UNIVERSITY OF MIAMI
EVELYN F. MCKNIGHT BRAIN INSTITUTE
ANNUAL PROGRESS REPORT
JANUARY 1, 2018 - DECEMBER 31, 2018

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

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UNIVERSITY OF MIAMI
EVE LIN F. MC KNIGHT BRAIN INSTITUTE

ANNUAL PROGRESS REPORT
JANUARY 1 – DECEMBER 31, 2018
1. Summary of Scientific and Educational Achievements Since Last Report

Introduction

We start the summary of our achievements with (1) the changes occurring after the formal appointment of Scientific Director, (2) accomplishments towards the goals set forth for the last year, (3) followed by our notable scientific and educational activities, and (4) concluding with the description of the first phase of the Evelyn F. McKnight Brain Institute (MBI) strategic planning completed in 2018.

1.1. Appointment of Scientific Director

In January 2018, Tatjana Rundek, MD, PhD was formally appointed as Scientific Director of the Miami Evelyn F. McKnight Brain Institute, after she served as Interim Scientific Director and after the national search for a new Scientific Director was concluded. She was considered to be a competitive and best-suited candidate for the position by the Search Committee. She immediately started in her role as Scientific Director with great enthusiasm and rigorous plans for a successful year. At the first McKnight research meeting there was a sense of excitement and camaraderie, which continued and grew throughout the year. Regular weekly staff and research meetings entailed briefings on progress of current projects, brainstorming of new ideas, mentoring and planning of research projects for all members, from the trainees to junior and mid-level faculty. Dr. Rundek made the McKnight Brain Institute’s members, collaborators and trainees eager to morph their interests and expertise into important science and collaborative research projects around the common theme of age-related memory loss and brain health. Plans for abstracts, posters, manuscripts and/or grant submissions were reviewed for science and feasibility, realistic research goals were set and the progress towards these goals was frequently reviewed. Although these meetings were productive and organized, she always fostered a free forum to explore ideas, encouraged junior members to participate in discussions and share their views, and hear group opinions.

Dr. Rundek successfully recruited collaborative partners from other departments, centers and institutes and fostered more productive multi-disciplinary collaborations within our McKnight Brain Institute and across the University of Miami. From multiple discussions with the Evelyn F. McKnight Executive Director Dr. Ralph L. Sacco and McKnight research team, the Scientific Advisory Board members, the leadership of the Miller School of Medicine including the new Dean and senior Executive Dean for Research, leaders of the Brain Bank, Center for Cognitive Neuroscience and Aging, the Miami Project, and Chairs of the Department of Psychology, Geriatrics and Genomics, it was clear that the direction, vision and mission, branding, and future research and educational plans for our McKnight Brain Institute needed to be revised and revitalized with important input from a broad range of scientists, partners, collaborators and
stakeholders interested in ameliorating age related memory loss and improving brain health. In order to accomplish this objective, we prepared and conducted the first phase of the McKnight Brain Institute strategic planning in June of 2018 with the help and coaching provided by the Miami Clinical Translational Science Institute (CTSI). This was the first strategic plan conducted for our MBI and its continuation to the next phase with clear definition of our strategic goals and their implementation, measurable outcomes and timeline will continue to be the focus of our MBI major activities in 2019.

Through the team and collaborative vision of Dr. Rundek, our Executive Director Dr. Sacco, the Scientific Advisory Board members and the conclusion of the first phase of our strategic planning, our McKnight Brain Institute’s first order of business was to extend our Scientific Advisory Board and develop a unified framework of cognitive aging and brain health. We will capitalize on the scientific strengths of our McKnight Brain Institute, UM Centers and Institutes, and to leverage our institutional infrastructure and resources, as well as the recently developed University of Miami Miller School of Medicine Research Strategic Plan. Our research focus on vascular, metabolic, and sensory drivers of cognitive aging and brain health is our major strength that will define our scientific framework, steer research and educational directions, and set research and educational goals and priorities to further the mission of our MBI.

PRESS RELEASE:
Dr. Tatjana Rundek Named Scientific Director of Evelyn F. McKnight Brain Institute

Tatjana Rundek, M.D., Ph.D., FAAN, professor of neurology and public health sciences and executive vice chair for research and faculty affairs in the Department of Neurology, has been named scientific director of the Evelyn F. McKnight Brain Institute and Evelyn F. McKnight Chair for Learning and Memory in Aging at the University of Miami Miller School of Medicine. She has served as the interim scientific director since October 2016.

The Evelyn F. McKnight Brain Institute at the University of Miami was established in 2007 with a donation from the McKnight Brain Research Foundation and a match from the Schoninger Foundation and other UM donors. Its mission is to discover and explore normal memory changes that happen with age, investigate the causes of age-related disorders of brain function and memory, and develop ways to prevent them.

“I am dedicated to our McKnight Brain Institute’s mission to accelerate discovery of the causes, treatment, and prevention of age-related memory loss and cognitive decline, and to enhance brain health through translational and patient-oriented research,” said Rundek, who also serves as director of the Clinical Translational Research Division in Neurology, and director of the Master of Science Degree in Clinical Translational Investigations.

"Dr. Rundek is a wonderful choice as scientific director,” said Ralph L. Sacco, M.D., M.S., executive director of the McKnight Brain Institute, professor and chair of neurology, Olemberg Chair in Neurological Disorders, senior associate dean for clinical and translational science and director of UM’s Clinical and Translational Science Institute. "Her passion for team science and developing new ideas in a truly collaborative manner is very special. I am looking forward to great things under Dr. Rundek’s leadership."

As interim director Rundek created the Miami McKnight Brain Institute Small Pilot Collaborative Award. The program gave small grants to junior faculty or post-doctoral trainees with promising potential to become successful investigators in age-related memory loss and cognitive decline, supporting research and advancing the McKnight Brain Institute collaborative research project pipeline.

“Dr. Rundek’s background and training, both as a clinician and a research scientist, make her uniquely qualified to advance the research initiatives in cognitive aging leading to the understanding of and alleviation of age-related memory loss, not only at the University of Miami, but throughout the universal scientific community,” said J. Lee Dockery, M.D., chair of the Board of Trustees for the McKnight Brain Research Foundation.
1.2. Accomplishments Towards Last Year Goals

In our previous Annual Progress Report, we included several goals and aspirations for our McKnight Brain Institute (MBI) for 2018. We have accomplished all the planned goals and more since last year’s progress report, including:

- First, we planned to reassess and revise our MBI research and education program. We have immediately started several new initiatives for our research direction in collaboration with the newly named Center for Cognitive Neuroscience and Aging (previously: Center for Aging) under the new leadership of Dr. David Loewenstein, PhD. Dr. Rundek and Dr. Loewenstein have established bi-monthly meetings to continue our current collaborations and discuss and strategize new avenues of research and educational collaborations. As Dr. Loewenstein is a co-Director of the Clinical Core of the 1FL ADRC (PI: Todd Golde, UF) he introduced Dr. Rundek to Dr. Ranjan Duara, (Mt. Sinai, Miami Beach) a Director of the 1FL ADRC Clinical Core and both Dr. Rundek and Dr. Loewenstein have established monthly research meetings with the research team at Mt. Sinai. These collaborations have already resulted in a successful grant application.

- Our major objective was to prepare and conduct the strategic planning meeting and align our MBI strategic goals with the recently completed University of Miami Miller School of Medicine Strategic plan. We conducted the MBI retreat and completed the first phase of MBI strategic planning with the help of coaching experts from our Clinical Translation Science Institute (Section 1.4).

- As a result of our retreat, we have immediately expanded the McKnight Scientific Advisory Board to include a broader representation of scientists, leaders, partners and collaborators focused on age-related cognitive functioning and brain health to help extend our research and educational mission and accomplish our strategic goals.

- We have successfully continued our current research and educational projects by focusing on successful and promising projects and collaborations, including an extension of the McKnight Frailty Registry (as a subset of the Cognitive Disorders Clinical and Biorepository Registry) led by Dr. Bonnie Levin, the small vessel disease project (brain and eye) led by Dr. Noam Alperin in Radiology and Dr. Hong Jiang in Neuro-ophthalmology; sleep disorders and cognition led by Dr. Alberto Ramos, and neuroplasticity assessment using Transcranial Magnetic Stimulation (TMS) led by Dr. Joyce Gomes-Osman. Our basic science projects continued to focus on treatments for improving cognitive outcomes using novel white matter stroke behavioral models in rats (Dr. Kunjan Dave and Dr. Miguel Perez-Pinzon). We have continued evaluating synergistic effects of physical exercise and resveratrol treatment on post-stroke cognitive function in middle aged rats with the goal of improving post-stroke cognitive function. In parallel, our clinical research has expanded to the investigation of the effect of aerobic exercise on synaptic functioning using TMS assessments.
• Two grants that were submitted to the NIH last year using preliminary data from the McKnight Frailty Registry (Dr. Jiang’s retinal and brain hemodynamic proposal, and Drs. Alperin/Rundek’s proposal on MR imaging of cerebral small vessel perfusion), received excellent scores but were not funded and will be resubmitted this year.

• Two R21 grant proposals on *sleep and cognitive performance across the lifespan* submitted last year (both by Dr. Alberto Ramos) were awarded funding by the NHLBI. A R01 using a large cohort from the Hispanic Community Health Study-Study of Latinos (HCHS-SOL) and based on the framework of these R21 grants was just submitted. It includes institutions that are homes to national leaders in sleep medicine (University of Miami, University of Chicago, Albert Einstein in NY, UCSD and MGH).

• In collaboration with other McKnight Brain Institutes, we successfully continued our collaborative projects, including the MBAR-McKnight Brain Aging Registry. Drs. Bonnie Levin and Sarah Getz (Co-Investigators) were awarded the first MBRF Cognitive Aging and Memory Intervention Core Inter-institutional Pilot Grant in collaboration with UF and the University of Arizona for the research project *Uncovering Risk Profiles of Deception and Mitigating Susceptibility to Scamming in Midlife and Older Age: A Novel Intervention Tool.*

• As part of other collaborations, we successfully continued with projects on cognitive trajectories in aging in NOMAS (Northern Manhattan Study) and the Brain Hemodynamic Study in the Einstein Aging Study in the Bronx. We would like to highlight the investigations on the associations between subclinical brain infarcts (SBI) and white matter hyperintensity volume (WMHV), cognition and functional trajectories. The results showed that SBI moderated the association between cognition and functional trajectories, with 3-fold greater functional decline among those having SBI compared to those not having SBI. This highlights the strong and independent association between subclinical brain imaging markers and patient-centered functional trajectories over time. This work will continue in the next year by including the network of inflammation biomarkers as important mediators between cognitive performance and functional trajectories over time.

• In the last year we have successfully started new research initiatives. These involved collaborations with the Center for Cognitive Neuroscience and Aging (Director: Dr. Loewenstein) and the Mount Sinai Wien Center (Dr. Duara) on two major initiatives that include (1) investigations of brain vascular phenotypes in cognitive decline, and (2) a collaboration on 1FL ADRC Clinical Core and Educational Component. We have submitted the proposal on *Brain Vascular Imaging Phenotypes (VIP) and cognitive and neurodegenerative profile* to the Florida DOH and just received the notification of an award for 2-year funding (PI: Dr. Rundek). In respect to the 1FL ADRC, UM will apply for the competitive renewal together with UF in May of 2019. The current 1FL ADC Clinical Core under the direction of Dr. Duara (Mt. Sinai) will be extended and will include a Co-Director at UM (Dr. Loewenstein) with Dr. Rundek as a co-investigator. In addition, Dr. Rundek will serve on the 1FL ADC Recruitment Core. One of the main changes in the 1FL ADC re-submission is in the Educational/Training Core leadership, where Dr. Rundek will serve as an educational/training Co-Director together with Dr. Glenn Smith from UF.
Another novel research initiative our MBI started last year included *novel functional interventions to improve synaptic functioning and cognitive performance in aging* using oral supplementation (Souvenaid) that increases brain levels of DHA, choline and uridine. This exciting new research initiative is led by Dr. Christian Camargo, our prior MBI fellow, under the mentorship of Dr. Rundek and Dr. Richard Wurtman, our recently appointed voluntary professor Emeritus. Dr. Richard J. Wurtman, MD who has been Professor Emeritus at MIT for over 40 years is known as the father of ‘the melatonin role in sleep’.

We have extended our MRI capabilities by partnering with the Department of Psychology (Dr. Phil McCabe, Department Chair) at the Coral Gables Campus where a research 3T MRI resides. We have started our MRI scans in that facility, which significantly increased a number of available MRI slots for our studies and reduced waiting and scheduling time for our participants that we experienced in the clinical MRI facilities at the Medical School Campus. We have also started a *new collaboration on resting brain networks* using resting state MRI in collaboration with Dr. Roger McIntosh, PhD from the Department of Psychology, who is an expert in fMRI. Dr. McIntosh is now our newest MBI collaborator.

