered by University of Miami	\$33,900

Note, Ralph Sacco has indicated that he can cover the cost for MRIs for this effort.



Proposal
McKnight Brain Research Foundation
Poster Reception
Washington, DC
October 25, 2020

Background

The Society for Neuroscience (SfN) has an annual convention giving members an opportunity to gather and share their research with others. 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 topics ranging from molecular signaling in the brain to systems neuroscience and neurodegenerative disorders. 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 and discuss ideas.

Beginning in 2008, the McKnight Brain Research Foundation has sponsored a poster reception in conjunction with SfN. The event 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 in a casual setting.

In recent years, SfN has rotated between the cities of San Diego, California; Chicago, Illinois; and Washington DC.

2019 Progress Report – Chicago, Illinois

The 12th Annual McKnight Brain Research Foundation Poster Reception was held at the Loews Chicago Hotel in Chicago, Illinois on Sunday, October 20, 5:00 – 7:00 p.m.

There were 177 recorded guests, along with 68 registered posters and 2 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.

Registered posters included representation from all four McKnight Brain Institutes. Abstracts for the submissions, can be found at:

https://www.uab.edu/medicine/mbi/images/Booklet_2019_1.pdf

First place was awarded to Yuliya Voskobiyuk from the University of Alabama at Birmingham, second place was awarded to Jolie Barter from the University of Florida and third place was awarded to Daniel Gray from the University of Arizona. Pradyumna Bharadwaj and Lindsey Crown both from the University of Arizona and Brittany Yelga from the University of Florida received honorable mention awards for their posters.

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 also in attendance. Posters were displayed and an assortment of refreshments 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 2020 McKnight Brain Research Foundation Poster Reception will be held in Washington, DC on Sunday, October 25, 2020. Pending budget approval, an event will be planned at one of the local venues. 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

Venues normally charge rental fees for conference rooms, however, the room rental fee can usually be waived for large events with a (pre-tax and service) minimum food/beverage commission. 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 make sure 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	\$ 700	\$ 700	\$ 700
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 of Display Signs, Name Tags, and Shipping Costs	\$ 500	\$ 500	\$ 500
Subtotal Miscellaneous Costs	\$ 7,200	\$ 7,200	\$ 7,200
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	\$13,000	\$15,000	\$17,000
Estimated Grand Total	\$20,200	\$22,200	\$24,200

Ronald A. Cohen, PhD, ABPP-cn
Evelyn F. McKnight Endowed Chair
Center for Cognitive Aging and Memory
1225 Center Drive
Professor, Department of Clinical and Health Psychology
PO Box 100165
Gainesville, FL 32610

December 1, 2019

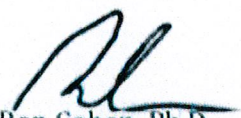
McKnight Brain Aging Registry: Neuroimaging and Cognitive Cores
Progress Report to the Trustees of the Evelyn F. McKnight Brain Research Foundation

Dear Trustees,

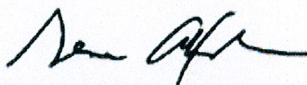
We are pleased to provide an update on our progress in establishing the McKnight Brain Aging Registry (MBAR) and its Neuroimaging and Cognitive Cores. This initiative has a primary goal of facilitating cross-institute collaborations across the four McKnight Brain Institutes, while advancing the collective mission of enhancing our understanding of cognitive and brain aging to support the development of interventions for age-related cognitive decline. Despite experiencing some significant challenges during the early start-up phases of the project, we have continued to make considerable progress over the last reporting period, and data collection continues to be fully underway. In this report, we summarize our ongoing scientific progress and plans for the coming year. Consistent with our last progress report, we have combined our reports on the Neuroimaging and Cognitive Cores, as the activities of these cores have been integrated to accomplish the collaborative MBAR mission. To the extent there are activities specifically related to one of the two cores, we have indicated this in the report.

We wish to express our sincere appreciation for your continued support in establishing the MBAR and both the neuroimaging and cognitive cores.

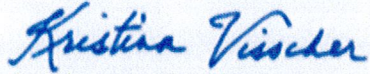
Sincerely,



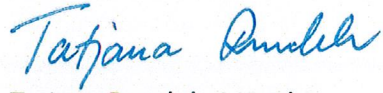
Ron Cohen, Ph.D.
Professor, Evelyn F. McKnight Chair for
Clinical Translational Research in
Cognitive Aging and Memory
Director, Center for Cognitive Aging and
Memory
Evelyn F. McKnight Brain Institute
University of Florida



Gene E. Alexander, Ph.D.
Professor and Director,
Brain Imaging, Behavior, & Aging Lab
Psychology, Psychiatry, Neuroscience and
Physiological Sciences &
Evelyn F. McKnight Brain Institute
University of Arizona



Kristina Visscher, Ph.D.
Associate Professor and Co-Director,
Civitan International Neuroimaging Laboratory
Department of Neurobiology &
Evelyn F. McKnight Brain Institute
University of Alabama, Birmingham



Tatjana Rundek, MD PhD
Professor of Neurology
Director, Clinical Translation Division
Scientific Director,
Evelyn F. McKnight Brain Institute
University of Miami



Bonnie E. Levin, Ph.D.
Alexandria and Bernard Schoninger Professor of Neurology
Director, Division of Neuropsychology
University of Miami Miller School of Medicine

McKnight Brain Aging Registry Update: Neuroimaging and Cognitive Cores

Vision

A Successful Aging Research Network that will facilitate multi-institutional collaborations across the McKnight Brain Institutes (MBI) to enhance our understanding of cognitive and brain aging and to identify intervention targets to ameliorate age-related cognitive decline.

Mission

Establish and maintain the necessary multi-institutional infrastructure to support and implement a Brain Aging Registry of the oldest old, which includes assessments of particular importance to the field of cognitive aging, including neuroimaging, extensive cognitive and functional assessments, and blood-based biomarkers.

Scientific Progress

The principal investigators, along with co-investigators and study coordinators involved in both the MBAR Neuroimaging and Cognitive Cores have continued to work hard to advance the project and considerable progress has been made over the current reporting period. To date, we have enrolled 141 participants who have been recruited across the four MBI sites, approaching 75% of our targeted enrollment, and who have been fully engaged in the registry, providing clinical, neuropsychological, and brain imaging data. It is anticipated that recruitment and assessments will be completed by the end of the next fiscal year with enrollment of the originally planned cohort of 200 MBAR oldest old participants.

