

UNIVERSITY OF MIAMI
MILLER SCHOOL OF MEDICINE
EVELYN F. MCKNIGHT
BRAIN INSTITUTE



UNIVERSITY OF MIAMI EVELYN F. McKNIGHT BRAIN INSTITUTE

ANNUAL PROGRESS REPORT
JANUARY 1ST – DECEMBER 31ST, 2019

UNIVERSITY OF MIAMI
MILLER SCHOOL OF MEDICINE
EVELYN F. McKNIGHT
BRAIN INSTITUTE



January 16th, 2020

Michael L. Dockery, M.D.
J. Lee Dockery, M.D.
Richard S. Isaacson, M.D.
Susan Pekarske, M.D.
Gene R. Ryerson, M.D.
Madhav Thambisetty, M.D., Ph.D.
Robert M. Wah, M.D.
Trustees, The Evelyn F. McKnight Brain Research Foundation, Inc.
SunTrust Banks, Inc.
Foundations & Endowments Specialty Practice
333 Garland Avenue
15th Floor
Orlando, FL 32801

Dear Trustees,

In her first year as both the *Evelyn F. McKnight Brain Institute's Scientific Director* and *Evelyn F. McKnight Endowed Chair for Memory and Learning in Aging*, Dr. Tatjana Rundek has led the University of Miami McKnight Brain Institute to expand collaborations, formalize and expand its advisory council, apply for outside grants and create the first draft of a strategic plan among other new initiatives.

We would like to thank you for your support and we are pleased to send this report for 2019 entailing our accomplishments, achievements, awards and research updates. In addition, we have included our goals and plans for 2020.

Thank you for your attention.

Yours Sincerely,

A blue ink signature of Ralph L. Sacco.

Ralph L. Sacco, M.D., M.S.
Executive Director
Evelyn F. McKnight Brain Institute

A blue ink signature of Tatjana Rundek.

Tatjana Rundek, M.D., Ph.D.
Scientific Director
Evelyn F. McKnight Brain Institute

RLS/TR/SSM/bd

cc: Amy Porter
Melanie Cianciotto
Susan Fox Rosellini
Stacy Merritt

LAST YEAR'S GOALS

SUMMARY OF SCIENTIFIC AND EDUCATIONAL ACHIEVEMENTS

SECTION 1



Introduction

Under the leadership of our Executive Director Dr. Ralph Sacco, Scientific Director Dr. Tatjana Rundek and the multi-disciplinary Scientific Advisory Board, this has been a tremendous year in which we are proud of our progress and accomplishments. Our McKnight Brain Institute achieved great academic success. Drs. Sacco and Rundek fostered and promoted the achievements of junior faculty and trainees through their dedication, leadership and mentorship. With their support, they have engendered a culture of multi-disciplinary cooperation, collaboration and team science in our Institute and beyond.

This report provides an opportunity to showcase our work at the University of Miami Evelyn F. McKnight Brain Institute in the past year. The report begins with an overview of our progress towards last year's goals. It is followed by several notable scientific and educational achievements, including our involvement in McKnight Brain Research Foundation events. The remainder of the report follows the MBRF template and details what we accomplished this year.

Overview of our Institute's Progress Toward Last Year's Goals

- Our main goal for 2019 was to create our five-year MBI Strategic Plan. The second phase of our [**Strategic Plan**](#) was ongoing throughout the year. This included bi-monthly meetings to prioritize and finalize our goals and to assess and brainstorm the availability and attainability of needed resources. With these goals in mind, we set forth to determine what our strategies and tactics for each goal would entail. The University of Miami Miller School of Medicine (UMMSOM) has been working on its strategic plan and is moving to its final phase this year. It is encouraged that entities within the medical school align their individual strategic plans with the overall plan of our Medical School. [**Drs. Sacco and Rundek**](#) participate in the (UMMSOM) strategic plan and will communicate our plan to Dean Henry Ford and the Dean for Research, Carl Schulman, once their strategic plan is completed and our strategic plan aligned. (See [**Appendix II**](#))
- [**Dr. Ralph Sacco**](#), director of the University of Miami Clinical Translational Science Institute (UM CTSI) completed the first year of the newly funded grant cycle. In 2019, the Miami CTSI successfully reached 1,900 individuals throughout the Hub and across the region, and it collaborated with 11 other CTSAs institutions across the country. See [**Section 9**](#) for more information on the success of the UM CTSI.
- [**Dr. Ralph Sacco**](#) and collaborators furthered their analysis this year on the longitudinal NOMAS program (See [**Section 9**](#)). They expanded their focus on the role of the immune mechanisms in vascular cognitive impairment and dementia. They enhanced their methods to explore inflammation networks in cerebrovascular disease as determinants of cognitive trajectories and functional decline. As a result, key research data and findings were published.
- [**Drs. Tatjana Rundek**](#) and [**David Loewenstein**](#) in collaboration with Dr. Todd Golde at the University of Florida successfully competed for renewal of the 1FL ADRC (newly named ADC). Dr. Rundek will co-lead the Research Educational Core with Dr. Glenn Smith from UF. Dr. Loewenstein will lead the UM Clinical Site. Both Drs. Rundek and Loewenstein will participate in the 1FL ADC Steering Committee and Recruitment Core. Details are provided in [**Section 9**](#).
- [**Drs. Bonnie Levin**](#) and [**Katalina McInerney**](#) continued building the registry for The McKnight Frailty Project. Our McKnight Frailty Registry is **unique** to the University of Miami and presents a critical research source for our young investigators to develop their clinical research skills, present and publish results and plan future research grants. The Registry

now includes clinical and neurocognitive data for over 500 clinic and community participants from diverse backgrounds, ranging in age from 50 to 95+. (See [Section 9](#))

- [Dr. Xiaoyan Sun](#), Director of our McKnight Education program expanded the scope of the program at the University of Miami and in the community of South Florida. Partnerships with the city of Miami were strengthened and new collaborations formed. Educational training geared towards residents, fellows and students was enhanced. Through our education and outreach program, we reached over 400 community members. We organized new brain cutting sessions with the Department of Pathology with multi-disciplinary team education. More details are presented in [Section 12](#).
 - We started planning [The Evelyn F. McKnight Brain Research Foundation 12th Annual Inter-Institutional Meeting](#) in Miami, April 1st - 3rd, 2020. The hotel rooms, meeting space and logistics are confirmed. Discussions on topics and presenters took place and the draft agenda is prepared and will soon be finalized. We are looking forward to hosting the McKnight Brain Research Foundation Trustees, other McKnight Brain Institutes, and the *McKnight Clinical Translational Research Scholars in Cognitive Aging and Age-related Memory Loss* fellows and their mentors.
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Notable Scientific and Educational Achievements

13th International Conference of Cerebral Vascular Biology

The UM McKnight Brain Institute (MBI) was one of the organizers and sponsors of the [13th International Conference of Cerebral Vascular Biology](#), held in Miami, June 25-28, 2019. [Dr. Ralph Sacco](#) was one of the keynote speakers and [Dr. Tatjana Rundek](#) was a moderator of a session on the *aging brain and age-related memory los*. [Dr. Vladimir Hachinski](#), a renowned cognitive neurologist from London, Ontario, Canada, was our MBI guest speaker at the conference.

CEREBRAL VASCULAR BIOLOGY
13th INTERNATIONAL CONFERENCE
CVB2019
MIAMI
June 25th – 28th

Keynote speaker:
Dr. Ralph L Sacco
Expanding the neuroscience frontier of brain health

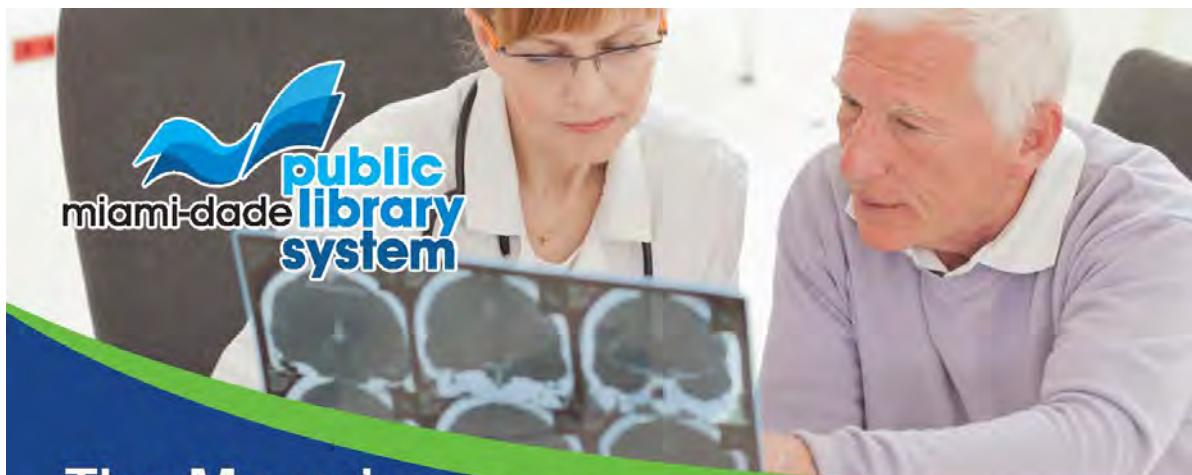
Session 5. (T Rundek, Moderator)
Cerebrovascular pathology of the aging brain,
age-related memory loss and cognitive decline

Dr. Vladimir Hachinski
*VCI: Can we prevent some types
of dementias beginning now?*

[Dr. Vladimir Hachinski](#) was one of our prestigious external speakers invited to our MBI seminar series, June 29th. Dr. Hachinski gave an interactive workshop on vascular ischemic cognitive scales and discussed the Hachinski Ischemic Risk Score with our MBI leaders, members, collaborators and trainees. The potential collaborations were discussed, particularly with a focus on global brain and vascular health, as a recently proclaimed global mission by the World Stroke Organization.

The Mayor's Initiative on Aging: Your Brain

As part of the UM MBI education mission, **Dr. Xiaoyan Sun** and **Stacy Merritt** forged a partnership with the Miami-Dade Mayor's office. We participated in **The Mayor's Initiative on Aging: Your Brain**_program by developing a seminar series presented in the community to teach how aging affects the brain and what to expect, as well as prevention and best practices.



The Mayor's Initiative on Aging: Your Brain

Join us for a series of discussions on how aging affects your brain, including what to expect, prevention and best practices.

Presented by the University of Miami Miller School of Medicine.

Ages 55 yrs.+

Tuesdays,
5 - 7 p.m.

October 8
Joyce Gomes-Osman, Pt, PhD
Exercise for brain health, from evidence to practical advice.

October 15
Sarah Getz, PhD
The aging brain and decision making.

October 22
Christian Camargo, MD
How our brain changes as we age.

October 29
Erika Marulanda-Londono, MD
How stroke affects the brain. What you need to know, before, during and after.

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Miami-Dade County Mayor Carlos A. Gimenez's Initiative on Aging provides resources and information on programs and activities for older adults throughout the County.

Miami-Dade County provides equal access and equal opportunity in employment and services and does not discriminate on the basis of a disability. If you need an accommodation such as a sign language interpreter or material in an alternate format, contact the Branch Manager at least 7 business days in advance. Systemwide TDD available via the Florida Relay Service at 711.

Friends of the Miami-Dade Public Library

CFAR HIV & Aging SWG Symposium

The University of Miami Center For AIDS Research (CFAR) had its inaugural [HIV & Aging Scientific Working Group \(SWG\) Symposium](#) this year. It was organized as part of a CFAR Scientific Working Group led by **Dr. Tatjana Rundek** and Dr. Pallikkuth from CFAR. The UM McKnight Brain Institute was one of the sponsors. Sessions covered HIV and the aging brain and biology and risk factors with aging. The symposium was a great success.

CFAR HIV & Aging SWG Symposium

Thursday, December 5, 2019, 8:30 am-4:00 pm
Don Soffer Clinical Research Center (CRB)
1120 NW 14th Street, CTSI Training Center, Suite 710

	Suresh Pallikkuth, PhD Co-Director, HIV & Aging SWG Research Assistant Professor Microbiology & Immunology		Tatjana Rundek, MD, PhD Co-Director, HIV & Aging SWG Professor of Neurology Scientific Director, Evelyn F. McKnight Brain Institute Chair, Learning and Memory in Aging
	Savita Pahwa, MD Director Center for AIDS Research, Miami Professor, Microbiology & Immunology (Pediatrics and Medicine) <i>"Introduction and Overview"</i>		Dana Gabuzda, MD Professor of Neurology (Microbiology) Dept. of Cancer Immunology and Virology Dana-Farber Cancer Institute Harvard Medical School <i>"Accelerated Aging in HIV Infection: Biology of Risk and Resilience"</i>
	Scott Letendre, MD Professor of Medicine and Psychiatry in Residence University of California, San Diego <i>"HIV and the Aging Brain"</i>		Marco Pahor, MD Director University of Florida Institute on Aging Professor & Founding Chair, (Aging & Geriatric Research) University of Florida <i>"Geriatric physical performance outcomes in persons with HIV"</i>
	Monty Montano, PhD Scientific Director, Boston Pepper Principal Investigator, Harvard Medical School Brigham and Women's Hospital <i>"Preclinical evidence for functional decline in People Living with HIV"</i>		Vincent Marconi, MD Director, Infectious Disease Research Professor of Medicine, Infectious Diseases (Medicine) Emory University <i>"Inflammaging: Discover the Fountain of Youth"</i>

UHealth
UNIVERSITY OF MIAMI HEALTH SYSTEM

EVELYN F. MCKNIGHT BRAIN INSTITUTE
UNIVERSITY OF MIAMI
Preserving memory, enhancing life

CTSI

To attend in person - email Amy Stewart axs3173@med.miami.edu (Seating is limited)

To attend online - Register in advance at

<https://zoom.us/meeting/register/4a61aa27c973b65d8c34be5db4a05ad8>

After registering to attend, you will receive a confirmation email containing information about joining the meeting.

"We acknowledge support from the Miami Center for AIDS Research (CFAR) at the University of Miami Miller School of Medicine funded by a grant (P30AI073961) from the National Institutes of Health (NIH)". For more information, contact Amy Stewart, 305-243-8125; axs3173@med.miami.edu

Additional Notable Scientific and Educational Achievements

- **Dr. Ralph Sacco** was elected to serve on the Steering Committee of the national network of Clinical and Translational Science Awards (CTSA) program at the National Center for Advancing Translational Sciences (NCATS). He also received the prestigious honor as the 2019 C. Miller Fisher Visiting Professor from Massachusetts General Hospital.
- **Dr. Tatjana Rundek** formally became a Contact Principal Investigator of the Miami CTSI KL2 mentored research training award program at NCATS to support newly trained clinicians in successful clinical and translational research.
- We were able to fund a new **Cognitive and Behavioral Neurology Fellow**, **Dr. Michelle Marrero** in the Neurology Department at the McKnight Brain Institute. Trainees in this field are lacking but greatly needed. Our program trains physician-scientists in skills needed to translate research findings to clinical practice and treat the ever-growing aging population. **Section 12**.
- **The Florida Stroke Registry** (**Drs. Sacco** and **Rundek**) program was awarded its third round of state appropriated funds to manage and maintain the Stroke Registry across hospitals treating stroke patients in Florida. Since last year, the Registry has added 34 new hospital members increasing the total number of participating Florida stroke centers to 114 (out of a total of approximately 160). The ongoing collection of Florida stroke cases (from 2010 to current) has collected clinical and outcome data on approximately 290,000 stroke patients to date. **Section 9**.
- **Drs. Jinhua Wang** and **Hong Jiang** received a NIH NINDS R01 grant on retinal changes in aging and small vessel brain disease. They were also awarded a grant for the project “Retinal biomarkers for monitoring vascular contributions to Alzheimer’s Disease” from the Ed and Ethel Moore Alzheimer’s Disease Research Program through the Florida Department of Health (DOH).
- **Dr. Joyce Gomes-Osman** was selected from a competitive pool of early career investigators at the University of Miami to be among the 4 participants to attend the prestigious *11th Annual International Certificate Course, Eureka Institute for Translational Medicine* in Syracusa, Italy. Eureka is a weeklong immersive program that focuses on the fundamentals of translational medicine and trains scientists to be leaders in the translational medicine field through coaching, networking and mentorship opportunities. More information can be found in **Section 9**.
- **Michelle Caunca**, our MD/PhD student received the P.E.O. Sisterhood award for the 2019-2020 academic year. Michelle is one of 150 women in the US and Canada to receive this merit-based award for women pursuing a doctoral-level degree at an accredited college or university. Recipients are a select group of women chosen for their high level of academic achievement and their potential for having a positive impact on society. Michelle began her third year of the program after defending her dissertation last summer. Her thesis research work, “A Population Neuroscience

Approach for Analyzing Regional Structural Brain MRI Data in Cognitive Aging,” under the mentorship of **Dr. Tatjana Rundek**, has won many awards, including the Ruth L. Kirschstein National Research Service Award Fellowship (F30 Award) funded by the National Institute of Neurological Disorders and Stroke (NINDS).

- Several grants and awards were given to these McKnight researchers in the basic and translational sciences, **Drs. David Della-Morte**, **Miguel Perez-Pinzon** and **Kunjan Dave**. See **Section 6.2**.
 - **Drs. Sarah Getz** and **Bonnie Levin** submitted an application for an AAN McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss for the project “Neurocognitive correlates of scam susceptibility in age-related hearing loss.” (Principal Investigator: Sarah Getz, Mentors: Drs. Levin and Rundek).
 - **Dr. Bonnie Levin** participated in a widely publicized press conference, which described the findings and explored the energy source producing hearing loss and cognitive impairments among diplomats in Cuba.
-

Participation in McKnight Brain Research Foundation Events

McKnight Clinical Translational Research Scholars in Cognitive Aging and Age-related Memory Loss Dinner

We have organized the first ***McKnight Clinical Translational Research Scholars in Cognitive Aging and Age-related Memory Loss Dinner*** in conjunction with the American Academy of Neurology (AAN) Meeting in Philadelphia, PA, May 4th, 2019.

Attendees:

2018 Scholars and Mentors

Brice McConnell, MD, PhD (Scholar – University of Colorado, Denver)
Benzi Kluger, MD, MS (Mentor – University of Colorado, Denver)

2019 Scholars and Mentors

Christian Camargo, MD (Scholar – University of Miami)
Richard Wurtman, MD (Mentor)

Guests

Jane Ransom, Executive Director, American Brain Foundation
Suzi Johnson, Program Officer, Research and Digital Grants, American Brain Foundation

UM Evelyn F. McKnight Brain Institute Representation

Tatjana Rundek, MD, PhD
Ralph Sacco, MD, MS
Susan Fox-Rossellini, MBA
Stacy Merritt, MA
Raphaelle Depuhl (Christian Camargo's Guest)

McKnight Brain Research Foundation Representation

Richard Isaacson, MD
Gene Ryerson, MD
Amy Porter

The Evelyn F. McKnight Brain Research Foundation 11th Annual Inter-Institutional Meeting

We participated at ***The Evelyn F. McKnight Brain Research Foundation 11th Annual Inter-Institutional Meeting*** at the University of Florida in Gainesville, April 10-12th.

Tatjana Rundek, MD, PhD provided the “Interventional Core Pilot Program” introduction and served as moderator of the “Cognitive Aging and Memory Interventional Core Updates” Session.

Sarah Getz, PhD presented “Detecting Deceptive Information in Scamming Paradigms: A Training Intervention.”

Bonnie Levin, PhD was the moderator for the “Mechanisms of Cognitive Decline” session.

Christian Camargo, PhD presented “Improving Cognition in Cognitive Aging: A Synaptic Approach.”

We have participated in **Session I - the McKnight Brain Aging Registry (MBAR)**, where preliminary results were presented on:

“Patterns of Daily Activity in the Oldest Old: Findings from MBAR”

“Cognition and Brain Volume in the Oldest Old: Findings from MBAR”

“Relationship of Brain Functional Connections to Behavior in the Oldest Old”

“Frontal GABA Concentrations in the Oldest Old in the MBR: An Update”

McKnight Brain Research Foundation 10th Poster Reception

We participated in the ***McKnight Brain Research Foundation 10th Poster Reception*** at the Society for Neuroscience (SFN) Meeting, October 20th.

Posters Presented by the University of Miami McKnight Brain Institute:

- “Exercise Barriers, Motivators, and Self-efficacy in Sedentary Aging Adults: An Ongoing Trial”
- “Effects of 8-weeks of Aerobic Exercise Intervention on Fitness and Neuroplasticity in Aging Adults: Preliminary Results of an Ongoing Trial”
- “Red blood cell-derived microparticles treatment improves post-intracerebral hemorrhage in long-term outcomes in rats”
- “Ethnicity moderates the relationship between sleep quality and learning and memory”
- “Fatigue, Adverse Childhood Experiences, and Frailty in Later Life”
- “Chronic nicotine exposure hinders whole body vibration therapy induced ischemic protection in the brain of reproductively senescent female rats”
- “Ethnicity moderates the relationship between sleep quality and learning and memory”
- “Effects of endogenous estrogen fluctuations on the post-ischemic innate inflammation in the brain of female rats”

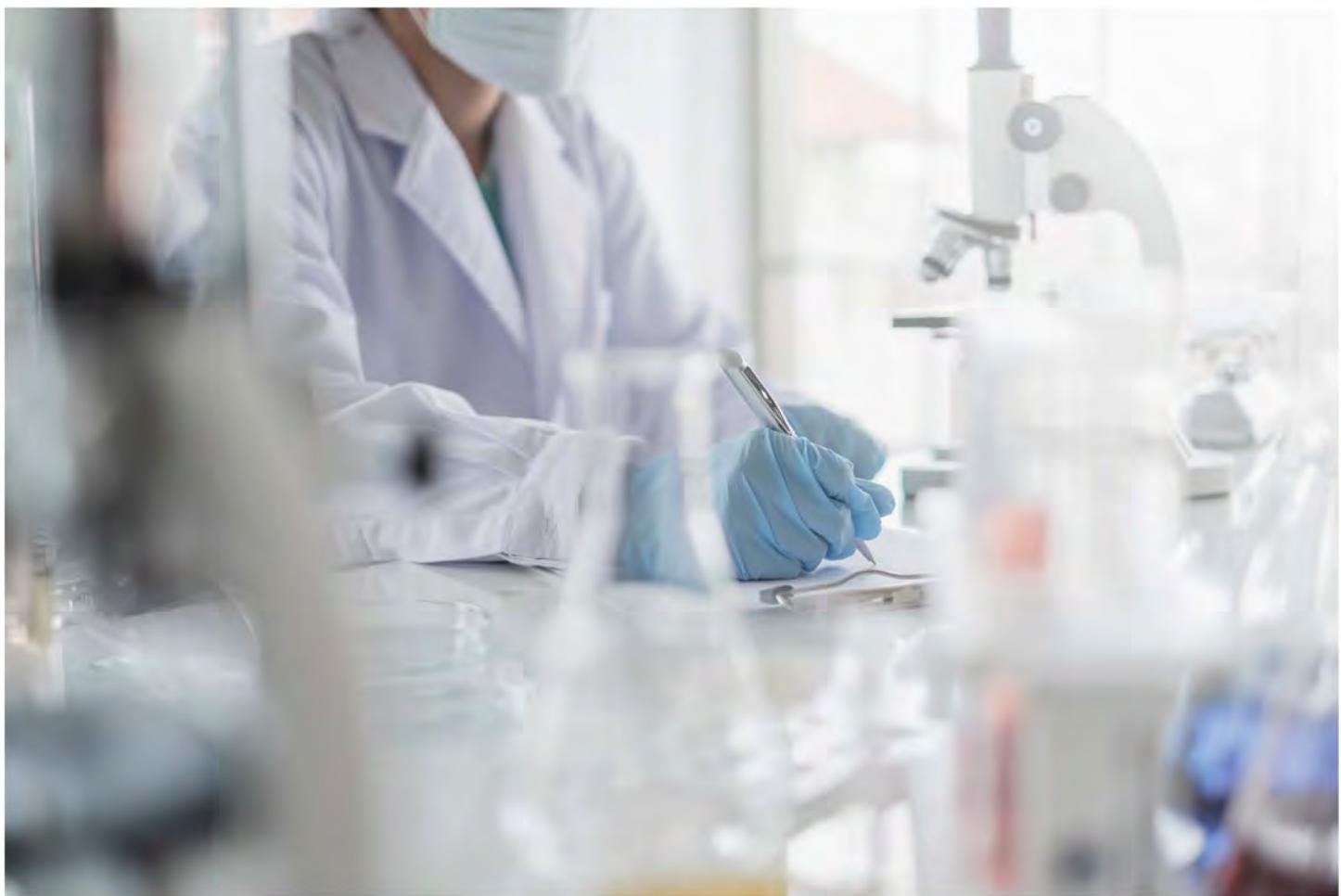
- “Prior exposure to recurrent hypoglycemia causes post-ischemic ER stress via increased free radical production in treated diabetic rats”
- “Measuring Frailty in Middle and Later Years and its Association with Cognition”
- “Post-stroke physical exercise reduces ischemic brain damage and improves cognition in reproductively senescent female rats”

McKnight Brain Institute Collaborative Inter-Institutional Posters:

- “Characterizing the Healthy Oldest Old: The McKnight Brain Aging Registry”
- “Age related decreases in cortical GABA concentrations assessed over the lifespan in cognitively intact adults over 85 years of age”
- “Relation of daily activity patterns to cortical gray matter maps in the healthy oldest old: Findings from the McKnight Brain Aging Registry”
- “Functional connectivity in the healthy oldest old: Findings from the McKnight Brain Aging Registry”

PUBLICATIONS AND PRESENTATIONS

SECTIONS 2-5



McKnight Brain Research Foundation 10th Poster Reception at the Society for Neuroscience (SFN) Meeting in Chicago, Illinois, October 20th, 2019.