Another important and *major partnership and collaboration* is currently in progress with the University of Arizona MBI under the leadership of Dr. Carol Barnes. She leads a large U19 application to the NIA (deadline: Jan 25, 2019) to investigate main drivers of cognitive aging across the lifespan: *Precision Aging Network (PAN): Closing the Gap Between Cognitive Healthspan and Human Lifespan*. Dr. Rundek and Dr. Levin will lead the Miami Clinical Project (*In-depth Profiles of Resilience and Risk*) and serve on the PAN Executive committee.

Lastly, with the respect of our educational goals, we have enrolled the second MBI research fellow last July (Dr. Anita Seixas Dias Saporta, MD) after Dr. Christian Camargo completed his MBI clinical and research fellowship. Anita has a strong clinical background in MRI and electrophysiology with a particular research interest in multimodality brain imaging and aging. She will continue her fellowship for another year. As our McKnight trainee Michelle Caunca, MD/PhD Student successfully obtained a F30 NIH award last year (primary mentor: Dr. Rundek) we have resources to accept another MD/PhD student to our McKnight cognitive graduate training program. Dr. Rundek serves on the MD/PhD Program Admission Committee and has already interviewed a number of candidates for the MD/PhD program and identified a highly promising MD/PhD candidate to join our MBI on the cognitive aging projects and work on her PhD thesis in our MBI. Her MBI appointment is pending official admission to the MD/PhD program at the University of Miami, Miller School of Medicine.

Dr. Joyce Gomes-Osman has just been awarded a *NCATS CTSI KL2 award*. This is a 2-year training award that will protect 75% of Joyce’s time to obtain research training and provides some funds for resources needed to conduct research on *Assessing cognitive improvements, brain neuroplasticity and the role of genetic factors after aerobic exercise in sedentary adults*. Joyce’s primary mentor is Dr. Rundek.

Dr. Christian Camargo has been retained and advanced to a faculty position of an Instructor in the Department of Neurology. He has submitted a grant on the use of Souvenaid to improve synaptic functioning in cognitive aging to the AAN/McKnight funding. He just
received a provisional award notice for 2-year funding (pending responses to the reviewers’ comments with the deadline of Jan 18). Christian’s primary mentor is Dr. Rundek.

- As we are currently planning and preparing a major education/training application to the NIA as a part of the 1FL ADC Educational Core in collaboration with UF, we have postponed our plans for a T32 training grant proposal in cognitive aging and brain health. Our Scientific Advisory Board also recommended that we postpone this application after reviewing our current educational activities.

1.3. Notable Scientific and Educational Activities

In the following section we provide more details on several of our noteworthy MBI progress and accomplishments in 2018.

1.3.1. MBI Related Grants and Other Prestigious Awards

Drs. Bonnie Levin and Sarah Getz (Co-Investigators) were awarded the first McKnight Brain Foundation Inter-Institutional Collaborative Pilot Grant in 2018 for the research project *Uncovering Risk Profiles of Deception and Mitigating Susceptibility to Scamming in Midlife and Older Age: A Novel Intervention Tool.*

The University of Miami neuropsychologists Bonnie Levin, PhD and Sarah Getz, PhD were awarded a grant for this important research project at the Evelyn F. McKnight Brain Institute. The research is a collaboration with the McKnight Brain Institutes at the Universities of Florida and Arizona. This collaboration will specifically examine scamming in middle and older life, a pressing public health problem associated with decreased functional independence, increased financial dependency, lower quality of life and a host of negative health outcomes. This project will attempt to understand the cognitive, socio-affective and neurobiological mechanisms underlying increased susceptibility to being deceived and poor decision-making. Currently, there are no effective interventions to reduce scam susceptibility and the goal of this multi-site collaboration is to develop and validate a decision-supportive device to reduce online scam susceptibility in late midlife and older age.

Dr. Joyce Gomes-Osman is awarded a Mentored Translational Research Scholars Program Award (KL2) from the University of Miami Clinical Translational Science Institute (CTSI)

Congratulations to Dr. Joyce Gomes-Osman for being awarded a Mentored Translational Research Scholars Program Award (KL2)! This program is designed to support the research career development of early stage investigators at the assistant professor level for two years and will include: (1) 75% salary support up to the NIH Salary Cap; (2) $2,500 for travel and training-related activities; (3) $30,000 for research expenses. Joyce’s primary mentor is Dr. Rundek.

Dr. Joyce Gomes-Osman is leveraging the preliminary data from her previously awarded *McKnight Pilot Grant* for an innovative study that will investigate mechanisms...
underlying cognitive benefits after an 8-week exercise intervention in sedentary adults over 55 years of age. In this study, she will combine the use of a non-invasive assessment of synaptic neuroplasticity by Transcranial Magnetic Stimulation (TMS), neuropsychological outcome measures, and examine potential effect modifications by genetic brain-derived neurotrophic factor (BDNF) and apolipoprotein E (APOE) factors.

This KL2 Award will greatly help her advancing academic career by protecting her time for research, enabling additional training and mentorship from a multi-disciplinary group of established researchers at UM Miller School of Medicine (Drs. Rundek and Loewenstein) and Harvard (Dr. Alvaro Pascual-Leone), combining the fields of clinical and translational research in aging, genetics, neurophysiology and cognition.

Dr. Christian Camargo just received a provisional award notice for 2-year funding from the AAN McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age Related Memory Loss (pending responses to the reviewers’ comments with the deadline of Jan 18) to study the effect of an oral nutrient on synaptic function and cognition in aging: Reducing the Effects of Aging on Cognition with Therapeutic Intervention of an Oral Nutrient - The REACTION Study. He is proposing 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 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. Christian’s primary mentor is Dr. Rundek.

Dr. Rundek just received a notice of award from FL DOH for a 2-year funding to study vascular contribution to neurodegeneration: Brain Vascular Imaging Phenotypes (VIP) and cognitive and neurodegenerative profile - The VIP Study. This research was a result from a new initiative and collaboration with the Center for Cognitive Neuroscience and Aging (Director: Dr. Loewenstein) and the Mount Sinai Wien Center (Director: Dr. Duara) started in 2018. The objective of the proposal is to determine the impact of novel brain vascular imaging phenotypes (VIP) of small vessel disease and modifiable vascular comorbidities on cognitive and neurodegenerative profiles. To achieve this goal, the investigators will leverage brain MRI, clinical and neurocognitive data from the NIH-funded 1FL ADRC control population. This unique study will determine the impact of the modifiable vascular risk factors, comorbidities and vascular brain imaging phenotypes on cognition and the signatures of AD pathology in the ‘non-AD affected’ 1FL ADRC population. The proposed study is of high impact for the health of the Florida population, as it will help to close the gap in our understanding of the mechanisms by which vascular phenotypes contribute to neurodegeneration and inform strategies to reduce AD risk specifically tailored to high vascular risk individuals in the diverse Florida population.

Dr. Ralph Sacco was elected to the prestigious National Academy of Medicine (NAM) this year. This extraordinary honor reflects his height of professional achievement and commitment to
service in health and medicine. Dr. Sacco received the honor “for his instrumental involvement in policies promoting ideal cardiovascular health, brain health, stroke prevention, and non-communicable disease targets,” according to the Academy. See Section 22 for additional information and the press release.

Dr. Rundek just received the 31st annual In the Company of Women Outstanding Woman in Science and Technology award. She was one of 2 winners who are sharing this year’s award. The award is given to recognize Miami-Dade County women leaders and their contributions to the community. Awardees are women who exemplify professional development, community responsibility, leadership and vision, who made contributions to women’s progress and the promotion of pluralism.

1.3.2. Participation in MBRF Inter-Institutional Events

The Miami Evelyn F. McKnight Brain Institute participation in the 10th Annual McKnight Inter-Institutional Meeting at the University of Alabama at Birmingham, April 5-6, 2018.

These were the presentations given by our Trainees, Collaborators and Members:

- Intervention Opportunities for Cognitive Decline: Report from the National Academy of Medicine, Ralph Sacco, MD, MS, FAHA, FAAN
- McKnight Brain Aging Registry I: Clinical Update, Bonnie Levin, PhD
- Cognitive, Cultural and Affective Dimensions of Frailty, Katalina McInerney, PhD, Assistant Professor and Sarah Getz, PhD Neuropsychology Postdoctoral Fellow
- Sleep and Neurocognitive Aging in Population Based Studies, Alberto Ramos, MD, MSPH, Associate Professor and Sleep Research Director
- Retinal Microvascular and Microstructural Changes in Normal Aging and Alzheimer’s Disease Hong Jiang, MD, PhD Assistant Professor of Clinical Neuro-ophthalmology & Neurology
- Post-Stroke Physical Exercise Improves Cognitive Outcomes in Young and Elderly Animals, Kunjan Dave, PhD, Research Associate Professor

The Miami MBI participation in the McKnight Brain Research Foundation Poster Reception at the Society for Neuroscience (SFN) meeting, San Diego, CA, November 4th, 2018.

Below are the poster presentations given by our Trainees, Collaborators and Members:

- Dr. Ami Raval “Monitoring post stroke frailty in nicotine exposed female rats”
- Dr. Milena Pinto “Lack Of Cytochrome C In Adult Forebrain Neurons In Vivo Leads To A Decrease In Cytochrome C Oxidase, Increased Oxidative Stress But No Overt Cell Death”
- Ashish Rehni mentored by Dr. Kunjan Dave “Exposure to recurrent hypo-glycemia modulates endoplasmic reticulum stress in hippocampus of insulin treated diabetic rats”
• **Austin Choi** mentored by **Dr. Antoni Barrientos** “Biogenetic features and function of the mitochondrial ribosome in health and mitochondrial encephalomyopathies”

• **Jordyn Rice** mentored by **Dr. Joyce Gomes-Osman** “Dual-task performance is related to a neurophysiological measure of plasticity in individuals with memory disorders”

• **Jordyn Rice** mentored by **Dr. Joyce Gomes-Osman** “Effects of a 4-week Aerobic Exercise Intervention on TMS Neuroplasticity Measures and Cognition in Healthy Sedentary Adults: an Ongoing Pilot Study”

• **Jordyn Rice** mentored by **Dr. Joyce Gomes-Osman** “Timed Up-and-Go Performance and Dual-Task Effects are Correlated with Distinct Neuropsychological Measures of Executive Function in Healthy Older Adults”

• **Kristen Sanders** mentored by Dr. Tasuku Akiyama "Anxiety-like behavior and Fos expression in amygdala elicited by itch mediators in mice"

### 1.3.3. Clinical and Population-Based Research

**Dr. Joyce Gomes-Osman’s** paper *Exercise for cognitive brain health in aging: A systematic review for an evaluation of dose* was published in *Neurology: Clinical Practice* in June 2018. It received wide coverage internationally from newspapers and magazines as well as radio and television interviews. See Section 9.1 for further information.

Under the direction of **Dr. Bonnie Levin**, significant work was done on the Cognitive Disorders Clinical and Biorepository Registry (referred to in the remainder of this report as the McKnight Frailty Registry). This database holds almost 400 records of subjects with memory complaints. Each participant who met study inclusion criteria was evaluated by Dr. Levin’s team with a detailed cognitive and frailty assessment battery and is included in the database. This database presents a valuable resource for generating research hypotheses relevant to age-related memory loss and cognitive decline and have already led to a great number of posters, presentations, abstracts and grant and manuscript submissions in 2018.

**Dr. Tatjana Rundek** received an NIH award to conduct a Family Study of Carotid Atherosclerosis and Stroke Risk (the 3rd cycle of funding). We propose to expand our prior genetic investigations to conduct a methylome-wide-association-study (MWAS) to identify differential DNA methylation regions (DMRs) associated with subclinical stroke precursors, stroke and CVD. The proposed investigations would provide new insights relevant to the development of novel clinical strategies for prevention and treatment of stroke and CVD, as our ultimate goal is to reduce stroke risk and race-ethnic disparities in stroke and CVD. Besides clinical aims, we plan to evaluate the functional impact of DNA sequence variation and DMRs using CRISPR-Cas9 technology. To achieve our goals we will leverage the rich data already collected in the past cycle of Family Study and add new data collection to detect vascular events (stroke, myocardial infarction, vascular death). We will validate the findings in an independent sample from the ongoing longitudinal Northern Manhattan Study (NOMAS). The innovative aspects of our proposal include novel discoveries of modifiable epigenetic sites for stroke, CRISPR-Cas9 technology to model specific genome-editing, a unique population of Dominicans, a family study design, and an available independent population for validation studies. Findings from our study may lead to the most promising molecular strategies for risk stratification, prevention and
treatment of stroke. The plan is to extend our genomic and epigenetic investigations to age-related cognitive performance in high-cerebrovascular-risk families.

Dr. Noam Alperin’s paper *Effect of Sleep Quality on aMCI Vulnerable Brain Regions in Cognitively Normal Elderly Individuals* was accepted for publication in the leading sleep journal, SLEEP. It describes the first assessment of the effect of poor sleep quality on several MRI phenotypes in cognitively intact elderly subjects. 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, cognition, and dementia disorders is still poorly understood. His study reports that patterns of cortical and deep gray matter atrophy related to poor sleep quality impact in AD–prone regions of the cortex even in a population rigorously deemed unaffected by cognitive impairment, psychological disorders or dementia. The study emphasizes a role for sleep intervention in fighting neurodegeneration and potentially slowing age-related cognitive decline.