Since the MBAR and neuroimaging cores were approved by the MBRF and funding began in January 2015, weekly conference calls have been held to discuss and implement the comprehensive assessments for collection of multi-modal neuroimaging, cognitive, and functional data from older adults over the age of 85 years who have been screened to exclude those with MCI or dementia and are showing evidence of successful cognitive aging. Over the last reporting period, the MBAR research activities have been mainly focused on our ongoing recruitment, execution of the data acquisition protocols, database modifications and data entry, and conducting interim data analyses for meeting presentations and development of submissions for publication. Weekly conference calls were held to discuss MBAR related issues. These were organized to include bi-weekly conference calls, attended by the PIs along with the study coordinators and MR physicists at each site. These calls focused on resolving any logistical, procedural, and data management issues or questions that may have arisen. A great deal of effort has been directed to insure harmonization of acquisition methods and data across sites to optimize quality assurance and quality control procedures. On alternate weeks, we held additional regular conference calls which were either focused on specific project-related discussions on neuroimaging and cognitive issues or were dedicated for our monthly MBAR Scientific Advisory Committee (SAC) call. The SAC is a representative committee of MBAR PIs and investigators, fully familiar with the MBAR cohort and data collection, with approximately two representatives from each MBAR MBI participating site. The SAC calls provide for discussions of broader issues related to the registry, including plans for new grant

submissions, identifying priorities for data analyses and lead investigators for MBAR manuscripts, and plans for enhancing use and accessibility of the growing MBAR dataset.

With our MBAR database infrastructure established, the REDCAP dataset continues to be fully operational and is actively being populated with data from each participant across all MBI sites. MRI data is uploaded from each site to the HiPerGator super-computer at UF, where it is pre-processed into a unified format enabling different imaging modalities to be more easily examined simultaneously. Cognitive and clinical data are uploaded to UM, where it is double entered into REDCAP with ongoing reliability checks. Data from the physical activity actigraph recordings are sent to Dr. Alexander at UA for processing and analyses. Blood specimens are sent to UF for storage in freezers located in the phlebotomy laboratory. All study coordinators have been trained in use of the database, including how to enter test scores and other clinical information. Several of the tests that are being employed require processing of scores and formatting prior to data entry. We have devoted effort in the last reporting period to further develop these tools for automatic data processing. All data is double entered into the REDCAP database, and quality control checks are conducted on a regular basis. Data sharing agreements and coordinated IRB approvals have been previously obtained for each site to support sharing data across MBI sites. In the sections below, additional progress relative to each core and component of the MBAR project are described.

Neuroimaging Core Progress

- 1) The MBAR neuroimaging protocol is fully operational. As described previously, we are collecting multimodal structural, functional, and metabolic neuroimaging data that includes: T1 images for cortical and subcortical volumetric and thickness measures; FLAIR-white matter hyperintensity lesion load; Diffusion Tensor Imaging for white matter integrity and tractography; MRS for cerebral metabolite concentrations, including GABA and glutamate; resting state fMRI functional brain activity at rest to measure functional connectivity; and MRI phase contrast scans for measures of cerebral vascular pulsation and blood flow analyses.
- 2) MR standardization: This has been accomplished and continues with all sites following standard procedures for the MRI protocols and order of administration.
- 3) MRI quality control: Each site sent data from pilot participants for each imaging modality to assess any scanner specific sources of artifact and to ensure that all metrics being obtained were consistent across sites. This involved each site processing a particular modality of data. For example, MRS data from each site was processed at UF, while resting state fMRI was processed at UAB. Considerable effort was directed at specific neuroimaging data types with novel applications for cognitive aging (see MRS below).
- 4) MRS spectroscopy: We have successfully implemented megapress MRS across sites, and have overcome technical challenges that occurred at certain sites. Dr. Porges has been conducting ongoing quality control of the GABA and other metabolite measures that have been obtained. Data quality has been excellent.
- 5) Time constraints: The neuroimaging protocol can typically be executed with acquisition within 60 minutes. We have not encountered complaints from the participants about the length of the MRI scan. For the most part they do not report finding this assessment burdensome nor do they describe significant discomfort. We believe this protocol

provides the opportunity for innovative and cutting-edge measures of brain structure, function, network connectivity, and neurometabolic and cerebral hemodynamic health.

- 6) Neuroimaging data collection continues to be well underway and imaging quality assurance across the sites is ongoing.
- 7) The neuroimaging data being acquired in the MBAR project is unique for the field of cognitive aging. There have not been other studies of people over the age of 85 that have assessed participants with such an extensive multimodal MRI scan battery.

Cognitive Core Progress

The Cognitive Core has continued to integrate their conference calls into the regular weekly calls described above to facilitate group communication across the cores and MBI sites. Most discussions have focused on resolving any data entry and analytic questions, as well as occasional queries from the study coordinators regarding minor procedural and scoring questions. However, most of the focus has been on strategic planning regarding the sequence of analyses to be conducted. There have also been ongoing discussions to consider adding a few additional cognitive measures or rating scales that might provide added value for the cognitive assessments. During the past year we achieved numerous objectives in this core as outlined below:

- 1) Identified cognitive parameters: We have continued to implement the battery of cognitive tests to address assessment of the proposed cognitive domains.
- 2) Battery refinement: We have continued to use our finalized main cognitive and clinical assessment battery.
- 3) Standardization of cognitive and clinical assessment procedures: We continued to use our training manuals, training videos that include test administration and scoring, and other tools to insure consistency of the assessment approach across sites and testers. Examples of the manuals and videos we created can be accessed at: <https://labs.uab.edu/visscher/2-uncategorised/48-mbarresearchtraining>
- 4) Certification program: Study coordinators have been certified to insure standardization. To achieve this standardization, we set up a procedure whereby one person (e.g., research associate) at each site is certified for cognitive and clinical test administration and scoring. This, in addition to ongoing oversight by investigators, gives us confidence that the study protocol is implemented in a systematic and uniform manner across sites.
- 5) NIH-Toolbox expanded domains: These measures continue to be collected, including measures from the motor and sensory domains.
- 6) Expanded memory assessment: The Face-Name Association Test and the Mnemonic Similarities Test continue to be implemented with data being collected on an ongoing basis at all sites.
- 7) Actigraphy: We continue to implement the use of Actigraph actigraphy watches to assess physical activity in our oldest old cohort for a 7-day period, consistent with the Center for Disease Control (CDC) standard research protocol. Processing and analysis software have been developed and applied at the UA with preliminary testing completed and initial results presented at the 2019 SFN McKnight Reception (see below).
- 8) NACC battery: Measures developed and employed by National Alzheimer's Coordinating Centers (NACC) continue to be collected following standardized procedures for all participants and are being used for clinical screening and adjudication

of cases with questionable MCI. This data will enable future harmonization with data collected in the NIA Alzheimer's Disease Centers and memory disorder programs at the MBI sites.

Laboratory Measures: Blood Biobanking

The MBAR is also collecting blood samples from participants. These samples are obtained using standard protocols and procedures across sites and are stored for future use for genetic, metabolic, and other analyses.

- 1) Blood samples from participants are being drawn on most participants across the MBI sites. These samples are centrifuged, frozen, and then sent to UF for central storage in the CAM freezers.

We have continued to make great progress over the past year. The time and effort directed at the MBAR project has resulted in the collection of important clinical, cognitive and neuroimaging data that should make a significant contribution to the clinical neuroscience of cognitive and brain aging. With the accumulation of the MBAR data, we are planning initial interim manuscripts for submission as we continue to approach our target sample size of 200 participants. We further expect that a greater number of analyses and manuscripts will be developed towards the end of the next fiscal year using data from the fully recruited cohort.