Sara Nolin (UAB), Bonnie Levin, Kristina Visscher (UAB),
Tatjana Rundek (MBAR collaborators)

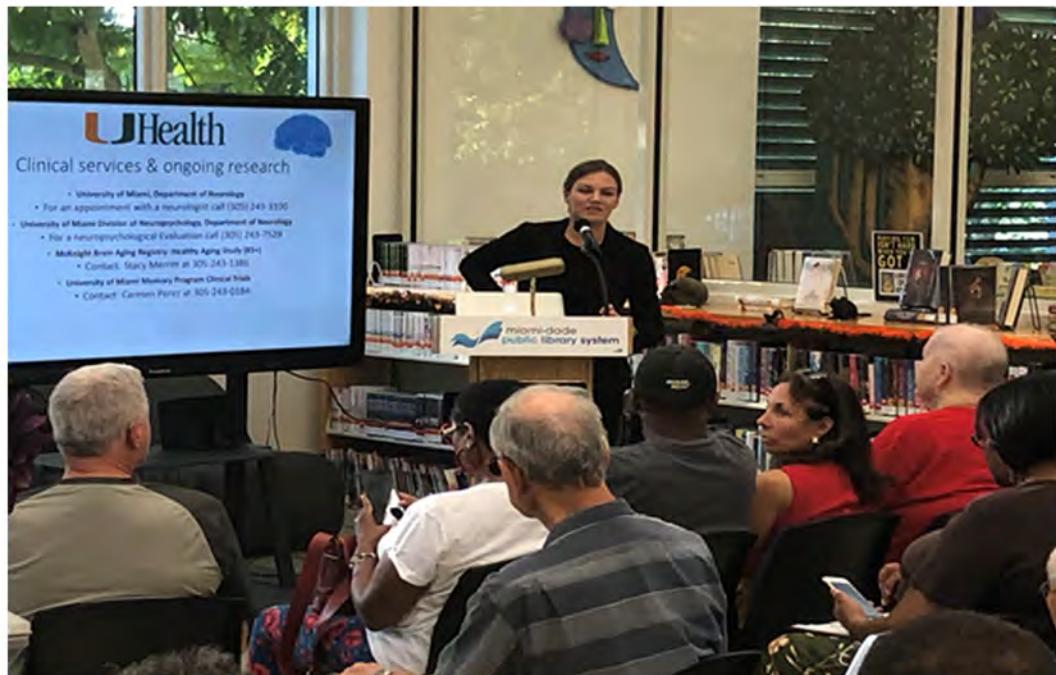


Sarah Getz



Ashish Rehni, Varun Reddy, Bonnie Levin,
Ami Raval, Tatjana Rundek, Sarah Getz,
Sunjoo Cho, Sharnikha Saravanan

Mayor's Initiative On Aging: Your Brain Seminar Series



Sarah Getz, PhD



Christian Camargo, MD
Stacy Merritt, MA



Joyce Gomes-Osman, PT, PhD

2. Publications in Peer Reviewed Journals

The names in bold are Members, Collaborators and Trainees at our MBI.

Trainee (as first authors) Publications

Banerjee N, McIntosh RC, Ironson G. Impaired Neurocognitive Performance and Mortality in HIV: Assessing the Prognostic Value of the HIV-Dementia Scale. AIDS and Behavior. 2019;1-11. DOI: 10.1007/s10461-019-02423-w.

Banerjee N, Slugh M, Kaur S, Suslow NS, McInerney KF, Sun X, Levin BE. Neuropsychological correlates of subjective fatigue in non-demented older adults and the moderating effect of physical activity. Aging Neuropsychology & Cognition. 2019;1-16.

Cabral DF, Rice J, Morris TP, Rundek T, Pascual-Leone A, Gomes-Osman J. Exercise for Brain Health: An Investigation into the Underlying Mechanisms Guided by Dose. Neurotherapeutics, 2019.

Caunca MR, Gardener H, Simonetto M, Cheung YK, Alperin N, Yoshita M, DeCarli C, Elkind MSV, Sacco RL, Wright CB, Rundek T. Measures of obesity are associated with MRI markers of brain aging: The Northern Manhattan Study. Neurology. 2019;Aug;93(8). :e791-e803. PMCID: PMC6711659.

Caunca MR, Simonetto M, Alperin N, Elkind MSV, Sacco RL, Wright CB, Rundek T. Measures of Adiposity and Alzheimer's Disease-Related MRI Markers: The Northern Manhattan Study. J Alzheimers Dis., Jul 8, 2019. doi: 10.3233/JAD-190092. [Epub ahead of print] PubMed PMID: 31306120.

Del Brutto VJ, Chaturvedi S, Diener HC, Romano JG, Sacco RL. Antithrombotic Therapy to Prevent Recurrent Strokes in Ischemic Cerebrovascular Disease: JACC Scientific Expert Panel. J Am Coll Cardiol, Aug 13, 2019. PMID: 31395130.

Getz SJ, Rooks J, McInerney KF, Banerjee NS, Levin BE (Under review). Fatigue as a powerful influence in the relationship between childhood exposure to adversity and frailty in later life.

Kaur S, Banerjee N, Miranda M, Slugh M, Sun-Suslow N, McInerney KF, Sun X, Ramos AR, Rundek T, Sacco RL, Levin BE. Sleep quality mediates the relationship between frailty and cognitive dysfunction in non-demented middle aged to older adults. Int Psychogeriatr. 2019;Apr 22:1-10. PMID: 31006402.

Rehni AK, Shukla V, Navarro Quero H, Bidot C Jr, Haase CR, Crane EAA, Patel SG, Koch S, Ahn YS, Jy W, **Dave KR**. Preclinical Evaluation of Safety and Biodistribution of Red Cell Microparticles: A Novel Hemostatic Agent. *J Cardiovasc Pharmacol Ther.* 2019;24(5):474-483.

Rehni AK, Shukla V, **Perez-Pinzon MA**, **Dave KR**. Blockade of Acid-Sensing Ion Channels Attenuates Recurrent Hypoglycemia-Induced Potentiation of Ischemic Brain Damage in Treated Diabetic Rats. *Neuromolecular Med.*, 2019. (In press).

Simonetto M, Infante M, **Sacco RL**, **Rundek T**, **Della-Morte D**. A Novel Anti-Inflammatory Role of Omega-3 PUFAs in Prevention and Treatment of Atherosclerosis and Vascular Cognitive Impairment and Dementia. *Nutrients*. 2019;Sep 23;11(10).

Sur NB, Wang K, Di Tullio MR, Gutierrez CM, Dong C, Koch S, Gardener H, García-Rivera EJ, Zevallos JC, Burgin WS, Rose DZ, Goldberger JJ, Romano JG, **Sacco RL**, **Rundek T**. Disparities and Temporal Trends in the Use of Anticoagulation in Patients With Ischemic Stroke and Atrial Fibrillation. *Stroke*. 2019;Jun;50(6):1452-1459. 2019. PMCID: PMC6538423.

Cross-Disciplinary and Collaborative Publications

Abou Shousha M, **Wang J**, Kontadakis G, Feuer W, Canto AP, Hoffmann R, Perez VL. Corneal epithelial thickness profile in dry eye disease. *Eye (lond)*. 2019. Epub ahead of print.

Abulafia C, Fiorentini L, **Loewenstein DA**, Curiel-Cid R, Sevlever G, Nemeroff CB, Villarreal MF, Vigo DE, Guinjoan SM. (2019) Executive functioning in cognitively normal middle-aged offspring of late-onset Alzheimer's disease patients. *Journal of Psychiatric Research*. 2019;11:23-29.. <https://doi.org/10.1016/j.jpsychires.2019.02.016>.

Chen D, Chen Q, Wu Y, Yu X, Shen M, Zhuang X, Tian Z, Yang Y, **Wang J**, Lu F, Shen L. Deep perifoveal vessel density as an indicator of capillary loss in high myopia. *Eye (lond)*. 2019. Epub ahead of print.

Alperin N, Wiltshire J, **Lee HS**, et al. Effect of Sleep Quality on anMCI Vulnerable Brain Regions in Cognitively Normal Elderly Individuals. *Sleep*. 2019 ;Mar;42(3). pii: zsy254. doi: 10.1093/sleep/zsy254.

Alperin N, Wiltshire J, Lee SH, **Ramos AR**, Hernandez-Cardenache R, Curiel RE, **Rundek T**, **Loewenstein DA**. Effect of Sleep Quality on aMCI Vulnerable Brain Regions in cognitively Normal Elderly Individuals. *Sleep*. 2019;1;42(3). pii: zsy254. doi: 10.1093/sleep/zsy254.

Arriga R, Pacifici F, Capuani B, Coppola A, Orlandi A, Sciolli MG, Pastore D, Andreadi K, Sbraccia P, Tesauro M, Di Daniele N, Sconocchia G, Donadel G, Bellia A, **Della-Morte D**, Lauro D. Peroxiredoxin 6 is a key antioxidant enzyme, in modulating the link between glycemic and lipogenic metabolism. *Antiox Long Med*. 2019. (In press).

Asdaghi N, Yavagal DR, Wang K, Mueller-Kronast N, Bhatt N, Gardener HE, Gutierrez CM, Marulanda-Londoño E, Koch S, Dong C, **Oluwole SA**, Hanel R, Mehta B, Robichaux M, Nobo U, Zevallos JC, **Rundek T**, **Sacco RL**, Romano JG. Patterns and Outcomes of Endovascular Therapy in Mild Stroke. *Stroke*. 2019;Aug;50(8):2101-2107. 2019. PMCID: PMC6646058.

Bademci G, Abad C, Incesulu A, Elian F, Reyahi A, Diaz-Horta O, Cengiz FB, Sineni CJ, Seyhan S, Atli EI, Basnak H, Demir S, Nik AM, Footz T, Guo S, Duman D, Fitoz S, Gurkan H, **Blanton SH**, Walter MA, Carlsson P, Walz K, Tekin M. FOXF2 is required for cochlear development in humans and mice. *Hum Mol Genet*. 2019;Apr 15;28(8):1286-1297. doi: 10.1093/hmg/ddy431. PMCID: PMC6452198 [Available on 2020-04-15].

Barba A, Urbina C, Maili L, Greives MR, Blackwell SJ, Mulliken JB, Chiquet B, **Blanton SH**, Hecht JT, Letra A. Association of IFT88 gene variants with nonsyndromic cleft lip with or without cleft palate. *Birth Defects Res*. 2019 Apr 5. doi: 10.1002/bdr2.1504. [Epub ahead of print]. PMID: 30953423.

Barbanti P, Guadagni F, De Marchis ML, Ialongo C, Egeo G, Fofi L, Aurilia C, Lovero D, **Della-Morte D**, Ferroni P, Palmirota R. Dopamine-beta-hydroxylase 19-bp insertion/deletion polymorphism affects medication overuse in patients with chronic migraine. *Neurol Sci*., Aug;40(8):1717-1724. 2019.

Bhatt N, Marulanda-Londoño ET, Atchaneeyasakul K, Malik AM, Asdaghi N, Akram N, D'Amour D, Hesse K, Zhang T, **Sacco RL**, Romano JG. Target Stroke: Best Practice Strategies Cut Door to Thrombolysis Time to <30 Minutes in a Large Urban Academic Comprehensive Stroke Center. *Neurohospitalist*, Jan;9(1):22-25. 2019. doi: 10.1177/1941874418801443. Epub 2018 Oct 3. PMCID: PMC6327242

Brainin M, Feigin V, Bath PM, Collantes E, Martins S, Pandian J, **Sacco R**, Teuschl Y. Multi-level community interventions for primary stroke prevention: A conceptual approach by the World Stroke Organization. *Int J Stroke*. 2019 Sep 9. PMID: 31500553.

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Wang Y, Ye J, Shen M, Yao A, Xue A, Fan Y, Huang S, **Wang J**, Lu F, Sha Y. Photoreceptor degeneration is correlated with the deterioration of macular retinal sensitivity in high myopia. *Invest Ophthalmol Vis Sci*. 2019;60(8):2800-2810.

Wu O, Winzeck S, Giese AK, Hancock BL, Etherton MR, Bouts MJRJ, Donahue K, Schirmer MD, Irie RE, Mocking SJT, McIntosh EC, Bezerra R, Kamnitsas K, Frid P, Wasselius J, Cole JW, Xu H, Holmegaard L, Jiménez-Conde J, Lemmens R, Lorentzen E, McArdle PF, Meschia JF, Roquer J, **Rundek T**, **Sacco RL**, Schmidt R, Sharma P, Slowik A, Stanne TM, Thijs V, Vagal A, Woo D, Bevan

S, Kittner SJ, Mitchell BD, Rosand J, Worrall BB, Jern C, Lindgren AG, Maguire J, Rost NS. Big Data Approaches to Phenotyping Acute Ischemic Stroke Using Automated Lesion Segmentation of Multi-Center Magnetic Resonance Imaging Data. *Stroke*. 2019 Jul;50(7):1734-1741. PMCID: PMC6728139.

Wu Y, Tu Y, Bao L, Wu C, Zheng J, Wang J, Lu F, Shen M, Chen Q. Reduced retinal microvascular density related to activity status and serum antibodies in patients with Graves' ophthalmopathy. *Curr Eye Res*. 2019;9:1-9.

Wu O, Winzeck S, Giese AK, Hancock BL, Etherton MR, Bouts MJRJ, Donahue K, Schirmer MD, Irie RE, Mocking SJT, McIntosh EC, Bezerra R, Kamnitsas K, Frid P, Wasselius J, Cole JW, Xu H, Holmegaard L, Jiménez-Conde J, Lemmens R, Lorentzen E, McArdle PF, Meschia JF, Roquer J, **Rundek T, Sacco RL**, Schmidt R, Sharma P, Slowik A, Stanne TM, Thijs V, Vagal A, Woo D, Bevan S, Kittner SJ, Mitchell BD, Rosand J, Worrall BB, Jern C, Lindgren AG, Maguire J, Rost NS. Big Data Approaches to Phenotyping Acute Ischemic Stroke Using Automated Lesion Segmentation of Multi-Center Magnetic Resonance Imaging Data. *Stroke*. 2019 Jul;50(7):1734-1741. PMCID: PMC6728139.

Xu J, Khouri N, Jackson CW, Escobar I, Stegelmann SD, Dave KR, Perez-Pinzon MA. Ischemic Neuroprotectant PKC ϵ Restores Mitochondrial Glutamate Oxaloacetate Transaminase in the Neuronal NADH Shuttle after Ischemic Injury. *Transl Stroke Res*. 2019 (In press).

3. Publications (other)

Assuras S, Levin BE. Special considerations for the neuropsychological interview of older adults. In L. Ravdin and H. Katzen (eds- Second Edition) *Handbook on the Neuropsychology of Aging and Dementia*. New York, Springer Publishing, 2019, 1-9.

Bacman SR, Williams SL, Pinto M, Moraes CT. Methods in Enzymology, Mitochondrial Function, Edited by Anne Murphy & David Chan (book chapter).

Cho S, Fuchs P, Sarmah D, Kaur H, Bhattacharya P, Dave KR. Cerebral ischemia in diabetics and oxidative stress., in: V. R. Preedy (Ed.), *Oxidative Stress and Dietary Antioxidants in Diabetes*. 2nd Edition, Elsevier Inc., San Diego, CA, 2019 (In press).

Denkova E, Zanesco A, Morrison AB, Rooks J, Rogers S. L, Jha AP. (In press). Strengthening attention with mindfulness training in workplace settings. In D. Siegel & M. Solomon, *Mind, Consciousness, and the Cultivation of Well Being*. New York, NY: W. W. Norton & Company, Inc.

Kichev A, Baburamani AA, **Vontell RT**, Gressens P, Burkly L, Thornton C, Hagberg H. TWeAK receptor Deficiency has Opposite effects on Female and Male Mice subjected to neonatal hypoxia-ischemia, In: Preventing Developmental Brain Injury – From Animal Models To Clinical Trials, M Tsuji, SV Sizonenko, O Baud ed., 73-85 Frontiers Media. ISBN 978-2-88963-075-2.

McIntosh RC, Lobo JD. (2019) Correlates of Executive Dysfunction in HIV. In: Ardila A, Fatima S, Rosselli M. (eds) Dysexecutive Syndromes. Springer, Cham pp. 281 – 264.

Nazmi A, Albertsson AM, Rocha-Ferreira E, Zhang X, **Vontell RT**, Zelco A, Rutherford M, Zhu C, Nilsson G, Mallard C, Hagberg H, Lai JCY, Leavenworth JW, Wang X. lymphocytes contribute to the Pathophysiology of neonatal Brain injury, In: Preventing Developmental Brain Injury – From Animal Models To Clinical Trials, M Tsuji, SV Sizonenko, O Baud ed., 282-293 Frontiers Media. ISBN 978-2-88963-075-2.

4. Presentations at Scientific Meetings

Aldraiwiesh S, **Rice J**, Cassidy N, Tiozzo E, **Flothmann M**, **Simonetto M**, **Sacco R**, Koch S, **Rundek T**, **Gomes-Osman J**. Assessing dual-task performance and characterizing task prioritization in individuals post-stroke Combined Sections Meeting American Physical Therapy Association. Poster January 23-26, 2019. Washington, DC.

Andreadi A, **Della-Morte D**, Pacifici F, Coppola A, Romano M, Sabato M, D'Amato C, Spallone V, Bellia A, Lauro D. Questionario Frax: Considerare Modificare Il Questionario Utilizzato Per Il Calcolo Della Probabilita Della Frattura In Pazienti Con Osteopenia/Osteoporosi? 40° National Congress of the Italian Society of Endocrinology (SIE) Rome, May 29-June 1, 2019.

Brown SC, Lombard J, Wang K, Toro M, Byrne MM, **Rundek T**, Dong C, Nardi M, Kardys J, Szapocznik J. *Neighborhood Greenness, Active Living Opportunities, and Alzheimer's Disease among 249,405 U.S. Medicare Beneficiaries*. Poster presented at the Active Living Research Conference, Poster Session 1, Charleston, South Carolina, February 17, 2019.

Brown SC, Wang K, Lombard J, **Rundek T**, Dong C, Marinovic Gutierrez C, Byrne MM, Toro M, Nardi MI, Kardys J, Szapocznik J. *The Relationship of Neighborhood Greenness to Heart Disease in 249,405 US Medicare Beneficiaries*. Poster presented at the American Heart Association-EPI/Lifestyle Scientific Sessions, Poster Session 1, Houston, Texas, March 5, 2019.

Cabral DLF, Ramon SV, Teixeira OT, **Rice J**, Kirk-Sanchez N, **Gomes-Osman J**, Oliveira AC. A brief, personalized intervention increases physical activity in sedentary older adults with memory complaints. Society for Neurosports Conference. Poster November 16th, 2019. Deerfield Beach, FL.

Cabral DLF, Rice J, Nunez C, Abel D, Van Deusen K, Moustafi B, Kitaigorodsky M, Loewenstein D, Cahalin L, Rundek T, Pascual-Leone A, Gomes-Osman J. Effects of 8-weeks of Aerobic Exercise Intervention on Fitness and Neuroplasticity in Aging Adults: Preliminary Results of an Ongoing Trial. Evelyn F. McKnight Poster Reception at Society for Neuroscience Meeting. Poster October 19th, 2019. Chicago, IL.

Cabral DLF, Rice J, Nunez C, Abel D, Van Deusen K, Moustafi B, Kitaigorodsky M, Loewenstein D, Cahalin L, Rundek T, Pascual-Leone A, Gomes-Osman J. Exercise Barriers, Motivators, and Self-efficacy in Sedentary Aging Adults: an Ongoing Trial. Evelyn F. McKnight Poster Reception at Society for Neuroscience Meeting. Poster October 19th, 2019. Chicago, IL.

Camargo CJ. A clinician's conundrum: The role of Amyloid in defining Alzheimer's disease. Oral Presentation. International Symposium on Pathomechanisms of Amyloid Diseases. Abstract. Miami, FL, December 18-20, 2019.

Camargo CJ, Rundek T. Design and Early Insights of the AREPAS (A Role for Evaluation of PET Amyloid Status) Study. International Symposium on Pathomechanisms of Amyloid Diseases. Abstract. Miami, FL, December 18-20, 2019.

Coppola A, Capuani B, Pacifici F, Pastore D, Arriga R, Rea S, Bellia A, Tesauro M, **Della-Morte D**, Sconocchia G, Lauro D. Proinflammatory Cytokine HMGB1 Increased Leptin Secretion with a TLR2/TLR4 Mechanism In Type 2 Diabetes Related Inflammation. 40° National Congress of the Italian Society of Endocrinology (SIE) Rome, May 29-June 1, 2019.

Coppola A, Capuani B, Pacifici F, Pastore D, Arriga R, Rea S, Bellia A, Tesauro M, **Della-Morte D**, Sconocchia G, Lauro D. Proinflammatory Cytokine HMGB1 Increased Leptin Secretion with a TLR2/TLR4 Mechanism In Type 2 Diabetes Related Inflammation. 55th EASD Annual meeting, Barcelona 16-20 September 2019.

Coppola A, Capuani B, Pacifici F, Pastore D, Arriga R, Rea S, Bellia A, Tesauro M, **Della-Morte D**, Sconocchia G, Lauro D. HMGB1 Increases Leptin Levels through a TLR2/TLR4 Based Mechanism. 40° National Congress of the Italian Society of Endocrinology (SIE) Rome, May 29-June 1, 2019.

D'Ippolito I, De Carli E, Andreadi A, Romano M, Galli A, Capria A, Massaro A, Sbraccia P, **Della-Morte D**, Bellia A, Lauro D. Effetti A Lungo Termine Del Dapagliflozin Su Disfunzione Diastolica E Reattività Vascolare In Pazienti Con Diabete Mellito Di Tipo 2 In Prevenzione Primaria Cardiovascolare. 40° National Congress of the Italian Society of Endocrinology (SIE) Rome, May 29-June 1, 2019.

Dave KR, Rejni AK, Navarro Quero H, Cho S, Jy E, Desai D, Koch S, Ahn YS, Perez-Pinzon MA, Jy W. Red blood cell-derived microparticles treatment attenuates intracerebral hemorrhage-induced behavioral deficits in rats. Brain 2019 (29th International symposium on Cerebral blood flow, metabolism and function) Conference held at Yokohama, Japan July 2019. Abstract number BS04-3. Abstract was refereed.

Donadel G, Arriga R, Marchetti V, Pastore D, Coppola A, Pacifici F, Scioli Mg, Orlandi A, **Della-Morte D**. Treatment with Human Placental Lactogen (hPL-A) Improves Glucose Homeostasis One Year after Pancreatic Islets Transplantation in Mice Anterior Eye Chamber. American Diabetes Association (ADA), 79th scientific sessions, San Francisco, June 7 - 11, 2019.

Dueker N, Gardener H, Gomez L, Beecham A, Wang L, **Blanton SH**, Dong C, Tom S, **Sacco RL**, **Rundek T**. Executive function GWAS in a multi-ethnic cohort implicates region on chromosome 1. Poster Presentation at the 69th Annual Meeting of the American Society of Human Genetics (ASHG), Houston, Texas, October 15-10, 2019 (#2046/W).

Gamerio GR, **Jiang H**, Shi C, Delgado S, Hernandez J, **Wang J**. Most vulnerable focal thinning of the ganglion cell-inner plexiform layer related to visual function and disability in patients with MS (poster). America's Committee for Treatment & Research in Multiple Sclerosis (ACTRIMS) Forum 2019. Dallas, TX, Feb 28-March 2, 2019.

Guo S, Bademci G, Huang J, **Blanton S**, Tekin M. Comparisons between whole exome sequencing and whole genome sequencing in 25 individuals with autosomal recessive non-syndromic deafness. Poster Presentation at the 69th Annual Meeting of the American Society of Human Genetics (ASHG), Houston, Texas, October 15-10, 2019 (#2824/T).

Jiang H. Retinal microvasculature manifestations of central nerve system neurodegenerative disorders. Singapore National Eye Research Institute, Singapore, Singapore, August 21, 2019.

Jiang H. Topographical thickness mapping of intraretinal layers in aging and neurologic disorders. Guangzhou Eye Center, Guangzhou, China. August 17, 2019.

Jiang H, Gameiro GR, Porciatti V, Hu HL, Monsalve P, Hernandez J, Delgado S, **Wang J**. Association between pattern electroretinogram and intraretinal layer thickness in patients with multiple sclerosis (paper). The North American Neuro-Ophthalmology Society 45th Annual Meeting, Las Vegas, Nevada, March 16-21, 2019.

Jiang H, Liu Y, Delgado S, Lin Y, Hernandez J, Deng YQ, Gamerio GR, Gregori G, **Wang J**. Retinal volumetric vessel density in multiple sclerosis (poster). America's Committee for Treatment & Research in Multiple Sclerosis (ACTRIMS) Forum 2019. Dallas, TX, Feb 28-March 2, 2019.

Jing X, **Natalie K**, Samuel DS, **Kunjan D**, **Miguel A Perez-Pinzon**. The Ischemic Neuroprotectant Protein Kinase C Epsilon, Phosphorylates Enzymes in Neuronal NADH Shuttle and Regulates Mitochondrial Respiration and Glycolysis. International Stroke Conference 2019 (February 2019) held at Honolulu, Hawaii. Abstract WP337. Abstract was refereed.

Kannan-Sundhari A, Abad C, Maloof M, Ayad N, Young J, **Blanton S**, Liu XZ, Walz K. Investigating the role of the epigenetic reader Brd4 in hearing and development of the inner ear. Poster Presentation at the 69th Annual Meeting of the American Society of Human Genetics (ASHG), Houston, Texas, October 15-10, 2019 (#3311/F).

Lane Alves Frias C, Pacifici F, Capuani B, Sinibaldi Salimei P, **Della-Morte D**. Inhibition of Adipogenesis and Induction of Lipolysis by Hydroxytyrosol and Tyrosol in 3T3-L1 Adipocytes. GANEPAO 2019, San Paolo, Brazil, June 14, 2019.