Dr. Sun Xiaoyan our MBI Educational Director has taken on a significant role in the University of Miami Brain Bank. She became a Co-Director of the Brain Bank and took a lead in making the final disease diagnosis from the brain pathology specimens and available clinical information. Dr. Sun’s new position will help in establishing a strong partnership between our MBI and the Brain Bank in research proposals and educational activities.

Dr. Elizabeth Crocco was named the Clinical Director of the Center for Cognitive Neuroscience and Aging (CNSA) directed by Dr. David Loewenstein.

Dr. David Loewenstein and his NIA-supported team of researchers at the Center for Cognitive Neurosciences and Aging and the University of Miami developed the *Loewenstein-Acevedo Scales for Semantic Interference and Learning (LASSI-L)* test. Traditional memory measures are subject to individual differences in learning strategies, cognitive reserve and other sources of variability that may effectively lower the signal-to-noise ratio, hampering the assessment of the earliest stages of cognitive deficits in AD, and the ability to track changes over time. The LASSI-L is a sensitive cognitive ‘stress’ test that overcomes these challenges and can assess cognitive deficits associated with early biological changes in neurodegeneration. The preliminary findings using LASSI-L show that semantic intrusion on the LASSI-L could differentiate amnestic MCI patients with high and low amyloid loads and may have significant implications for screening for enrollment in novel clinical trials for cognitive improvements. The results were published in the September 4, 2018 issue of *Neurology*.

### 1.3.4. Basic and Translational Science Research

Dr. Milena Pinto has resubmitted her K01 award project in and will receive notice regarding funding in 2019.

Dr. Ami Raval was appointed Associate Research Professor.
1.4. The Evelyn F. McKnight Brain Institute Strategic Planning

Our major goal set last year was to hold a one-day Evelyn F. McKnight Brain Institute Strategic Planning Retreat, in order to steer our Institute’s research and educational priorities for the next 5 years, focus energy and resources towards these priorities, strengthen clinical oriented research in age-related memory loss, ensure that our research team members and collaborators work toward the common goals, and to assess and adjust the Institute's direction in response to a changing research and funding environment.

1.4.1. Development of MBI Strategic Plan

Preparation for the Strategic Planning Retreat began immediately after Dr. Rundek was appointed as Scientific Director in Jan 2018. Dr. Rundek spent a significant amount of time to conduct a thorough search across departments, disciplines, centers, institutes and schools to learn about the age-related research being done at all University of Miami campuses. She explored potential research partnerships and collaborations with our MBI and identified key players and leaders within the University as potential partners for advancing our MBI mission and programs. She met with most of these leaders and scientists personally and invited them for collaborations with our research and education programs in age-related memory loss and cognitive decline.

Multiple disciplines were considered including geriatrics and public health, psychology, psychiatry, radiology, nuclear medicine, basic science, genetics, exercise physiology, aging/neuroscience, psychology, and representative partners were invited to be part of the MBI Strategic Planning Retreat.

Task Force Working Groups

We have created 3 task force working groups consisting of multi-disciplinary teams and based on their expertise in aging and cognitive function, leadership ability and propensity to brainstorm and bring forth novel ideas. The three task force groups were (members of the each group are listed below - ‘Today’s exercise’):

(1) Clinical Interventions
(2) Translational/Genetics/Brain Bank
(3) Imaging

These 3 task force groups consisted of scientists and leaders in age-related research across UM campuses and our MBI members and collaborators, as listed below. The task force groups had an experienced group leader-scientist in age-related research, who are also leaders of one of the UM Centers, Institutes or Departments. In addition, each working group had a facilitator experienced in research administration and coaching. We also included a junior faculty or trainee in each working group to foster their learning experience and include them in discussions, decision-making and research networking.
The Retreat was held on June 1st, 2018. **Phase I of our MBI Strategic Plan was completed.**

The Retreat was structured in 3 parts:

1. It started with an initial group meeting and presentation of the history, mission and vision and current state of our MBI programs, preliminary SWOT analysis, and a charge to the 3 task force working groups (Clinical Interventions, Translational/Genetics/Brain Bank and Imaging),

2. Breakout sessions with each group directed to review our MBI vision and mission, SWOT, and to propose several goals and strategies for their achievement, tactics and metrics, and milestones, and

3. It ended with all regrouping to share and review each group’s goals and strategies.

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**TODAY’S EXERCISE**

**Goals**

1. Discuss and add to SWOT analysis – 30 minutes
2. Fill out template for each Focus Area
3. Give 15 minute presentation to the group

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<th>Translational/Genetics/Brain Bank (Rm. 1340)</th>
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<td>Joyce Gomes-Osman</td>
<td>Pradip Pattany</td>
<td>Savita Pahwa</td>
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<td>Neil Schneiderman</td>
<td>Alberto Ramos</td>
<td>Milena Pinto</td>
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<td>Joe Signorile</td>
<td>Anita Saporta</td>
<td>Ami Raval</td>
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<td>Adina Zeki Al Hazzouri</td>
<td>Xiaoyan Sun</td>
<td>Peggy Pericak-Vance</td>
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University of Miami
Evelyn F. McKnight Brain Institute
Strategic Planning Meeting
June 1st, 2018

AGENDA

8:30am - 9:00am  Breakfast

9:00am - 9:15am  Introduction - Sacco, Rundek, Attendees

9:15am - 9:30am  McKnight Brain Research Foundation (MBRF) and IOM Report - Sacco

9:30am - 9:45am  McKnight Brain Institute History, Mission and Vision - Rundek/Sacco

9:45am - 10:00am  Miller School of Medicine Neuroscience Strategic Plan - Sacco/Ransford/Dominguez

10:00am - 10:30am  SWOT Analysis - Rundek
Assignment of Working Groups - Rundek/ Ransford/Dominguez/Rosellini
- Clinical/Intervention Group
- Imaging Group
- Translational/Biomarker/Brain Bank

10:30am - 12:00pm  Working Group Meetings

12:00pm - 12:45pm  Working Lunch/Prepare Presentations
1.4.2. Strategic Plan - Phase I

In Phase I of our Strategic Plan each working group accomplished the following:

- Reviewed the MBI vision and mission and the group SWOT analysis
- Established strategic SMART objectives (Specific, Measurable, Achievable, Realistic and Time-based) for the next 3-5 years; and
- Proposed a ‘big picture’ strategy for achievement of the SMART objectives.

Objective #1:
In the group discussion at the end of the Retreat, the main objective was to expand our MBI Scientific Advisory Board to include a broader cross-disciplinary representation of investigators and leaders involved in age-related memory research across our medical school Departments, Centers and Institutes, and across the schools at UM.

Completed Action:
In addition to the current Board members (Dr. Sacco, Dr. Rundek, Dr. Levin, Dr. Sun and Dr. Perez-Pinzon) the new MBI Scientific Advisory Board Members are:

- **Dr. David Loewenstein, PhD**, Professor, Director of the Center for Cognitive Neuroscience & Aging
- **Dr. Phillip McCabe, PhD**, Professor and Chairman of the Department of Psychology
- **Dr. William Scott, PhD**, Professor of Human Genetics, Neurology and Public Health Sciences, Director of the Brain Bank, and Vice Chair for Education and Training of the John P. Hussman Institute for Human Genomics; and
- **Dr. Olveen Carrasquillo, MD, MPH**, Professor of Medicine and Public Health Sciences, Chief of General Internal Medicine Division, Director of Community Engagement, UM CTSI.

These new Board Members were chosen based on their ability to complement the Board’s current Members and their knowledge-base; to employ novel approaches to identifying funding opportunities and challenges in age-related cognitive research; to be well-versed on memory and cognition changes in aging; to execute research on the aging population; and to possess experience in forming multi-disciplinary and multi-institutional collaborations. Their NIH biosketches are included with this report.
The entire Scientific Advisory Board was assembled in August and reconvened in November of 2018. The MBI Scientific Advisory Board has been charged to help conduct Phase II of the Strategic Planning in 2019, to align our Strategic Plan with the recently completed Miller School of Medicine Research Strategic Plan and to successfully lead the implementation of our Strategic Plan in the next 5 years.

**Objective #2:** to develop a unified framework of cognitive aging and brain health capitalizing on the scientific strengths of our McKnight Brain Institute, UM Centers and Institutes, and leveraging institutional infrastructure and resources and recently developed University of Miami Miller School of Medicine Research Strategic Plan.

**Action:** Development of our unified scientific framework of cognitive aging and brain health is in development. We focus on clinical and translational investigations of vascular, metabolic and sensory drivers of cognitive aging and brain health, that unifies the major strengths of our MBI and Institution and that will define our scientific framework, steer research and educational directions, and set research and educational goals and priorities to further the mission of our McKnight Brain Institute.

The 3 task force working groups have created a set of preliminary goals and strategies that will be discussed, revised and adopted in *Phase II of the MBI Strategic Plan* in 2019:
We have already started to develop and implement some of the identified goals.

For example:

- **Clinical Interventional working group Goal #3**: We have established multiple mentorship teams across disciplines for several of our trainees: Dr. Gomes-Osman (Mentors: Drs. Loewenstein, Rundek) and Dr. Camargo (Mentors: Drs. Levin, Wurtman, Rundek) who have been successful in obtaining training and research grants in 2018;

- **Imaging working group Goal #1**: We have already started utilizing the research MRI facilities at the Coral Gables campus;

- **Translational working group Goal #3**: We have devised our preliminary unified framework and Logic Model around age-related memory loss, cognitive aging and brain health, which will be presented, discussed and finalized in the Phase II Strategic Planning and included in our MBI Strategic Plan document.
1.4.3. UM Medical School Research Strategic Plan

In November of 2017, Dean Dr. Edward Abraham at the time (now Chief Executive Officer of UHealth) charged our Research Deans and Leadership to execute the Miller School of Medicine Research Strategic Plan. Our new Dean, Dr. Henri Ford (appointed in June 2018) is now in charge of the Plan implementation.

Under this plan, Brain Health, Aging, and Degenerative Diseases are areas of focus under the Neuroscience pillar, one of the main strategically focused areas.

Alignment of our MBI Strategic Plan with the Miller School of Medicine Research strategic plan will create new opportunities for our McKnight Brain Institute to advance the goals and mission through strategically targeted collaborations and partnerships and by leveraging institutional infrastructure, resources and research support.

The next step is to conduct Phase II of the MBI Strategic Retreat in 2019, where the Phase I Retreat attendees will meet in smaller groups to review and refine the goals, priorities, strategies and tactics based on proposed goals and resources, the Medical School Strategic Plan, and feasibility. The Scientific Advisory Board will lead and implement the final strategies and directions of our MBI in the next 5 years. After completion of the Phase II Strategic Plan in 2019, we plan to prepare a separate document, The MBI Strategic Plan Document, where the details on unified goals, action plans, milestones and timelines will be provided.
1.5. The McKnight Brain Research Foundation Visits the University of Miami and the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging Ceremony

In October of 2018, the MBRF Trustees visited our MBI, attended the UM Evelyn F. McKnight Research Symposium, and installed the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging.

Dr. Rundek has received the second Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging at the University of Miami.

The Endowed Chair Ceremony was led by Dr. Sacco with participation of the UM President Dr. Julio Frenk, Dean of the University of Miami Miller School of Medicine Dr. Henri Ford, and the MBRF Trustee, Dr. Lee Dockery.