Deliverables

Leveraging the infrastructure and opportunities for inter-institutional collaborations provided by the MBAR over the past year, the MBAR leadership and investigators have had a number of achievements, including collaborative grant awards, manuscript publications, presentations at scientific meetings, and the roll out of a MBRF pilot project program. In addition, please note that many MBAR investigators from each of the MBI sites have benefited from the inter-institutional interactions facilitated by the MBAR effort, leading to numerous grant submissions and manuscripts that are not reflected by the cross-institutional grants and papers listed below. The specific deliverables showing cross-institutional collaboration are described below:

Frontiers in Aging Neuroscience Special Edition: The core and affiliated faculty of the four MBIs have generated a special edition, with additional articles submitted for publication in the last year, of the journal focusing on the use of neuroimaging for the study and assessment of cognitive and brain aging. The editors for this special edition include several PIs and investigators for MBAR (Cohen, Alexander, Visscher, Wright, Woods). All but one of the manuscripts planned for this special edition have already been published. An additional overview article by the special edition editors is in preparation.

Augmenting Cognitive Training in Older Adults (ACT) Project Update: This five-year, \$5.7M NIA-funded, R01 multicenter Phase III RCT continues to be actively recruiting the planned 360 healthy older adults between the ages of 69-90 years. This project utilizes the infrastructure created by MBAR for this multisite trial between the MBIs at UF and UA (MPIs: Cohen, Marsiske, Woods; UA Site PI: Alexander). The effects of transcranial direct current stimulation (tDCS) given in conjunction with cognitive training is being examined to determine if

tDCS increases neuroplasticity (as measured using neuroimaging methods) and ultimately whether it leads to improved cognitive outcomes as measured by the NIH-Toolbox. This study is the largest tDCS study of its kind ever conducted or supported by NIH. This study fits fully with the MBAR mission and the MBRF more broadly, and is a direct byproduct of the inter-institute collaborative work initiated within the MBAR. It is a major deliverable resulting from this inter-institute collaboration. A manuscript describing this cross-institutional, collaborative RCT protocol has been published (Woods et al., 2018; see below). In addition, collaborative manuscripts for journal publication (Hausman et al., submitted; Kraft et al., submitted) and presentations at the International Neuropsychological Society meeting (Boutzoukas et al., January, 2020; Evangelista et al., January, 2020; Hardcastle et al., January, 2020; Hausman et al., January, 2020; Kraft et al., January, 2020), using the baseline assessment and neuroimaging data, have been submitted (see references below).

Near Infrared Brain Stimulation Study: A new \$3.8M NIA R01 RCT grant proposal was awarded in August, 2019 to examine the effects of near infrared brain stimulation on cognitive and brain function in older adults to determine its ability to augment cognition during aging. This highly innovative multisite proposal between UF and UA (MPIs: Woods, Alexander, Bowers) directly utilizes the collaborative, multi-institutional infrastructure created by MBAR and represents the largest study to apply this novel method to enhance brain and cognitive performance during aging.

Vagal Nerve Stimulation Study: As part of the McKnight Interventions Core, a pilot study was awarded in October, 2019 by the MBRF to investigate the potential for using vagal nerve stimulation to enhance cognitive function in healthy older adults. This work directly leverages the infrastructure established as part of the MBAR with UF (Williamson (PI), Cohen, Woods, Lamb, Porges) and UA (Alexander) MBI teams, to support the investigation of this novel intervention pilot study. With the essential pilot data from this study, we would plan to pursue a larger scale subsequent NIA grant submission.

MBI Inter-Institute MBAR Grant Initiative: The MBI sites are discussing plans for new grant proposals to NIA that will expand on findings from MBAR. Following discussions and recommendations from NIA program, the MBAR PIs have been working to establish access to PET imaging and neuropathology follow-up across MBI sites to enhance this proposal effort. We are planning to develop this initiative into one or more NIA grant submissions in the coming year.

Manuscripts: With the MBAR sample now reaching well over 100 participants, we are currently also planning two manuscripts for publication from the MBAR data. One manuscript will be led by Dr. Alexander and his team on the physical activity data using actigraphy in relationship to cognitive and brain aging. A second analysis is underway examining the initial GABA MRS data in this cohort. Additionally, a graduate student working with Dr. Visscher is planning her dissertation research with the MBAR data, which is expected to lead to three new manuscripts for publication. We anticipate a series of additional manuscripts based on data from the registry to be developed in the coming year.

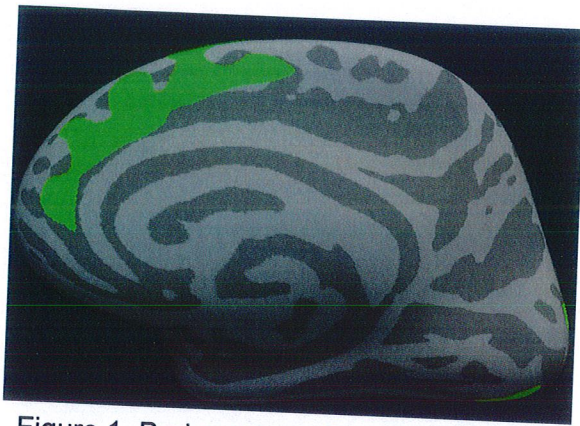


Figure 1. Brain regions showing greater medial frontal cortical volume with greater exercise in the MBAR cohort.

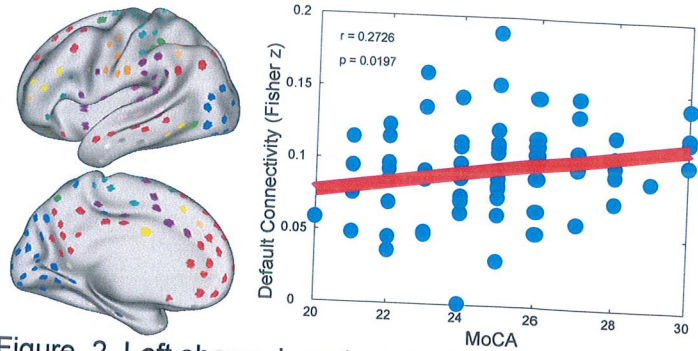


Figure 2. Left shows, in red, cortical regions that are part of the Default Mode Network. Plot on the right shows that the strength of functional connectivity of those Default Mode regions correlates with performance on MoCA, a test of cognitive function.

Meeting Presentations: Progress for the MBAR was presented at the 2019 McKnight Inter-institutional meeting at UF with slide presentations by Drs. Alexander (UA), Porges (UF), and Visscher (UAB), reporting recent efforts and progress in the recruitment and acquisition of neuroimaging and cognitive data for the registry cohort. Posters with research findings were presented during the 2019 SFN McKnight Reception meeting in Chicago, IL with interim results on actigraphy measures of moderate to vigorous exercise in relation to regional cortical thickness, area, and volume maps from structural MRI scans, on magnetic resonance spectroscopy findings, and on resting state functional connectivity analyses in the MBAR oldest old cohort. This work showed support for increased engagement in aerobic activity associated greater cortical volume in regions of medial frontal cortex in oldest-old individuals from the MBAR cohort (Raichlen et al., November, 2019; see Figure 1). Additionally, posters were presented showing analyses with resting state functional connectivity scans (Visscher et al., November, 2019; see Figure 2) and magnetic resonance spectroscopy data (Porges et al., November, 2019) in the MBAR cohort, supporting these novel brain imaging measures in the evaluation of successful cognitive aging.