Millan C, **Saporta ASD** et al. "Volumetric measurements of hippocampal formations: Is it time to replace the manual method by an automated method?" American Epilepsy Society 72nd Annual meeting. New Orleans, LA. Dec 3rd, 2018.

McIntosh RC, Quadir D, Paparozzi J. (2019, June). Hypertension status associated with cerebral blood flow and volumetric reduction in the central executive network. Poster presented at Cerebral Vascular Biology, Miami, Fl.

McIntosh RC, Lobo J. Paparozzi J, Dukenik D, Hurwitz B. (2019, June). Relationship between bone-marrow derived endothelial cells and intracranial brain volume in HIV. Poster presented at Cerebral Vascular Biology, Miami Fl.

Nunez C, **Rice J, Cabral DLF**, Kitaigorodsky M, **Loewenstein D, Gomes-Osman J**. The relationship between proactive semantic interference and gait speed in aging individuals- preliminary results of an ongoing trial. University of Miami Neuroscience Day. Poster December 1st, 2017. Miami, FL.

Pacifici F, Arriga R, Pastore D, Capuani B, Coppola A, Andreadi K, Frontoni S, Spallone V, Sconocchia G, Donadel G, Bellia A, **Della-Morte D**, Lauro D. Caloric Restriction Delays Senescence Processes by Improving Glucose Homeostasis and Mitochondrial Function in a Mice Model of Aging. 40th National Congress of the Italian Society of Endocrinology (SIE) Rome, May 29-June 1, 2019.

Pacifici F, **Della-Morte D**, Capuani B, Pastore D, Arriga R, Coppola A, Donadel G, Bellia A, Lauro D. Peroxiredoxin6 is a Novel Promoter of Pancreatic beta cells survival. American Diabetes Association (ADA), 79th scientific sessions, San Francisco, June 7 - 11, 2019.

Pacifici F, Pastore D, Arriga R, Capuani B, Coppola A, Rea S, Andreadi A, Donadel G, Abete P, Bellia A, **Della-Morte D**, Lauro D. Peroxiredoxin6 plays a Crucial Role in the Crosstalk between Diabetes and Aging in the Development of Sarcopenia. 55th EASD Annual meeting, Barcelon 16-20 September 2019.

Patel S, Diaz F, **Raval AP**. Nicotine alters brain energy metabolism and exacerbates ischemic injury in female rats. Program No. 540.10. 2019 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience.

Raval AP, Furones CF, Zhao WZ, **Dave KR, Perez-Pinzon MA**. Resveratrol treatment reduces ischemic brain damage in reproductively senescent female rats. Program No. 448.08. 2019 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience.

Raval AP, Moreno WJ, Sanchez J, Kerr NA, Furones-Alonso OE, Dietrich WD, Bramlett HM. Chronic nicotine exposure hinders whole body vibration therapy induced ischemic protection in

the brain of reproductively senescent female rats. Program No. 540.09. 2019 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience

Raval AP, Moreno WJ, Sanchez-Molano J, Kerr N, Furones-Alonso O, **Rundek T**, Dietrich WD, Bramlett HM. Whole body vibration therapy after ischemia reduces brain damage in reproductively senescent female rats. Brain and Brain PET 2019 held in Yokohama, Japan 4-7 July 2019. (Refereed)

Reddy VG, Furones CF, de Rivero Vaccari JP, **Raval AP**. Effect of endogenous estrogen fluctuations on the post-ischemic innate inflammation in the brain of female rats. Program No. 390.12. 2019 Neuroscience Meeting Planner. Poster Session at Society for Neuroscience, Chicago, IL, October 21, 2019.

Rehni AK, Navarro H, Bidot Jr. C, Shukla V, Koch S, **Perez-Pinzon MA**, Ahn YS, Jy W, **Dave KR**. Use of red cell microparticles to limit hematoma growth following intracerebral hemorrhage. International Stroke Conference 2019 (February 2019) held at Honolulu, Hawaii. Abstract # WP460. Abstract was refereed.

Rice J, Corp D, Swarowsky A, **Gomes-Osman J**. Dual-task performance is related to a neurophysiological measure of plasticity in individuals with memory disorders. Combined Sections Meeting American Physical Therapy Association. Poster January 23-26, 2019. Washington, DC.

Rice J, Dabrowski K, Modera P; Lisenbee M, Muro O, Morris T, **Gomes-Osman J**. Does a single session of moderate intensity cycling modulate plasticity in healthy adults? Combined Sections Meeting American Physical Therapy Association. Poster January 23-26, 2019. Washington, DC.

Rice J, **McInerney K**, Corp D, Cahalin L, Swarowsky A, **Gomes-Osman J**. Timed Up-and-Go Performance and Dual-Task Effects are Related to Distinct Cognitive Measures. World Confederation for Physical Therapy Congress. Poster May 13-19, 2019. Geneva, Switzerland.

Sacco RL. C Miller Fisher Lecture, Forecasting a Brighter Future for Preventing Stroke and Cognitive Decline. Massachusetts General Hospital, Harvard Medical School, Boston, MA, April 18, 2019.

Sacco RL. Expanding the Neuroscience Frontier of Brain Health, Cerebral Vascular Biology 13th International Conference, Miami, FL, June 25, 2019.

Sacco RL. Forecast for a Brighter Future for Stroke Prevention, International Stroke Conference, Honolulu, Hawaii, February 6, 2019.

Sacco RL. Neurology Update & Stroke Intensive 2019, Embolic Stroke of Undetermined Source: Diagnosis and Management, Miami, FL, February 2, 2019.

Sacco RL. Our American Academy of Neurology: Addressing Challenges to our Profession, Philadelphia Neurological Society, Philadelphia, PA, October 16, 2019.

Sacco RL. Presidential Address at the Annual Meeting of the American Academy of Neurology, Neurology: Challenges, Opportunities, and the Way Forward, Philadelphia, PA, May 5, 2019.

Sacco RL. Stanley Wissman Neuroscience Symposium 2019 - Past, Present and Future Treatment and Prevention of Stroke, Fort Wayne, IN, October 3, 2019.

Sacco RL. Third Annual Cerebrovascular Symposium, Cryptogenic Stroke/Embolic Stroke of Undetermined Source, Boca Raton, FL, October 25, 2019.

Sacco RL. Third Annual Cerebrovascular Symposium, Risk Factor Management for Preventing Stroke and Improving Brain Health, Boca Raton, FL, October 25, 2019.

Saravanan S, Furones CC, Zhao W, **Dave KR, Perez-Pinzon MA**, AP Post-stroke physical exercise reduces ischemic brain damage and improves cognition in reproductively senescent female rats. Brain 2019 (29th International symposium on Cerebral blood flow, metabolism and function) Conference held at Yokohama, Japan July 2019. Abstract number PB02-Q08. Abstract was refereed.

Tandon B, Yuan Q, Maili L, **Blanton SH**, Eisenhoffer GT, Letra A, Hecht JT. Role of MMP2 in early craniofacial development in zebrafish. Platform Presentation at the 69th Annual Meeting of the American Society of Human Genetics (ASHG), Houston, Texas, October 15-10, 2019 (#148).

Wang L, Dueker N, Beecham A, **Blanton SH, Sacco RL, Rundek T.** Targeted sequencing of linkage region in Dominican families implicates PRIMA1 and the SPATA7-PTPN21-ZC3H14-EML5-TTC8 locus in carotid-intima media thickness and atherosclerotic events. Poster Presentation at the 69th Annual Meeting of the American Society of Human Genetics (ASHG), Houston, Texas, October 15-10, 2019 (#2697/W).

Wang J. Age related changes in retinal microvasculature, microcirculation and microstructure. Bascom Palmer Eye Institute Research Talk, University of Miami, June 6, 2019.

Wang J. Ophthalmic imaging for clinical research. Shenzheng Eye Hospital. Shenzhen, China. August 8, 2019.

Wang J. Topographical thickness mapping of intraretinal layers in aging and neurologic disorders. Singapore National Eye Research Institute, Singapore, Singapore, August 21, 2019.

Wang J, Delgado S, Liu Y, Lin Y, Hernandez J, Deng YQ, Gameior GR, **Jiang H**. Retinal tissue hypoperfusion in multiple sclerosis (poster). America's Committee for Treatment & Research in Multiple Sclerosis (ACTRIMS) Forum 2019. Dallas, TX, Feb 28-March 2, 2019.

Wang J, Lin Y, Liu Y, Gameior GR, Dong CH, **Rundek T, Jiang H**. Age-related reduction in retinal tissue perfusion in a healthy population (poster). The North American Neuro-Ophthalmology Society 45th Annual Meeting, Las Vegas, Nevada, March 16-21, 2019.

Xiaoyan S. Invited speaker for CME activity for the update of Alzheimer's disease in the Alliance of North American Chinese Physicians Annual Meeting in Sep. 2019.

McKnight Brain Research Foundation 10th Poster Reception at the Society for Neuroscience (SFN) Meeting in Chicago, Illinois, October 20th, 2019.

Ami P. Raval, William Javier Moreno, Juliana Sanchez, Nadine Kerr, Ofelia E. Furones-Alonso, W. Dalton Dietrich, Helen M. Bramlett. Chronic nicotine exposure hinders whole body vibration therapy induced ischemic protection in the brain of reproductively senescent female rats.

Ashish K. Rejni, Sunjoo Cho, Kunjan R. Dave. Prior exposure to recurrent hypoglycemia causes post-ischemic ER stress via increased free radical production in treated diabetic rats.

Danylo Cabral, Jordyn Rice, Christina Nunez, Danielle Abel, Kaylee Van Deusen, Baabak Moustafi, Marcela Kitaigorodsky, **David Loewenstein**, Lawrence Cahalin, **Tatjana Rundek, Joyce Gomes-Osman**. Exercise Barriers, Motivators, and Self-efficacy in Sedentary Aging Adults: An Ongoing Trial.

Danylo Cabral, Jordyn Rice, Christina Nunez, Danielle Abel, Kaylee Van Deusen, Baabak Moustafi, Marcela Kitaigorodsky, **David Loewenstein**, Lawrence Cahalin, **Tatjana Rundek, Joyce Gomes-Osman**. Effects of 8-weeks of Aerobic Exercise Intervention on Fitness and Neuroplasticity in Aging Adults: Preliminary Results of an Ongoing Trial.

Joshua J. Rooks, Nikhil Banerjee, Z. Goodman, Katalina F. McInerney, Sarah Getz, Sonya Kaur, Bonnie Levin. Measuring Frailty in Middle and Later Years and its Association with Cognition.

Krizia Crespo, **Sonya Kaur, Katalina McInerney, Joshua Rooks**, Marina Sarno, Mitchell Slugh, **Sarah Getz**, Annelly Bure-Reyes, Nikhil Banerjee, **Tatjana Rundek, Bonnie Levin**. Ethnicity moderates the relationship between sleep quality and learning and memory.

Sarah J. Getz, Joshua Rooks, Katalina F. McInerney, Nikhil S. Banerjee, **Bonnie E. Levin**. Fatigue, Adverse Childhood Experiences, and Frailty in Later Life.

Sharnikha Saravanan, Concepcion C. Furones, Weizhao Zhao, Kunjan R. Dave, Miguel A. Perez-Pinzon, Ami P Raval. Post-stroke physical exercise reduces ischemic brain damage and improves cognition in reproductively senescent female rats.

Sunjoo Cho, Ashish K. Rejni, Hever Navarro Quero, Carolyn J. Keatley, Shyam Gajavelli, Sebastian Koch, Yeon S. Ahn, Miguel A. Perez-Pinzon, Wenche Jy, Kunjan R. Dave. Red blood cell-derived microparticles treatment improves post-intracerebral hemorrhage in long-term outcomes in rats.

Varun Reddy, Concepcion Furones, Juan Pablo de Rivero Vaccari, Ami Raval. Effects of endogenous estrogen fluctuations on the post-ischemic innate inflammation in the brain of female rats.

5. Presentations at Public (Non-scientific) Meeting or Events

Blanton S. Ad hoc member of the NIH study section, Genetics of Health & Disease, (02/25/19-02/26/2019).

Blanton S. Scientific organizer for the annual meeting of the International AMD Genomics Consortium, which took place November 7-8, 2019, in Jerusalem, Israel.

Brown SC, Bachin RF. "Health Disparities and Population Health: *Built Environment, Behavior and Health.*" Invited speaker at the Introduction to the Medical Profession Course (taught to first-year medical students at the University of Miami), University of Miami Miller School of Medicine, Miami, FL, August, 2019.

Brown SC. "Built Environment, Behavior and Health." Invited Speaker at the Evelyn F. McKnight Brain Institute at the University of Miami, Miami, FL, August, 2019.

Brown SC. "The Relationship of Neighborhood Greenness to Heart Disease in 249,405 U.S. Medicare Beneficiaries." Invited Speaker and Panel Discussant for Geographic Information System (GIS) Day, at the University of Miami Richter Library, Coral Gables, FL, November, 2019.

Bulotsky-Shearer R, Delgado C, **Brown SC**, Bachin RF. "U-LINK: Using Big Data to Understand and Improve Child Health and Well-being." Invited speakers at Pediatric Grand Rounds, Mailman Center for Child Development, University of Miami, Miami, FL, September 2019.

Buré-Reyes A, Sarno M, Miranda M, **McInerney KF**. Normal and abnormal aging: The need for neuropsychological assessment. Invited speakers at the Latino Center for Aging, Miami Lakes, FL, April 2019.

Camargo C. "How our brain changes as we age." The (Miami-Dade) Mayor's Initiative on Aging: Your Brain Seminar Series. Pinecrest, FL, October 22nd, 2019.

Getz J. "How the aging brain can make us vulnerable and affect decision-making." The (Miami-Dade) Mayor's Initiative on Aging: Your Brain Seminar Series. Pinecrest, FL, October 15th, 2019.

Gomes-Osman J. Exercise for Brain Health: From Evidence to Practical Advice. Health and Wellness Series at the Vi Aventura. Aventura, FL, November 8th, 2019.

Gomes-Osman J. Exercise for Brain Health: From Evidence to Practical Advice. The (Miami-Dade) Mayor's Initiative on Aging: Your Brain Seminar Series. Pinecrest, FL, October 8th, 2019.

Gomes-Osman J. Exercise for Brain Health: From the Neuroscience to the Practical Advice. Society for Neurosports Conference. Poster November 16th, 2019. Deerfield Beach, FL.

Gomes-Osman J. Exercise for Neuroplasticity in Aging: Translating Animal Evidence into Human Interventions. Miami Project Seminar Series. Miami, FL, September 18th, 2019.

Gomes-Osman J. Exercise for Neuroplasticity in Aging: Translating Animal Evidence into Human Interventions. Dean's Interdisciplinary Research Seminar Series - Research Mentoring. Miami, FL, November 22nd, 2019.

Kaur S. Epilepsy Boot Camp Lecture Series, University of Miami Miller School of Medicine. August 2019.

Kaur S, Slugh M, Rey, G. Introduction to Neuropsychology. University of Miami Miller School of Medicine, Neurology Resident Lecture Series. 2019.

Lobo J. FSL Course Overview & Introduction to FSLeyes. Invited speaker for Brain Cognition and Connectivity Lab Meeting, Florida. Miami, January 12th, 2019.

Lobo J. NKI dataset & Neuroimaging formats and Successful Agers. Invited speaker for Integrative Health and Mind-Body Biomarker Laboratory Standing Lab Meeting, UC San Diego. California, San Diego, July 12th, 2019.

Lobo J. Resting-state Brain Connectivity & Cardiovascular Disease risk of Successful Agers. Invited speaker for HIV Neurobehavioral Research Program, UC San Diego. California, San Diego, July 12th, 2019.

Loewenstein D. New Methods for Detection of Early Alzheimer's Disease, Florida Department of Health-Plenary Statewide Presentation, November, 2019.

Loewenstein D. Novel Cognitive Stress Paradigms, Brain Biomarkers and Early Detection of Alzheimer's Disease, Neurology Grand Rounds, March, 1st, 2019.

Marulanda-Londono E. "How stroke affects the brain, what you need to know about stroke, before during and after." The (Miami-Dade) Mayor's Initiative on Aging: Your Brain Seminar Series. Pinecrest, FL, October 29th, 2019.

McInerney KF. Presented at McKnight Journal Club in September, 2019 on recruiting the oldest old for clinical research.

McIntosh RC. NIMH workshop titled "Mood Disorders in People Living with HIV," Bethesda, MD. July, 2019.

Sacco RL. Dean Ford's Inaugural Distinguished Lecture Series, Forecasting a Brighter Future for Preventing Stroke and Cognitive Decline. University of Miami Miller School of Medicine, Miami, FL, January 30, 2019.

Sacco RL. Forecasting a Brighter Future for Preventing Stroke and Cognitive Decline, Grand Rounds, Wake Forrest School of Medicine, Winston-Salem, NC, May, 17, 2019.

Sacco RL. Forecasting a Brighter Future for Preventing Stroke and Cognitive Decline, Grand Rounds, University of Chicago, Chicago, IL, October 10, 2019.

Sacco RL. Improving Stroke Quality and Reducing Health Disparities. Lecture to Residents, Massachusetts General Hospital, Harvard Medical School, Boston, MA, April 18, 2019.

Sacco RL. Improving Quality and Reducing Disparities: Florida Stroke Registry, Grand Rounds, University of Miami, Miami FL, November 15, 2019.

Vontell R. (presentation) Blood Vessel Regulation and White Matter Pathology. McKnight Research Meeting. Miami FL., May 15 2019.

Vontell R. (presentation) Return of Neuropathology Reports to the Families and Physicians: Challenges and Best Practices. NIH NeuroBioBank Directors Meeting. Bethesda Maryland, October 28, 2019.

GRANTS AND AWARDS

SECTION 6



6. Grants and Awards

6.1. Trainee Grants and Awards

Dr. Ralph Sacco has mentored the following trainees who have received funding awards.

- Fellows

Nicole Sur, MD received funding as a Florida Stroke Registry Fellow.

Victor Del Brutto, MD received funding as a NINDS StrokeNet Fellow.

- Graduate Student

Michelle Caunca was given an F30 Fellowship Award and the P.E.O. Sisterhood award.

Dr. Tatjana Rundek has been mentoring the following trainees who received grants and funding.

- Fellows

Dr. Anita Saporta - UM Evelyn F. McKnight Research Fellow grant recipient

Dr. Michelle Marrero - UM Department of Neurology Cognitive Behavioral Fellow

- Junior Faculty

Dr. Joyce Gomes-Osman - recipient of a KL2 award and EUREKA.

Dr. Christian Camargo - recipient of the AAN McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss

Tali Elfassy - recipient of a KL2 award, R01 and Prevention Medicine Award from AHA.

Dr. David Loewenstein trains and mentors the following trainees who have received funding awards.

- Training

Michelle Caunca - Neurology candidate on Dissertation Committee funded by F30 Fellowship Award and the P.E.O. Sisterhood award

Maya Elias, PhD School of Nursing Mentoring F32 Grant Application

- Mentoring

Joyce Gomes-Osman, PhD - recipient of a KL-2 award

Miriam Rodriguez, PhD - recipient of a KL-2 award

Drs. Sonya Kaur mentored by **Bonnie Levin** and **Alberto Ramos**, received funding from the American Academy for Sleep Medicine Foundation to attend the Young Investigator's Research Forum in Bethesda, MD in April 2019.

Jing Xu, a graduate student mentored by **Dr. Miguel Perez-Pinzon**, began her work on the American Heart Association pre-doctoral fellowship award.

Dr. Joyce Gomes-Osman's PhD student **Jordyn Rice** won a prestigious Promotion of Doctoral Studies (PODS) II Scholarship award from the Foundation for Physical Therapy Research for her dissertation work, supervised by Dr. Gomes-Osman (Principal Investigator). The project is "Assessing Factors Related to Dual-Task Performance in Aging Adults."

Dr. Ami Raval mentors **Sharnikha Saravanan** who received funding from the Miami Project Summer Fellowship for Undergraduates.

Dr. Milena Pinto's Post-Doc **Amanda Ferreira Neves**, received a Lois Pope LIFE Fellowship Foundation research award.

6.2. Faculty Grants and Awards

Dr. Ralph Sacco received significant recognitions. Dr. Sacco is serving as Immediate Past President of the American Academy of Neurology. He is serving his first year as member of the National Academy of Medicine. He was honored with the Distinguished Alumnus Award, Boston University and listed among the Top 40 Graduates of the Class of 1979, Cornell University. He was also honored with the Neurologist Pioneering Award, Society of Vascular and Interventional Neurology.

Dr. Tatjana Rundek was elected to the Dr. M. Lee Pearce Foundation Board. She is Incoming President of the Intersocietal Accreditation Committee, the largest national accreditation organization that accredits clinical imaging laboratories (CT, MRI, Ultrasound, cardiac catheterization, Echo). She is also a formal KL2 training director at the Miami CTSI awarded by NCATS.

Dr. Joyce Gomes-Osman was selected to participate in the prestigious *11th Annual International Certificate Course*, Eureka Institute for Translational Medicine that took place April 7th - 13th, 2019 in Syracuse, Italy.

Dr. Jinhua Wang was awarded an NIH NINDS R01 grant (MPI: Detre at UPENN and Wang at UM) to study the microvasculature in the eye and brain in healthy populations and patients with small vessel diseases. His novel techniques for imaging the tissue perfusion of the retina and brain are applied to refine vascular biomarkers of small vessel disease. **Dr. Hong Jiang** is a Co-Investigator.

Dr. David Loewenstein was Appointed Associate Director for the 1Florida Alzheimer's Disease Research Center (1Florida ADRC).

Dr. Christian Camargo was promoted from Instructor in the Department of Neurology to Assistant Professor.

Dr. Sarah Getz served as a member of the Women in Academic Medicine Scholarship Committee, University of Miami Miller School of Medicine.

Dr. Roger McIntosh completed the second year of his K01 award for his K01 HIV-Related Changes in Brain Function and Hypertensive Risk, funded by NHLBI.

Dr. Sonya Kaur, who completed her Post-doctoral Fellowship under **Dr. Bonnie Levin** was hired as an Instructor as part of the Schoninger Neuropsychology Program in the Department of Neurology.

Dr. Scott Brown received an Ed and Ethel Moore Alzheimer's Research Grant to evaluate the relationship of neighborhood greenness (e.g., parks) and greening interventions (e.g., tree planting) to Alzheimer's Disease in Medicare beneficiaries residing in low-income Miami neighborhoods. He also received a Sylvester Cancer Center Pilot Grant from the University of Miami's Sylvester Cancer Center to investigate the relationship of neighborhood greenness (e.g., parks; tree canopy) to cancer diagnoses in Miami Medicare beneficiaries. He was named Faculty Advisory Committee Member of the Abess Center for Ecosystem Science and Policy, at the University of Miami.

Dr. David Della-Morte received substantial funding and prestigious accolades this year. He received funds from the European Social Fund, under the Italian Ministries of Education, University and Research to study personalized medicine for innovative strategies in neuropsychiatric and vascular diseases. He was recognized for the best Research and Scientific contribution by the APSEN 50 GANEPAO, San Paolo, Brazil and received the CICERONE AWARD, International Award by the MARCO TULLIO CICERONE FOUNDATION for Renowned Scientific Contribution and Dissemination. Lastly, he received a Rome Foundation Grant.

Dr. Miguel Perez-Pinzon received an R21 grant from the National Center for Complementary & Integrative Health.

Dr. Kunjan Dave received a discovery grant from the James and Esther King Biomedical Research Program, Florida Department of Health (DOH).

FACULTY AND TRAINEES

SECTIONS 7-8



LEADERSHIP

Ralph L. Sacco, M.D., M.S., FAHA, FAAN

Evelyn F. McKnight Brain Institute Executive Director and Scientific Advisory Board Member

Professor and Oleberg Chair of Neurology
Director, Clinical and Translational Science Institute
Senior Associate Dean for Clinical and Translational Science
President, American Academy of Neurology 2017-2019
University of Miami, Miller School of Medicine



Tatjana Rundek, M.D., Ph.D. FANA

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Director, Clinical and Translational Research Division
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Evelyn F. McKnight Brain Institute Cognitive Core Director, and Scientific Advisory Board Member

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Noam Alperin, Ph.D.

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Miguel A. Perez-Pinzon, Ph.D.

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Vice-Chair for Basic Science (Neurology)
Director, Cerebral Vascular Disease Research Laboratories
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Susan Fox-Rosellini, M.B.A.

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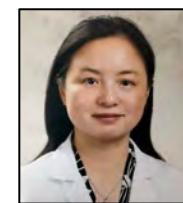
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Chuanhui Dong, Ph.D.

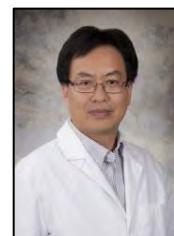
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Ami Pravinkant Raval, Ph.D.

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Jianhua Wang, M.D., Ph.D.

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Associate Professor

Department of Ophthalmology Bascom Palmer Eye Institute

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Faculty (Members)

Biosketches are provided at the end of the report.

Name	Center Role	Area of Expertise
Noam Alperin, PhD	Member	Radiology, Physics (MRI)
Christian Camargo, MD	Member	Neurology
Kunjan R. Dave, PhD	Member	Neurobiology, Basic Science
David Della Morte, MD, PhD	Member	Neurology
Joyce Gomes-Osman, PhD, PT	Member	Physical Therapy, Neurology
Hong Jiang, MD, PhD	Member	Neuro-ophthalmology, Neurology
Bonnie Levin, PhD	Cognitive Core Director, Scientific Advisory Board Member	Neuropsychology
Miguel Perez-Pinzon, PhD	Member, Scientific Advisory Board Member	Neuroscience
Tatjana Rundek, MD, PhD	Scientific Director, Scientific Advisory Board Member	Neurology, Epidemiology
Ralph L. Sacco, MD, MS	Executive Director, Scientific Advisory Board Member	Neurology, Epidemiology, Genetics
Xiaoyan Sun, MD, PhD	Educational Director, Scientific Advisory Board Member	Neuroscience, Biochemistry

Faculty (Collaborators)

Biosketches are provided at the end of the report.