October 30th - 31st, 2018
The McKnight Brain Research Foundation Trustees,
Dr. Sacco, Dr. Rundek and the
UM President Julio Frenk and Medical School Dean Henri Ford
University of Miami Miller School of Medicine
Evelyn F. McKnight Brain Institute
Research Symposium and Chair Installation
October 31st, 2018

Don Soffer Clinical Research Center
Michael S. Gordon Center for Research in Medical Education
1120 NW 14th Street, 1st Floor, Miami, Florida 33136

8:00am - 8:30am            Breakfast

8:30am - 8:50am            Welcome, Introduction and Scientific Director Transition
Ralph L. Sacco, MD, MS, FAHA, FAAN
Professor and Olemberg Chair of Neurology
Executive Director, Evelyn F. McKnight Brain Institute
Director, Clinical and Translational Science Institute
Senior Associate Dean for Clinical and Translational Science
University of Miami, Miller School of Medicine
President, American Academy of Neurology 2017-2019

Edward Abraham, MD
Executive Vice President for Health Affairs and Chief Executive Officer
of UHealth, University of Miami, Miller School of Medicine

J. Lee Dockery, MD
McKnight Brain Research Foundation Trustee

8:50am - 9:05am            Scientific Overview
Tatjana Rundek, MD, PhD
Professor of Neurology
Scientific Director, Evelyn F. McKnight Brain Institute
Executive Vice Chair of Research and Faculty Affairs
Director, Clinical and Translational Research Division
Department of Neurology
Director, Master of Science in Clinical and Translational Investigation

Research Update Session

9:05am - 9:20am            A Treatment Strategy for Age-Related Cognitive Decline: Accelerating
Synapse Formation with the Oral Multi-Nutrient Souvenaid
Christian Camargo, MD
Collaborator, Evelyn F. McKnight Brain Institute
Instructor, Clinician Department of Neurology
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<th>Time</th>
<th>Session Topic</th>
<th>Speaker and Affiliations</th>
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| 9:20am - 9:35am | Resting-State Functional Brain Connectivity: A Potential Biomarker of Risk For Age-Related Cognitive Decline | Roger McIntosh, PhD  
Collaborator, Evelyn F. McKnight Brain Institute  
Assistant Professor, Department of Psychology, Health Division |
| 9:35am - 9:50am | Susceptibility to Deception: Decreasing Vulnerability in Age Related Memory Loss | Sarah Getz, PhD  
Collaborator, Evelyn F. McKnight Brain Institute  
Instructor, Department of Neurology |
| 9:50am - 10:05am | Exercise for Brain Health: Neuroplasticity and the Pursuit of Data-driven, Dose-specific Recommendations | Joyce Gomes-Osman, PT, PhD  
Member, Evelyn F. McKnight Brain Institute  
Assistant Professor, Department of Physical Therapy and Neurology |
| 10:05am - 10:20am | Sleep Quality Mediates the Relationship Between Cognitive Dysfunction and Frailty in Non-demented Older Adults | Sonya Kaur, PhD  
Neuropsychology Research Fellow, Department of Neurology |
| 10:20am - 10:35am | Subjective Fatigue and Cognition in Non-demented Older Adults | Nikhil Banerjee  
Predoctoral Psychology Trainee, Clinical Health Psychology |
| 10:35am - 10:50am | Whole Body Vibration Therapy after Ischemia Reduces Brain Damage In Reproductively Senescent Female Rats | Ami Raval, PhD  
Collaborator, Evelyn F. McKnight Brain Institute  
Associate Research Professor, Department of Neurology |
| 10:50am - 11:00am | Questions | |
| 11:00am - 11:15am | Break | |
| 11:15am - 11:45am | Chair Presentation | Henri Ford, MD, MHA  
Dean and Chief Academic Officer  
University of Miami, Miller School of Medicine  
Chair Presentation  
President Julio Frenk, MD, MPH, PhD  
University of Miami, Miller School of Medicine |
|             | | J. Lee Dockery, MD  
McKnight Brain Research Foundation Trustee  
Tatjana Rundek, MD, PhD  
Professor of Neurology  
Scientific Director, Evelyn F. McKnight Brain Institute  
Executive Vice Chair of Research and Faculty Affairs  
Director, Clinical and Translational Research Division  
Department of Neurology  
Director, Master of Science in Clinical Translational Investigations |
1.5.1. Overview of the Evelyn F. McKnight Brain Institute Research Symposium

October 31, 2018

We decided to provide an opportunity for our MBI trainees and junior faculty to participate in the MBI Research Symposium, present their research and show their enthusiasm to be a part of the Symposium and our MBI.

Dr. Rundek presented the MBI scientific update with the current research portfolio and introduced our junior speakers.

Here are the highlights of the McKnight Research Symposium presentations:

**A Treatment Strategy for Age-Related Cognitive Decline: Accelerating Synapse Formation with the Oral Multi-Nutrient Souvenaid**

*Presented By Christian Camargo, MD*

Christian presented a pilot study of a multi-nutrient oral supplement for improved cognitive performance in participants with age-related cognitive complaints. The study is designed to test the feasibility and safety of Souvenaid for improvements in cognitive performance in age-related cognitive decline (ARCD).

Recent research has suggested that the underlying mechanism behind age-related cognitive decline is a *loss of synaptic plasticity*, the dynamic ability of synapses to strengthen or weaken their connections. Synaptic plasticity is essential for learning, memory and the formation of memory engrams in part, through its effects on dendritic spine morphology. A
landmark study has recently described the biological basis of memory engrams by utilizing Souvenaid, a specific oral multi-nutrient, as an example of a treatment to increase synaptic plasticity. The formulation is based on the biochemical properties of synaptic membranes intimated after years of rigorous research.

Resting-State Functional Brain Connectivity: A Potential Biomarker of Risk For Age-Related Cognitive Decline

Presented By Roger McIntosh, PhD

Roger eloquently presented some of our resting state functional brain connectivity research, addressing the risk for cognitive aging that was recently submitted for publication. His first study evidenced preserved resting state functional connectivity (rsFC) of the hippocampus and parietal lobes in Super-Agers, versus age-matched controls, as it relates to lower cardiovascular disease risk. His second study demonstrated that poorer performance on the Trails-making task was linked to aberrant patterns of intrinsic rsFC in the executive control network of individuals self-reporting high sleep disturbance versus those endorsing low sleep disturbance. He also presented results from an Honor's Thesis Study of one of his students, addressing whether cardiorespiratory fitness relates to differential patterns of intrinsic rsFC of the default mode network in post-menopausal women.

Susceptibility to Deception: Decreasing Vulnerability in Age Related Memory Loss

Presented By Sarah Getz, PhD

Sarah presented on the project scamming in elderly. Scamming, the cheating of people out of money or information, is a pressing public health problem associated with decreased quality of life, functional dependence and negative health outcomes. Individuals in late middle and late adulthood are at particular risk for scamming, but the cognitive, socio-affective, and neurobiological mechanisms underlying this increased risk with advanced age are unclear. There are currently no effective interventions to reduce scam susceptibility in these age groups. Therefore, the long-term goal of this research is to implement an effective intervention to reduce online scam susceptibility in late midlife and old age. Her specific goal is to quantify the cognitive, physical, and socio-affective correlates deception susceptibility, among cognitively healthy late middle and older adults. Within this aim, she will measure participants’ actual behavioral response when faced with deceptive stimuli and their scam susceptibility. She will employ a selected test battery to identify correlates of self-reported level of scam susceptibility. She hypothesize that high scam susceptibility will be associated with evidence of executive dysfunction, increased frailty symptoms, and lower scores on affective ratings of social wellbeing (e.g., more negative affect, more loneliness).
**Exercise for Brain Health: Neuroplasticity and the Pursuit of Data-driven, Dose-specific Recommendations**  
*Presented By Joyce Gomes-Osman, PT, PhD*

Joyce spoke about the theoretical concept of brain plasticity, defined as the capacity of the nervous system to adapt and change in response to changes in the environment and lifespan. She expanded upon this concept by presenting a more practical scientific paradigm used to quantify brain plasticity using non-invasive transcranial magnetic brain stimulation (TMS). In addition, she presented the preliminary results of our first McKnight pilot study that was awarded to her last year in which she investigated changes in brain plasticity in aging adults following a 4-week aerobic exercise intervention. Finally, she shared the results of an extensive quantitative systematic review that she carried out with the objective of outlining dose-specific recommendations of exercise to promote cognitive brain health.

**Sleep Quality Mediates the Relationship Between Cognitive Dysfunction and Frailty in Non-demented Older Adults**  
*Presented By Sonya Kaur, PhD*

Sonya presented on the association of frailty with a host of negative outcomes including cognitive decline in older adults and how sleep quality may play an important role in understanding this association in older adults. Her results showed that the relationships between frailty severity and measures of executive function, learning and memory were significantly mediated by poor sleep quality. Based on her research, interventions to improve sleep quality may be promising avenues to prevent or potentially reverse cognitive decline in frail older adults.

**Subjective Fatigue and Cognition in Non-demented Older Adults**  
*Presented By Nikhil Banerjee*

Nick presented the association between self-reported fatigue and neuropsychological functioning in middle-aged and older adults, and the moderating role of physical activity. He showed that higher levels of fatigue were significantly associated with poorer attention/information processing, executive functioning, and psychomotor speed, even after controlling for depression, sleep quality, grip-strength, and gender. Participants endorsing moderate-severe fatigue faced higher odds of exhibiting attention/information processing and psychomotor speed/dexterity impairments than those without after controlling for covariates. Moderation analyses showed that fatigue was related to attention/information processing and psychomotor speed deficits among those reporting mean or lower levels of activity, but not high levels. Overall, these findings highlight fatigue as a distinct and important clinical marker of select cognitive deficits in non-demented older adults. High levels of physical activity may buffer this relationship, suggesting a potential avenue for targeted intervention efforts to promote healthy cognitive aging.
1.5.2. The Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging Ceremony (October 31, 2018).

Dr. Tatjana Rundek was deeply honored by receiving the second *Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging.*

PRESS RELEASE:

*Dr. Tatjana Rundek was Awarded the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging*

![Image of Dr. Tatjana Rundek and others at the ceremony]

L-r, back row: Michael Dockery, M.D., Madhav Thambisetty, M.D., Ph.D., Richard Isaacson, M.D., Gene Ryerson, M.D., and Amy Porter. L-r, front row: Dean Henri R. Ford, M.D., MHA, Ralph Sacco, M.D., MS, Tatjana Rundek, M.D., Ph.D., Lee Dockery, M.D., Melanie Cianciotto, President Julio Frenk

At a ceremony before many of the nation’s most prominent neurologists, renowned researcher, epidemiologist, mentor, and educator Tatjana Rundek, M.D., Ph.D., formally became the holder of the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging.

Dr. Rundek, who is also the scientific director of the Evelyn F. McKnight Brain Institute (MBI) at the University of Miami Miller School of Medicine, said she is excited to lead the dedicated team of physician-scientists who are committed to understanding how aging influences memory.

“I am dedicated to the McKnight Brain Research Foundation [MBRF] mission of improving cognitive brain health,” said Dr. Rundek, professor of neurology and public health, executive vice chair of research and faculty affairs, director of the Clinical Translational Research Division in Neurology, and director of the Master of Science degree program in clinical translational investigations. “I see myself as a catalyst, along with the MBI team, to advance our innovative research and educational programs.”
One of four McKnight Institutes nationwide, MBI was established in 2002 with a generous donation from the MBRF and a match from the Bernard and Alexandria Schoning Foundation and other UM donors to investigate and treat age-related cognitive decline. Through an additional gift, MBRF then established the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging to support the scientific director of the institute, providing them the freedom to further their research in the field.

“Today’s installation is a well-deserved honor for Dr. Rundek and stands as a testament to the generosity of the Evelyn F. McKnight Brain Research Foundation,” said University of Miami President Julio Frenk. “We are so appreciative of their extraordinary philanthropy.”

“An endowed chair is one of the highest academic honors that we can confer on a faculty member,” said Henri R. Ford, M.D., MHA, dean and chief academic officer of the Miller School. “It is a tribute to the faculty member’s achievements and our sincere and utmost confidence that this individual is going to continue on a path of excellence.”

J. Lee Dockery, M.D., chair of the board of trustees of MBRF, said Mrs. McKnight would have been delighted with Dr. Rundek’s appointment as chair holder.

“Mrs. McKnight was a great champion of women and had a very successful career as a nurse, serving as a captain in the United States Air Force and as a Nurse in United States Congress — she created great things,” Dr. Dockery said. “Dr. Rundek would have certainly been her choice to take on this challenge.”

Ralph L. Sacco, M.D., MS, professor and chair of the Department of Neurology, has been Dr. Rundek’s colleague for 20 years. He said she embodies a commitment to excellence that is critical to the department’s success.

“Thanks to her innovation, her insight, and her collaboration, Tatjana truly embraces team science,” said Dr. Sacco, who is also the Olemberg Family Chair in Neurological Disorders and executive director of the institute. “She does it with grace and in a way that makes everyone feel a part of the team.”

While accepting the honor, Dr. Rundek thanked those who spoke on her behalf, as well as members of MBRF, her research team, and collaborators. “I like to say, ‘If you want to go fast, go alone. But if you want to go far, go together.’ This has been my motto,” Dr. Rundek said. “I look forward to working with all to do great things.”
2. Publications in Peer Reviewed Journals

Trainee (as first authors) Publications


**Denotes corresponding author


Khoury N, Koronowski KB, Young JI, Perez-Pinzon MA. The NAD(+)-Dependent Family of Sirtuins in Cerebral Ischemia and Preconditioning. Antioxid Redox Signal. 2018;28(8):691-710.


Cross-Disciplinary and Collaborative Publications


*AZ and MRC shared first authorship.


Curiel RE, **Crocco EA**, Raffo A, Guinjoan SM, Nemeroff CB, Pina D, Penate A, **Loewenstein DA**. Failure to recover from proactive semantic interference differentiates amnestic mild cognitive impairment and PreMCI from normal aging after adjusting for initial learning ability. Advances in Alzheimer's Disease. 2018;7(02):50.


Reid KJ, Weng J, et al. (Ramos AR). Impact of shift work schedules on actigraphy-based measures of sleep in Hispanic workers: results from the Hispanic Community Health Study/Study of Latinos ancillary Sueno study. Sleep. 2018;41(10).