Challenges and Barriers

While we have been quite productive and achieved many of our MBAR goals for the past year, we have had to overcome several challenges and barriers that impeded our progress in the early stages of the project. However, we believe the study is well underway and continues to run efficiently, and we are on target to reach our original goal of 200 MBAR participants in the coming year. To reach this goal and to maintain our throughput of new potential recruits of cognitively unimpaired oldest old adults, we have collectively continued to enhance our community outreach, use newspaper ads, and use population databases in the public domain (e.g., voter registration rolls) or other sources for targeted mailings. Going forward we plan to leverage the data collected to support new publications that will contribute to the scientific literature, will advance translation and implementation of the assessments for clinical use, and will support the development of multiple inter-institute grant proposals that capitalize on the unique McKnight dataset of successful aging oldest old adults.

Summary

Despite past challenges, the MBAR continues to be fully operational with recruitment ongoing and data for the registry continues to be actively collected. We fully expect that our substantial progress will continue over the coming year. To support our goals and plans for the MBAR cohort, we are kindly requesting a no cost extension for the combined Neuroimaging and Cognitive Cores through the next fiscal year, so we can continue our MBAR progress to reach our original target enrollment goal at no additional cost through December 31, 2020. During this time, we will also continue to examine in conjunction with the Clinical Interventions Core, opportunities for new and emerging studies, manuscripts, and grant proposals that fully leverage the collaborative inter-institutional infrastructure and expertise created by the MBAR.

Cited References

- Boutzoukas EM, O'Shea A, Evangelista ND, Hausman HK, Kraft JN, Porges E, Hishaw GA, Wu S, DeKosky S, Alexander G, Marsiske M, Cohen R, Woods AJ. (January, 2020) Contribution of region specific white-matter hyperintensities in cognitive aging. Abstract for presentation at the International Neuropsychological Society meeting, Denver, CO.
- Evangelista ND, O'Shea A, Kraft JN, Hausman HK, Boutzoukas E, Hardcastle C, Porges E, Alexander GE, Marsiske M, Cohen R, Woods AJ. (January, 2020) Independent contributions of dorsolateral prefrontal structure and function to working memory in older adults. Abstract for presentation at the International Neuropsychological Society meeting, Denver, CO.
- Hardcastle C, O'Shea A, Kraft JN, Hausman HN, Evangelista ND, Boutzoukas EM, Porges E, Alexander GE, Marsiske M, Cohen R, Woods AJ. (January, 2020) Lateralized hippocampal contributions to cognition in healthy older adults. Abstract for presentation at the International Neuropsychological Society meeting, Denver, CO.
- Hausman HK, O'Shea A, Kraft JN, Boutzoukas EM, Evangelista ND, Van Etten EJ, Bharadwaj PK, Smith SG, Porges E, Hishaw GA, Wu S, DeKosky S, Alexander GE, Marsiske M, Cohen R, Woods AJ. (January, 2020) The role of resting-state network functional connectivity in cognitive aging. Abstract for presentation at the International Neuropsychological Society meeting, Denver, CO.
- Hausman HK, O'Shea A, Kraft JN, Boutzoukas EM, Evangelista ND, Van Etten EJ, Bharadwaj PK, Smith SG, Porges E, Hishaw GA, Wu S, DeKosky S, Alexander GE, Marsiske M, Cohen R, Woods AJ. The role of resting-state network functional connectivity in cognitive aging. Manuscript Submitted.
- Kraft JN, O'Shea A, Albizu A, Evangelista ND, Hausman HK, Boutzoukas E, Porges E, Alexander GE, Marsiske M, Cohen R, Woods AJ. (January, 2020) Structural neural correlates of speed of processing. Abstract for presentation at the International Neuropsychological Society meeting, Denver, CO.

- Kraft JN, O'Shea A, Albizu A, Evangelista ND, Hausman HK, Boutzoukas E, Nissim NR, Van Etten EJ, Bharadwaj PK, Song H, Smith SG, Porges E, DeKosky S, Hishaw GA, Wu SS, Marsiske M, Cohen R, Alexander GE, Woods AJ. Structural neural correlates of speed of processing. Manuscript Submitted.
- Raichlen DA, Bharadwaj PK, Franchetti MK, Sims SA, Rezaei RF, Merritt SS, Jessup CJ, Porges EC, Geldmacher D, Hishaw GA, Alperin N, Trouard TP, Wadley VG, Levin BE, Woods AJ, Rundek T, Visscher KM, Cohen RA, Alexander GE. (November, 2019) Relation of daily activity patterns to cortical gray matter maps in the healthy oldest old: Findings from the McKnight Brain Aging Registry. Abstract presented at the Society for Neuroscience meeting, Chicago, IL.
- Porges EC, Bharadwaj PK, Franchetti MK, Sims SA, Rezaei RF, Forbes MA, Merritt SS, Jessup CJ, Raichlen DA, Geldmacher D, Hishaw GA, Alperin N, Trouard TP, Wadley VG, Levin BE, Woods AJ, Rundek T, Visscher KM, Cohen RA, Alexander GA, Jensen G, Foster B, Puts NAJ. (November, 2019) Age-related decreases in cortical GABA concentrations assessed over the lifespan abate in cognitively intact adults over 85 years of age. Abstract presented at the Society for Neuroscience meeting, Chicago, IL.
- Visscher KM, Stewart P, Sims SA, Bharadwaj PK, Franchetti MK, Rezaei RF, Merritt S, Jessup CJ, Raichlen DA, Porges EC, Geldmacher D, Hishaw GA, Trouard TP, Alperin N, Wadley VG, Levin BE, Woods AJ, Rundek T, Cohen RA, Alexander GE. (November, 2019) Functional connectivity in the healthy oldest old: Findings from the McKnight Brain Aging Registry. Abstract presented at the Society for Neuroscience meeting, Chicago, IL.
- Woods AJ, Cohen R, Marsiske M, Alexander GE, Czaja SJ, Wu S. (2018) Augmenting cognitive training in older adults (The ACT Study): Design and methods. Contemporary Clinical Trials, 65, 19-32.