Name	Center Role	Area of Expertise
Antoni Barrientos, PhD	Collaborator	Neuroscience, Genetics
Susan Blanton, PhD	Collaborator	Genetics
Scott Brown, PhD	Collaborator	Public Health
Elizabeth Crocco, MD	Collaborator	Psychiatry
Chuanhui Dong, PhD	Collaborator	Epidemiology, Biostatistics
Sarah Getz, PhD	Collaborator	Neuropsychology
David Loewenstein, PhD	Collaborator, Scientific Advisory Board Member	Neuropsychology
Katalina McInerney, PhD	Collaborator	Neuropsychology
Roger McIntosh, PhD	Collaborator	Psychology
Teshame Monteith, MD	Collaborator	Headache Science
Carlos Moraes, PhD	Collaborator	Neuroscience
Milena Pinto, PhD	Collaborator	Neuroscience
Alberto Ramos, MD	Collaborator	Neurology, Sleep Medicine
Ami P. Raval, PhD	Collaborator	Neuroscience, Epidemiology
Regina Vontell, PhD	Collaborator	Neurology
Jianhua Wang, MD, PhD	Collaborator	Neuro-ophthalmology, Neurology

Trainees

Name	Center Role	Area of Expertise
Saeed Alahmari	MS CTSI Student	Physical Therapy
Shatha Aldraiwiesh, PT	PhD Student	Physical Therapy
Nikhil Sebastian Banerjee	Intern	Neuropsychology
Myriam Bourens, PhD	Associate Research Scientist	Neuroscience
Jabari-Ture Ghingo Brooks	Post-Bac Student	Neuroscience
Kyle Andrade-Bucknor	Undergrad Student	Pre-Med
Danylo Cabral, BS, PT	PhD Student	Physical Therapy/Cognition
Nicholas Cassidy	Undergrad Student	Neurology
Michelle Caunca, PhD (MD Student)	Formal McKnight Trainee	Neurology
Austin Choi	PhD Student	Neurobiology
Charles Cohan, PhD	Postdoctoral Fellow	Neurology
Crizia Crespo, PhD	Postdoctoral Fellow	Neuropsychology
Samuel Del'Olio, BS	PhD Student	Pharmacology
Brett Doliner	MD Student	Neurology
Carolina Flores	Post-Bac Student	Physical Therapy
Olivia Gardner	PhD Candidate	Genetics
Chelsey Guastucci	Undergrad Student	Basic Science Neurology
Alison Headley, MD	Resident	Neurology
Jason Hokenson	Undergrad Student	Physical Therapy
Sonya Kaur, PhD	Instructor	Neuropsychology
Nathalie Khoury, BS	PhD Student	Neuroscience
Hyun-Jun Kim	PhD Student	Neuroscience
Kevin Koronowski, BS	MD/PhD Student	Neuroscience
Cril Larhsen	Undergrad Student	Physical Therapy
Diego Lasso	Undergrad Student	Biology

Suzanne Lippman	MD Student	Neurology
Che Liu	Graduate Student	Neuroradiology
Judith Lobo	Graduate Student	Cognitive Behavioral Neuroscience
Ava Marsh	Undergrad Student	Biology
Alejandro McCluskey	Post-Doctoral Trainee	Neurology
Amanda Neves	Post-Doctoral Trainee	Basic Science Neurology
Qismat Niazi	Student	Neuroscience
Eva Nyvtova, PhD	Post-Doctoral Trainee	Biochemistry
Sofia Oluwole	MD/PhD Student	Neurology
Sabrina Pastore	Undergrad Student	Physical Therapy
Pujan Patel	Undergrad Student	Neuropsychology
Sonya Patel	Undergrad Student	Neuroscience
Maya Pinjala	Graduate Practicum Student	Neuropsychology
Andy Hinojo-Perez	Undergrad Student	Biology
Adele Raymo	Undergrad Student	Physical Therapy
Varun Reddy	Student	Neuroscience
Ashish Rehni, PhD	Post-Doctoral Fellow	Neuroscience
Jordyn Rice, PT, DPT	DPT, PhD Student	Physical Therapy/Cognition
Joshua D. Rooks, PhD	Postdoctoral Fellow	Neuropsychology
Anita Seitas Dias Saporta, MD	McKnight Fellow	Neurology, Imaging
Sharnikha Saravanan	Undergrad Student	Neuroscience
Kasra Sarhadi	MD MPH Student	Physical Therapy/Cognition
Marc Schatz	MD Student	Neurology
Vibha Shukla, PhD	Postdoctoral Fellow	Neurology
Nikhil Sikha	Undergrad Student	Biology
Marialaura Simonetto, MD	Resident	Neurology
Hesley Solano	Undergrad Student	Neuroscience
Chantel Sorochuk	Graduate Practicum Student	Neuropsychology
Courtney Sparger	Undergrad Student	Neuroscience
Holly Stradecki, MS	MD/PhD Student	Neuroscience
Alba Timon, PhD	Post-Doctoral Trainee	Biotechnology

Kristopher Wolford, MPH	Undergrad Student	Public Health
Jing Xu, BS	PhD Student	Neuroscience
Michelle Zambik	Post-Bac Student	Physical Therapy, Cognition
Rui Zeng	PhD Student	Neuroscience
Hui Zhong, BS	PhD Student	Biochemistry

CLINICAL AND TRANSLATIONAL PROGRAMS

SECTION 9



9. Clinical/Translational Programs

9.1. Update on MBI Directly Related Clinical Translational Studies

Section 9 consists of the following sub-sections. (1) **An update on the following:** MBI Directly Related Clinical Translational Studies; McKnight Brain Institute Inter-Institutional Collaborative Projects; Clinical Translational and Population-Based Research Projects; Other MBI Projects; Schoninger Neuropsychology Program; Neuroimaging MBI Core; Other MBI Research Performed by Trainees; and Basic and Translational Science Research (2) **Future/upcoming research plans** for the following: Clinical Translational and Population-Based Research; Basic and Translational Science Research; and Education Program.

McKnight Frailty Project - The McKnight Frailty Project is unique to the University of Miami and includes clinic and community participants from diverse backgrounds ranging in age from 50 to 95+. The frailty and cognitive testing battery has been validated in both English and Spanish. The registry is well balanced, with an equal representation of Hispanic and Non-Hispanic males and females. Under the supervision of **Drs. Katalina McInerney** and **Bonnie Levin**, the McKnight Frailty Project includes demographic, medical/clinical, neuropsychological, imaging and psychosocial data. This registry is the foundation for expanding our McKnight collaborations with other disciplines (such as imaging, medicine, PT). It also serves as an important resource for pilot data and new grants.

This year **Dr. Katalina McInerney** took on the enormous endeavor of enhancing the McKnight Frailty database to take advantage of its research potential. She organized and led meetings and brainstorming sessions on an ongoing basis to extrapolate novel approaches to researching/defining frailty as it relates to cognition and aging. With the plan mapped out to move forward with the project upgrade, **Drs. Bonnie Levin, Katalina McInerney** and their capable team of volunteers, students and fellows worked hard to optimize the database. This entailed adding itemized scores of four full behavioral assessments (BDI-II, BAI, ACE, FAQ) into the REDCap database. There are over 500 records in the database of which, approximately 350 have close to complete records. It is expected that Drs. Katalina McInerney and Bonnie Levin's efforts will continue to lead to fruitful and robust research. This wide-ranging data will be instrumental in obtaining funding and establishing collaborative partnerships across disciplines. **The McKnight Frailty database** is directly translatable in the clinic as it leads to patient treatment recommendations and referrals. Most importantly, it leads to preventative care, thereby addressing risk factors for physical and cognitive decline and memory loss in older adults.

Dr. Christian Camargo is the Principal Investigator and **Dr. Katalina McInerney** is the Co-Investigator for **Reducing the Effects of Aging on Cognition with Therapeutic Intervention of an**

Oral Nutrient - The REACTION Study, which is funded by the AAN McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss. It is a pilot study with a parallel group design of a multi-nutrient oral supplement on improved cognitive performance in participants with age-related cognitive complaints and age-matched participants without cognitive complaints. The nutrient being used, Souvenaid is an example of such a treatment to increase synaptic plasticity. Its key ingredient, Fortasyn-Connect, contains a patented combination of phospholipids, DHA and choline. The formulation is based on the biochemical properties of synaptic membranes intimated after years of rigorous research by one of his mentors, Dr. Richard Wurtman from MIT. Dr. Christian Camargo's primary mentor is **Dr. Tatjana Rundek**. The project has been given IRB approval and enrollment will begin in 2020.

Dr. Christian Camargo continued working on his novel pharmacological interventions (e.g., HDAC inhibitors) for cognitive aging treatment. He implemented the study A Role for Evaluating PET-Amyloid Status (AREPAS) as part of the Key Hallmarks of Amyloid Tracer as an Ideal Biomarker (KHATIB) study. It is halfway done with enrollment and is so far, very successful showing great feasibility.

Drs. Christian Camargo and **Katalina McInerney** are two of the Co-Investigators for A Phase I, Prospective, Open-Labeled Trial to Evaluate the Safety, Tolerability and Exploratory Outcomes of Multiple Allogeneic Human Mesenchymal Stem Cell (MSC) Infusions in Patients with Mild to Moderate Alzheimer's Disease. Dr. Bernard Baumel, Cognitive Division Director, is PI of the study.

Dr. Katalina McInerney is a Co-Investigator for A Phase I, Prospective, Randomized, Double-Blinded, Placebo-controlled Trial to Evaluate the Safety and Potential Efficacy of Longeveron Allogeneic Human Mesenchymal Stem Cell (LMSC) Infusion Versus Placebo in Patients with Alzheimer's Disease. Dr. Bernard Baumel, is PI and Longeveron LLC is the Sponsor.

9.1.1. Update on McKnight Brain Institute Inter-Institutional Collaborative Projects

McKnight Brain Aging Registry (MBAR) at the University of Miami – This is a collaborative research project with all four McKnight Brain Institutes participating. It is designed to study those who are 85 years or older and have aged 'successfully'. Successful aging refers to physical, mental and social well-being in older age. It incorporates cognitive, physical and emotional domains, and the way the aging process affects them.

Our site began the year with 35 subjects enrolled and it ended with a total of 52 participants. Thirty-three have completed all study procedures and the end goal is to have 50 completed subjects. This is a promising goal as there are several subjects in different stages of the study at this time and we continue to receive calls from potential candidates. **Marti Flothmann**, the MBAR study coordinator has been coordinating the study visits and taking great care of our truly special participants. This is a unique cohort with a wide breadth of knowledge and experience.

Dr. Christian Camargo has taken the time to converse with each study participant this year while conducting neurological exams. There is no doubt that his role in the study has added to subject satisfaction with our research and aided with study subject retention. **Dr. Sonya Kaur** has been one of our neuropsychologists along with **Dr. Katalina McInerney** who conducted testing sessions with the MBAR participants. They spend at least six hours with each participant during the study. Their hard work and diligence has been tantamount to our success.

The bi-weekly conference calls in which study teams at all sites join, continued through 2019. These are productive calls even though the study has been underway and protocols are set. All sites have an opportunity to discuss recruitment strategies, challenges, solutions, and to maintain a sense of camaraderie.

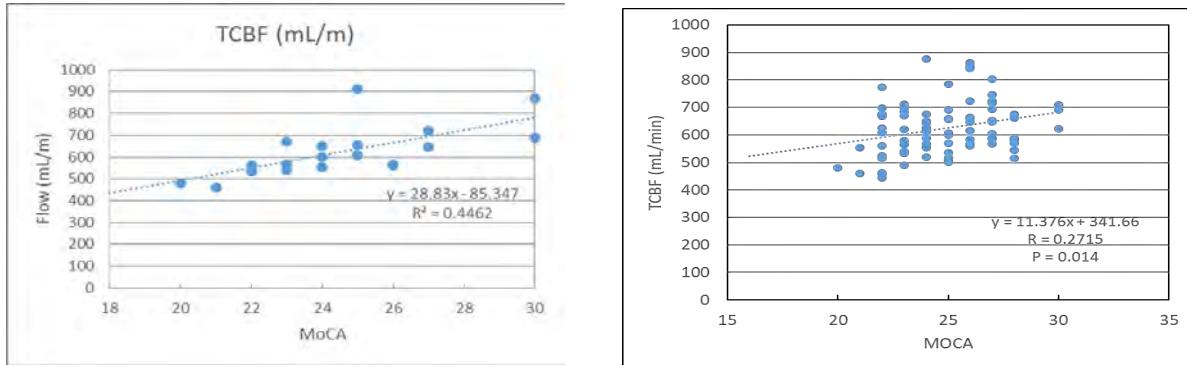
Stacy Merritt continued the recruitment efforts by sending out more flyers to the community as well as to almost every church in the Miami vicinity. MBAR flyers are displayed across the Miami-Dade library system. Additionally, the community outreach and education events, which she plans and attends, have been a promising forum for recruiting. We have developed a following of former MBAR subjects who we invite to the events. And as such, each community event has become a reunion. Subjects are eager to participate if there is a follow-up of any kind to the MBAR project.

Drs. Bonnie Levin and **Katalina McInerney** remain actively involved and lead the MBAR behavioral studies by monitoring the quality control and accuracy of data entry into the REDCap database from all sites. They have been leaders in data analyses for preliminary and pilot results for presentations and upcoming abstract and manuscript submissions.

Dr. Noam Alperin and **Sang Lee, MS** of the MBAR Neuroimaging Core have been an integral part of the study team. Having an MRI is the more difficult portion of the study for the participants. Though their focus is on ensuring the quality of the scans, the neuroimaging team ensures a comfortable experience for this older cohort and establishes a gentle rapport with each subject. Despite the challenge of limited access to the MRI scanner, which impedes scheduling of MRI scans, thirty-four study subjects were successfully scanned to date. We note the dedication and effort of our research coordinator, **Marti Flothmann** to overcome scheduling and imaging procedure obstacles.

Our MBAR site has been responsible for specific imaging of cerebral blood flow and has generated preliminary blood flow analyses. **Dr. Noam Alperin** and his team have completed a review of the 126 data sets obtained at the four McKnight study sites to date. Eighty-four data sets of blood flow dynamics were of good or fair quality and were included in the data analysis. The significant correlation between total cerebral blood flow (tCBF) and cognitive performance as measured by the MoCA test has been identified and verified using the larger cohort. The MBAR study is one of the few aging related studies that includes the measure of tCBF as part of the imaging protocol. Here we highlight these important preliminary findings.

The initial results with 18 subjects from the UM site and the most current results with 84 subjects from all sites are highlighted in the figures below, respectively.



Scatter plots of the total CBF measurements vs MoCA (at UM site- left and in the total MBAR sample-right). A significant correlation was found between tCBF and MoCA scores.

Che Liu, a post-doctoral trainee in **Dr. Noam Alperin's** laboratory has investigated gender-related differences in neural activity and brain activation patterns in the idling brain using rest-state fMRI in a cognitively intact oldest old cohort. The work is summarized in a publication titled "Gender differences in brain function in the cognitively intact oldest old: resting-state fMRI findings from McKnight Brain Aging Registry (MBAR)." An important observation of this work is that age related differences between men and women is smaller in the oldest old cohort, compared with younger cohorts. Gender differences in brain activity patterns subside with aging. Based on these results, Dr. Noam Alperin submitted the following abstracts which have been accepted for presentation at the upcoming Cognitive Aging Conference in Atlanta, Georgia in 2020: "Gender Differences in Brain Morphology and Blood Flow in the Cognitively Intact Oldest Old from McKnight Brain Aging Registry"; and "Gender Differences in Resting Brain Activity and Connectivity in the Cognitively Intact Oldest Old from McKnight Brain Aging Registry."

McKnight Brain Aging Registry (MBAR) Update Across Sites - Our mission is to establish and maintain the 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.

MBAR 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.

We held additional regular bi-weekly 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. Blood specimens are sent to UF for storage in freezers located in the phlebotomy laboratory. The detailed report on MBAR for all sites has been submitted to the Trustees by the Inter-Institutional MBAR investigators. It is included in [Appendix I](#).

Uncovering Risk Profiles of Deception and Mitigating Susceptibility to Scamming in Midlife and Older Age: A Novel Intervention Tool - Drs. Sarah Getz and Bonnie Levin continue to work in close collaboration with Drs. Grilli and Wilson (UA) and Dr. Ebner (UF) on this McKnight funded intervention pilot study that aims to identify correlates of susceptibility to deception and scamming in the elderly. IRB approval has been obtained for the cross-institutional study. Our team meets regularly via collaborative conference calls monthly and often, bi-monthly calls are initiated to discuss specific aspects of our ongoing projects. We have collectively submitted an NIH R21 proposal, "The Neuroeconomics of Phishing Susceptibility in Younger and Older adults." We have also written a manuscript entitled, "Evaluating the cognitive mechanisms of phishing detection with PEST, an ecologically valid lab-based measure of phishing susceptibility" and it is currently under review (*Journal of Experimental Psychology*). Our team is also developing a number of other data driven manuscripts as well as additional grant applications. The University of Miami team will spearhead a review paper on the status of susceptibility to deception and scamming among the vulnerable aging. Currently, we are preparing our pilot study of the "Assessment of Situational Judgment" for publication, which will be followed up with a larger psychometric study showing its reliability and validity in a sample of 200+ participants. Data collection is projected to be completed in 2020, with plans to submit a larger R01 to the NIH.

9.1.2. Update on Clinical Translational and Population-Based Research Projects

Dr. Ralph Sacco is PI and leads several important federally funded research projects involving stroke and cognitive decline. These studies have continued to make tremendous progress this year. Summaries are detailed below.

Dr. Ralph Sacco is the Principal Investigator of [The Northern Manhattan Study \(NOMAS\)](#). Drs. Tatjana Rundek, Bonnie Levin and Xiaoyan Sun are Co-Investigators. This longitudinal study [Risk Factors for Stroke and Cognitive Decline in a Tri-Ethnic Region](#) is currently in its 27th year and in 2019 is in the 5th cycle of funding. The aims of this funding cycle have focused on addressing gaps in knowledge related to the risks and determinants of stroke, **cognitive impairment and dementia** by advancing research on: (1) specific neuro-immune and inflammation-related molecules and networks and their association with accelerated cognitive trajectories; (2) regional white matter volumes, lobar volumes, hippocampal volume,

perivascular spaces, dolichoectasia and collateral variants and their association with accelerated cognitive trajectories and dementia; (3) vascular risk factors, including immune biomarkers and networks and their significance as determinants of dementia; (4) individual vascular risk factors and global vascular risk scores and their ability to predict trajectories of functional outcomes and quality of life independent of stroke; and (5) vascular risk factors and varying effects for specific ischemic stroke subtypes.

In this past year, [Dr. Ralph Sacco](#) and team have begun to explore the **association between cognitive trajectories and biomarkers/networks** (assayed with neuro-immune and neuro-inflammatory biomarker panels). Using a multiplex immunoassay panel, they completed measurement of concentrations of 60 neuroimmune-inflammatory markers in plasma samples from 1,179 participants. They explored associations of these neuroimmune signatures with neuropsychological testing and MRI volumetric data. Preliminary findings showed significant associations of specific sets of immune markers with cognition overall and with scores in individual domains, as well as with white matter hyperintensity volume (WMHV). These findings have been presented in plenary and poster presentations at the 2019 American Association of Neurology (AAN) meeting. Manuscripts are in preparation.

NOMAS has also produced findings **associating regional brain arterial diameters with cognitive performance localized to the vascular territory supplied by such arteries**. [Dr. Ralph Sacco](#) and team reported cross-sectional non-linear associations between left middle and anterior cerebral artery mean diameter and semantic memory, and left posterior cerebral artery/left posterior communicating artery (PCA/Pcomm) mean diameter and episodic memory. In these cross-sectional models, diameters were inversely associated with cognitive scores. Longitudinally, surviving participants with the largest left PCA/Pcomm mean diameter had greater decline in all-domain Z-scores, as well as in semantic memory and possibly episodic memory compared with participants with more average diameters. Furthermore, dilated brain arteries are effect modifiers in the relationship between measures of systemic arterial stiffness and brain perivascular spaces.

Through work from [Michelle Caunca](#) (MD/PHD student mentee), [Drs. Rundek and Sacco](#), this year they were able to report on **associations between brain imaging parameters, vascular risk factors and cognitive performance** in manuscripts describing: (1) Greater Body Mass Index is Associated with Smaller Cortical Thickness in the Alzheimer Disease-Signature Regions (PMID31341005); (2) Cholinergic White Matter Lesion Load is Associated with AD Signature Cortical Thickness (PMID31306120); and (3) Machine learning-based estimation of cognitive performance using regional brain MRI markers (PMC6711659). They also reported that more ideal cardiovascular health, as defined by the American Heart Association (AHA), was associated with less white matter hyperintensity volume (WMHV) and greater total cerebral volume as well as lower odds of subclinical brain infarct (PMC6201403).

Using other available NOMAS data, [Dr. Ralph Sacco](#) and team have also demonstrated the **association between cerebrovascular disease and cognitive trajectories**. Using generalized estimating equation models, they evaluated subclinical brain infarcts and functional decline independent of intervening clinical vascular events and other vascular risk factors. A strong and independent association was found between subclinical markers of cerebrovascular injury and important clinical, person-centered functional trajectories (PMC6235693). In another study, the

measurements of periventricular WMHV was analyzed in 1,280 participants, summarized as a function of distance from the ventricular wall. Results found that greater skewness and kurtosis (a summary measure of thickness of the tail of a distribution) were associated with steeper decline in functional status over the long term, independent of overall WMHV and vascular risk factors, and events (PMC6235693).

Dr. Ralph Sacco has continued to lead the analysis of the **relationships between risk factors and functional outcome**, with studies on the relationship between anterior WMHV and lower scores on the Short Physical Performance Battery (SPPB), a well-validated mobility scale, indicating that prevention of subclinical cerebrovascular disease is a potential target to prevent physical decline in the elderly (PMC6093792). Other studies have examined associations between inflammatory biomarkers (interleukin-6 (IL6) and lipoprotein-associated phospholipase A2 (LpPLA2)) and long-term functional trajectories. They found that IL6 levels were associated with decline in Barthel Index (BI) over time, LpPLA2 activity levels were associated with baseline BI but not with change over time, and LpPLA2 mass levels were not associated with either (PMC6443177).

This year NOMAS researchers have followed up on reports about the relationship between carotid intima media thickness (cIMT) and its association with greater burden of cerebral WM lesions independent of demographics and traditional vascular risk factors. They found that increased stiffness (as a functional measure of the arterial wall's resistance to pressure deformation during the cardiac cycle) was associated with increased cIMT and carotid artery dilatation with greater plaque burden (PMC5911635). Their other studies show that the APOE-IMT relationship was not modified by race-ethnicity, and that APOE-ε4 carriers had elevated cIMT independent of demographics and vascular risk factors including LDL levels (PMC5811383).

NOMAS continues to track the cognitive status of survivors in the cohort and had initiated a dementia adjudication system to classify all subjects into no cognitive impairment, mild cognitive impairment and dementia. Over the next year, we will evaluate vascular, inflammatory, and immune biomarkers as risk factors for dementia and cognitive decline. The project will also investigate the role of gut microbiome in stroke and vascular cognitive impairment.

Dr. Ralph Sacco is the Principal Investigator for [The University of Miami Stroke Prevention Intervention Research Program \(SPIRP\), Florida-Puerto Rico Collaboration to Reduce Stroke Disparities \(FL-PR CReSD\)](#). This year marks the close out of NIH funding for the project which has successfully established a stroke registry unique among others in its focus on disparities in the quality of care and outcomes. Throughout the NIH funded period, the FL-PR CReSD stroke registry collected and collated data from (up to 94) Florida and (up to 15) Puerto Rico stroke centers using the American Heart Association/American Stroke Association Get With The Guidelines- Stroke (GWTG-S) program. The registry has been and continues to be a rich source for the exploration and review of disparities in acute stroke care, thus far having provided the foundation for multiple FL-PR CReSD Registry manuscripts describing race/ethnic and sex disparities in stroke care (i.e., changes in disparities over time (PMC5639478; PMC5523741; PMC5039084), disparities in mortality and long-term outcomes after stroke (PMC6405703), and

disparities in the use of emergency response system and disparities in transportation times (PMC6483889).

Through the NIH funded award, the project developed several interventions/initiatives to evaluate and reduce disparities in stroke performance metrics such as: 1) Quality improvement tools (the Annual Hospital Disparities Dashboards which visualize hospital performance data by race/ethnicity and sex, are hospital-specific, provide state and regional benchmarks for performance evaluation, and serve as a self-monitoring tool for hospitals); 2) Educational tools (the interactive educational Door-to-Needle time intervention, which focused on reducing arrival time to treatment and arrival time to imaging for ischemic stroke patients, an area of disparity in stroke care identified by the FL-PR CReSD); and 3) Stakeholder outreach (quarterly conference calls, listserv postings, twitter, a dedicated website, and the Annual Stakeholder Meeting providing formal project presentations, panel discussion, sharing of best practices to improve the quality of care).