**Denotes corresponding author
**Denotes corresponding author


3. Publications (other)


Della-Morte D. Interview for Italian scientific magazine Oggiscienza: “Aggiustare i mitocondri per curare malattie” July 10th 2017.


4. Presentations at Scientific Meetings


Brito, Y, CC Pedraza, AR Abreu, **AR Ramos.** Poster presentation: The Case for Spino-cerebellar Ataxia with Insomnia and Comorbid Obstructive Sleep Apnea. SLEEP41, A418-A418.


Caunca MR, Simonetto M, Alperin N, Elkind MSV, Sacco RL, Wright CB, Rundek T. Greater Body Mass Index is Associated with Smaller Cortical Thickness in the Alzheimer Disease-Signature Regions: The Northern Manhattan Study. Oral Data Blitz Presentation and Poster at the American Neurological Association Annual Meeting, Atlanta, GA.


44th Annual Eastern-Atlantic Student Research Forum, held at the University of Miami, February 2018. Abstract was not refereed.


Perez E, Caunca M, Montero D, Reyes-Iglesias Y. The Importance of Neurology as a Required Third-Year Clerkship: a Medical Student Survey. Poster at the American Academy of Neurology Annual Meeting, Los Angeles, CA.


Raval A. Society for neuroscience (SFN) 2018 annual meeting and McKnight Brain Research Foundation 2018 Poster Reception. San Diego, California.

Rehni AK, Shukla V, Dave KR. Potential role of endoplasmic reticulum stress in mediating recurrent hypoglycemia-induced increase in ischemic brain damage in treated diabetic rats. 9th annual Postdoctoral research day, University of Miami Miller School of Medicine, March 2018.


Sacco RL. 2018 Evelyn F. McKnight Brain Institute Inter-Institutional Meeting, Birmingham, AL, April 4 – 6, 2018.

Sacco RL. Hypertension, Small Vessel Disease and Cognition, The Heart & Brain Symposium, Chicago, IL, June 29, 2018.


Sacco RL. 11th World Stroke Congress Stroke Congress, Life's Simple Seven Determinants of Stroke and Brain Health, Montreal, Canada, October 17, 2018.


Sacco RL. The Annual Israeli Neurological Association Meeting 2018, Neurology Challenges and Future Opportunities, Tel Aviv, Israel, December 11, 2018.

Sacco RL. The Annual Israeli Neurological Association Meeting 2018, Preventing Stroke and Promoting Brain Health, Tel Aviv, Israel, December 11, 2018.


Watanabe M, Bhattacharya P, Khan A, Hare JM, Perez-Pinzon MA, Raval AP, Yavagal DR. Multiple intra-arterial dosing of the mesenchymal stem cells reduces ischemic brain injury in a rat stroke model. International Stroke Conference healed at Los Angeles, January 23rd 2018. (Refereed)
5. Publications at Public (Non-scientific) Meeting or Events


Caunca M. Freesurfer Workshop, October 2018, Boston, MA.

Caunca M. Epidemiology Journal Club, October 2018. LASSO Regression and Prediction Modeling using Biomarker Data.

Dave K. The McKnight brain research foundation, 10th inter-institutional meeting, University of Alabama at Birmingham April 2018.


Loewenstein D. Lecture: Nurturing Your Brain in Middle Age and Beyond, Broward Women's Health Forum, October 17, 2018.


Gomes-Osman J. Exercise for Brain Health: Plasticity, and the pursuit of Data-Driven, Dose-Specific Recommendations. Massachusetts General Hospital Institute of Health Professions, Department of Physical Therapy, Boston, MA, April 2018.


Kaur S. Didactic titled "Using existing medical data collection systems for cardiovascular disease surveillance," University of Miami.


Perez-Pinzon M, Dave K International Stroke Conference 2018 held at Los Angeles, California, January 2018.

Perez-Pinzon M, Dave K. 10th International Symposium on Neuroprotection Neurorepair 2018 held at Dresden, Germany October 2018.

Perez-Pinzon M, Dave K. The 5th International Symposium on Conditioning Medicine 2018 held at Beijing, China November 2018.


Ramos AR. Sleep and cognitive impairment lecture. Baptist Health System Sleep Symposium. Miami, FL November 3rd, 2018, 0.25 CME.

Ramos AR. Sleep and Women’s Health Conference. The NIH and its different institutes wanted to highlight the most important sleep science of the last 10 years emphasized in sleep and women’s health. It was attended by close to 300 people at the NIH headquarters in Bethesda, Maryland and seen by close to 1300 people in the live webcast (link below). The video for Day 1 is up: https://videocast.nih.gov/PastEvents.asp?c=1 I also got some media attention in their twitter account: https://twitter.com/nih_nhlbi/status/105228963027456000 https://twitter.com/nih_nhlbi/status/1052227674805014529?s=20 and also provided two national telephone interviews (one for CNN Español) and one TV interview for Univision (link to follow). See attached emails with NIH staff requesting to complete these interviews.


Sacco RL. Preventing Stroke and Cognitive Decline, Neurology Grand Rounds, UT Southwestern Medical Center, December 5, 2018.

6. Awards (other)

6.1. Trainee Awards

Dr. Anita Seixas Dias Saporta is our second McKnight Fellow. She has experience in clinical and translational neuroscience research. Her previous research work includes brain neuroimaging from the neonatal period to adulthood and utilizing multiple imaging modalities to analyze brain function and structure (PET, MRI, DTI, MRS). She also has experience with large database management and development of clinical tools. Since her clinical training in child neurology in Rio de Janeiro, Brazil, she developed an increased interest in the normal and pathological development of the brain, behavior and cognition. She pursued research training in neuroimaging in reference centers including the PET Center at Wayne State University (Detroit, MI) and the Neonatal Brain Disorders Lab at UCSF (San Francisco, CA). Her current research interests include the neuroimaging and electrophysiology markers of epilepsy severity and of normal and pathological aging.

Since she joined us in June, Anita has been processing MRI scans of subjects enrolled in the McKnight Frailty Registry, which is going to be added to the registry dataset and will be available for further use in future projects of the multidisciplinary research group.

The MRI processing techniques she uses are described below:
Regional brain volumes: Regional analysis is being done on the 3D T1 MPRAGE images with FreeSurfer 5.3 (http://surfer.nmr.mgh.harvard.edu) (Soon, with Freesurfer 6.0 as well). 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 pipeline will be applied to the MRI scans to produce 115 cortical and subcortical volumetric measures. These 115 regional volumes will be corrected for head size variation using FreeSurfer’s estimate of total intracranial volume (TIV), which has been shown to be highly accurate in adults. Currently, the focus on studying the aging brain is on volumetric changes in bilateral hippocampal volumes as well as other structures affected early in those at AD risk (e.g., precuneus, entorhinal cortex, anterior cingulate and posterior cingulate) and volumetric changes in the ventricular spaces that have been shown to be early markers as well. Hippocampal volumes derived from FreeSurfer are comparable to manually traced regions of interest and provide a practical method for big data studies.

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.

Dr. Christian Camargo, formerly the McKnight Brain Institute Cognitive Fellow, was appointed Instructor, with the plan to be appointed Assistant Professor in Clinical Neurology in July 2019.

Dr. Sarah Getz received a UM Miller School of Medicine Medical Faculty Association travel award to present McKnight Frailty research at the 2018 Annual Meeting of the International Neuropsychological Society in Washington DC. She is mentored by Dr. Bonnie Levin, and has been appointed Instructor of Neuropsychology in the Department of Neurology at the University of Miami.

Dr. Marina Sarno who is mentored by Dr. Bonnie Levin has been appointed Instructor of Neuropsychology in the Department of Neurology at the University of Miami.

Dr. Annelly Buré-Reyes who is mentored by Dr. Bonnie Levin has been appointed Assistant Professor of Neurology in the Department of Neurology at the University of Miami.

Michelle Caunca, our McKnight MD/PhD student received the following awards and honors:

- The following grant went into effect in 2018: Ruth L. Kirschstein National Research Service Award (NRSA) Fellowship for Students at Institutions with NIH-Funded Institutional Pre-doctoral Dual-Degree Training Programs (F30)
- Delta Omega Honors Society
- PEO International Scholar Award Nominee
- Travel Award, American Neurological Association Annual Meeting
- Best Poster, 10th Annual Medical Scientist Training Program (MSTP) Student Symposium
- Medical Faculty Association Travel Award, University of Miami
- Young Investigator Scholarship, Annual Meeting, American Academy of Neurology (AAN)

Jing Xu (Graduate student in Dr. Miguel Perez-Pinzon’s laboratory) received the American Heart Association (AHA) pre-doctoral fellowship award.
Ashish Rehni (Post-doc in Dr. Kunjan Dave’s laboratory) received the American Heart Association (AHA) Post-doctoral fellowship award.

Andrea Ruetenik (Ph.D. Student in Dr. Antonio Barrientos’ laboratory) has received Huntington’s Disease Human Biology Project Fellowship from the Huntington’s Disease Society of America on The protective role of NAD salvage pathway proteins against mutant huntingtin toxicity.

6.2. Faculty Grants and Awards

Dr. Ralph Sacco is serving his second and last year as President of the American Academy of Neurology.

Dr. Ralph Sacco was elected to the National Academy of Medicine. (See Section 22)

Dr. Ralph Sacco is PI for the NIH/NCRR/NIMHD UL1 (Clinical and Translational Science Award) to facilitate translational research at the University of Miami which was awarded a five-year renewal.

Dr. Ralph Sacco is Co-PI for the NIH/NINDS U10 (Miami Regional Coordinating Center for NINDS -StrokeNET), which was awarded a five-year renewal to: a) provide a robust and efficient infrastructure to implement high-quality research clinical trials that address acute stroke treatment, prevention and recovery; b) to leverage the internal and regional resources to enhance the Stroke Trials Network; and c) to train the next generation of stroke clinical and translational researchers.

Dr. Ralph Sacco and Dr. Tatjana Rundek are Co-Investigators for the NIH/NINDS U10 (University of Miami: Network of Excellence in Neuroscience Clinical Trials -NEXT), which was awarded a 5-year renewal to (a) function effectively as a NEXT consortium trial site, (b) to enhance quality and efficiency of NEXT and other NINDS trial implementation at the University of Miami and (c) to leverage institutional strengths to enhance NEXT consortium activities.

Dr. Ralph Sacco is Co-Chair and Co-I for the NIH/NINDS U01 (NSTN National Clinical Coordinating Center,StrokeNET), which was awarded a 5-year renewal to coordinate NINDS-funded trials in stroke prevention, acute therapy, and recovery. He serves as the co-chair of the Stroke Prevention Committee.

Dr. Hong Jiang received the Dean’s NIH Bridge program award for “Novel retinal microvascular biomarkers of vascular contribution to dementia.”

Dr. Joyce Gomes-Osman was selected to participate in the prestigious Training for Grantsmanship in Rehabilitation Research (TIGRR) funded by the NIH/NICHD and hosted by the Medical University of South Carolina, Charleston, SC.
**Dr. David Della-Morte** and Dr. Guadagni received a European Social Fund, under the Italian Ministries of Education, University and Research (PNR 2015-2020 ARS01_01163) PerMedNet award to study personalized medicine for innovative strategies in neuropsychiatric and vascular diseases.

**Dr. David Della-Morte** and Dr. Lauro and received a Rome Foundation award for Diabetes Mellitus, Regenerative and Reparative Processes, and Improvement of Pancreatic Beta Cell Function: Role of Bone Marrow-Mesenchymal Stem Cells, Micrornas, M2 Macrophages and Myeloid Derived Suppressor Cells.

**Dr. David Della-Morte** and Dr. Suhrud submitted an ITS proposal to study the role and the therapeutical approach for mitochondrial sirtuins in noise-induced hearing loss.

**Dr. David Loewenstein** (PI) has received funding from the National Institute on Aging (NIA) R01AG061106: for his research proposal: *A Novel Computerized Stress Designed for Clinical Trials in Early Alzheimer’s: Relationship with Multimodal Imaging Biomarkers in Diverse Cultural Groups.*

**Dr. David Loewenstein** (PI) has received funding from the State of Florida #9AZ24: to study *Middle-aged Offspring of late Alzheimer’s Probands: Novel Cognitive and Biomarker Assessment.*

**Dr. David Loewenstein** (PI) received funding from State of Florida Ed and Ethel Moore Grant #8AZ23 for the Program: *New Cognitive Stress Tests and Multimodal Imaging Diverse Ethnic/Cultural Groups.*

**Dr. David Loewenstein** (Co-Investigator) is included on an NIH/NIA grant: *Precision-Based Assessment for Detection of MCI in Older Adults.*

**Dr. David Loewenstein** (PI) received funding from the State of Florida Ed and Ethel Moore Grant # 7AZ18 Program: to research *Cognitive Stress Tests and Amyloid Load in Diverse Ethnic/Cultural Groups.*

**Dr. David Loewenstein** (PI) received funding from NIH/NIA for the research study: *Novel Detection of Early Cognitive and Functional Impairment in the Elderly grant.*

**Dr. David Loewenstein** (PI) received an R01 grant for the: *Non-Pharmacological Intervention for Patients with Alzheimer’s Disease and Family Caregivers.*

**Dr. David Loewenstein** (PI of scientific project and Co-PI of the clinical core) received a grant from the Florida Alzheimer’s Disease Research Center (ADRC) to explore novel cognitive measures/biomarkers for early detection of Preclinical Alzheimer’s in English/Spanish speaking elderly.