Budget Expenditures

For expenses from November 1, 2018—September 30, 2019

University of Arizona Expenditures

Personnel:

Co-Investigator	\$ 315
Research Coordinator	\$ 4,855
Research Assistant	\$ 4,316
Graduate Research Assistant	\$ 2,859

Other:

Research Supplies	\$ 517
Advertising & Mailing	\$ 786
MRI & Blood Collection	\$ 23,466
Subject Pay & Parking	\$ 3,295

University of Arizona total expenditures this period: \$40,409

For expenses from November 1, 2018—September 30, 2019

University of Alabama at Birmingham Expenditures

Personnel:

Co-Investigator	\$ 7,379.65
Neurologist	\$ 17,153.36
Research Coordinator	\$ 7,346.48
Graduate Research Assistant	\$ 34,578.13

Other:

Research Supplies	\$ 1,511.55
Mailing	\$ 835.82
Copying and Printing	\$141.34
MRI & Blood Collection	\$3,125
Subject Pay & Parking	\$2,770.48
Staff Travel	\$633.91
Phone Service	\$77.13

*paid by an internal UAB CCTS grant obtained

University of Alabama at Birmingham total expenditures this period: \$ 75,552.85

For expenses from November 1, 2018—September 30, 2019

University of Florida Expenditures

Personnel:

Co-Investigator	\$ 00,000.00
Neurologist	\$ 00,000.00
Research Coordinator	\$ 53,913.86
Research Assistant	\$ 20,588.32
Test Development Research Assistant	\$ 00,000.00
Graduate Research Assistant	\$ 00,000.00

Other:

Research Supplies	\$ 2,441.25
Advertising	\$ 606.91
Mailing	\$ 193.23
MRI & Blood Collection	\$ 10,500.00
Subject Pay & Parking	\$ 2640.00

University of Florida total expenditures to date: \$ 90,883.57

For expenses from November 1, 2018—September 30, 2019

University of Miami Expenditures

Given the University of Miami MBAR funds have been expended, all MBAR efforts for this budget period were completely covered by complementary UM institutional funds. Of course, please note that we are fully committed to continuing to support our UM MBAR efforts with our UM institutional funds to complete the originally planned target enrollment.

For expenses from November 1, 2018—September 30, 2019

University of Florida Expenditures

Personnel:

Co-Investigator	\$ 00,000.00
Neurologist	\$ 00,000.00
Research Coordinator	\$ 53,913.86
Research Assistant	\$ 20,588.32
Test Development Research Assistant	\$ 00,000.00
Graduate Research Assistant	\$ 00,000.00

Other:

Research Supplies	\$ 2,441.25
Advertising	\$ 606.91
Mailing	\$ 193.23
MRI & Blood Collection	\$ 10,500.00
Subject Pay & Parking	\$ 2640.00

University of Florida expenditures to date: \$ 90,883.57

Cianciotto.Melanie

From: Cianciotto.Melanie
Sent: Monday, December 16, 2019 5:09 PM
To: 'Amy Porter'
Subject: FW: Requesting a No Cost Extension for funds not utilized
Attachments: 12 03 2019 _MBAR Financials Template Nov 2018 - Sept 2019.docx
Importance: High

Hi Amy,

Dr. Cohen is asking for a no cost extension of the MBAR program. He requested this in 2017 and Lee told me to approve the no cost extension. Dr. Cohen also asked for one in December of last year. Lee provisionally approved it and then ran it by the trustees at the February 2019 meeting.

Is it okay if I tell Dr. Cohen it is provisionally approved and then add it to the agenda or do you want to run it by the research committee?

Please let me know.

Thanks!
Melanie

Melanie A. Cianciotto
First Vice President, Foundations and Endowments Specialty Practice
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From: Lacy,Tina L [<mailto:tinalacy@php.ufl.edu>]
Sent: Friday, December 13, 2019 5:07 PM
To: Cianciotto.Melanie
Cc: Cohen,Ronald A
Subject: FW: Requesting a No Cost Extension for funds not utilized
Importance: High

Good Afternoon Melanie,

Dr. Cohen has asked to follow up on the request to extend the projects here at the University of Florida.

If you approve the extension of the projects a reply to Dr. Cohen's email (or this one) affirming the projects can continue as outlined below will suffice.

Thanks in advance for your help with this matter. Please reach out to me and/or Dr. Cohen if you need any further information or clarification.

Kind Regards, Tina

Tina L. Lacy
Administrative Coordinator
Center for Cognitive Aging and Memory (CAM)
Phone: 352-294-5841
Email: tinalacy@ufl.edu

From: Cohen, Ronald A <roncohen@ufl.edu>
Sent: Thursday, December 5, 2019 2:24 PM
To: Melanie.Cianciotto@SunTrust.com
Cc: Lacy, Tina L <tinalacy@phhp.ufl.edu>
Subject: Requesting a No Cost Extension for funds not utilized
Importance: High

Hi Melanie,

RE: UF Projects for MBAR (P0039221 & P0039224)

Hope all is well. My CAM administrator (Tina) indicated that I should write to you regarding continuation of the MBRF funding for the MBAR Cognitive/Neuroimaging cores.

Our annual progress report for the MBAR project across the four McKnight Brain Institute sites is being finalized this week. However the internal financial systems at UF are set up to have project expiration dates. Accordingly, the University of Florida MBAR projects are set to expire on 12/31/2019 and we are not able to continue research operations beyond that date with approval from the MBRF.

I am requesting a no-cost extension with an end date of 12/31/2021, so that we can continue with our current work. We are anticipating completing the study over the coming year, but wanted extend to 2021 for analysis and publications in case these are not all completed in 2020.

If additional information is needed, I am can provide specific details or answer questions about our fund expenditure.

Thanks ,
Ron

Ron Cohen, PhD, ABPP, ABCN
Evelyn McKnight Chair of Clinical Translation in Cognitive Aging
Professor, Clinical and Health Psychology, Neurology and Psychiatry
Director, Center for Cognitive Aging and Memory
University of Florida
352-294-5840
roncohen@ufl.edu

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

Funded by the McKnight Brain Research Foundation through the American Brain Foundation,
and the American Academy of Neurology

Application Deadline: October 1, 2019

This award aims to encourage young investigators in clinical studies relevant to age-related cognitive decline and memory loss. The award also recognizes the importance of rigorous training in clinical research and encourages young investigators in seeking opportunities to establish future careers in the area of human cognitive aging. **Please note: the focus should NOT be solely on a neurodegenerative dementia (e.g. Alzheimer's disease); however, proposals that focus on combined study on cognitive aging and a neurodegenerative dementia may be considered.**

Each award will consist of a commitment of \$65,000 per year for two years, plus a \$10,000 per year stipend to support education and research-related costs for a total of \$150,000.

HOW TO APPLY

1. Visit AAN.com/view/ResearchProgram
2. Select "2020 McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss"
3. Select "Apply now"

Please only submit one application - applicants are not allowed to submit applications for more than one award. Your application may be considered for another category at the discretion of the review committee, however, the system will only allow one application per person. Visit the [Frequently Asked Questions](#) portion of the website for more information.

IMPORTANT DATES

October 1, 2019: Application deadline – Note that this is the deadline for all documents, including those from references, the mentor, and the chair. Applications will be declined if this information is not submitted by October 1.
January 2020: Notification of recipients
July 1, 2020: Funding begins

ELIGIBILITY

1. For the purpose of this scholarship, research is defined as "patient-oriented research conducted with human subjects, or translational research specifically designed to develop treatments or enhance diagnosis of age-related cognitive decline and memory changes. These areas of research include epidemiologic or behavioral studies, clinical trials, studies of disease mechanisms, the development of new technologies, and health services and outcomes research." Disease related studies not directly involving humans or human tissue are also encouraged if the primary goal is the development of therapies, diagnostic tests, or other tools to prevent or mitigate neurological diseases. This award is also appropriate for junior investigators interested in an academic career in translational-based research in neurology.
2. Recipient must be interested in an academic career in neurological research who has completed a residency or a PhD degree no more than 5 years prior to the beginning of this award (July 1, 2020). If you completed a fellowship of any kind after residency, your eligibility is still based on the date you finished residency.