Through the NINDS Parent Grant and Administrative Supplement awards, significant work was accomplished to evaluate post-hospital stroke outcomes (30-days post-stroke and long-term) and the benefits of hospital use of quality improvement programs, through a linked FL-PR CReSD registry and CMS post-hospital dataset (with a 64% match rate). We have recently reported race/ethnic disparities for 30-day and 1-year mortality, but not in-hospital mortality. We also found lower mortality among FL and PR Medicare beneficiaries treated for stroke in hospitals utilizing a quality improvement program such as GWTG-S hospitals vs. those treated in non-GWTG hospitals. This study reported less race/ethnic disparities for in-hospital mortality among stroke patients treated at FL-PR CReSD hospitals that utilize the GWTG-S tool (PMC6405703). This year the CMS data has been applied to explore racial/ethnic disparities in 30-day all-cause readmission after stroke. The study revealed that all-cause readmission did not vary significantly by race/ethnicity (although Florida non-Hispanic blacks and Florida Hispanics were less likely to be readmitted for cerebral artery interventions, *J. Stroke and CVD*, in press). These findings reinforce the continued need to evaluate healthcare approaches to transitions of care after stroke and to identify opportunities to eliminate disparities in acute stroke care.

Though this project is completed, resulting accomplishments remain pertinent as they are the foundation to the amended Florida Stroke Act in 2017, which authorizes the existing Florida Stroke Registry (to be discussed below). Additionally, the collaborations and partnerships developed under the SPIRP FL-PR CResD have established an interdisciplinary group of stakeholders (researchers, clinicians, patients, caregivers, policy makers) strongly invested in the improvement of the quality of care and reduction of disparities.

Dr. Ralph Sacco oversees The Florida Stroke Registry. **Dr. Tatjana Rundek** is the Data Management and Analytics Primary Investigator. In 2019, the University of Miami Department of Neurology was awarded its third round of state appropriated funds to manage and maintain the Florida Stroke Registry (the Registry). Since last year, the Registry has added 34 new hospital members increasing the total number of participating Florida stroke centers to 114 (out of a total of approximately 160). The ongoing collection of Florida stroke cases (from 2010 to current) has collected approximately 290,000 to date. This data has been used to produce Florida Stroke Registry derived Self-Monitoring Tools (Hospital-specific Disparities Dashboards;

Regional Dashboards, Statewide Dashboards) which allows tracking and measuring of quality of care performance and stroke outcomes.

The Registry has also impacted the implementation of Florida state policy in 2019. Through evidence-based results provided by the Registry, the Florida Stroke Act was revised to mandate hospital adherence to obtain national certification in order to be identified as a state accredited stroke center. Data provided by the Florida Stroke Registry demonstrated that nationally certified stroke centers perform better in important time sensitive stroke treatment measures than non-nationally certified hospitals. As a result of the evidence-based findings, and with the support of Florida Stroke Registry stakeholders, legislation passed in 2019 stating that *Florida stroke centers are to become accredited through nationally recognized certifying organizations which provide independent stroke care verification, based on nationally recognized stroke guidelines, with a process stringent enough to protect the health, safety and welfare of Florida citizens.*

Also influencing policy at a regional level and possibly eventually at a state level are the Florida Stroke Registry Regional Dashboards. These reports offer hospitals within a county (or defined area/region) a quarterly snap-shot of relative performance for thrombolytic and endovascular treatment. As a tool for hospital quality improvement, the Regional Dashboards were developed to support the collaboration between Emergency Medical Services and stroke centers in an effort to improve local transportation policies. This year reports were added for Miami Dade and Pinellas counties, with plans to include Tampa and Jacksonville. These Registry hospitals may access their self-monitoring tools at the registry website (www.floridastrokecollaboration.org) and may choose to share and utilize the reports as they see fit. The dashboard initiatives serve as examples of the registry's capability to inform a variety of target audiences and different phases of stroke care.

The evolution of the Florida Stroke Registry from its first iteration (described in the section above) involves the expansion of its focus and analytic capacity to involve not only "in-hospital" data, but also "pre- and post-hospital" stroke performance/stroke outcome data. The enhanced shift converts the Registry into a multi-dimensional quality improvement tool, capable of informing systems of stroke care as well as all stroke stakeholders including health care givers, patients/caregivers, researchers and policymakers.

Drs. Ralph Sacco and Tatjana Rundek are Co-Investigators for the [Transitions of Care Stroke Disparity Study \(TCSD-S\)](#). The study, now in its third year of NIH funding, aims to identify disparities in transitions of stroke care and key factors associated with effective transitions of care. This year strong efforts have been placed on increasing and facilitating enrollment by doubling the number of participating sites to twelve (stroke centers throughout Florida). Efforts are ongoing to finalize the inclusion of new sites into the project. Meanwhile, active study sites continue to enroll and collect data through TCSD-S structured telephone interviews conducted by the stroke coordinators to assess patient medication adherence, healthy lifestyle, utilization of rehabilitation interventions and medical follow-up 30 and 90 days after hospital discharge to home. We have also begun to match the collected follow-up data with corresponding AHA GWTG-S data (baseline in-hospital data) to initiate the exploration of predictors of disparities in transitions of care.

The project has also begun to identify patient/caregivers and health care professionals to nominate to the Intervention Advisory Committee. The committee is patient-centered and will involve health care professionals such as nurses, physical therapists, stroke coordinators and community health navigators. Early conversations about committee initiatives include the development of a “stroke support group” modeled after a support group spearheaded by one of the TCSD-S patient Intervention Advisory Committee members. Through the “stroke support group” innovative feedback may be offered towards patient-centered interventions to address transitions of care, as well as a citizen scientist perspective on strategies to improve patient participation in clinical trials. Discussions on this topic among others will commence once health care professional members have been fully confirmed within the committee.

9.1.3. Update on Other MBI Projects

Dr. Ralph Sacco is Director of the [**University of Miami Clinical Translational Science Institute \(UM CTSI\)**](#). It is a university-wide institute dedicated to accelerating and transforming culturalized clinical and translational science. Created to be an indispensable resource for researchers and stakeholders, the Miami CTSI serves as the Miami Hub of the national Clinical and Translational Science Award (CTSA) consortium, which works to advance scientific discoveries into improved health care. Together with Hub partners that include the entire University of Miami as well as Jackson Health System, Miami VA Healthcare System, OneFlorida Clinical Research Consortium, Health Choice Network and Health Council of South Florida, the Miami CTSI focuses on clinical and translational research infrastructure, translational workforce development and stakeholder engagement and culturalization.

Over the two years of the newly funded grant cycle, the Miami CTSI promoted multi-level alignment locally - throughout the University of Miami and UHealth, regionally - across Hub partners, and nationally through key consortium partnerships. Over the course of fiscal year 2019, the Miami CTSI successfully reached 1,900 individuals throughout the Hub and across the region, collaborated with 11 other CTSA institutions across the country, appointed 4 new mentored career scholars, awarded 10 pilot and collaborative projects, had 17 active students in the MS in Clinical and Translational Investigation program, provided more than 1,200 hours of biostatistical and methods consultations, supported more than 3,800 active REDCap users, held 54 education and training events with a total of 765 attendees, enrolled more than 110,000 UHealth patients in the Consent to Contact for Research program, had 38 participants attend I-Corps entrepreneurial training, launched a new interdisciplinary research seminar series in collaboration with the Miller School of Medicine dean, expanded URIDE – a de-identified clinical data service, and held 7 meetings of the Connection for Research Career Enhancement, which brings together more than 50 mentees and mentors.

Dr. Tatjana Rundek is the Principal Investigator of the [**Family Study of Stroke Risk and Carotid Atherosclerosis**](#) study that was ongoing in 2019. The major goal of this study is to evaluate heritability and genetic linkage of novel vascular risk factors such as carotid intima-media thickness among the families of high-risk Caribbean Hispanics. It is an R01 and is funded by NIH/NINDS. In 2019, Dr. Rundek has secured additional NIH funding to extend this study towards cognitive assessments in collaboration with Dr. Ron Lazar, MBI Director at UAB. This study is currently in IRB and contracting process between the UM and UAB.

Dr. Tatjana Rundek is the Principal Investigator for the [Disparities in Stroke Outcomes and Care Delivery in Patients with Atrial Fibrillation: FLIPE-R-AF Study](#) which continued in 2019.

This study examines race-ethnic and sex disparities in health care delivered to stroke patients with atrial fibrillation and their outcomes after acute stroke hospitalization. It is funded by ARISTA-USA.

Dr. Tatjana Rundek is the Principal Investigator for the Transcranial Doppler Ultrasound (TCD) Core of [The Albert Einstein Study \(AES\) Program Project in Aging](#), a collaborative project. This is a Cerebral Hemodynamics Study of Aging of the AES program project aimed to study the vascular mechanisms of normal aging, MCI and dementia using TCD challenge test. It is funded by NIH/NIA.

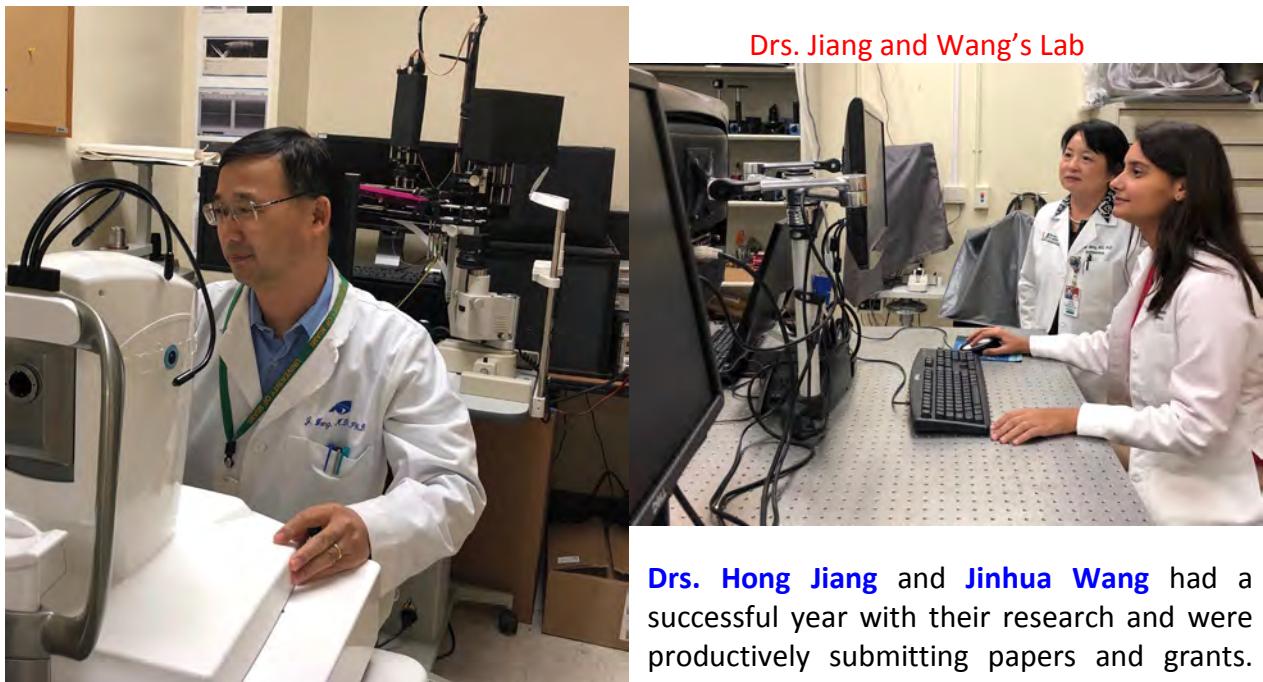
Dr. Tatjana Rundek is a Co-Investigator of the [Oral Infections, Carotid Atherosclerosis and Stroke \(INVEST\)](#) study, a study of a cohort study that examines the effect of chronic periodontal disease and inflammation as a risk factor for stroke and carotid atheroma progression at Columbia University (CU) in New York. Dr. Moise Desvarieux at CU is the PI (funded by NIH/NIDCR), and currently the extension of this study to assess cognitive performance and risk of periodontal disease on cognitive decline is under review at NIA.

Dr. Tatjana Rundek is the Stroke Adjudication Core investigator for the [Hispanic Community Health Study -Study of Latinos \(HCHS-SOL\)](#) Miami Field Center. The HCHS/SOL is a multi-center epidemiologic study designed to determine the role of acculturation in disease prevalence and to identify health risk factors in Hispanics/Latinos. Dr. Neil Schneiderman is PI. It is funded by the NIH/NHLBI.

Brain Vascular Imaging Phenotypes (VIP) and cognitive and neurodegenerative profile (VIP study) - **Drs. Tatjana Rundek** and **David Loewenstein** completed their first year of work in 2019. This year was spent preparing MRI scans for the completion of their first aim. Dr. Tatjana Rundek and team have dedicated maximum effort for the quality checks and assurance of the quality of the MRI acquisition and data completeness. They set up a quality assurance procedure and corrections for MRI data. The imaging team continued to prepare post-processing of the MRI data and a series of scripts for automatic and semi-automatic approaches for brain parcellations and reads. This process will speed up the MRI data analyses and interpretation. In addition, this is a critical step towards the fulfillment of all of the aims. Dr. Tatjana Rundek is the PI of the VIP study. Funded by FL DOH.

The [1FL ADRC](#) (Alzheimer's Disease Research Center) is a collaborative project between the University of Florida (Dr. Todd Golde), Mt. Sinai Medical Center in Miami Beach (Dr. Ranjan Duara), Florida International University and Florida Atlantic University. It was up for competitive renewal and was successfully funded this year. **Drs. Tatjana Rundek, David Loewenstein** and **Xiaoyan Sun** are the UM Investigators. The overall goal of the 1Florida Alzheimer's Disease Research Center (ADRC) is to advance the understanding of Alzheimer's disease and Related Disorders (ADRDs), especially in underrepresented minority groups, by leveraging the large numbers and diversity of older adults in Florida. Clinical Core activity at UM will focus on phenotyping African American participants. The Clinical Core will be a major source of support for developmental studies, grants, clinical trials, publications and training opportunities, as well as for integration into the National ADRC network. The 1FL ADRC educational Core will provide

resources to foster training and career development of upcoming clinicians and researchers. It will also provide educational activities relevant to ADRDs with the goals of improving knowledge and skills and building stronger coalitions to deliver better diagnoses and care to patients and their families.



Drs. Jiang and Wang's Lab

Drs. Hong Jiang and Jinhua Wang had a successful year with their research and were productively submitting papers and grants. Their "Clinical Applications of Ophthalmic Imaging" study has 137 study subjects enrolled. Analysis continues as well as the preparation for possible publications. The primary results may also be used in writing further grant applications. They have submitted a number of manuscripts, including: "Focal alteration of the intraretinal layers in neurodegenerative disorders" to the journal *Annals of Eye Science*; "Age-related focal thinning of the ganglion cell-inner plexiform layer in a normal population" to the journal *Aging and Disease*; "Characterization of the retinal vasculature in fundus photos using the PanOptic iExaminer System" and "Nutritional and Medical Food Therapies for Diabetic Retinopathy (a review)" to *Eye and Vision*. They submitted a proposal titled "The effect of circuit resistance training on retinal vascular and neuronal functions" to the University of Miami Scientific Awards Committee (SAC) of the Leonard M. Miller School of Medicine. They also received funding to research "Retinal biomarkers for monitoring vascular contributions to Alzheimer's Disease" from the Ed and Ethel Moore Alzheimer's Disease Research Program through the Florida Department of Health (DOH).

Dr. David Loewenstein is the Director of the Center for Cognitive Neuroscience at the

University of Miami Miller School of Medicine. He is involved in and leads an array of important research as follows: A Novel Computerized Cognitive Stress Test Designed for Clinical Trials in early Alzheimer's Relationship with Multimodal Imaging Biomarkers in Diverse Cultural Groups, funded by the National Institute on Aging (NIA) (PI); Middle-aged Offspring of late Alzheimer's Probands: Novel Cognitive and Biomarker Assessment, funded by the State of Florida (PI); New Cognitive Stress Tests and Multimodal Imaging Diverse Ethnic/Cultural Groups, funded by the State of Florida Ed and Ethel Moore Program (PI); Cognitive Stress Tests and Amyloid Load in Diverse Ethnic/Cultural Groups Project, funded the State of Florida Ed and Ethel Moore Grant Program (PI); Novel Detection of Early Cognitive and Functional Impairment in the Elderly Research study, funded by the NIH/NIA (PI); Data Core and Biostatistician for the Center on Research and Education for Aging and Technology Enhancement (CREATE IV), which is a multidisciplinary research project aimed at understanding how age-related changes in function impacts a person's ability to interact successfully with technical systems. It is funded by the NIH/NIA (Co-I); and A Precision-Based Assessment for Detection of MCI in Older Adults project, funded by the NIH/NIA (Co-I).



Dr. Loewenstein's Team at the Center for Cognitive Neuroscience and Aging

Dr. Elizabeth Crocco, our collaborator, has been working on several research studies sponsored by state and federal funds and pharmaceutical sponsored clinical trials. These include: Treatment of Psychosis and Agitation in Alzheimer's Disease (Lithium Study), funded by the NIA (PI for UM Site); Novel Detection of Cognitive and Functional Impairment in the Elderly, funded by the NIA (Co-I); A Consortium to Study Precision-based Computerized Assessment for the Detection of Mild Cognitive Impairment in Older Adults, funded by the State of Florida Department of Health, Ed and Ethel Moore AD Research Program (Co-I); A Non-pharmacological intervention for Patients with Alzheimer's Disease and Family Caregivers, funded by the NIA (Co-I); Precision-based assessment for the Detection of Mild Cognitive Impairment in Older Adults, funded by the NIA (Co-I); Non-invasive Ocular Screening Approach to Identify Early Biomarkers in AD study, funded by the Alzheimer's Association (Co-I); A randomized double-blind, placebo controlled, parallel group study to evaluated the efficacy and safety of CNP520 in participants at risk for the onset of clinical symptoms of Alzheimer's Disease, funded by Novartis (PI); A Randomized, Double-Blind, Parallel-Group, Placebo-Controlled, Dose-Rannfing study of Piromelatine in patients with mild dementia due to Alzheimer's disease, funded by Neurim Pharmaceuticals (PI); and A randomized, double-blind, placebo-controlled, two cohort parallel group study to evaluate the efficacy of CAD106 and CNP520 in participants at risk for the onset of clinical symptoms of Alzheimer's disease, funded by Novartis (PI).

Dr. Elizabeth Crocco is the Director of the University of Miami Memory Disorders Clinic (MDC), which is funded by an ongoing state of Florida Department of Elder Affairs (DOEA) Alzheimer's Disease Initiative (ADI) contract. As the Principal Investigator and Director of the clinic, she provides clinical and diagnostic services, research and training for individuals and caregivers about Alzheimer's disease or related disorders, and conducts clinical memory disorders research.

Dr. Regina Vontell's studies focus on perinatal brain injury and researching the white matter malformations that result in cerebral palsy and the additional cognitive impairments. The research concentration is on the cellular response to focal injury seen after white matter injury and how it cascades to secondary atrophy in regions such as thalamic and internal capsule. She has also correlated white matter injury with toll-like receptor (TLR) and microglia activation, which then might provide insight as to how these structures cope with inflammatory responses. In this research she shows that increases in both mRNA and protein expression leads to intracellular signals that can increase cytokine production and excessive autophagy. She is also working on a collaborative project with King's College London, assessing the morphology and pattern of radial glial expression in Trisomy 21 and euploid aged-matched brains. Recently, they found that from mid-gestation the pattern of expression of radial glia markers had subtle deviations from aged-matched euploid fetal brains. Future plans are to use Dr. Vontell's expertise in white matter injury and glial expression to investigate if other cells, such as lipid laden macrophages can be correlated with neuronal stress and/or loss.

Dr. Regina Vontell is a Co-Investigator and **Dr. William Scott** (a McKnight Scientific Advisory Board member) the Principal Investigator of The NIH NeuroBioBank and Tissue Repository at the University of Miami. It is one of six designated brain and tissue biorepositories in the nation. It was up for a competitive renewal this year and was successfully funded.

9.1.4. Update on the Schoninger Neuropsychology Program Directed by Dr. Bonnie Levin



Dr. Sacco and Dr. Levin's Team

Dr. Bonnie Levin and her team of post-doctoral fellows, undergraduate and graduate students had an accomplished year.

- **Drs. Sarah Getz** and **Bonnie Levin** continue to work in close collaboration with Drs. Grilli and Wilson (UA) and Dr. Ebner (UF) on a funded McKnight intervention pilot study that aims to identify correlates of susceptibility to deception and scamming in the elderly. Data collection will be completed in 2020, with plans to submit a larger R01 to the NIH.
- **Dr. Bonnie Levin** is co-investigator on a grant funded by FL- DOH (Govind Varan- PI) that is examining associations between measures of gut microbial dysbiosis and markers of intestinal permeability and microbial translocation with brain inflammation markers (e.g., myo-inositol), peripheral amyloid oligomers, lipopolysaccharides (LPS) and inflammation markers, and cognitive function in patients clinically-diagnosed with mild AD (n=25) and age-matched healthy controls (n=25).
- **Drs. Sarah Getz** and **Bonnie Levin** are co-investigators for the project Treatment options for age-related hearing loss that was submitted to the Patient-Centered Outcomes Research Institute. (PI: Sandra Prentiss, University of Miami Miller School of Medicine)
- **Dr. Sonya Kaur** received funding from the American Academy for Sleep Medicine Foundation to attend the Young Investigator's Research Forum in Bethesda, MD in April 2019.
- **Dr. Sonya Kaur** was hired as an Instructor in the Department of Neurology in November 2019. She has also become a fellow on a federally funded grant on Epigenetics of atherosclerosis and cognition (**Dr. Tatjana Rundek**, PI).
- **Dr. Bonnie Levin** is a co-investigator on a project funded by the Study of Latinos (SOL) entitled, The Effects of CBD + Hu211 in MTBI. She is in charge of clinical outcomes examining whether a combination therapy of CBD and HU211 influences recovery following a mild TBI. The purpose of the study is to develop a novel treatment that is readily available for mild to moderate TBI, that has a wide therapeutic window, can be administered orally after an injury, and has been demonstrated to be safe and effective with a low side effect profile.

Dr. Bonnie Levin's Cognitive Team published several manuscripts and two book chapters in 2019. The research themes are listed below (full citations in **Sections 2 and 3** of the report).

- The independent effect of subjective fatigue on neurocognitive function in middle aged to older adults.
- A history of adverse childhood events is uniquely associated with the fatigue subcomponent of the frailty syndrome in later life.
- The Phishing Email Suspicion Test, in which participants rate a series of phishing and non-phishing emails according to their level of suspicion. Together our task and model provide a framework for studying the cognitive neuroscience of email phishing detection in the lab.

- The link between mindfulness training (MT) programs and the working memory (WM) brain system. It suggests that given the centrality of WM in processes such as emotion regulation, problem solving, and learning, MT programs may be well positioned to promote desired outcomes.
- Findings that sleep quality accounts for most of the relationship between frailty and cognitive outcomes in middle aged to older adults without dementia.
- Do elevated mood symptoms lead to poorer outcomes following Deep Brain Stimulation (DBS) surgery? Findings indicated that preoperative mood symptoms were not associated with worsening cognitive, emotional or motor functioning following DBS surgery.
- The use of large data sets to understand the multi-faceted health trajectories associated with the aging process and the need to understand individualized profiles of risks and protective factors.
- The demographics of deep brain stimulation (DBS) surgery and underscored the need to reach out to women with PD who are underserved.
- The acute effects of a mysterious unidentified exposure, presumably stemming from a sonic origin that produced a pattern of hearing loss and cognitive dysfunction.

Dr. Bonnie Levin and her Fellow **Dr. Joshua Rooks**, et al. wrote the book chapter “Strengthening attention with mindfulness training in workplace settings” being published in *Mind, Consciousness, and the Cultivation of Well Being*. This chapter reviews current evidence on the effects of mindfulness training on cognitive and emotional functioning among those in high demand workplace settings. A summary of current research suggests that mindfulness may lead to greater well-being and strengthened attention for those in the workplace.

Dr. Bonnie Levin and colleague wrote the chapter “Special considerations for the neuropsychological interview of older adults” that was published in the *Handbook on the Neuropsychology of Aging and Dementia*. This chapter examines the focused interviewing techniques in the evaluation of the older adult with special attention on physical, behavioral and cognitive changes associated with advanced age.

Dr. Bonnie Levin and her trainees including students and fellows, presented several posters in 2019 which are listed below: (full citations in **Section 4** of the report)

- “Neuropsychological correlates of subjective fatigue in non-demented older adults and the moderating effect of physical activity” This poster presentation highlighted the independent effect of subjective fatigue on neurocognitive function in middle aged to older adults.
- “Ethnicity moderates the relationship between sleep quality and learning and memory” This poster presentation demonstrated that while poor sleep quality (as measured by the Pittsburgh Sleep Quality Index) predicted cognitive dysfunction in Non-Hispanic/Latinx older adults, these findings were not apparent in Hispanic/Latinx adults. These differences corroborate recent publications by Dr. Ramos highlighting a longer sleep phenotype as predictive of cognitive dysfunction in Hispanic/Latinx older adults.

- “Fatigue, Adverse Childhood Experiences, and Frailty in Later Life” This poster presentation demonstrated that a history of adverse childhood events is uniquely associated with the fatigue subcomponent of the frailty syndrome in later life.
- “Detecting Deceptive Information in Scamming Paradigms: A Training Intervention” This presentation highlighted the researchers’ achievements (including the development of an ecologically valid scam questionnaire, neuropsychological battery to assess scam detection profiles, and two IRB protocols) who were awarded the McKnight Inter-Institutional Pilot grant.
- “Relationship between sleep quality, frailty and cognitive dysfunction in non-demented middle aged to older adults” This poster presentation highlighted findings that sleep quality accounts for most of the relationship between frailty and cognitive outcomes in middle-aged to older adults without dementia.
- “Measuring frailty in middle and later years and its association with cognition” This poster presentation demonstrated support for the construct validity of the frailty phenotype among those in both mid-life and older age and that its negative effects on cognitive functioning are commensurate across the age spectrum.
- “Characterizing the Healthy Oldest Old: The McKnight Brain Aging Registry” This poster presentation was prepared by the investigators and collaborators of the four McKnight Brain Institutes involved in the McKnight Aging Registry (MBAR) study. It showcased data collected from cognitively unimpaired adults aged 85 and older enrolled in the McKnight Brain Aging Registry (MBAR).
- “System Segregation is related to Cognition in the Healthy Oldest Old: Findings from the McKnight Brain Aging Registry” This poster presentation was prepared by the investigators and collaborators of the four McKnight Brain Institutes involved in the McKnight Aging Registry (MBAR) study. It represents the collaborative efforts from the four McKnight sites examining the relationship between cortical network integrity and generalized cognition in the later stages of life.