**Dr. David Loewenstein** has been appointed Director of the Center for Cognitive Neuroscience and Aging, Department of Psychiatry & Behavioral Sciences.
Dr. David Loewenstein has been appointed as a Member of the University of Miami Scientific Advisory Board of the Evelyn F. McKnight Brain Institute, Department of Neurology.

Dr. David Loewenstein has been appointed Co-Director of the Integrating Special Populations Program-Older Adults at the UM Clinical and Translational Science Institute (CTSI).

Dr. David Loewenstein’s paper published in Neurology was highlighted on the National Institute on Aging website showing that semantic intrusion on the LASSI-L could differentiate amnestic MCI patients with high and low amyloid loads significant implications for screening into novel clinical trials.

7. Faculty

Our MBI Faculty is categorized to those receiving direct support from the Institute (Members) and those with whom the Institute is collaborating across the University of Miami (Collaborators).

A Table with our McKnight Brain Institute Faculty and their biosketches are provided at the end of the report.
8. Trainees

A table with our trainees is provided at the end of the report.

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9. Clinical/Translational Programs

9.1. Update on Existing Clinical Studies

9.1.1. Update on Population-Based Research

McKnight Brain Aging Registry (MBAR) - This study is a collaborative research project with our fellow McKnight Brain Institutes on 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 (thinking abilities), physical and emotional areas and the way the aging process affects them. (A detailed report on MBAR has been submitted to the Trustees by the Inter-Institutional MBAR investigators in a separate document).

This year, the majority of research activity has been directed toward our ongoing recruitment. Substantial effort was made to increase the enrollment from 9 subjects to 35. We had the help of Marti Flothmann who was still responsible for another study but made tremendous efforts to help with MBAR recruitment as well as study coordination. Dr. Bonnie Levin’s team of neuropsychologists, Dr. Katalina Mclnerney, Dr. Marina Sarno and Dr. Sonya Kaur worked an incredible amount of time administering and scoring assessments while fitting in the many clinical patients they see. Together with Dr. Rundek, Dr. Christian Camargo performed the neurology exams engaging each participant in meaningful conversation. Dr. Noam Alperin and Sang Lee made it possible to schedule and conduct several MRIs in a very short period of time. Additionally, a summer volunteer worked in the community to recruit study subjects. The group effort led by Stacy Merritt enabled our site to get our enrollment numbers on par with all sites. Our main recruitment strategy this year was to obtain a public list of registered English speaking voters over 84 in Miami-Dade County. About 600 envelopes were stuffed with flyers, hand stamped and mailed out. Several respondents were ineligible because they were not old enough
or were unable to have an MRI. Participants have truly enjoyed the study and being able to refer to themselves as ‘successful agers.’

Operationally, we had bi-weekly conference calls attended by Dr. Rundek, Dr. Levin, Dr. Alperin, Stacy Merritt and Dr. McInerney. These calls focused on resolving any logistical, procedural and data management issues that may have arisen. On alternative weeks, we held additional conference calls that were either focused on specific project-related discussions on neuroimaging and cognitive issues or were dedicated for our newly implemented MBAR Scientific Advisory Committee (SAC) call. The SAC consists of an eight-member committee of MBAR PIs and investigators, fully familiar with the MBAR cohort and data collection, with two representatives from each MBAR MBI participating site. The SAC calls provide for monthly meetings 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. Dr. Rundek and Dr. Levin are our MBAR SAC members.

With our MBAR database infrastructure established, the REDCap dataset is now fully operational and 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 is uploaded to UM, where it is double entered into REDCap with ongoing reliability checks.

- **MBAR Neuroimaging Core Progress:** The neuroimaging protocol is now finalized and fully operational. MR standardization across all sites has been accomplished following standard procedures for the MRI protocols and order of administration. Neuroimaging data collection is well underway and imaging quality assurance across the sites is ongoing.

  **Dr. Noam Alperin** has dedicated significant time in 2018 working on the neuroimaging core of the McKnight Brain Aging Registry (MBAR) study. During this period the recruitment of subjects for the MBAR study has grown substantially largely due to the dedication of our research team led by Stacy Merritt. A comprehensive MRI protocol and scans were successfully completed on 20 MBAR subjects.

  **Preliminary Analyses of blood flow scans** Measurement of blood flow dynamics are unique for the MBAR study protocol. In a preliminary study testing the quality of the scans we tested the relationships between total cerebral blood flow (tCBF) and 1) Cognitive scores (MMSE and MoCA), and 2) Brain gray matter volume. The results are described in the figures below.

  **Figure 1:** Scatter plot of the total CBF measurements vs MMSE (left) and MoCA (right). A strong and significant ($P=0.002$) correlation was found between tCBF and MoCA scores. No significant correlation was found with MMSE suggesting that MoCA provide a more sensitive and comprehensive measure of cognitive performance than MMSE.
Figure 2: The inter-relationship between blood flow, cognitive performance, and GM brain volume. The initial results suggest that in cognitively normal elderly subjects the tCBF is more strongly correlated with cognitive performance than with GM brain volume. Thus tCBF may be a stronger predictor of cognitive performance than brain GM volume.

- **MBAR Cognitive Core Progress**: The Cognitive Core has also integrated 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 planning of the sequence of analyses to be conducted in the next year. There has also been ongoing discussion to consider adding a few additional cognitive measures or rating scales that might provide added value for the cognitive assessments. Dr. Bonnie Levin, Dr. Katalina McInerney and their UM team continued implementation of neuropsychological testing for the UM MBAR study as well as led the data analyses and organized the MBAR cognitive and behavioral database for all the McKnight sites. Dr. Levin works closely with Dr. McInerney and the other members of the Division of Neuropsychology in leading the data cleaning, monitoring for quality control and overseeing the MBAR site entries in order to prepare the data set for collaboration with our McKnight and MBAR collaborators.

**McKnight Frailty Project** - Under the supervision of Drs. Katalina McInerney and Bonnie Levin, the McKnight Frailty Project is unique to the University of Miami and includes clinic and community dwelling participants from diverse backgrounds ranging in age from 50 to 95+. The
The frailty database has yielded 7 abstracts this year and we anticipate many more going forward, as well as peer-reviewed publications. The Frailty Project has been strengthened through collaborations with the Department of Psychology.

Dr. McInerney holds bi-weekly meetings with our MBI team of research assistants to address issues related to data management and quality control of the McKnight Frailty database. All neuropsychology Post-doctoral Fellows and graduate students are actively engaged in the project. Dr. Levin leads a weekly research rounds on the Frailty and Normative Aging Project, being driven from the McKnight Frailty Registry. This meeting focuses exclusively on research topics related to frailty and normative aging. Our database, which is now approaching 400 participants, has become for the first time, a wonderful resource for generating new hypotheses and preliminary data for grant applications regarding cognitive aging and functional ability for our MBI Trainees and faculty to propose. However, it requires continued quality control and maintenance. Therefore, we are still largely focused on data check and entry into the REDCap database, data management and monitoring quality control.

**Uncovering Risk Profiles of Deception and Mitigating Susceptibility to Scamming in Midlife and Older Age: A Novel Intervention Tool** - Drs. Bonnie Levin and Sarah Getz work with Drs. Ebner and Oliveriera (UF) and Grilli and Wilson (UA) on susceptibility to deception tools and the collection of pilot data. Our team has been meeting via monthly conference calls. The UM team has organized a battery to examine targeted domains and generate a more comprehensive understanding of susceptibility profiles. This battery assesses areas that have been shown to be highly relevant to scamming, and include measures of cognition (emphasizing memory and executive functioning and utilizing the NIH toolbox), mood and emotional wellbeing, and socio-affective functioning. Dr. Getz drafted the IRB protocol to carry out the Miami portion of the multisite collaboration with the Universities of Florida and Arizona. Data collected in this protocol will lay the foundation for a future R01 proposal in which we will study the efficacy of an online intervention tool in the real world and extend the investigation of cognitive and socio-affective risk profiles to neurobiological factors contributing to scam susceptibility in midlife and old age.

**The Northern Manhattan Study (NOMAS)** - Dr. Ralph Sacco is the Principal Investigator (Drs. Rundek, Levin and Sun are co-Investigators). Stroke Incidence and Risk Factors in a Tri-Ethnic Region, currently in its fourth year of funding for cycle 5, is a 26-year-old longitudinal study. Through the continued participation of the now aging NOMAS cohort, the project is addressing gaps in knowledge related to the risks and determinants of stroke, as well as cognitive impairment and dementia. In collaboration with Columbia University, the project is 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, this study has successfully accomplished obtaining data necessary to conduct various analyses to explore the association between cognitive trajectories and biomarkers/networks (assayed with neuro-immune and neuro-inflammatory biomarker panels). Approximately 200 more participants have provided a 3rd data point for cognitive trajectories by completing a 10-year follow-up neuropsychological evaluation this year. The same cohort (now reaching almost 400) has provided plasma samples and all baseline samples have been processed with the biomarker panels enabling the study team to conduct cross-sectional analysis to define the relationship between biomarkers and cognitive status at baseline.

The project has also begun to assemble a NOMAS dementia cohort. Through the dementia adjudication protocol, a data-driven algorithm validated this year, the dementia adjudication committee reviews cases that have not meet the algorithmic criteria to be categorized as “normal cognition”. Dementia adjudication includes the review of all available cognitive performance data via a centralized REDCap database application.

Using other available NOMAS data, multiple studies have been completed this year yielding at least 12 published manuscripts demonstrating the association between cerebrovascular disease and cognitive trajectories. We have recently reported on the association of brain arterial diameters with cognitive performance demonstrating that NOMAS participants with larger brain arterial diameters, particularly in arteries supplying domain-specific territories had greater cognitive decline. We studied the association of small and large vessel cerebrovascular disease and vascular cognitive impairment and found that white matter lesions are associated with a regional pattern of gray matter atrophy that is mitigated by blood pressure control, exacerbated by aging, and associated with cognitive performance. This study extends and support work from last year, in which explored the regional patterns of gray matter atrophy using a neuroimaging technique, which applies gray matter voxel-based morphometry with the scaled sub-profile model. We found that the pattern of reduced gray matter volume was associated with white matter lesion load in bilateral temporal-parietal regions with relative preservation of volume in the basal forebrain, thalami and cingulate cortex. This pattern was expressed most in those with uncontrolled hypertension and least in normotensives. Expression of this pattern was associated with worse performance in executive function and memory.

This year we have also accomplished a series of studies testing the effects of vascular risk factors and global vascular risk scores on trajectories of functional outcomes. We tested the hypothesis that white matter hyperintensity volume (WHMV) asymmetry may be an important predictor of long-term functional status. Greater WHMV asymmetry in the parietal lobes and temporal lobes was associated with lower overall function. Greater WHMV asymmetry in the parietal lobes was also independently associated with accelerated functional decline (Regional WMHV was also predictive of functional decline, with periventricular WMHV particularly associated with accelerated functional decline. In another analysis, we reported a strong and independent association between the subclinical markers pathology-informed subclinical brain infarct (PI-SBI) and WMHV and trajectories of patient-centered outcomes over time. Though PI-SBI was independently associated with steeper functional decline, over and above the decline due to aging, WMHV did not moderate the relationship between cognitive performance and function.
Our findings suggest that WMHV may function through mechanisms distinct from SBI to affect ongoing functional decline independently of processes that determine cognitive ability.

Other NOMAS studies this year have explored healthy behaviors, cardiovascular health, and cognitive aging. We reported a relationship between greater depressive symptoms and worse episodic memory, smaller cerebral volume, and silent infarcts. We have shown also that physical inactivity predicted slow gait speed, and that white matter hyperintensity volume particularly in the anterior cerebral regions was associated with lower mobility scores suggesting that prevention of subclinical cerebrovascular disease might be a potential target to prevent physical decline in the elderly. Our studies also show that having a greater number of ideal cardiovascular health factors is associated with a reduced burden of biomarkers of brain aging, including silent brain infarcts, white matter hyperintensity volume, and brain atrophy, which supports the American Heart Association's recommended use of the Life's Simple 7 metric in adulthood as an important predictor of optimal brain health.

Finally, this year we have initiated studies examining the associations between inflammatory biomarkers and long-term functional trajectories. Specifically, we focused on tumor necrosis factor (TNF) receptors, as the TNF pathway has been found to play a role in acute and chronic cerebrovascular disease. We found that higher TNFR1 levels were associated with lower baseline functional status, as well as accelerated decline over time. As data becomes available, we look forward to reporting on more studies exploring the relationship between biomarkers/networks assayed with neuro-immune and neuro-inflammatory biomarker panels and cognitive trajectories.