EVALUATION AND SELECTION

Applications are evaluated by reviewers based on the following criteria:

- Applicant's ability and promise as a clinician-scientist based on prior record of achievement and career plan, letters of reference, and NIH Biosketch (30 percent)
- Quality and nature of the training to be provided and the institutional, departmental, and mentor-specific training environment (30 percent)
- Quality and originality of the research plan for cognitive aging and age-related memory loss (40 percent)

ANNUAL AND FINAL PROGRESS REPORTS

An annual progress report is due in May of the first year. Renewal of the award in year two is contingent upon presentation of a satisfactory progress report. Additionally, a final research report and a final expenditure report are due within 60 days following the close of the grant term. The final expenditure report must be prepared by the institution's financial office.

REQUIRED ATTACHMENTS FOR APPLICATION

1. PDF of three-page Research Plan, including brief statements of aims, background, methodology, and any supporting preliminary data/figures. References do not count toward the page limit. The research plan should be written by the applicant and should represent his/her original work. However, the applicant is expected and encouraged to develop this plan based on discussion with the proposed mentor. It is appropriate, but not required, for the proposed work to be specifically related to the mentor's ongoing research.
2. PDF of Applicant's NIH Biosketch. See this [link](#) for the most recent NIH Biosketch template.

Once the above information is fully completed and submitted by the applicant:
3. The **chair** will receive an email with a link asking them to check a box confirming that that applicant's clinical service responsibilities will be restricted to no more than 20 percent of their time. The chair will NOT be asked to submit a letter.
4. Two **references**, identified by applicant, will receive an email with a link to submit a letter of reference supporting the applicant's potential for a clinical, academic research career and qualifications for the scholarship.
5. The **mentor** will receive an email with a link to submit a letter of reference detailing his/her support of and commitment to the applicant and the proposed research and training plan. The letter should specifically indicate the mentor's role in the development and preparation of the applicant's research plan and should include:
 - How the proposed research fits into the mentor's research program
 - Expertise and experience in the area of research proposed and the nature of the mentor's proposed time commitment to the supervision and training of the applicant
 - Mentor's prior experience in the supervision, training, and successful mentoring of clinician scientists
 - Potential for applicant's future research career and comparison of applicant among other residents
6. The **mentor** will also be required to upload a NIH Biosketch.
7. Applications will not be processed or reviewed until the letters of recommendation are submitted. The applicant will receive an email confirmation upon receipt of each support letter. To send a reminder email to the letter writer, log back into the application and select "Re-send Recommendation Request" located in the Support Information section of the application.

CONTACT INFORMATION

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Research Partnership in Cognitive Aging

A report to the McKnight Brain Research Foundation

October 7, 2019

Foundation for the National Institutes of Health

Plasticity and Mechanisms of Cognitive Remediation in Older Adults is the centerpiece of a Research Partnership in Cognitive Aging between the McKnight Brain Research Foundation (MBRF) and the National Institute on Aging (NIA), coordinated by the Foundation for the National Institutes of Health (FNIH). The partnership—now more than a decade long—currently supports an NIA grant for a multicenter clinical research trial on remediating age-related cognitive decline through mindfulness-based stress reduction and exercise, the MEDEX trial.

The FNIH is pleased to present this 2019 report to the MBRF. It provides updates from the NIA on the MEDEX trial, as well as information on three other trials investigating plasticity and mechanisms of cognitive remediation in older adults that the NIA supports with grant awards stimulated by the MBRF/NIA partnership. A report of outcomes from the Cognitive Aging Summit III, held in 2017, is also provided.

“Plasticity and Mechanisms of Cognitive Remediation in Older Adults”
RFA-AG-14-016 (R01)

Remediating Age-related Cognitive Decline: Mindfulness-based Stress Reduction and Exercise (MEDEX)

The MEDEX clinical trial (R01 AG049369), awarded to Eric Lenze, M.D. at Washington University, has completed enrollment. All participants have completed the first 6-month follow-up. The study is slated to be completed in August 2020; publication of the results should follow sometime in 2021.

The abstract for the grant:

DESCRIPTION (provided by applicant): The vast majority of older adults will suffer declines in cognitive functions such as memory and cognitive control (or executive function), interfering with their ability to participate and engage in meaningful activities. Importantly, the recent observation that the brain retains plasticity late into life suggests that timely and personalized interventions might remediate age-related cognitive decline. Two promising interventions are Mindfulness-Based Stress Reduction and Exercise, each of which appears to act in multi-modal ways to make plastic changes in CNS function to improve memory and cognitive control in older adults. Our research team has conducted several studies of these interventions, supporting their benefits and pathways to improved cognitive functioning. We propose a 2x2 factorial design RCT to definitively test MBSR and exercise for remediation of age-related cognitive decline. We will randomize 580 healthy community-living adults aged 65+ to one of four conditions: MBSR alone, exercise alone, MBSR + exercise, or health education (a control condition). Participants will receive protocolized interventions for a six-month acute period, followed by a 12-month maintenance period. We will examine (1) cognitive improvements using a well-validated and sensitive neuropsychological battery focusing on memory and cognitive control; (2) mechanistic changes such as reduced cortisol and improved insulin sensitivity (3) neuroimaging markers of plasticity: structural and functional connectivity changes indicating plastic CNS changes underlying the cognitive improvements (4) individual variability that predicts response to the interventions. Our main goal is to carry out a high-quality clinical trial, such that data and biosamples will become a resource for the scientific community. Then, we can not only improve the lives of older adults in the near-term by matching individuals to readily available interventions that most benefit them, we can also understand the mechanisms of neuroplastic changes with interventions to rescue cognitive decline with aging, leading to a more active and vital senior community. PUBLIC HEALTH RELEVANCE: The world is graying, and the vast majority of older adults will have declines in cognitive function, interfering with function,

quality of life, and engagement in valued activities. We will test two promising interventions - Mindfulness Based Stress Reduction (MBSR) and Exercise - for their ability to remediate age-related cognitive decline. MBSR and exercise are both inexpensive, well-tolerated, safe, and highly scalable interventions; therefore our project can demonstrate how effective they are, for whom, and by what mechanisms, in the near term older adults could receive lifestyle strategies that would benefit their brain and cognitive functioning, staving off disability and dependence on others and maintaining engagement in life's most valued activities.

Updated information from the Principal Investigator, Dr. Lenze, is provided below. He agreed that this information may be shared with the MBRF board:

Recruitment and Retention: Recruitment is complete, yielding a racially diverse sample (see Table), and all participants completed the 6-month follow-up assessment as of August 2019; the entire study will be completed by August 2020. A total of 585 participants were randomized. As of October 2019, the retention rate in the 18-month study is 94%, and the successful MRI scanning rate is 99%. Adherence to the interventions is high. We have also completed genotyping and data cleanup for cognitive and neuroimaging outcomes through month 6 for all participants.