[Dr. Bonnie Levin](#) and her team submitted and participated in the following grant proposals in 2019:

- **Dr. Bonnie Levin** is co-investigator on a NIH grant that is under review (Goldberg, PI) examining the relationship between copper homeostasis and cognitive performance in the Diabetes Prevention Program Outcomes Study (DPPOS), the long-term follow-up study to the Diabetes Prevention Program (DPP).
- **Dr. Bonnie Levin** is a co-investigator on a grant that is in the Department of Defense’s (DOD) pre-award budget review/audit process. The proposal, “A portable method for objective of fitness for return to duty,” is being supported through the “Transitional Technology for the Warfighter” program from the DOD. This project is designed to examine associations between vestibular dysfunction, audition and cognition.
- **Drs. Sarah Getz** and **Bonnie Levin** were consultants for “The Neuroeconomics of Phishing Susceptibility in Younger and Older adults” an R21 submitted to the NIH. (PI: Robert Wilson, University of Arizona).

- Drs. Sarah Getz, Katalina McInerney and Bonnie Levin were selected for the University of Miami Miller School of Medicine's limited internal submission competition for the Florida Department of Health's (DOH) Ed and Ethel Moore Alzheimer's Disease Research Program.
- Drs. Sarah Getz, Katalina McInerney and Bonnie Levin submitted "Detection and reduction of scam susceptibility amongst individuals with mild cognitive impairment and Alzheimer's disease: Calculating risk and educating caregivers," a pilot grant submitted for the Ed and Ethel Moore Alzheimer's Disease Research Program (PI: Dr. Sarah Getz).
- Drs. Sarah Getz and Bonnie Levin submitted the project "Neurocognitive correlates of scam susceptibility in age-related hearing loss," submitted for the McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss (PI: Dr. Sarah Getz, Mentor: Dr. Bonnie Levin).

9.1.5. Update on Neuroimaging MBI Core

Dr. Noam Alperin has been involved in writing 5 important manuscript publications this year. (Full citations in **Section 2** of the report). He describes the importance of these publications below:

- These papers are based on methodology we have developed to qualify different aspects of the distribution of white matter hypersensitive load (markers of small-vessels disease and impaired transependymal flow of CSF) within the brain. Our team applied this analysis to the NOMAS MRI database. The first author Michelle Caunca obtained an NIH grant to identify the potential of these markers and their link to other risk factors such as obesity.
- This work was enabled by a method our lab has developed to segment and qualify the morphology and sizes of the cerebral blood vessels. This work investigates the link between vascular morphology and cerebral hemodynamics.
- Our group has reported the first brain volumetry imaging-based study of the effect of poor sleep quality on brain atrophy of MCI signature regions in cognitively intact elderly subjects. These regions were significantly smaller (on the order of 7%) in poor sleepers compared with good sleepers. This finding in conjunction with unpublished results identifies that this pre-symptomatic phase is the most beneficial for the application of sleep intervention. The onset of symptoms is found to be the most beneficial for intervention. The finding from this study led to a follow up proposal we submitted to the FL DOH to assess the efficacy of cognitive behavior therapy to slow down rate of brain tissue loss in cognitively critical regions. Faced with aging global populations, the medical community has become increasingly interested in developing interventions to slow or prevent age-related cognitive decline. Sleep quality has been targeted as a factor that may help modulate the course of amnestic mild cognitive impairment and Alzheimer's, but the relationship between sleep and dementia disorders is still poorly understood. Our study reports that patterns of cortical and deep gray matter atrophy related to poor sleep quality impact Alzheimer's disease-related regions of the cortex

even in a population rigorously deemed unaffected by cognitive impairment, psychological disorders or dementia.

9.1.6. Update on Other MBI Research Performed by Trainees

Dr. Joyce Gomes-Osman has been working to develop a precision medicine approach to the delineation of effective exercise dose to achieve maximal cognitive benefits for older adults. She continues to work very effectively at different projects related to brain plasticity, cognitive health and walking function. The past year has been exciting and very productive for her. She has authored 3 additional peer-reviewed publications and presented her preliminary work in 8 posters at national meetings. In addition to the professional activities outlined below, she has welcomed her first son, Danilo Gomes Osman to her family. A summary of her professional activities is below.

- She has continued to make progress on her University of Miami Evelyn F. McKnight Pilot Grant. This project aims to examine the influence of a 4-week aerobic exercise regimen (moderate versus high intensity) on neurocognitive performance and neuroplasticity, or the brain's ability to adapt to changes imposed by experience, environment and aging itself. The study is ongoing with 12 participants having completed the program. Recruitment is anticipated to wrap up by the summer of 2020, with a goal of manuscript preparation for the Fall of 2020.
- In taking active steps toward examining dose-response relationships for exercise and cognition in aging adults, **Dr. Joyce Gomes-Osman** continues to make progress on the project that is part of her Career Development Award (KL2) by the Miami Clinical and Translational Science Institute. In this project, aging adults are participating in a 2-month exercise intervention, and she is examining neuroplasticity, neurocognitive performance, exercise capacity and genetic modification of response. Currently, 30 participants have enrolled, 16 have completed (with a goal of 80 total by December 2020.)
- **Dr. Joyce Gomes-Osman** was selected from a competitive pool of early career investigators at the University of Miami to be among the 4 participants at the prestigious *11th Annual International Certificate Course*, Eureka Institute for Translational Medicine that took place April 7th - 13th, 2019, in Syracusa, Italy. Eureka is a weeklong immersive program, that focuses on the fundamentals of translational medicine that trains scientists to be leaders in the translational medicine field through coaching, networking and mentorship opportunities. The Eureka Institute's vision is to develop translational medicine to address unmet needs. Its mission is to build and foster a global community of translational medicine professionals for the tangible benefit of patients and society as a whole. Its strategy is to catalyze, integrate and impact education, research and policy making in an international translational medicine ecosystem that benefits society.
- **Drs. Joyce Gomes-Osman** and **David Loewenstein** were selected as a model mentee-mentor pair to participate in an important research mentoring training and certification

program with the goal to set standards of prerequisite research mentoring training, developing mentoring skills and building successful relationships between mentors and mentees. CTSI Research Mentoring Program. December 2019-April 2020, Miami, FL.

- **Dr. Joyce Gomes-Osman** was invited to move her Neuromotor Plasticity Laboratory to the prestigious Miami Project to Cure Paralysis, at the Lois Pope Life Center. This move not only allowed more physical space for her team to conduct their research activities, but also many opportunities for collaboration and potential synergies with many other clinical and translational investigators.
- **Dr. Joyce Gomes-Osman** has been collaborating with **Dr. Tatjana Rundek** and the remainder of the University of Miami Bugher team investigating brain plasticity changes in individuals post-stroke who are undergoing combined exercise and cognitive training, exercise in isolation or stretching exercises. She is currently working on two manuscripts from this work to be submitted in 2020.
- **Dr. Joyce Gomes-Osman** is collaborating with the Alagoas State University for Health Sciences, in Brazil and is overseeing a study to evaluate the influence of an exercise literacy workshop to improve engagement in physical activity and cognitive performance in older adults. Thirty participants have completed the study and data analysis and manuscript preparation are underway.



Dr. Gomes-Osman's Team

Dr. Joyce Gomes-Osman's success in 2019 is related to her KL2 Career Development Award from the UM Clinical and Translational Science Institute (CTSI). She is grateful that her career trajectory changed, and this is the reason. The award has allowed her protected time to conduct research while being formally mentored by distinguished leaders in the field. The mentorship has exceeded any expectations in time and generosity. (**Drs. Tatjana Rundek & David Loewenstein** and Alvaro Pascual-Leone at Harvard). She is compiling important pilot data that will be the foundation of her independence as an investigator.

Dr. Scott Brown published two major peer-reviewed research papers on neighborhood greenness (e.g., vegetative presence such as tree canopy, parks) and health outcomes in ~250,000 Medicare beneficiaries: 1) *Wang et al. (2019, J. Am. Heart Assoc.)* linked higher levels of greenness to lower odds of four forms of heart disease (ischemic heart disease; heart failure; acute myocardial infarction; atrial fibrillation); 2) *Perrino et al. (2019, Brit. J. Psychiatry)* linked greenness to lower odds of depression. He continued research on his existing Robert Wood Johnson Evidence for Action Grant (funded 2018) on impacts of neighborhood greenness (e.g., parks) and greening interventions (e.g., tree-planting) to odds of six cardiovascular disease (CVD) diagnoses (e.g., heart disease; stroke) over time in low-income Miami Medicare beneficiaries. Given that cardiovascular disease is a risk factor for age-related cognitive decline, should findings suggest that greenness lowers the risk of CVD, then this might also suggest that greening (tree-planting) may be a possible intervention for reducing age-related cognitive decline at the population level.

Dr. Roger McIntosh has been working extensively on two projects. His first project is conducting research outside of HIV, which has shown that disruption of the anterior insula is associated with increased incidence of hypertension, arrhythmia and stroke, along with sympathetic over-arousal. Sympathetic-parasympathetic imbalance is frequently observed in older age and is linked to elevated cardiovascular risk. Although sympathetic-parasympathetic imbalance has been observed since the beginning of the HIV epidemic, there has been no formal investigation into the central etiology of autonomic dysfunction. While functional neuroimaging may be useful in determining the extent to which HIV or hypertension (HTN) disease state can predict dysautonomia, cytometric-based analyses might allow us to examine the role of sympathetic nervous system communication with bone marrow as it relates to endothelial cell health, function and vascular disease.

His second project is a proposed study that aims to first address this gap by using functional magnetic resonance imaging (fMRI) to identify patterns of brain activity and connectivity that confer lower HRV and higher blood pressure reactivity during rest, mental stress and psychological distress. Individual differences in patterns in cardio-autonomic reactivity will be compared between groups as a function of HIV and pre-hypertensive (HTN) status. Seventy-two HIV+ men and women on stable antiretroviral therapy will be recruited along with a matching sample of HIV- negative controls based on JCN-7 criteria for hypertension.

9.1.7. Update on Basic and Translational Science Research

Drs. Miguel Perez-Pinzon and **Kunjan Dave** led a team studying [Post-cerebral Ischemia Cognitive Impairment](#). Here is a detailed account of the research experiments that Dr. Kunjan Dave supervised. In order to understand the neurobiological mechanisms by which physical exercise (PE) protects and restores cognitive abilities after cardiac arrest (CA), Dr. Kunjan Dave and his lab team investigated the effect of PE on gene expression following CA in rats. Adult, male Sprague-Dawley rats were acclimated to treadmill walking (5 m/min for 5 min) for 8 days. They were then induced global cerebral ischemia by 8-minute asphyxia cardiac arrest. Physiological parameters were maintained within normal ranges during surgery. After 3 full days of recovery from surgery, rats were separated into sham or exercise subgroups. The exercise

subgroup ran on a treadmill set at 15 m/min for 30 minutes a day for 5 days while the sham group was exposed to a stationary treadmill for the same amount of time. Thirty minutes after the last treadmill session, rats were sacrificed, and the hippocampus collected for RNA preparations. Dr. Kunjan Dave's group then performed RNA-seq to assess genome-wide changes in hippocampal gene expression induced by PE post CA (five samples per group).

Analysis of the data resulted in 63 genes that were significantly upregulated and 32 genes that were significantly downregulated by PE post-CA. Validation of the RNA-seq data was performed by qRT-PCR analysis (n=5 per group) for 15 differentially regulated genes. To functionally categorize the genes differentially induced by PE post-CA, **Dr. Kunjan Dave** and team analyzed their data with Genevestigator software (<https://genevestigator.com/gv/index.jsp>). Unbiased analysis of the conditions that particularly affect the expression of the genes differentially induced by PE post-CA identified Alzheimer disease as the most significant neurological disorder associated with their gene list. Approximately 40% of the genes differentially induced by PE post-CA have been linked to Alzheimer's. Interestingly, 30% of the genes have also been shown to be related to physical exercise. There is a large overlap between the genes differentially induced by PE post-CA associated with Alzheimer's and exercise.

To functionally categorize the differentially expressed genes, GO analysis was performed with the EnrichR software. The most significantly enriched GO terms in the list of upregulated genes induced by PE post-CA are related to neuroinflammation, plasticity (long-term memory, p= 0.00007), cell death and transcriptional regulation (regulation of transcription, p=0.0004, and histone H3 deacetylation, p =0.02). Examples of upregulated genes involved in neuroinflammation include Stat1 and Egr1, transcriptional activators of post-ischemic inflammation that are also known to be involved in Alzheimer's neuropathology. Upregulated plasticity genes include Arc and Sgk1, also suggested to participate in the pathogenesis of Alzheimer disease through amyloid-beta regulation of synaptic activity. For the genes downregulated after PE post-CA, the most significantly enriched GO term was extracellular matrix organization. Thus, PE post-CA initiates a program that promotes plasticity and transcriptional reprogramming.

Exposure to recurrent hypoglycemia (RH) is common in diabetic patients receiving glucose-lowering therapies and is implicated in causing cognitive impairments. Despite the significant effect of RH on hippocampal function, the underlying mechanisms are currently unknown. **Dr. Kunjan Dave's** goal was to determine the effect of RH exposure on hippocampal metabolism in treated streptozotocin-diabetic rats. Hyperglycemia was corrected by insulin pellet implantation. Insulin-treated diabetic (ITD) rats were exposed to mild/moderate RH once a day for 5 consecutive days.

The effect of RH on hippocampal metabolism revealed 65 significantly altered metabolites in the RH group compared to controls. Several significant differences in metabolite levels belonging to major pathways (e.g. Krebs cycle, gluconeogenesis and amino acid metabolism) were discovered in RH-exposed ITD rats when compared to a control group. Key glycolytic enzymes including hexokinase, phosphofructokinase, and pyruvate kinase were affected by RH exposure. These results demonstrate that the exposure to RH leads to metabolomics alterations in the hippocampus of insulin-treated streptozotocin-diabetic rats. Understanding

how RH affects hippocampal metabolism may help attenuate the adverse effects of RH on hippocampal functions.

Dr. David Della-Morte is a **collaborator** on the following research projects:

- **Drs. David Della-Morte** and **Miguel Perez-Pinzon** are investigating the interaction of Peroxiredoxin 6 and Sirtuin 1 in inducing age-related neurodegeneration by using mice model of Prdx6 knockout. The experiments are ongoing and preliminary data analysis results will be used to submit a NIH R01 grant.
- **Dr. David Della-Morte** and Dr. Hung Wen Lin, Louisiana State University, New Orleans, are collaborating on a project aimed to determine the role of serum/glucocorticoid-regulated kinase 1(SGK1) in protecting against neuroinflammation and neurodegeneration. This project is funded with an AHA SDG grant. Experiments are ongoing to translate the preliminary data on cognitive diseases.
- **Dr. David Della-Morte** and Dr. Suhrud Rajguru, Department of Otolaryngology and Biomedical Engineering, University of Miami, have an open collaboration to investigate the role of hypothermia and antioxidant therapies against cochlear damage. Experiments are ongoing and as well as preliminary data collection. They resubmitted a NIH R01 project to develop applications of early-targeted temperature management strategies for hair cell and neuro-protection, and long-term preservation of hearing function. They also aim to submit an AHA Collaborative Grant in the next cycle.
- **Dr. David Della-Morte** and Dr. Camillo Ricordi are collaborating on the POSEIDON Trial to potentially translate therapy with high doses of Omega-3 and Vitamin D also to type 2 diabetes based on the promising results obtained in type 1 diabetes. A grant proposal has been submitted to the Italian Minister of Heath and the recruitment of patients is ongoing.
- **Drs. David Della-Morte** and **Tatjana Rundek** are collaborating on a project aimed to evaluate the association between a well-established biomarker of systemic inflammation the Arachidonic Acid/Eicosapentaenoic Acid (AA/EPA) ratio with biomarkers of carotid atherosclerosis and biomarkers of cognitive degeneration, in the MRI sub-study cohort from the Northern Manhattan Study (NOMAS). A NIH R21 grant proposal is projected for submission in February 2020.

Dr. David Della-Morte is **leading** the following projects: Role of SGK-1 in regulating eNOS activity in HCAEC; Pro-inflammatory Cytokine HMGB1 Increase Leptin Secretion with a TLR2/TLR4 Mechanism In Type 2 Diabetes Related Inflammation; Insulin and Exendin-4 prevent mutated Huntingtin increase at neuronal level; Sarcopenia, Diabetes Mellitus and Aging: New Role of Peroxiredoxin6.

Dr. Ami Raval continued with her research, which revealed that whole body vibration improves stroke outcome in nicotine-exposed rats. Additionally, post-stroke physical exercise reduces ischemic brain damage and improves cognition in reproductively senescent female rats. Lastly, nicotine alters brain energy metabolism and exacerbates ischemic injury in female rats.

Dr. Milena Pinto is expanding her knowledge and research of the role of mitochondria in neurodegenerative diseases. Her research methods and analyses are explained here. Neuronal

OXPHOS deficiency has been associated with a variety of late-onset progressive neurodegenerative diseases. She induced mitochondrial defects in different neuronal subpopulations, mimicking the mitochondrial function decline that occurs naturally with aging. In the work published this year, she induced OXPHOS deficiency in adult neurons by knocking out Cytochrome c (Cyt c). Cyt c is a heme-containing mitochondrial protein, with critical functions in both respiration and apoptosis. Consistent with these vital functions, somatic Cyt c mouse knockout is embryonic lethal. In order to investigate the sensitivity of postnatal neurons to Cyt c depletion, she developed a neuron-specific conditional knockout model. Neuron-specific Cyt c KO mouse (nCytcKO) was created by crossing the floxed Cyt c mouse with a CamKIIα-cre transgenic mouse, which deletes the floxed alleles postnatally. NCytcKO mice were normal at birth but developed an abnormal phenotype with weight loss, tremor, decreased sensorimotor coordination and sudden death between 12 and 16 weeks.

Histological analysis did not show major neuronal degeneration. Analyses of oxidative phosphorylation showed a specific reduction in complex IV levels. Markers of oxidative stress were also increased. This novel model showed that neuronal complex IV is destabilized in the absence of Cyt c. It also showed that ablation of Cyt c in neurons leads to severe behavioral abnormalities and premature death without detectable neuronal loss, suggesting that neurons have the potential to survive for extended periods of time without a functional OXPHOS.

Even though **Dr. Pinto's** main line of research is focused on neurodegenerative disorders, her contribution has also been essential in other fields where mitochondrial dysfunctions plays an important role, like aging, age-related cachexia, and mitochondrial diseases (Leber's hereditary optic neuropathy plus dystonia).

Dr. Milena Pinto is collaborating with Dr. Barry Baumel on the use of mesenchymal stem cells (MSCs) in the treatment of Alzheimer's disease. In recent years, the use of stem cells to reverse neurodegeneration has raised hopes toward a long-lasting treatment. In particular, mesenchymal stem cells are an attractive therapeutic possibility, due to their ease of isolation, low immunogenicity, and their ability to target multiple pathways involved in neuronal regeneration. The long-term goal of this project is to characterize the neuroprotective function of MSCs in a mouse model of Alzheimer's disease. The achievement of this goal will make it possible to build a "basic science" platform based on animal models at the University of Miami that can be translated directly into clinical practice at Jackson Memorial Hospital.

To achieve the goals of this study they used the following approach: they extracted and expanded MSCs from a healthy mouse donor, injected the cells into a mouse model of AD and followed the progression of the pathology in presence or absence of MSCs. In 2018 **Dr. Milena Pinto** completed most of the experiments planned and then started a new session of treatments this year. **Dr. Barry Baumel** and Dr. Milena Pinto are working with a new Post-Doc **Amanda Neves**, who will continue and finalize the project. This research will make a strong and lasting impact on our understanding of the use of MSCs as a new neuroprotective agent.

9.2. Future Research Plans

9.2.1. Upcoming Clinical Translational and Population-Based Research

Dr. Ralph Sacco will be working on the competitive renewal for NOMAS to begin to address other vascular and non-vascular contributors to cognitive decline and dementia.

Dr. Ralph Sacco submitted a Research Infrastructure proposal entitled, “Infrastructure Core Alliance for Research and Education for Stroke (iCARE for Stroke)” to create an innovative bioinformatic tool that will facilitate multidisciplinary and collaborative research. It is currently pending review.

Drs. Tatjana Rundek and **David Loewenstein** will continue working on the newly funded award from the Florida Department of Health (DOH) for the research project *Brain Vascular Imaging Phenotypes (VIP) and cognitive and neurodegenerative profile (or the VIP study)*.

Drs. Tatjana Rundek, David Loewenstein and **Xiaoyan Sun** will continue collaborating on the 1FL ADRC (newly named ADC) with the University of Florida (PI: Todd Golde) and start a new collaboration on the Clinical and training Core across 1FL ADC. They will participate in the 1FL ADC Clinical Core, Recruitment Core and co-direct Educational/Training Core in conjunction.

Dr. Xiaoyan Sun will be preparing a manuscript on the relationship between pulse pressure and cognition. She will be starting her new project on the reduction of neurogranin expression in post-mortem brains of Alzheimer’s disease.

The large grant application to the NIH/NIA titled Sleep in Neurocognitive Aging and Alzheimer’s Research (SANAR) that **Dr. Alberto Ramos** submitted this year is on target to be resubmitted for funding in 2020.

Dr. Noam Alperin along with **Drs. David Loewenstein** and **Alberto Ramos** submitted a grant application to the Florida Department of Health (DOH) this year. It is a follow up grant to a currently funded grant focusing on the role of sleep quality in aging related progression to dementia. The project title is “Lifestyle Stressors of Hippocampus and AD related brain regions: Potential for Intervention.” The two main aims of the project are to (1) Assess the differences in the “rate” of volume loss in these and other brain regions between the poor and good sleeper using follow up scans (already available through another study) taken approximately 2 years after the initial baseline scan used to obtain the above results. They will compare the age effect with the sleep quality effect on these volumes. This information will be useful for the development of morphological references for the assessment of the impact of sleep intervention. (2) The second aim is to assess the impact of a proven intervention to improve sleep quality based on cognitive behavior therapy (CBT).

Dr. Roger McIntosh will be working on a project that will comprise 36 virally-suppressed Latinas living with the Human Immunodeficiency Virus (LLWH). They will be randomized to either the English or Spanish arms of a written emotional disclosure (WED) intervention or writing about non-trauma related daily events. Psychosocial surveys, neurocognitive testing, functional

magnetic resonance imaging (fMRI), blood and saliva will be collected before and after the 4-week intervention period. It is hypothesized that compared to the English-WED and the non-WED writing conditions Spanish-WED will be associated with greater decline in PTS, greater verbal learning and memory, as well as lower neuroendocrine and inflammatory-immune reactivity to trauma recall-evoked stress.

In 2020, **Dr. Scott Brown** will start his research on the two new grants he received as Principal Investigator this year: 1) an Ed and Ethel Moore Alzheimer's Research Grant to examine the relationship of neighborhood greenness (e.g., parks) to risk for Alzheimer's disease in Medicare beneficiaries residing in low-income Miami neighborhoods; and 2) a Sylvester Cancer Center Pilot Grant from the University of Miami Sylvester Cancer Center to investigate the relationship of greenness to five cancer diagnoses in ~250k Medicare beneficiaries.

Dr. Scott Brown submitted two R01 proposals as Principal Investigator to the National Institutes of Health (NIH), which proposed to evaluate the relationship of neighborhood greenness (e.g., tree canopy) to health outcomes over time: (1) NHLBI (National Heart, Lung, Blood Institute) R01 proposal to investigate the relationship of greenness to cardiometabolic health outcomes (e.g., blood pressure; blood glucose) in the Study of Latinos (SOL); and (2) NIA and NINDS R01 proposal to investigate the relationship of greenness to stroke, cardiovascular disease and cognitive decline in the Northern Manhattan Study (NOMAS). The SOL R01 proposal received a score in the top 12%ile and he is currently investigating the possibility of funding by NHLBI/NIH. He is hoping for funding to work on these projects next year.

In 2020 **Dr. Anita Saporta** will conduct structural analysis with Freesurfer 5.3 and 6.0 of all available cases in the [McKnight Frailty Project](#). Once the primary focus of the MRI analysis is finished, she plans to do further research and write her first project (**Dr. Tatjana Rundek** as mentor) on exploring the brain aging processes in **normal aging** and in pathological conditions through the study of the cerebellum, using Freesurfer analysis. Her interest in this brain structure has arisen from the knowledge that the cortical contributions to age-related declines in motor and cognitive performance are well known, while the potential contributions of the cerebellum are less clear. The diverse functions of the cerebellum that go beyond motor function and include emotion, language and cognition, make it an important structure to investigate in aging.