The University of Miami American Heart Association/Bugher Center of Excellence - Dr. Ralph Sacco is the Center Director and Dr. Tatjana Rundek is the Training Director. In its final year of funding, the project and nears completion of its complementary clinical and basic science research aimed to enhance scientific knowledge base on the recovery of brain health following stroke.

In the clinical arm of the project, Dr. Sebastian Koch leads the pilot randomized clinical trial designed to identify methods to improve cognitive recovery and quality of life after stroke through the exploration of the combined benefits of cognitive and physical exercise. The study team is currently finalizing analysis towards the study’s primary outcome of safety and feasibility and will present the results at the 2019 International Stroke Conference in Hawaii. Preliminary results show that the Cognitive and Resistance Exercise Training protocol is feasible among stroke survivors. These promising feasibility results will provide needed preliminary data to propose a larger and more definitive study to improve functional and cognitive recovery after stroke.

Other preliminary study results address issues related to socioeconomic status and mental health as important contributors to physical well-being, quality of life, and cognition. Because all participants in the study underwent detailed psychosocial evaluation, the complex interactions of social and psychological factors on cognitive recovery was available for examination within the Bugher cohort, all of which had recently experienced a stroke. Our preliminary findings confirm the high prevalence of depression and cognitive impairment following stroke. At baseline the average Montreal Cognitive Assessment score was 20, significantly below the threshold of 26,
indicating a significant cognitive impairment. Depression is highly prevalent in our stroke subjects and particularly in women whose scores on depression (Clinical Epidemiological Scale-Depression) were significantly lower than in men. Our follow-up results demonstrate that both depression and cognition improved for the group as a whole over the course of the cognitive and physical exercise intervention. Interestingly, the improvement of mood in women was greater than in men.

While it may not be readily apparent, we are not aware of any adverse events related to depression. We have also not found depression to negatively influence adherence with the study intervention. However, a final more quantitative analysis may reveal a detrimental effect on compliance with the intense exercise and cognitive training intervention, as well as the effect of these interventions on stroke recovery. Only on rare occasions, we had to intervene and provide treatment and appropriate referrals for mental health management. Our careful attention to monitoring depression and cognition post stroke shows that brain and mental health remain a priority for our overall Bugher program. We hope that exercise and cognitive training may provide non-pharmacological means of treating neuropsychiatric complications that may hinder recovery from stroke.

The complimentary basic science project, led by Dr. Miguel Perez-Pinzon, aims to provide insight into cellular mechanisms underlying stroke-mediated damage and repair in an animal stroke model. Pre-clinical studies conducted in Dr. Perez-Pinzon’s lab are intended to lay the foundation for future clinical trials. This year, the basic science project describes new results for work including female rats. Ongoing studies to increase the total study numbers have been conducted in both young and aged rats to determine how exercise intensity effects cognitive deficits following focal cerebral ischemia. It was found that moderate intensity physical exercise provided the most beneficial impact on cognitive recovery compared to other exercise intensities. Specifically, these experiments revealed not only that exercise at varying intensities post stroke is feasible in young and aged rats, but also that (moderate) exercise ameliorates cognitive deficits following a stroke in young rats, while in aged rats exercise reduced cognitive deficits following stroke. The results suggest that exercise improves plasticity following stroke in young and aged rats. The ongoing animal studies are also utilizing pharmacological agents with and without exercise that will provide preliminary pre-clinical data for other human intervention studies.

The University of Miami Stroke Prevention Intervention Research Program, Florida-Puerto Rico Collaboration to Reduce Stroke Disparities (FL-PR CReSD) - Dr. Ralph Sacco is the Principal Investigator. It is in its final year of NIH funding (through a No Cost Extension). The project has successfully addressed its aims to identify race-ethnic and sex disparities in acute stroke care and to inform hospital quality improvement. Our recent study, linking pre-hospital emergency service data with the FL-PR CReSD data reinforced the potential of our data to inform improvement of quality of care beyond the acute in-hospital phase. The study identified race-ethnic differences in the time to call 9-1-1 services following acute stroke onset suggesting the need to explore innovative strategies to improve public education regarding stroke symptoms and immediate 9-1-1 system activation. Another study published this year reflects post-hospital outcomes and compares benefits to hospital participation in quality improvement programs. The study showed that disparities in outcomes were less common in hospitals participating in the FL-PR CReSD than in hospitals that did not participate in any sort of quality improvement program. The results from
our study support the benefits of quality improvement programs, particularly those focusing on race/ethnic disparities. These observations also demonstrate the need to design and implement evidence-based interventions that continue beyond the acute hospitalization period in order to reduce disparities in longer term outcomes after stroke. Although NIH funding for the project is complete, the value of the project and the data compiled is recognized by its continuation through new funds described in the next section.

The Florida Stroke Registry - Dr. Ralph Sacco is the Principal Investigator. In 2018, the University of Miami, Department of Neurology, was awarded its second round of state appropriations funds to manage and maintain the Florida Stroke Registry (the Registry). Originating from the NIH funded Florida Puerto Rico Collaboration to Reduce Stroke Disparities (described above), the Registry currently consists of 80 participating Florida stroke center hospitals. Actively engaged in recruiting all Florida stroke center hospitals, approximating 160 stroke centers in total, the Registry aims to obtain a standardized and comprehensive dataset.

The Registry currently consists of at least 250,000 Florida stroke cases obtained since 2010 to current from the 80 participating Florida hospitals. Data is downloaded quarterly, thereby increasing the number of cases included in the Registry at every download. Analyses of the data offers hospital level reports that facilitate participating hospitals to track and measure their quality of stroke care performance. As a state registry, systems of care may be addressed and ultimately improved. Alternatively, the Regional Dashboards, provide a self-monitoring tool that improves the quality of care at a local level in collaboration with EMS. This reporting tool, which in this past year have been phased out of “pilot” to the “live” implementation stage, is now being actively used in two Florida counties (of the 65 in Florida). The Regional Dashboards allow participating hospitals to review their performance against nearby hospitals on measures specifically related to endovascular treatment, an increasingly utilized innovative and minimally invasive procedure. Though still very new, the Regional Dashboards are garnishing extensive attention statewide and even nationwide as a method to improve acute in-hospital care as well as potentially pre-hospital care.

The Transitions of Care Stroke Disparity Study (TCSD-S) - Drs. Ralph Sacco and Tatjana Rundek are Co-Investigators. This study aims to identify disparities in transitions of stroke care and key factors associated with effective transitions of care. In its second year of funding, the project has accomplished multiple operational milestones including the development of the TCSD-S follow-up protocol, accompanying Case Report Forms, Manual of Operations, and the final specification of Social Determent of Health data elements to be captured for the project. After having successfully trained collaborating sites’ coordinators, enrollment has begun. Coordinators are now actively conducting TCSD-S structured telephone interviews to evaluate medication adherence, healthy lifestyle, utilization of rehabilitation interventions and medical follow-up 30 and 90 days after hospital discharge to home. Within this stage of the project, data is being collected to identify race-ethnic and sex disparities in hospital-to-home transition of stroke care and stroke outcomes. We look forward to reporting future analyses and results from this study which will help in the development of effective hospital-centered system level initiatives to reduce these disparities, improve stroke outcomes and reduce readmissions.
The University of Miami Clinical Translational Science Institute (UM CTSI) - Recently awarded a second competitive grant cycle, and directed by Dr. Ralph Sacco, the University of Miami Clinical and Translational Science Institute (Miami CTSI) is a university-wide institute dedicated to accelerating and transforming culturalized clinical and translational science. Serving as an indispensable resource for researchers and stakeholders, the Miami CTSI serves as the Miami Hub of the national Clinical and Translational Science Award 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 Memorial Hospital, the Miami VA, OneFlorida Clinical Research Consortium, Health Choice Network, and Health Council of South Florida, the Miami CTSI focuses on translational workforce and career development, research infrastructure, methods and processes, team science, and community engagement.

The Miami CTSI strategy of “culturalizing” health sciences acknowledges that the region is composed of more than 85% racial and ethnic minorities. Through Miami CTSI programs, the research workforce are exposed to cultural competency skills and tools allowing the development of adaptable study techniques to better suit the culture, language, and norms of diverse groups to ensure their active participation and engagement in research. These programs effectively extend research opportunities to South Florida’s diverse and underrepresented communities to assure integration of special and underserved populations.

In 2018, the Miami CTSI successfully competed and awarded 4 KL2 career development awards, 9 pilot project awards, began integrating partner data for research use, participated in network trial activities, completed community health worker training across Florida and in three other states, was recognized for excellence in team science by NCATS, implemented grant writing support, held workshops for junior faculty, clinical research professionals, and multidisciplinary teams on research processes, best practices, innovation and entrepreneurship, and much more.

Drs. Sarah Getz and Bonnie Levin developed and piloted an online tool to assess susceptibility to scamming in the elderly. This tool has been translated in to French and is uniquely tailored to detect individual differences in ability to differentiate scams from legitimate scenarios. This tool has also been adapted to pen and paper format for administration among vulnerable minority populations.

Drs. Christian Camargo and Katalina McInerney have been collaborating on the design of the Souvenaid study and will continue once the project is funded. See Section 1.3.1. for project details.

Drs. Christian Camargo and Barry Baumel have been working on a stem cell study with Alzheimer’s Disease. Alzheimer’s disease (AD) is the most common progressive neurodegenerative disease causing dementia in the elderly. Alzheimer’s disease is irreversible and, depending on its stage, can interfere mildly or severely with a patient’s everyday activities. The symptoms are caused by neurodegeneration characterized initially by synaptic impairment followed by neuronal loss. This is accompanied by extracellular amyloid plaques, intracellular neurofibrillary tangles, neuroinflammation (astrogliosis and microglial cell proliferation), and impaired adult neurogenesis. Mesenchymal stem cells directly affect the pathophysiology of Alzheimer’s disease by reducing amyloid beta plaque burden, regulating inflammation, and
promoting neuro-restoration by increasing neurogenesis. Based on the existing preclinical literature, we believe there is a mechanistic argument for the use of mesenchymal stem cells in Alzheimer’s disease. Therefore, we will be conducting a Phase 1, open-label, single center investigation to demonstrate the safety of allogenic Mesenchymal Stem Cells in patients diagnosed with mild-to-moderate Alzheimer’s disease.

**Sponsored clinical trials related to cognitive outcomes and our MBI clinical translational program** - Dr. Katalina McInerney and Dr. Marina Sarno have been working together with Dr. Barry Baumel (Interim Director of Neurocognitive Division) on a series of clinical trials that investigate treatment for memory loss that are listed below:

- **Drs. Katalina McInerney and Marina Sarno** are Sub-Investigators in *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*. PI: Bernard Baumel, M.D. **Sponsor: Longeveron LLC.**

- **Drs. Katalina McInerney and Marina Sarno** are Sub-Investigators in *A Phase 3 Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of Aducanumab (BIIB037) in Subjects with Early Alzheimer’s Disease*. PI: Bernard Baumel, M.D. **Sponsor: Biogen MA Inc.**

- **Drs. McInerney and Marina Sarno** are Sub-Investigators in *A Randomized, Double-Blind, Placebo-Controlled and Delayed-Start Study of LY3314814 in Mild Alzheimer’s disease Dementia (The DAYBREAK Study)*. PI: Bernard Baumel, M.D. **Sponsor: Eli Lilly and Company.**

- **Dr. Katalina McInerney** is a Sub-Investigator in *A Seamless Phase 2A-B Randomized Double-Blind Placebo-Controlled Trial to Evaluate the Efficacy and Safety of BHV-4157 in Patients with Mild to Moderate Alzheimer’s Disease*. PI: Bernard Baumel, M.D. **Sponsor: Biohaven Pharmaceuticals Holding Company Limited.**

Dr. Noam Alperin has submitted manuscripts that are based on methodology he developed for regional quantitation of the white matter hyperintensities, which is a primary sign for a cerebral small vessel disease.

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 hard at different projects related to brain plasticity, cognitive health and walking function. Please see a summary below:

- The past year has been exciting and very productive for **Dr. Joyce Gomes-Osman**. She has continued to make progress on her University of Miami McKnight Pilot Grant. This project aims to examine the influence of a 4-week aerobic exercise regimen (moderate versus high intensity) on cognition and neuroplasticity, or the brain’s ability to adapt to changes imposed by experience, environment and aging itself. The study is ongoing, with 15 individuals enrolled and 9 individuals having completed the study.
• On the national level, Dr. Joyce Gomes-Osman was selected from a competitive pool of investigators from around the country to participate in the prestigious Training for Grantsmanship in Rehabilitation Research (TIGRR), an initiative continuously funded by the NIH for 20 years that recognizes outstanding young investigators in the Rehabilitation Research Community with high promise for research success. She completed this training successfully and with positive feedback from national leaders in the field.