With a supplement from NIA, we are also examining plasma amyloid (AB 40/42 ratio) in a large subsample of the study (n=140) at the month 0, 6, and 18 timepoints of the study. These assays are ongoing and should be available within 1-2 months.

We have also recruited most (~80%) of the MEDEX completers into a MEDEX extensions study with biyearly follow up cognitive assessments and monthly maintenance interventions.

Table 1. Baseline sociodemographic characteristics of the MEDEX study participants (randomized only)

	RCT (N = 585)
Age (Years), Mean (SD)	71.5 (4.8)
Gender, n (%)	
Male	161 (27.5)
Female	424 (72.5)
Ethnicity, n (%)	
Hispanic or Latino	39 (6.7)
Not Hispanic or Latino	546 (93.3)
Race, n (%)	
American Indian/Alaska Native	2 (0.3)
Asian	27 (4.6)
Black or African American	69 (11.8)
Native Hawaiian or Other Pacific Islander	0 (0.0)
White	477 (81.5)
More than one race	4 (0.7)
Unknown/Not Reported	6 (1.0)

Other grants supported by the NIA, originally in response to RFA-AG-14-016

Augmenting Cognitive Training in Older Adults – The ACT Grant (R01 AG054077)
Adam Woods, Ronald Cohen, Michael Marsiske (MPIs) – University of Florida

The trial is currently underway. Enrollment is going well. Trial completion anticipated in 2021 with publication of findings probably in 2022.

The abstract for the grant:

DESCRIPTION (provided by applicant): This randomized clinical trial will test whether transcranial direct current stimulation (tDCS) of frontal cortices enhances neurocognitive and functional outcomes achieved from cognitive training in older adults experiencing age-related cognitive decline. Change in well-validated measures of neurocognitive function and everyday abilities will serve as outcome measures. Functional and structural neuroimaging biomarkers of neural plasticity and learning (fMRI, GABA MRS, etc.) will measure intervention-associated alterations in specific brain regions impacted by cognitive aging. tDCS is a noninvasive brain stimulation method that facilitates neural plasticity and learning. Accordingly, when used as an adjunctive intervention, tDCS may augment cognitive training effects. This study will leverage existing multisite clinical trial infrastructure at McKnight Brain Institutes located in two of the states with the largest representation of older adults in the United States: University of Florida, University of Miami, and University of Arizona. Adults over the age of 65 represent the fastest growing group in the US population. As such, age-related cognitive decline represents a major concern for public health. Recent research suggests that cognitive training in older adults can improve cognitive performance, with effects lasting up to 10 years. However, effects are typically limited to the tasks trained, with little transfer to other cognitive abilities or everyday skills. Effects may also be reduced in people with Alzheimer's disease risk factors. A two-phase multisite randomized clinical trial will examine the individual and combined impact of pairing cognitive training with transcranial direct current stimulation (tDCS) in older adults experiencing age-related cognitive decline ($n = 360$; 120 per site). Participants will consist of elderly men and women 65-90 years of age with evidence of age-related cognitive decline, but not MCI or Alzheimer's disease ($\text{MoCA} \geq 25$). We will compare changes in cognitive and brain function resulting from CT and CT combined with tDCS using a comprehensive neurocognitive, clinical, and multimodal neuroimaging assessment of brain structure, function, and metabolic state. Functional magnetic resonance imaging (fMRI) will be used to assess brain response during working memory, attention, and memory encoding; the active cognitive abilities trained by CT. Proton magnetic resonance spectroscopy (MRS) will assess markers of neural plasticity, GABA concentrations, and cerebral metabolism. We hypothesize that: 1) tDCS will enhance neurocognitive function, brain function, and functional outcomes from CT; 2) Effects of tDCS on CT will be maintained up to 12 months following training, and 3) Neuroimaging biomarkers of cerebral metabolism, neural plasticity (GABA concentrations) and functional brain response (fMRI) during resting vs. active cognitive tasks will predict individual response to tDCS, with certain Alzheimer's risk factors (e.g., APOE4 genotype, family history of Alzheimer's disease) predicting poorer cognitive and functional outcome. To date, no studies have comprehensively examined combined CT and tDCS intervention in the elderly. This study will provide definitive insight into the value of combating cognitive decline in a rapidly aging US population using tDCS with cognitive training. PUBLIC HEALTH RELEVANCE: This randomized clinical trial examines the effect of augmenting cognitive training with transcranial direct current stimulation to maximize cognitive and functional outcomes older adults experiencing age-related cognitive decline. Change in well-validated measures of everyday abilities and neurocognitive function will serve as outcome measures. Functional and structural neuroimaging biomarkers of neural plasticity and learning (fMRI, GABA MRS, etc.) will measure intervention-associated alterations in specific brain regions impacted by cognitive aging.

Enhancing Cognitive Control Older Adults with Complementary Interventions (R01 AG054077)

Adam Gazzaley, Patricia Arean (MPIs) – UC San Francisco

The trial is currently underway. Trial completion anticipated in 2020 with publication of findings probably in 2021.

The abstract for the grant:

DESCRIPTION (provided by applicant): Deficits in cognitive control are at the core of many functional declines in healthy older adults. A fundamental contributor to these deficits is compromised regulation of both external and internal attention processes, which leads to a decreased ability to effectively engage in complex, goal-directed behavior. As a result, there is a critical need to develop targeted interventions to reverse or prevent declines in regulation of attention processes in healthy older adults. Targeted cognitive training and focused-attention meditation are two interventions that hold great promise for boosting attention and cognitive control abilities in healthy older adults, but we lack a firm understanding of the neural and physiological mechanisms that underlie this positive neuroplasticity. We also know little about whether such interventions might have multiplicative effects on cognition when administered in a combinatorial manner. The goals of the proposed research are threefold. First, we will determine the unique and synergistic effects of an externally oriented attention training paradigm and an internally oriented meditation paradigm on enhancing regulation of external and internal attention in healthy older adults, leading to improvements in functional outcomes. Second, we will examine the impact of potential genetic, physiological, and social moderators of the treatment effects in individuals and subgroups who show variability in their response to the interventions. Third, we will document the neural and physiological mechanisms underlying the unique and synergistic plasticity associated with each individual or combined intervention. To accomplish these aims, we will conduct a randomized clinical trial in healthy older adults of two novel cognitive training paradigms that are deployed on wireless mobile devices. We will collect data from two samples: a large (N = 1650) sample that will be recruited nationally who will complete the study entirely on mobile devices and a smaller (N = 225) local sample who will also complete more in-depth lab-based cognitive assessments, EEG, structural MRI, and functional MRI. The national sample will provide the numbers needed to examine individual and subgroup differences in treatment response in an extremely diverse sampling of the general population. The local sample will allow us to dive deeper into the underlying neural and physiological mechanisms that give rise to training effects. Both groups will complete baseline, immediate follow-up, and one-year follow-up assessments of cognitive and functional outcomes, while the local group will undergo neuroimaging at all three time points. We anticipate that the unique methodological approach and experimental design will significantly advance the development of rehabilitation programs directed at the broad range of cognitive abilities and functional outcomes in both healthy and clinical populations that suffer from problematic regulation of attention and cognitive control. PUBLIC HEALTH RELEVANCE: Cognitive deficits that occur with aging are a pervasive concern to older individuals and a growing public health issue. The goal of this project is to determine the neural and physiological mechanisms by which older adults reap cognitive and functional benefits from individual and combined cognitive and meditation training. This knowledge gained from this high-impact study will transform the field of cognitive interventions, leading to new methods that improve quality of life for older adults and individuals with cognitive impairment from neurological and psychiatric disease.