9.2.2. Upcoming Basic and Translational Science Research

Dr. Kunjan Dave will be leading research on the project explained below. Post-stroke cognitive decline remains a major issue and no treatment is available to enhance recovery for sub-acute and chronic stroke, emphasizing the need for new therapeutic developments. The vast body of literature suggests that physical exercise improves cognitive function and in a recent study **Dr. Kunjan Dave** and team demonstrated that post-stroke physical exercise (PE) significantly enhances cognitive recovery in rats. Studies have shown that the forced treadmill exercises can reduce ischemic brain damage and improve synaptic plasticity, and learning and memory after stroke. Recent studies from their laboratory have shown that a regimen of treadmill PE is able to ameliorate cognitive deficits following middle cerebral artery occlusion (MCAo; a well established rat model of ischemic stroke) in young and 11-14 month old male rats. However,

aged rats were unable to run at the same speeds of the younger cohort, suggesting that as rats age, higher exercise intensities will be more difficult to attain. In addition, they observed that in 12-month-old reproductive senescent female rats running at the same intensity as the corresponding age cohort of male rats did not exhibit cognitive recovery post MCAo. These data along with clinical data, suggests that to require ailing, elderly smoker MCAo patients to adhere to a chronic PE regimen presents a major obstacle. Therefore, the main goal of this project will be to determine whether PE along with other therapies can ameliorate cognitive deficits in older cohorts of rats (male and female) that ensue from MCAo (plus nicotine).

Because neurodegeneration is the cause of several progressive diseases, **Dr. Milena Pinto** will be working on a new project that involves the use of mesenchymal stem cells (MSCs) in the treatment of frontotemporal dementia. Using the same approach utilized for the study of Alzheimer's disease, she injected two mouse models of FTD with MSCs and followed the evolution of their pathology.

Dr. Milena Pinto also submitted a research study for the Alzheimer Drug Discovery Foundation grant that is in the review process. Pending the outcome, she may be working on this project in 2020.

Dr. Regina Vontell is seeking to enhance the understanding of the deviations in brain development that occur in cases of Trisomy 21 by closely investigating the complex interplay between radial glia and neuronal development. Whilst current therapies target childhood and adulthood, this research could lead to earlier intervention designed to improve cognition and delay later cognitive decline.

9.2.3. Upcoming Education Program

The Education and Training Core of the UM McKnight Brain Institute led by our McKnight Education Director **Dr. Xiaoyan Sun**, will aim to:

- Provide education on normal cognitive aging and memory related disorders to medical students, graduate students, fellows, neurology residents, faculty and staff;
- Foster collaborative educational efforts between faculty and staff at the McKnight Brain Institute and Center for Cognitive Neuroscience and Aging (CNSA), Departments of Psychology and Psychiatry and the Brain Endowment Bank to promote learning and research collaboration in the studies of cognitive aging;
- Develop community education and outreach programs that focus on the aging population and brain health and;
- Deliver education and training via invited Grand Rounds speakers, weekly Research Meetings, multi-disciplinary Research Seminar presentations and Journal Clubs on important and relevant publications.

Additionally **Dr. Xiaoyan Sun** will focus on the following:

- Coordinating a brain-cutting program with Dr. Garbin Di Luca and Dr. Gultekin.

- Helping to coordinate and oversee in conjunction with [Dr. Barry Baumel](#) and [Dr. Tatjana Rundek](#), an Individual Career Development Plan (IDP) consisting of clinical and research components that will be developed with our new **Cognitive Behavioral Fellow, Michelle Marrero**. It will focus on distinguishing the characteristics of normal aging and brain changes from those due to pathological etiologies. This will be key to understanding the challenges and thereby the precision needed for diagnoses in this patient population. She will learn how to design a research project and to submit it to the Institutional Review Board (IRB) and how to write grant proposals, abstracts and manuscripts. Lastly, her IDP will include forming collaborations with cross-disciplinary partners and learning principles of team science.
- Working with the Miami-Dade Mayor's office on the coordination of the "Miami-Dade Mayor's Initiative on Aging: Your Brain" seminar series that will take place again at a different location in the Miami-Dade area. Additionally, efforts will be made to conduct the series in Spanish.
- The McKnight Journal Clubs and Research Seminars which will be based on core topics and categories to focus more intently on specific areas of research. Additionally, an emphasis will be placed on mentor-mentee teams co-presenting. A "How to be a mentor" workshop will take place as well.
- Continuing the brain cutting sessions started this year, and plan for dissemination in partnership with the Research Component of our CTSI.
- Planning for a greater integration of our MBI trainees in CTSI research, education and training programs (through [Drs. Ralph Sacco](#) and [Tatjana Rundek's](#) roles in our CTSI). This will include applying for KL2, pilot and EUREKA awards, the Connection Club for research, and applying to our MS in Clinical Translational Investigation (MSCTI) directed by [Dr. Tatjana Rundek](#).
- Integrating our trainees with other award educational/training opportunities such as AAN, NeuroNext/StrokeNet, NIH Clinical trial course, 1FL ADC and others.
- Branching out further than Miami-Dade County with our community education and outreach program by forming partnerships in Broward and/or Palm Beach Counties.

10. Technology Transfer

N/A

EDUCATIONAL PROGRAMS

SECTION 12



12. Educational Programs Focusing on Age-Related Memory Loss

Section 12 consists of the following sub-sections. (1) **General Education Program** (Community Outreach), the Evelyn F. McKnight Brain Institute Community Educational Program and (2) **Education of Trainees: Undergraduate, Medical and Doctoral Students, Post-Doctoral Students, Residents and Fellows at UM**: Evelyn F. McKnight Brain Institute Fellows; Evelyn F. McKnight Education Program at UM; The Schoninger Neuropsychology Program at UM; and Mentoring, Training and Teaching by UM McKnight Members and Collaborators.

12.1. General Education Program (Community Outreach)

Evelyn F. McKnight Brain Institute Community Educational Program

In her role as the education director, **Dr. Xiaoyan Sun** continued to develop a community education and outreach program via seminars and presentations with relevant topics related to the aging brain and brain health. Our Research and Administration Director **Stacy Merritt** coordinated the community outreach education program. In total, we reached approximately 400 people through our program.

This year our McKnight Brain Institute Education and Outreach Program formed a partnership with the Miami-Dade Mayor's office. We participated in ***The Mayor's Initiative on Aging: Your Brain*** program. We developed a seminar series to teach how aging affects the brain, what to expect, prevention and best practices. The series was held at a library in Pinecrest in South Miami on four consecutive Tuesday nights in October. The seminar series titles and topics are below.

- **Dr. Joyce Gomes-Osman** presented "Exercise for brain health, from evidence to practical advice" It focused on these two topics: *Staying physically active can turn back the clock of aging in the brain* and *Exercise, what's right for me?*
- **Dr. Sarah Getz** presented "How the aging brain can make us vulnerable and affect decision-making" The talk discussed: *Vulnerability with aging, and its effects, Brain changes that affect decision-making* and *Scams, education and prevention, healthy tips.*
- **Dr. Christian Camargo** presented on "How our brain changes as we age" which focused on these two premises: *What to expect as part of normal brain changes* and *When to be concerned about memory/cognition changes and what to do.*
- **Dr. Erika Marulanda-Londono** from our stroke team presented "How stroke affects the brain, what you need to know about stroke, before during and after." The seminar addressed: *Healthy steps to prevention, Education on F.A.S.T. and Post-stroke intervention.*

Tremendous effort was made by **Dr. Xiaoyan Sun** and **Stacy Merritt** to directly reach the aging population. Building on existing partnerships and forging new ones, presentations were arranged to disseminate vital information about the aging brain such as dispelling myths and teaching the importance of maintaining cognition and memory through healthy lifestyles. There were eleven of these presentations (full citations in **Section 5** of the report).

- **Dr. Katalina McInerney** gave a presentation on “Normal and Abnormal Aging: The Need for Neuropsychological Assessment.”
- **Dr. Sarah Getz** gave a presentation on “The Aging brain and decision making.”
- **Dr. Joyce Gomes-Osman** gave **three** presentations on “Exercise for brain health, from evidence to practical advice” to various aging audiences.
- **Dr. Christian Camargo** gave **six** presentations on “Aging and the Brain” to various aging audiences.

Dr. Bonne Levin’s team spent time teaching current and future health professionals this year. They organized an extensive community workshop. This workshop was given by several junior faculty led by Dr. Levin that took place at a Latino Center for Aging. “The need for neuropsychological assessment” presentations were given to a variety of professionals including health care practitioners, reporters, politicians and philanthropists interested in serving Hispanic/Latino older adults. Its aim was to inform them of the differences between normal and abnormal aging, the benefit of neuropsychological evaluations and to promote ongoing research studies at our institution.

12.2. Education of Trainees: Undergraduate, Medical and Doctoral Students, Post-Doctoral Students, Residents and Fellows at UM

Evelyn F. McKnight Brain Institute Fellows

We had two Fellows as of the fall of 2019. Our Evelyn F. McKnight Research Fellow continued in her second year and we welcomed our first Cognitive and Behavioral Clinical Fellow.

Evelyn F. McKnight Research Fellow

Dr. Anita Saporta (IMG) began serving her second year as the Evelyn F. McKnight Research Fellow in 2019. She is trained in pediatric neurology and neuroimaging research in multimodalities (mainly MRI and PET) and she collaborates with multiple projects under the mentorship of **Dr. Tatjana Rundek** and her collaborators. Her main role with the McKnight Research team is in the post-processing of MRIs for subjects enrolled in the McKnight Frailty Registry and other MBI research utilizing structural MRI. These processing techniques focus on brain structural analysis as described below.



Regional brain volumes: Regional analysis is being done on the 3D T1 MPRAGE images with FreeSurfer 5.3 and 6.0 (<http://surfer.nmr.mgh.harvard.edu>). This MRI software package is comprised of a suite of automated tools for segmentation, re-construction, and derivation of regional volumes and surface-based rendering. The FreeSurfer 5.3 pipeline produces 115 cortical and subcortical volumetric measures, and 6.0 adds hippocampal subfields volumes (and other structures in its beta version). The primary focus of studying the aging brain is on exploring volumetric differences in hippocampal volumes as well as other structures early affected in those at AD risk (e.g., precuneus, entorhinal cortex, anterior cingulate and posterior cingulate regions), and in the volumetric changes in the ventricular spaces that have been shown to be early markers as well.

Regional cortical thicknesses: In addition to regional volumes, the FreeSurfer analysis also provides measurements of regional cortical thicknesses. This analysis provides the framework to study the relationship between the characteristics of cortical thinning and relate them to normal or abnormal aging changes, with or without cognitive decline. Over the past year, [Dr. Anita Saporta](#) has also started to collaborate on other projects, including the [Brain Vascular Imaging Phenotypes, Vascular Comorbidities and the Risk for Alzheimer Disease: The Florida VIP Study of AD Risk](#). For this project, she works under [Dr. Tatjana Rundek's](#) mentorship (Study PI) and the sub-investigators on not only MRI structural analysis with FreeSurfer software, but on the development of alternative methods to quantify silent cerebrovascular disease related lesions as white matter hyperintensities.

[Dr. Anita Saporta](#) also works on the [McKnight Frailty Project](#) under [Drs. Bonnie Levin](#) and [Katalina McInerney](#) conducting medical chart reviews.

University of Miami Department of Neurology, Cognitive and Behavioral Clinical Fellow

In late 2019, a new Cognitive and Behavioral Neurology Fellow was welcomed to the neurology department and the McKnight Brain Institute. [Dr. Michelle Marrero](#) earned a medical degree with Honors from the University of Puerto Rico School of Medicine. During those four years, she focused her research on the areas of neurology and behavioral sciences. She then completed a Neurology Residency Program at the University of Miami, Jackson Memorial Hospital. She is passionate about brain health and the integrative treatment of the person as a whole, taking into consideration the physical, emotional, nutritional, spiritual and environmental influences that contribute to health and brain wellness. [During her Fellowship](#), she will study and conduct research on memory disorders and the impact of neurological damage and disease on behavior, memory and cognition.



Evelyn F. McKnight Education Program at UM Directed by Dr. Xiaoyan Sun

Dr. Xiaoyan Sun organized and coordinated a number of educational and training activities including:

- Brain cutting teaching sessions including a session with **Dr. Regina Vontell** that was taught at the University of Miami Jackson Memorial Hospital (UM/JMH) Neurology Brain Cutting Conference ("A 51-year-old Man with progressive visual complaints"). Dr. Xiaoyan Sun worked with the chief resident of the neurology program and staff from the Brain Endowment Bank to initiate a brain cutting teaching program for resident and house staff.
- Multi-disciplinary Research Seminars (**Table 1**) and Journal Club interactive sessions (**Table 2**).
- Together with **Drs. Sacco and Rundek**, organized a neuroscience course to MD and MD MPH students in the spring of each year.
- Clinical shadowing and mentoring program in the Cognitive Neurology Fellows clinic. She also instituted the memory disorders clinic 2-week clinical rotation for 3rd and 4th year neurology residents. This rotation helps the residents understand memory-related disorders. Residents learn a systemic approach to diagnosis and treatment of patients with memory related disorders.
- Observership for neurology residents to learn neuropsychological testing and discuss the neuropsychological findings with our neuropsychologists.
- **Dr. Xiaoyan Sun** is a core faculty for the ACGME Accreditation Data System of UM, Neurology Resident Program. She also gives a lecture providing an overview of dementia to psychiatry residents every year.
- A lecture series in which cognitive neurology and geriatric psychiatry faculty give lectures to neurology residents about diagnosis and management of memory related disorders during cognitive neurology month.

As part of our goal to educate within the university across disciplines and departments, we hosted three prestigious outside invited speakers. Their presentations were geared towards educating students, trainees, post-doctoral fellows, medical residents, faculty and staff.

- **Our Special Invited Speaker Dr. Brian Kennedy, PhD** Yong Loo Lin School of Medicine, NUS, Singapore joined us on May 7th to present "Aging Interventions Get Human" and to host a collaborative dialogue about aging research afterwards. **Dr. Kennedy** is a distinguished professor, in the departments of biochemistry and physiology. He is the Director of the National University Health System (NUHS) Centre for Healthy Ageing in Singapore. He is a professor at Buck Institute for Research on Ageing, in Novato, California. He is also an adjunct professor at the Leonard Davis School of Gerontology, USC in Los Angeles, California. His research in the Kennedy lab is directed at understanding the biology of aging and translating research discoveries into new ways

of delaying, detecting, preventing and treating human aging and associated diseases. His research employs several research strategies to understand the biology of human aging and to develop translational approaches. He uses multiple model organisms and systems for these purposes, relying on non-vertebrates for discovery-based approaches to generate hypotheses regarding aging mechanisms and studies in mammals to test hypotheses and to develop translational strategies.

- **Our Special Invited Speaker Dr. Ron Lazar, PhD, FAHA, FAAN** University of Alabama, Birmingham joined us on June 7th to present “Vascular Cognitive Impairment: Insights from Vascular Interventions.” He is the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging and the Director of the Evelyn F. McKnight Brain Institute at UAB. As part of our commitment to partner with our Inter-Institutional McKnight colleagues, **Dr. Lazar** met with faculty from our department as well as with cross-disciplinary faculty to discuss future research and collaborations with emphases on reversible causes of cognitive decline, risk-factor modification to promote cognitive resiliency and recovery after stroke.
- **Our Special Invited Speaker Dr. Vladimir Hachinski, CM, MD,** University of Toronto, DSc, FRCPC, FRSC joined us on June 26th to present “Origin, Status and Future of the Hachinski Ischemic Score” which was followed by a lucrative roundtable discussion in which future collaborations with our McKnight members, collaborators and trainees were discussed. **Dr. Hachinski** has transformed the understanding, diagnosis, treatment and prevention of the two greatest threats to the brain: stroke and dementia. He co-discovered a link between Alzheimer's and stroke and introduced new concepts and a new clinical diagnosis tool; the Hachinski Ischemic Score for identifying the treatable components of dementia. He co-founded the world's first successful acute stroke unit, now the standard of care. Dr. Hachinski was Editor-in-Chief of *Stroke*, the leading publication in the field for an unprecedented 10 years (2000-2010).

The Schoninger Neuropsychology Program at UM Directed by Dr. Bonnie Levin

- **Drs. Bonnie Levin, Sarah Getz and Katalina McInerney** hold neuropsychology teaching rounds for the Schoninger Neuropsychology Program. Weekly teaching rounds provide an opportunity to review individual cases and address issues related to clinical care.
- **Dr. Bonnie Levin** mentored five Post-Doctoral Fellows this year. Additionally, she had 3 undergraduate and graduate students on her trainee team.
- **Dr. Bonnie Levin** gave lectures in the Department of Psychology to upper level PhD students in the Behavioral Medicine, Clinical and Neuroscience tracks.
- **Dr. Sonya Kaur** presented “Neuropsychology of Parkinson’s Plus Disorders” to the University of Miami Miller School of Medicine during Neuropsychology Rounds. This presentation aimed to educate junior neuropsychology fellows about the cognitive/behavioral sequelae of Parkinson’s Plus Disorders.

- **Dr. Sonya Kaur** presented “Neuropsychology of Alcohol & Alcohol Use” to the University of Miami Miller School of Medicine during Neuropsychology Rounds. This presentation aimed to educate junior neuropsychology fellows about the independent neurobiological and cognitive effects of alcohol use and alcohol use disorders.
- **Drs. Sonya Kaur** and Mitchell Slugh presented “Introduction to Neuropsychology” for the University of Miami Miller School of Medicine, Neurology Resident Lecture Series. This presentation aimed to educate junior neurologists about the role of neuropsychologists.
- **Dr. Sonya Kaur** presented “Neuropsychology in Epilepsy” for the Epilepsy Boot Camp Lecture Series at the University of Miami Miller School of Medicine. This presentation aimed to educate incoming epilepsy fellows about the role of neuropsychology in a comprehensive epilepsy center.
- **Dr. Katalina McInerney** presented “Recruiting the oldest old for clinical research.” This presentation reviewed various strategies for recruitment of the oldest old for research protocols and focused on those strategies that could be particularly beneficial in continued recruitment for the McKnight Brain Aging Registry (MBAR).
- **Dr. Sarah Getz** attended the University of Miami Miller School of Medicine Master’s in Clinical Translational Investigation grant writing course (“Introduction to Writing for Clinical and Translational Science”), led by **Dr. Tatjana Rundek**. This was a tremendous opportunity for her as a junior investigator to learn principles of scientific writing that have already helped her to prepare several grant submissions.

Mentoring, Training and Teaching by UM McKnight Members and Collaborators

Dr. Ralph Sacco mentors the following students (Mentees with funding are listed in **Section 6.1.**)

- **Michelle Caunca** our McKnight MD/PhD student recently obtained her doctoral degree in Epidemiology in May 2019 after successfully completing her dissertation (which was funded by an F30 Fellowship Award) entitled “Effects of White and Gray Matter Integrity on Cognition in a Multi-Ethnic Cohort.” Analysis of the regional WMHV and cortical thickness data is a major part of her dissertation work. This year she has been co-author on two NOMAS manuscripts and has presented her work at the American Neurological Association (AAN) 2018 in the Plenary Session “Vascular Contributions to Neurodegeneration,” and at the American Academy of Neurology 2019. She is currently finalizing dissertation-related manuscripts and is returning to complete her clinical clerkships (MD anticipated 2021).
- **Sofia Oluwole** an MD/PhD student, recently obtained her doctoral degree in Epidemiology in May 2019 having successfully defended her dissertation “Disparities in Acute Ischemic Stroke Care and In-hospital Outcomes.” She is currently finalizing dissertation-related manuscripts and is returning to complete her clinical clerkships (MD anticipated 2021).

Dr. Tatjana Rundek directs the Clinical Translational Research Division in the Department of Neurology. She is also Director of the MS degree in Clinical Translational Investigation, and Director of the KL2 program and translational workforce development at the UM CTSI. She is a career development and research mentor to junior faculty and trainees. She helps to develop their research and grant writing skills and to foster their careers in cognitive aging. This year, she has been involved in the mentoring of some talented junior faculty listed below.

- **Sonya Kaur, PhD** (MBI research instructor)
- **Sarah Getz, PhD** (MBI research instructor)
- **Tali Elfassy, PhD** (KL2 and K01 recipient)
- **Ayham Alkhachroum, MD** (AAN career development award candidate)
- **Christian Camargo, MD** (AAN/McKnight career development awardee)
- **Joyce Gomes-Osman, PT, PhD** (KL2 recipient)
- **Alejandro Mccluskey** (MSCTI student)
- **Saeed Alahmari** (MSCTI student)
- **Victor Del Brutto** (StrokeNet Scholar)
- **Jennifer Schmaus** (MS candidate in Psychology)
- **Olivia Gardner** (PhD candidate in Genetics)

Dr. Tatjana Rundek is the Training Director for the ongoing [University of Miami: Network of Excellence in Neuroscience Clinical Trials \(NeuroNEXT\)](#). The goals of this project are to enhance quality and efficiency of NIH trial implementation at the University of Miami and to leverage existing institutional strengths to enhance NeuroNEXT consortium activities. (PI Michael Benatar). It is funded by NIH/NINDS.

Dr. Tatjana Rundek continues to teach two classes at the Medical School MSCTI: *Team Science and Entrepreneurship* in the fall and *Introduction to Writing for Clinical and Translational Science* in the spring.

Dr. Tatjana Rundek is the Training Director for the [Miami Regional Coordinating Center for NINDS Stroke Trials Network](#). The major goal of this research is to function effectively as a Regional Coordinating Center for the NINDS stroke trials and to enhance quality and efficiency of NINDS stroke trial implementation at the Miami site. (PI Jose Romano; **Ralph Sacco**) It is funded by the NIH/NINDS.

Dr. Tatjana Rundek is a Co-Investigator for the [Mechanisms of Early Recurrence in Intracranial Atherosclerotic Disease \(MyRIAD\)](#) study. The research objective is to determine the mechanisms and predictors of stroke in patients with symptomatic Intracranial Atherosclerotic Disease. (PI Jose Romano) It is funded by the NIH/NINDS.

Dr. Elizabeth Crocco continues to educate students, Fellows and Residents. A description of her curricula follows.

- “Geriatric Psychiatry Lecture Series Jackson Memorial Hospital (JMH) General Psychiatry Residency Training Program” She develops and implements comprehensive geriatric specialty lectures in all 4 years of general psychiatric residency training. The topics include: normal aging, late-life schizophrenia, late-life depression, ECT, bereavement,

neurodegenerative disorders, Alzheimer's, Vascular, Lewy body disease and caregiving issues.

- “Weekly Case Conference Jackson Memorial Hospital (JMH) Geriatric Psychiatry Training Program” She coordinates and supervises all geriatric psychiatry fellows’ weekly presentations of patient case histories, including biological, psychological and sociological data and formulates an integrated treatment plan.
- “Weekly Journal Club Jackson Memorial Hospital (JMH) Geriatric Psychiatry Residency Training Program” She handles the weekly coordination and supervision of all geriatric psychiatry fellows with the objective of critical evaluation of peer-reviewed, original research articles and applies this knowledge to the care of their geriatric patients.
- “Geriatric Psychiatry Seminar Jackson Memorial Hospital (JMH) Geriatric Psychiatry Residency Training Program” She develops and implements weekly core curriculum-focused conferences that cover knowledge and skill areas that are necessary to the successful completion of the geriatric psychiatry training program and commonly seen diagnoses in geriatric psychiatry.
- “Doctoring II: Dementia Small Groups Miller School of Medicine University of Miami” She leads small groups of 20-25 medical students in diagnosis and evaluation of cognitive disorders.

Dr. David Loewenstein’s mentors these dissertation students.

- Kimberly Capp - Nova Southeastern University
- Ana Maria Diaz Santos - Carlos Albizu University

Dr. Roger McIntosh mentors **Judith Lobo, MA** a doctorate student on the functional neural correlates of super-aging.

Dr. Joyce Gomes-Osman is currently mentoring two PhD Students from the Department of Physical Therapy at the University of Miami Miller School of Medicine (Jordyn Rice, DPT, Danylo Cabral, PT), who have now been fully trained in data collection procedures involving non-invasive brain stimulation, functional walking and cognitive function testing. In addition, during this year she has mentored a Masters student who works as a research associate (Christina Nunez), supporting these efforts and learning about the exciting studies being carried out in Dr. Gomes-Osman’s lab.

Dr. Joyce Gomes-Osman taught a 3-credit graduate level class to physical therapy students - Neuroscience II 641. In this class, students learn about clinical neurophysiology and functional performance in the healthy nervous system and in neurologic conditions.

Dr. Ami Raval taught the following courses this year.

- Cellular and Molecular Neuroscience to undergraduate students
- Neural Mechanisms of Disease to undergraduate students
- Faculty Overview of Research and Undergraduate Mentoring
- Masters level course in the Department of Epidemiology - a new course, offered for the first time in the Spring of 2019
- Facilitator for MD-MPH Problem Based Learning for 1st and 2nd year medical students

Dr. Raval mentors three students who are all majoring in neuroscience.

- Qismat Niazi
- Sonya Patel
- Verun Reddy

Dr. Milena Pinto mentors three trainees. She is guiding a Post-Doc, Amanda Neves in the interpretation of research results and using them to prepare manuscripts and presentations. She mentors Chiara Villa, visiting from the University of Milan, Italy. She is also mentoring an undergraduate student Chelsey Guastucci.

This year **Dr. Milena Pinto** taught undergraduate students the principles of good laboratory practice (pipetting, solution preparation and calculations), as well as basic laboratory techniques (PCRs, Western Blots).

Dr. Regina Vontell mentors two graduate students in the Neuroscience Graduate Program.

Dr. Susan Blanton is the course director and lecturer for HGG 640, Family Based Studies and Analysis, and HGG 680, Genome Ethics and Public Policy.

Table 1. 2019 Evelyn F. McKnight Brain Institute Research Seminars

Speaker	Area of Expertise	Date	Title
Noam Alperin, PhD	Neuroradiology	January 23 rd	<i>MRI Analysis, White Matter Hyperintensities in the Aging Brain</i>
David Della-Morte, MD	Neurology	February 20 th	<i>Treatment With Insulin and Exendin-4 Reduces Apoptosis and Mutated Huntingtin Accumulation in Neurons</i>
Bonnie Levin, PhD	Neuropsychology	February 27 th	<i>2019 International Neuropsychological Society (INS) Meeting Research Current Research Topics</i>
Brian Kennedy, PhD <i>Special Invited Speaker</i>	Biology & Physiology	March 7 th	<i>Aging Interventions Get Human</i>
Che Liu	Neuroradiology	April 3 rd	<i>The influence of gender and age on rest state neural networks measured by fMRI: preliminary MBAR results</i>
Regina Vontell, PhD	Neurology	May 15 th	<i>Blood Vessel Regulation and White Matter Pathology</i>
Ron Lazar, PhD <i>Grand Rounds Speaker</i>	Neuropsychology	June 7 th	<i>Inter-Institutional Research Collaborations</i>
Andrew Dykstra, PhD	Auditory Cognitive Neuroscience	June 12 th	<i>Identifying physiological markers of conscious audition: "Progress, problems, and potential applications</i>
Vladimir Hachinski, MD <i>Special Invited Speaker</i>	Neurology	June 26 th	<i>Origin, Status and the Future of Hachinski Ischemic Score</i>
Joseph Signorile, PhD	Neurophysiology	July 24 th	<i>Muscle to Mind</i>
Scott Brown, PhD	Public Health	August 21 st	<i>The Role of Neighborhood Greenness & Greening Interventions in Successful Aging</i>
David Loewenstein, PhD	Neuropsychology	September 4 th	<i>New Methods of Quantifying Semantic Intrusions and Relation to Different Biomarkers in Alzheimer's Disease and Related Disorders</i>

Che Liu	Neuroradiology	October 16 th	<i>The Effect of Aging on Resting State Connectivity of Predefined Networks in the Brain</i>
Che Liu	Neuroradiology	October 23 rd	<i>Gender differences in brain morphology and function in the cognitively intact oldest old: MRI findings from McKnight Brain Aging Registry (MBAR)</i>
Sonya Kaur, PhD	Neuropsychology	November 6 th	<i>Neuropsychological Assessments: Fact And Fiction</i>
Bonnie Levin, PhD	Neuropsychology	November 13 th	<i>The MoCA and MMSE Assessments: What do they tell us?"</i>
Timothy Morris, PhD <i>Special Invited Speaker</i>	Physical Therapy & Cognitive Science	November 20 th	<i>Results From the Barcelona Brain Health Initiative - Exercise, Cognition and TMS-EEG in Healthy Aging</i>
Amanda Ferreira Neves, PhD	Neurology	December 4 th	<i>Mesenchymal stem cells treatment on a mouse model of Alzheimer's disease</i>
Eddie Tiozzo, PhD	Neurology	December 11 th	<i>The Bugher Study: The Challenges of a 4-Year Stroke Trial</i>

Table 2. 2019 Evelyn F. McKnight Brain Institute Journal Clubs

Speaker	Area of Expertise	Date	Title
Judith Lobo, MA	Cognitive Neuroscience	March 6 th	<i>Physical activity over a decade modifies age-related decline in perfusion, gray matter volume, and functional connectivity of the posterior default-mode network—A multimodal approach</i>
Josh Rooks, PhD	Neuropsychology	April 17 th	<i>Mindfulness</i>
Nik Banerjee	Neuropsychology	April 24 th	<i>LADIS study review</i>

Noam Alperin, PhD	Neuroradiology	June 23 rd	<i>Radiomics (The Genomics of Radiology)" "Radiomic Texture Analysis Mapping Predicts Areas of True Functional MRI Activity</i>
Xiaoyan Sun, MD, PhD	Neurology	July 10 th	<i>Different Relationship Between Systolic Blood Pressure and Cerebral Perfusion in Subject With and Without Hypertension that was in Hypertension</i>
Christian Camargo, MD	Neurology	August 14 th	<i>NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease</i>
Anita Seixas Saporta, MD	Neurology	August 28 th	<i>Brain volumes and cortical thickness on MRI in the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER)</i>
Katalina McInerney, PhD	Neuropsychology	September 11 th	<i>Recruiting the Oldest-Old for Clinical Research</i>
Joshua Rooks, PhD	Neuropsychology	September 23 rd	<i>A 2 year multi-domain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial</i>

COLLABORATIONS

SECTIONS 13-14



13. Collaborative Activities with other McKnight Brain Institutes, Institutions and Research programs

Drs. Tatjana Rundek and **Bonnie Levin** worked on the submission of a U19 grant entitled, Precision Aging Network: Closing the Gap Between Cognitive Healthspan and Human Lifespan, in collaboration with a team led by Carol Barnes and Lee Ryan at the University of Arizona. It was not funded and the resubmission is planned in the coming year.

McKnight Brain Aging Registry (MBAR) - **Dr. Tatjana Rundek**, the PI for the MBAR study together with other leaders at the University of Miami **Drs. Bonnie Levin** and **Noam Alperin**, collaborates with the 3 other McKnight Brain Institutes. **Section 9**. The collaborative MBAR report with information from all sites that was submitted to the Trustees can be found in **Appendix I**.

The McKnight Brain Institutes Inter-Institutional McKnight Brain Aging Registry (MBAR) Grant Initiative. The MBI sites are in the process of developing a proposal to the NIA that will expand on findings from the MBAR study. Following discussions with and recommendations from the 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 working to develop this initiative into an NIA grant submission for the coming year under the leadership of Dr. Gene Alexander and the MBAR Executive Committee (Drs. Gene Alexander, Ron Cohen, Ron Lazar, Kristina Visscher, **Bonnie Levin** and **Tatjana Rundek**). The Publication committee and publication policy has been developed and further scientific goals for MBAR have been discussed. The primary aims are in development.

The MBRF Cognitive Aging and Memory Intervention Core - **Dr. Tatjana Rundek** is involved in the McKnight funded pilot-study awards (2 per year) that require collaboration among two or more McKnight Brain Institute sites on a pilot-study that researches interventions to reduce age-related memory loss and cognitive decline. The goal is to facilitate grant submissions for extramural funding sources for multi MBI site cognitive aging and memory intervention trials.

Uncovering Risk Profiles of Deception and Mitigating Susceptibility to Scamming in Midlife and Older Age: A Novel Intervention Tool - **Drs. Sarah Getz** and **Bonnie Levin** continue to work in close collaboration with Drs. Grilli and Wilson (UA) and Dr. Ebner (UF) on this McKnight funded intervention pilot study that aims to identify correlates of susceptibility to deception and scamming in the elderly. **Section 9**.

The McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss - This award is funded by the McKnight Brain Research Foundation through the American Brain Foundation and the American Academy of Neurology. It aims to encourage

young investigators to engage 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.

The [1FL ADRC \(Alzheimer's Disease Research Center\)](#) study was up for a competitive renewal that was successfully funded. This is a collaborative project between the University of Florida (Dr. Todd Golde, PI), Mt. Sinai Medical Center in Miami Beach, Florida International University and Florida Atlantic University. **Drs. Tatjana Rundek, David Loewenstein** and **Xiaoyan Sun** are the UM Investigators and Core co-Leaders. [Section 9](#).

14. Collaborative Activities With Non McKnight Brain Institutes, Institutions and Research Programs

Drs. Ralph Sacco and **Tatjana Rundek** have active research programs with the NOMAS team at Columbia University in NY. Dr. Tatjana Rundek is a collaborative clinical researcher with established extensive collaborations on these large NIH-funded studies at Columbia University (INVEST and U01 eMERGE), at Albert Einstein in the Bronx (Einstein Aging Study), and national and international consortia (NINDS SiGN, ISGC).

Drs. Ralph Sacco and **Tatjana Rundek** have an active genetic research program as a part of the Family Study with **Dr. Susan Blanton** and Dr. Liyong Wang from the Miami Hussman Institute for Human Genomics.

Drs. Ralph Sacco and **Tatjana Rundek** participate and collaborate with the Hispanic Community Health Study- Study of Latinos (HCHS/SOL) with the Miami Site PI, Dr. Neil Schneiderman. They are also involved with Dr. Schneiderman's T32, one of the longest standing T32 training programs on cardiovascular risk funded by the NHLB.

The funding of the Florida Department of Health (DOH) grant through the [Ed and Ethel Moore Alzheimer's Disease Research Program Brain Vascular Imaging Phenotypes \(VIP\)](#) and cognitive and neurodegenerative profile (VIP study) has fostered our collaborative relationship with Mount Sinai Medical Center in Miami Beach, the University of Florida McKnight Brain Institute, Florida International University and Florida Atlantic University. **Dr. Tatjana Rundek** spent time this year overseeing the multi-institutional project. The study aims to determine (1) the burden of brain vascular imaging phenotypes (VIP) of small vessel disease; (2) the association of modifiable vascular factors and comorbidities with VIP; and to (3) Investigate the impact of VIP and vascular risk factors on cognitive performance. In the past year, most of time was spent on the preparation of MRI for analyses from high resolution structural T1 imaging, T2 weighted imaging, susceptibility weighted imaging (SWI), and diffusion-weighted imaging (DWI). In total, MR imaging datasets were acquired for 314 subjects that will be analyzed in this

study. This effort has been carried out in collaboration with the investigators at Florida International University, which is a Core member of the 1Florida ADRC consortium. Our team at the University of Miami (Dr. Mohammed Goryawala and Dr. Anita Seixas Dias Saporta) have been working towards the development of semi-automatic approaches towards the quantification of white matter hyper intensities using T2 weighted images.

The investigators from the University of Miami (Dr. Rundek as PI and other investigators) developed close relationships and collaborations with the investigators from the Mount Sinai's Wien Center for Alzheimer's Disease and Memory Disorders, the University of Florida and Florida International University. Specifically with:

- Mount Sinai's Wien Center for Alzheimer's Disease and Memory Disorders: Dr. Rundek (UM) together with Dr. Ranjan Duara (Mt Sinai) and his 1Florida ADRC research team have supervised the overall image data quality assurance process.
- University of Florida: Dr. David Loewenstein (UM) together with Dr. Kevin Hanson (UF) have supervised MRI data retrieval for this proposal to assure quality checks as recommended by the 1Florida ADRC consortium.
- Florida International University: Dr. Mohammed Goryawala (UM) and Dr. Malek Adjouadi (FIU) have performed MRI quality and data bias corrections. They were helped by two PhD students from Dr. Adjouadi's FIU laboratory, who learned the QC process of image quality checks and image bias corrections.

WHATS IN THE FUTURE?

RESEARCH AND CLINICAL INITIATIVES

SECTION 15



15. Briefly Describe Plans for Future Research and/or Clinical Initiatives

Upcoming Clinical Translational and Population-Based Research

- **Dr. Ralph Sacco** will be submitting a competitive renewal for his data rich longitudinal research project NOMAS to begin to address other vascular and non-vascular contributors to cognitive decline and dementia. He also may be working on the project “Infrastructure Core Alliance for Research and Education for Stroke (iCARE for Stroke)” to create an innovative bioinformatic tool that will facilitate multidisciplinary and collaborative research. It is currently pending review.
- **Drs. Tatjana Rundek** and **David Loewenstein** will continue researching *Brain Vascular Imaging Phenotypes (VIP) and cognitive and neurodegenerative profile* (or the VIP study). They will also continue collaborating on the 1FL ADRC with the University of Florida, starting a new collaboration on the Clinical and training Core across 1FL ADC.
- **Dr. Xiaoyan Sun** will be preparing a manuscript on the relationship between pulse pressure and cognition. She will be starting her new project on the reduction of neurogranin expression in post-mortem brains of Alzheimer’s disease.
- **Drs. Noam Alperin, David Loewenstein** and **Alberto Ramos** hope to be working on the follow-up grant to a currently funded grant focusing on the role of sleep quality in aging related progression to dementia. The project is *Lifestyle Stressors of Hippocampus and AD related brain regions: Potential for Intervention*.
- **Drs. Hong Jiang** and **Jinhua Wang** will be working on the 2 new grants they received in 2019 for the projects *Retinal biomarkers for monitoring vascular contributions to Alzheimer’s Disease* and *Retinal changes in aging and small vessel brain disease*.
- **Dr. Scott Brown** will start his research on the two new grants he received as Principal Investigator this year: 1) an Ed and Ethel Moore Alzheimer’s Research Grant to examine the relationship of neighborhood greenness (e.g., parks) to risk for Alzheimer’s disease in Medicare beneficiaries residing in low-income Miami neighborhoods; and 2) a Sylvester Cancer Center Pilot Grant from the University of Miami Sylvester Cancer Center to investigate the relationship of greenness to five cancer diagnoses in ~250k Medicare beneficiaries.
- In 2020 **Dr. Anita Saporta** will conduct structural analysis with Freesurfer 5.3 and 6.0 of all available cases in the [McKnight Frailty Project](#). Once the primary focus of the MRI

analysis is finished, she plans to do further research and write her first project (**Dr. Tatjana Rundek** as mentor) on exploring the brain aging processes in **normal aging** and in pathological conditions through the study of the cerebellum.

Upcoming Basic and Translational Science Research

- **Drs. Kunjan Dave, Miguel Perez-Pinzon** and team will be conducting research to determine whether physical activity along with other therapies can ameliorate cognitive deficits in older cohorts of rats that ensue from MCAo (plus nicotine).
- **Dr. Milena Pinto** will be working on a new project that involves the use of mesenchymal stem cells (MSCs) in the treatment of frontotemporal dementia. She may also be working on a project submitted for an Alzheimer Drug Discovery Foundation grant that's is in the review process.
- **Dr. Regina Vontell** will focus on seeking to enhance the understanding of the deviations in brain development that occurs in cases of Trisomy 21 by closely investigating the complex interplay between radial glia and neuronal development.

Upcoming Education Program

- **Dr. Xiaoyan Sun** will be coordinating a brain cutting program and working with the Miami-Dade Mayor's office on the coordination of the "Miami-Dade Mayor's Initiative on Aging: Your Brain" seminar series.
- Through **Drs. Ralph Sacco** and **Tatjana Rundek's** UM CTSI roles, they are planning for a greater integration of the UM MBI trainees in CTSI research education and training programs, including applying for KL2, pilot and EUREKA awards, Connection club for research, and to the MS in Clinical Translational Investigation (MSCTI) directed by **Dr. Rundek**. They also plan to integrate their trainees with other award educational/training opportunities such as AAN, NeuroNext/StrokeNet, NIH Clinical trial course, 1FL ADC and others.

Upcoming Plans for the McKnight Scientific Advisory Board

Future plans for the Scientific Advisory Board include defining the strategies and tactics for our strategic plan, addressing the addition of any new members and devising a timeline to move the strategic plan forward.

16. If applicable, please provide endowment investment results for the report period.

This is included in **Section 8 Budget Update and Growth Pool Results**.

17. Were any funds used for a Prohibited Purpose during the report period?

No funds were used for prohibited purposes.

18. Do you recommend any modification to the Purpose or mandates in the Gift Agreement?

No.

19. Did all activities during the report period further the Purpose?

Yes.

20. Please describe any negative events (loss of personnel, space, budget, etc.) that occurred during the report period and the possible impact on carrying out the Gift Agreement.

None

21. Please provide any general comments or thoughts not covered elsewhere – a response is not required. Please respond only if you would like to add something not otherwise covered elsewhere.

N/A

ACHIEVEMENTS OF THE YEAR

SECTION 22



22. What do you consider your most important scientific achievements this year?

Together, our McKnight Directors Drs. Sacco, Rundek, Sun and Levin along with Stacy Merritt and Susan Fox-Rosellini worked towards advancing our knowledge of the aging brain and promoting the mission and vision of the McKnight Brain Research Foundation. Our collaborative and talented researchers had a productive year, contributing copiously to our McKnight Brain Institute's repertoire of research and publications. In this last section of the report, we will review some of the important scientific contributions we made.

Dr. Ralph Sacco's projects reviewed in **Section 9** provide opportunities to explore and address the risk and determinants of neurologic conditions such as stroke, **cognitive decline, cognitive aging and dementia** among an ever-increasing aging diverse population. In particular, his longstanding NOMAS project with its well-studied aging cohort (mean age was 70 at baseline MRI) has produced reports this year that have received the attention of the general public and the press due to identified modifiable risk factors.

Dr. Ralph Sacco's study "The Association between Elevated Depressive Symptoms and Risk of Incident Ischemic Stroke: the Northern Manhattan Study (NOMAS)," led by one of our fellows **MariaLaura Simmonetto**, was presented at the 2019 American Academy of Neurology (AAN) in Philadelphia. The study reported that older adults who report an elevated number of depression symptoms may be more likely to have a stroke years later than people with no depression symptoms or a low number of depression symptoms. Depression not only relates to stroke, but is likely to affect cognitive aging and impairment. It also received some press and public attention.

Dr. Bonnie Levin's team had a prolific year. Her team's most notable achievements were (1) uncovering the common neural circuitry underlying vestibular function and cognition; (2) dissecting the individual components of the frailty model and showing how they each uniquely impact cognition; and (3) developing a model for detecting susceptibility for deception.

An important accomplishment this year was **Dr. Scott Brown's** research being published in the *Journal of the American Heart Association* (AHA) which was the first-ever publication to document a relationship of objectively-measured block level greenness (vegetative presence such as parks, tree canopy) to lower odds of heart disease. It did so using diagnoses of four forms of heart disease in ~250,000 Medicare beneficiaries in Miami-Dade County, FL.

Dr. Susan Blanton's research involving the identification of several new genes for hearing loss along with insights into their function is an important contribution to science this year.

Dr. David Della-Morte researched the role of Peroxiredoxin 6 on metabolism and aging phenotypes which may help better to understand the role of these antioxidant molecules

against chronic diseases. The link found between Prdx6 and Sirt1 in modulating cell survival is especially important as it may indicate a novel pathway to counteract age-related diseases, such as dementia.

Along with the successful achievements of our McKnight Members and Collaborators, many of our studies (such as those led by Dr. Sacco described in **Section 9**) have established extensive reach and immediate applicability. This year's most important scientific achievement though, has been to successfully guide and mentor the young professionals who lead our important studies. Our mentorship success has led to publishing key papers and obtaining numerous grants and awards.

Lastly, these notable publications have significantly added to our academic success in 2019:

***Michelle Caunca** our MD/PhD student led a team to study obesity and markers of brain aging. The abstract results showed that obesity appears to accelerate brain aging by a decade or more. They found that people with a wide waist circumference and higher body mass index (BMI) were more likely to have a thinner cerebral cortex, a condition that has previously been linked to a decline in brain function.*

Measures of obesity are associated with MRI markers of brain aging: The Northern Manhattan Study. **Caunca MR**, Gardener H, Simonetto M, Cheung YK, Alperin N, Yoshita M, DeCarli C, Elkind MSV, **Sacco RL**, Wright CB, **Rundek T**. Neurology. 2019 Aug 20;93(8):e791-e80.3

Working with our fellow McKnight Brain Institute at the University of Arizona, we worked on defining the drivers of cognitive education in this journal article.

Precision Aging: Applying Precision Medicine to the Field of Cognitive Aging. Ryan L, Hay M, Huentelman MJ, Duarte A, **Rundek T**, **Levin B**, Soldan A, Pettigrew C, Mehl MR, Barnes CA. Front Aging Neurosci. 2019 Jun 7;11:128. doi: 10.3389/fnagi.2019.00128. eCollection 2019. PMID:31231204.

***MariaLaura Simonetta's** important paper describes the link between atherosclerosis, vascular cognitive impairment and dementia (VCID) and inflammation, as well as how omega-3 polyunsaturated fatty acids supplements may be useful to prevent and treat inflammatory-related diseases.*

A Novel Anti-Inflammatory Role of Omega-3 PUFAs in Prevention and Treatment of Atherosclerosis and Vascular Cognitive Impairment and Dementia. **Simonetto M**, Infante M, **Sacco RL**, **Rundek T**, **Della-Morte D**. Nutrients. 2019 Sep 23;11(10). pii: E2279. doi: 10.3390/nu11102279. Review. PMID: 31547601.

***Dr. Joyce Gomes-Osman's** research on exercise and brain health found there is a need for learning whether these results are generalizable to aging adults. In this paper, she delved into discovering the effect of exercise and dose on aging adults.*

Exercise for Brain Health: An Investigation into the Underlying Mechanisms Guided by Dose. Cabral DF, Rice J, Morris TP, **Rundek T**, Pascual-Leone A, **Gomes-Osman J**. Neurotherapeutics. 2019 Jul;16(3):580-599. doi: 10.1007/s13311-019-00749-w. Review. PMID: 31197642.

Neighbourhood greenness has been associated with health and well-being but its relationship to depression in older adults is less studied. Dr. Scott Brown's research is important because understanding its relation to depression may inform and complement traditional depression interventions. This study examines greenness and depression diagnoses among older adults in Miami.

Neighbourhood greenness and depression among older adults. Perrino T, Lombard J, **Rundek T**, Wang K, Dong C, Gutierrez CM, Toro M, Byrne MM, Nardi MI, Kardys J, Szapocznik J, **Brown SC**. Br J Psychiatry. 2019 Aug;215(2):476-480. doi: 10.1192/bjp.2019.129. Epub 2019 Jun 13. PMID: 31190652.

While frailty is associated with cognitive decline in older adults, the mechanisms explaining the relationship aren't totally clear. Dr. Sonya Kaur's abstract below discusses how sleep quality may mediate the relationship between frailty and cognition.

Sleep quality mediates the relationship between frailty and cognitive dysfunction in non-demented middle aged to older adults. Kaur S, Banerjee N, Miranda M, Slugh M, Sun-Suslow N, McInerney KF, Sun X, Ramos AR, Rundek T, Sacco RL, Levin BE. Int Psychogeriatr. 2019 Jun;31(6):779-788. doi: 10.1017/S1041610219000292. Epub 2019 Apr 22. PMID: 31006402.

Michelle Caunca sought to examine associations between measures of adiposity with Alzheimer's disease (AD)-signature region cortical thickness and hippocampal volume. She found that greater BMI and waist circumference were related to cortical thinning within and outside the AD-signature region, suggesting a global effect not specific to AD.

Measures of Adiposity and Alzheimer's Disease-Related MRI Markers: The Northern Manhattan Study. Caunca MR, Simonetto M, Alperin N, Elkind MSV, Sacco RL, Wright CB, **Rundek T**. J Alzheimers Dis. 2019;70(4):995-1004. doi: 10.3233/JAD-190092.

23. Signature, date, and title of person submitting the report



January 14th, 2020

Tatjana Rundek, M.D., Ph.D.
Scientific Director
Evelyn F. McKnight Brain Institute

Date

Appendix I - UM McKnight Brain Aging Registry: Neuroimaging and Cognitive Cores Progress Report

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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.

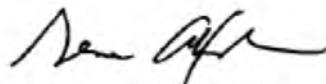
We wish to express our sincere appreciation for your continued support in establishing the MBAR and both the neuroimaging and cognitive cores.

Sincerely,

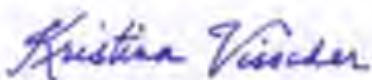


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McKnight Brain Aging Registry Update: Neuroimaging and Cognitive Cores

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.

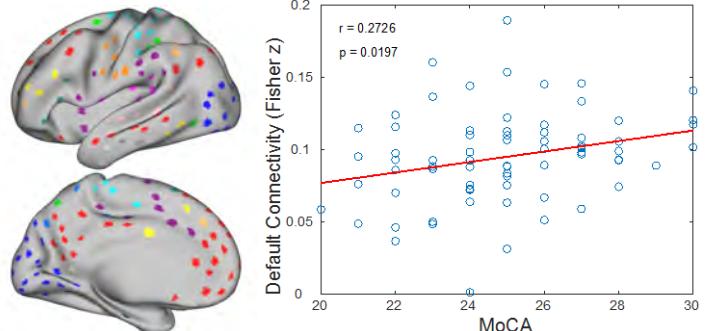


Figure 2. Left shows, in red, cortical regions that are part of the Default Mode Network. Plot on the right shows that the strength of functional connectivity of those Default Mode regions correlates with performance on MoCA, a test of cognitive function.

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.

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Appendix II - UM McKnight Brain Institute Strategic Plan

In early 2019 we convened for a second session with the expanded Advisory Board and a multi-disciplinary group of physicians, scientists and research administrators from the Departments of Neurology, Neurosurgery, Psychiatry, Radiology, Internal Medicine, Psychology, Kinesiology and Sport Sciences, as well as others to evaluate the current research and educational program and develop goals and strategies of our Institute over the next 5 years. The strategic plan is to evaluate and emphasize the strengths of our University of Miami Evelyn F. McKnight Brain Institute, to acknowledge weaknesses and to recognize challenges and opportunities so as to achieve our mission, vision and goals. Our Strategic plan will be aligned with the University of Miami Miller School of Medicine (UMMSOM) strategic plan that is currently in the final phase. It is expected the UMMSOM will be completed in 2020 and our plan will be completed immediately thereafter.

Our [Mission](#) and [Vision](#) are:

Mission: To accelerate discoveries of the causes and treatments of age-related memory loss and cognitive decline and to promote brain health through multi-disciplinary collaborations and partnerships; and to train new generations of skilled clinical and translational scientists specializing in age-related memory loss and cognitive decline

Vision: To become a leading center for clinical and translational research into the causes, treatments and prevention of age-related cognitive disorders

Our major [Goals](#) are:

Goal 1: Develop a scientific program directly related to the mission of our MBI and the McKnight Brain Research Foundation, focused on clinical translational research in age-related memory loss and translating discoveries into clinical practice.

Goal 2: Promote and provide a structure to share information on age-related memory loss across clinical translational research, education and clinical landscapes at UM as well as between MBIs focusing on our clinical and translational research strengths and areas highlighted in the UM Miller School of Medicine strategic plan.

Goal 3: Develop community outreach plan by leading community research in age-related memory loss and cognitive decline and providing and disseminating information on cognitive decline in communities.

Goal 4: Provide training and education in age-related memory loss and cognitive decline to our trainees and to all of our constituents including researchers, physicians and other health care professionals.

The UM MBI Executive Committee reconvened in the fall and decided that final strategies and tactics would be defined in early to mid 2020 when the University of Miami Miller School of Medicine Research strategic plan will be finalized.