Investigating Gains in Neurocognition in an Intervention Trial of Exercise (IGNITE) (R01 AG0532952)
Kirk Erickson, Jeffrey Burns, Arthur Kramer, Edward McAuley (MPIs) – University of Pittsburgh (parent site)

The trial is currently underway. Trial completion anticipated in 2021 with publication of findings probably in 2022.

The abstract for the grant:

Abstract Despite the ubiquity of normal age-related cognitive decline there is an absence of effective approaches for improving neurocognitive health. Fortunately, moderate intensity physical activity (PA) is a promising method for improving brain and cognitive health in late life, but its effectiveness remains a matter of continued skepticism and debate because of the absence of a Phase III clinical trial. Here we propose a Phase III multi-site randomized clinical trial called IGNITE (Investigating Gains in Neurocognition in an Intervention Trial of Exercise) to more definitively address whether exercise influences cognitive and brain health in cognitively normal older adults. We are proposing a 12-month, multi-site, randomized dose-response exercise trial (i.e., brisk walking) in 639 cognitively normal adults between 65-80 years of age. Participants will be randomized to a (a) moderate intensity aerobic exercise condition at the public health recommended dose of 150 minutes/week (N=213), (b) a moderate intensity exercise condition at 225 minutes/week (N=213), or (c) to a stretching-and-toning control condition for 150 minutes per week (N=213). Participants will meet 3 days/week for site-based exercise and do home-based activity on two more days of the week for 12 months. A comprehensive state-of-the-science battery of cognitive, MRI, amyloid imaging, physiological biomarkers, cardiorespiratory fitness, physical function, and quality of life measures will be assessed at baseline and after completion of the intervention. We have assembled a highly creative, productive, and interdisciplinary team with a long history of collaboration and experience conducting exercise interventions in older adults to test the following aims: Aim 1: Using a comprehensive neuropsychological battery and the NIH Toolbox, we will test whether a 12-month moderate intensity exercise intervention improves cognitive performance in older adults and (b) test whether the improvements occur in a dose-dependent manner. Aim 2: We will test whether a 12-month PA intervention augments MRI markers of brain health and whether these changes happen in a dose-dependent manner. Aim 3: We will test the hypothesis that cardiometabolic, inflammatory, and neurotrophic changes mediate improvements in brain and cognition. Aim 4: We will examine subgroups (i.e., individual differences) that attenuate or magnify the effect of the intervention on cognitive, brain, and physiological systems to better understand the factors that predict 'responders' versus 'non-responders' to the intervention. We will explore three categories of variables: (1) demographic (e.g., age) (2) genetic (e.g., APOE), and (3) baseline A β burden. Exploratory Aims: We will explore (a) whether baseline brain health metrics predict adherence and compliance to 12-months of PA, and (b) the utility of multi-modal brain imaging analytical approaches to more comprehensively understand the effects of PA on the aging brain. The results from this trial could transform scientific-based policy and health care recommendations for approaches to improve cognitive function in cognitively normal older adults. PUBLIC HEALTH RELEVANCE: In this Phase III randomized clinical trial, we will examine the effects of aerobic exercise on cognitive and brain function in late adulthood. We will be collecting a battery of cognitive, neuroimaging, amyloid, psychosocial, physical function measures, and blood-based biomarkers to examine the outcomes and mechanisms of the intervention.

Outcomes from the Cognitive Aging Summit III

A special issue of the journal *Neurobiology of Aging* is planned for publication in late November 2019, just after the Society for Neuroscience meeting. The issue will feature an introduction by the NIA's Molly Wagster, Ph.D. and Jonathan King, Ph.D., and 6 articles co-authored by the presenters and chairs of each of the 6 Summit sessions. (For a description of the Summit and an Executive Summary see <https://www.nia.nih.gov/research/dn/cognitive-aging-summit-iii>)

The NIA also has launched two research initiatives based on the set of recommendations 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. That recommendation is now an action. NIA's Intramural Research Program (IRP) will develop and conduct the longitudinal study with the name STARRRS—Successful Trajectories of Aging: Reserve and Resilience in RatS. The study will generate state-of-the-art neuroimaging, along with phenotypic results, non-invasive biological samples plus other indicators that could give insight into the mechanisms of healthy neurocognitive aging. STARRRS will create open-source data and a sample hub to be shared with the entire aging science community. The goal is to bring us closer to an understanding of the factors that contribute to successful versus unsuccessful neurocognitive aging.

For the NIA blog on this study see: <https://www.nia.nih.gov/research/blog/2019/06/cognitive-reserve-research-reaches-starrs>

- Another recommendation from the 2017 Summit was to develop uniform definitions of terms such as resilience, reserve, compensation, maintenance, etc. so that the research community, nationally and internationally, could advance the field and our knowledge base more rapidly and lead to a better understanding of how individuals can promote and sustain brain and cognitive health. In response to that recommendation, the NIA issued an RFA (RFA-AG-18-024), "Collaboratory on Research Definitions for Cognitive Reserve and Resilience to Alzheimer's Disease (R24-Clinical Trial Not Allowed)."

One award was made to Yaakov Stern and Columbia University Health Sciences for a network grant titled "Collaboratory on Research Definitions for Cognitive Reserve and Resilience" (R24 AG061421). The abstract for the grant:

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 to develop data sharing and information exchange platforms to help guide promote research in this area. PUBLIC HEALTH RELEVANCE: In order to achieve state-of-the-art definitions and research guidelines for key concepts associated with resilience against cognitive aging and Alzheimer's disease related dementia, 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.

The PI, Dr. Stern, and his Executive Committee (Marilyn Albert, Carol Barnes, Roberto Cabeza, Alvaro Pascual-Leone, Peter Rapp), have been very productive to date. They have developed a website for the effort <https://reserveandresilience.com/> and have organized and held the first workshop associated with this network grant (download the mobile app by accessing <https://my.yapp.us/RANDR> for agenda, details, and slides from the workshop). The next workshop is scheduled for September 14-15, 2020 in the Bethesda area. Over the coming year, workgroups formed at the first workshop will continue to meet and refine concepts and approaches in anticipation of the 2020 workshop.

A third recommendation from the 2017 Summit was approved by NIA Council as a concept for development—"Network for Identification, Evaluation and Tracking of Older Persons with Superior Cognitive Performance for Their Chronological Age." The draft funding opportunity announcement has been submitted to the NIH system for review for publication.