• Dr. Joyce Gomes-Osman has leveraged both, participation in TIGRR and the pilot data generated with the McKnight Pilot Grant, by securing funding for a Mentored Translational Research Scholars Program Awards (KL2) by the University of Miami Clinical and Translational Science Institute (CTSI). Dr. Tatjana Rundek is her primary mentor for this project, and Dr. David Loewenstein and Dr. Alvaro Pascual-Leone (Harvard) are her additional mentors. This proposal will examine the effects of an 8-week aerobic exercise intervention on cognition and brain plasticity, and additionally consider how genetic differences may modify the cognitive response to exercise.

• Dr. Joyce Gomes-Osman has recently published a large-scale systematic regression determining evidence-based recommendations of dose and type of exercise to promote cognitive gains in older adults. This manuscript was published in the high-impact journal Neurology: Clinical Practice, and featured in media releases in several major media outlets, including TIME Magazine, Medscape, CBS News, The London Times, and The Boston Globe, among others. Dr. Gomes-Osman asserts there’s no question that exercise is good for the body, and there is growing evidence that staying physically active can help slow the normal declines in brain function that come with age.

Dr. Joyce Gomes-Osman led the research to find an exercise prescription for the brain. She and her colleagues performed meta-analyses from nearly 100 existing studies that connected exercise with more than 122 different tests of brain function. Based on data that included more than 11,000 older people, they found that people who exercised about 52 hours over a period of about six months showed the biggest improvements in various thinking and speed tests. On average, people exercised for about an hour, three times a week. And the effect applied to both people without cognitive decline as well as those with mild cognitive impairment or dementia. People in the study showed the strongest improvements in their ability to solve problems and process information. The effect was not as robust in memory tests, but Dr. Gomes-Osman notes that most complex brain functions, from reasoning and processing speed to recall, are related.

What surprised the researchers was that the only strong correlation between exercise and brain function occurred when they looked at the overall time people spent being physically active. They did not find associations between improvements in thinking and the frequency, intensity or length of time people exercised. That may further support the idea that for brain health, the overall and cumulative effect of physical activity is what’s important. This suggests that exercise affects the brain in a variety of different ways, from preserving the brain’s nerve network that starts to decline with age, to boosting the function of neurons and improving blood flow to brain cells, as well as promoting the production of growth factors to help cells involved in higher level thinking tasks.
• **Dr. Joyce Gomes-Osman** has published a systematic review in *Frontiers in Aging Neuroscience* about Non-invasive Brain Stimulation in the Aging Brain in collaboration with Dr. Adam Woods, from the Evelyn F. and William L. McKnight Brain Institute at the University of Florida. In addition, she has authored 2 additional peer-reviewed publications, and presented her preliminary work in 6 posters at national meetings.

• In addition to the studies above, **Dr. Joyce Gomes-Osman** has been collaborating with **Dr. Tatjana Rundek** and the remainder of the University of Miami Bigher team investigating brain plasticity changes in individuals post-stroke who are undergoing combined exercise and cognitive training, exercise in isolation or stretching exercises. All data has been collected and processed, and manuscript preparation is underway.

• Furthermore, **Dr. Joyce Gomes-Osman** has collaborated with Dr. Sara Czaja on an NIH-funded project by Dr. Sara Czaja that consists of proposing an app-based intervention study for older individuals. Dr. Gomes-Osman has worked to create the content of this app. Finally, Dr. 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. Elizabeth Crocco** participated in and published research on the development of a novel cognitive assessment and its relationship to biological markers in Alzheimer’s Disease in Pre-MCI subjects.

**Dr. Elizabeth Crocco** has continued working on the following clinical trials that are sponsored by pharmaceutical companies aiming to be on the cusp of therapeutic breakthroughs:

• PI: 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*. **Sponsor: Novartis.**

• PI: *Randomized, Double-blind, Parallel-Group, Placebo-Controlled, Dose-ranging study of Piromelatine in Patients with Mild Dementia due to Alzheimer’s Disease* **Sponsor: Neurim Pharmaceuticals.**

• PI: 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*. **Sponsor: Novartis.**


• PI: *A Phase 3, multicenter, randomized, double-blind, placebo-controlled study to assess the efficacy, safety, and tolerability of AVP-786 (deuterated [d6]-dextromethorphan hydrobromide [d6-DM]/quinidine sulfate [Q]) for the treatment of agitation in patients with dementia of the Alzheimer’s type*. **Sponsor: Avanir Pharmaceuticals.**
• Co-Investigator: A Phase III, Randomized, Placebo-Controlled, Parallel-Group, Double-Blind Clinical Trial to Study the Efficacy and Safety of MK-8931 (SCH 900931) in Subjects with Amnestic Mild Cognitive Impairment Due to Alzheimer’s Disease (Prodromal AD) Sponsor: Merk & Co.

Dr. David Loewenstein (Co-Director, Data Core and Biostatistician) will continue his work with the Center on Research and Education for Aging and Technology Enhancement (CREATE IV) grant which is a multidisciplinary research project aimed at understanding how age-related changes in function impact a person’s ability to interact successfully with technical systems.

Dr. David Della-Morte and his team continued research on the association between different phenotypes of atherosclerosis and risk for cerebrovascular disease and neurodegeneration. Using data from an elderly multi-ethnic cohort from the Northern Manhattan Study (NOMAS), along with colleagues from the Departments of Neurology at the UM and Columbia University, he demonstrated a significant association between larger carotid intima media thickness and greater burden of cerebral white matter lesions independently of demographics and traditional vascular risk factors. Brain white matter hyperintensities (WMH) have been associated with increased risk of cognitive decline and dementia, therefore the results of this study may lead to a strategy to using ultrasound markers in order to prevent neurodegenerative diseases.

Also, by using the NOMAS dataset in another study, Dr. Della Morte investigated the associations between the different phenotypes of atherosclerosis: carotid plaque (CP), carotid intima media thickness (cIMT), and stiffness (STIFF), which may provide insight into the mechanisms to the increased risk of cardiovascular disease. He demonstrated that an increase in STIFF was associated with an increase in cIMT and carotid artery dilatation with greater plaque burden. Increased cIMT and plaque burden represent vascular remodeling that likely results from the two different age-related mechanisms, one that includes diffuse wall thickening (cIMT) with STIFF and another that incorporates focal atherosclerosis (plaque) with luminal dilatation. Understanding these phenomena may further elucidate the age-related mechanisms that underlie age-related cognitive decline.

Neighborhood Greenness and Alzheimer’s Disease in 249,405 U.S. Medicare Beneficiaries - We established a new collaboration with Scott Brown, PhD, a Research Associate Professor in the Department of Public Health Sciences at the University of Miami Miller School of Medicine. He is an expert in the impacts of neighborhood built (physical) and social environments on residents’ health and well-being across the lifespan. His research seeks to understand environmental policies and strategies that promote brain health for the most vulnerable residents (i.e., elders; the poor), particularly those at risk for physical inactivity, social isolation and behavioral health problems.

The overarching goal of Dr. Brown’s research is to inform policies pertaining to the built environment to enhance health in the most underserved populations and communities. Most recently, he collaborated with Dr. Rundek and conducted investigations linking higher levels of neighborhood greenness (e.g., tree canopy; parks) to lower risk for Alzheimer’s disease.
The results of this research were presented at the ‘Developing Topics’ poster session of the Alzheimer’s Association International Conference (AAIC) in Chicago, July 2018.

The results showed the following:
In a large CMS database, 5.5% (n=13,685) of Medicare beneficiaries had a diagnosis of Alzheimer’s disease. Higher levels of neighborhood greenness were significantly associated with lower odds of Alzheimer’s disease, even after adjusting for individual age, gender, race/ethnicity, and neighborhood income. These results showed that neighborhood greenness might reduce risk of Alzheimer’s disease among older adults. Environmental improvements, such as increasing trees and vegetation in neighborhoods – even to moderate levels — may be important modifiable factors for reducing Alzheimer’s disease and improving mental and general health in older populations. Dr. Brown together with Dr. Rundek just obtained funding from the FL DOH to conduct similar research in South Florida and extend these findings to MCI and other cognitive impairments in Medicare beneficiaries over the age of 65.

9.1.2. Update on Basic and Translational Science Research

Post-cerebral Ischemia Cognitive Impairment Research Program - Patients that have experienced cerebral ischemia suffer long-term disability, affecting both motor and cognitive function. The laboratory run by Drs. Kunjan Dave and Miguel Perez-Pinzon has been investigating strategies to improve post-cerebral ischemia cognitive impairments. As mentioned in earlier reports, they demonstrated that cerebral ischemia (both focal cerebral ischemia/stroke and global cerebral ischemia) impairs cognitive function, and moderate intensity physical exercise provides a beneficial impact on cognitive recovery in young and middle-aged male rats. In an earlier report they evaluated the effect of physical exercise on post-stroke cognitive function in reproductively senescent female rats. These results are now under peer-review in a manuscript submitted for publication in the journal Stroke.

Because it may be difficult for ailing elderly cerebral ischemia patients to adhere to a chronic physical exercise regimen, Drs. Dave and Perez-Pinzon are presently evaluating the impact of synergistic effects of sub-threshold intensity physical exercise and resveratrol (a well-established neuroprotective agent) treatment on post-stroke cognitive function in middle-aged rats. For this study, male rats were subjected to 90 minutes of transient middle cerebral artery occlusion (MCAO). Following 3-4 days of recovery post-stroke, rats were exposed to physical exercise (9 m / min on a treadmill) and / or resveratrol treatment (50 mg / kg / day) for five consecutive days. Cognitive outcomes were evaluated 22 days post-stroke using a contextual fear-conditioning test. They observed that the differences in percent freezing on day 2 from day 1 of contextual fear conditioning in rats belonging to MCAO + sham exercise + vehicle (DMSO), MCAO + sham exercise + resveratrol, MCAO + exercise + vehicle DMSO, and MCAO + exercise + resveratrol were 19, 25, 18, and 30%. None of the differences were statistically significant. As mentioned above, they intentionally used a sub-threshold exercise intensity (intensity that did not demonstrate
improvement in cognitive outcomes post-stroke) in this present study. The results indicate a
trend, although statistically non-significant, that exercise and resveratrol treatment has a
synergistic effect on cognitive outcomes post-stroke.

As mentioned in an earlier report, most ischemic injury research focuses on gray matter injury
despite 30% of strokes resulting in just subcortical white matter injury (WMI). Additionally, 90% of
individuals older than 65 develop white matter hyper-intensities, a marker of ischemic WMI.
The goal of this study was to characterize a model of WMI in young (3 months) and aged rats (12–18 months), using microinjections of the nitric oxide synthase inhibitor N5-(1-iminoethyl)-L-
or-nithine, dihydrochloride (L-NIO), and evaluate the impact of physical exercise on motor and
cognitive outcomes post-white matter stroke. This year, Drs. Dave and Perez-Pinzon completed
those studies and are now preparing a manuscript.

Dr. Ami Raval has continued her research to determine if whole body vibration improves stroke
outcome in nicotine-exposed rats. Her research reveals that post-stroke physical exercise
reduces ischemic brain damage and improves cognition in reproductively senescent female
rats. Another finding thus far is that Nicotine alters brain energy metabolism and exacerbates
ischemic injury and alters cognition in female rats.

Dr. Antoni Barrientos’ laboratory has made major advances in three lines of research focusing
on defining mechanisms of neuroprotection against human neurodegenerative proteinopathies,
with a focus on Huntington’s disease (HD). Research: Major advances on the role of (1) NAD
enzymes as neuroprotective chaperones, (2) several new encephalocardiomyopathy
mitochondrial assembly factors, and (3) discovery of several GTPases required for the biosynthesis
of mitochondrial ribosomes.

(1) Catalytically inactive forms of NAD+ salvage pathway proteins retain protective activity
against 103Q toxicity in yeast
Previously, Dr. Barrientos observed that multiple proteins that belong to the yeast NAD+ salvage
pathway were able to protect against the growth deficit that occurs with 103Q mutant huntingtin
expression in a yeast model of Huntington’s disease. Furthermore, upon deletion of one of the
essential genes of the yeast NAD+ salvage pathway, NPT1, they saw that the overexpression of
the other NAD+ salvage pathway proteins maintained their ability to protect against 103Q
expression, indicating that a functional NAD+ salvage pathway was unnecessary for protection
by these NAD+ salvage pathway proteins (REF). To further study what aspects of these NAD+
salvage pathway proteins are required to confer protection against 103Q toxicity, they mutated
the catalytic core of each of the NAD+ salvage pathway proteins as reported on to disrupt their
catalytic activity. Then they performed serial dilution tests alongside yeast cells overexpressing
the wild-type NAD+ salvage pathway proteins to see whether disruption of catalytic function
impaired the ability of the NAD+ salvage pathway proteins to protect against 103Q toxicity.

Furthermore, his lab collected cell extracts from these yeast strains, ran the extracts on SDS-PAGE
gels, and probed with antibodies that detect the 103Q mutant huntingtin fragment Figure. In
cells expressing 103Q alone, over time, large oligomers form that are unable to enter the gel at
all, seen by antibody binding within the wells of the stacking gel. However, in cells expressing
either wild-type yeast NAD+ salvage pathway proteins or their catalytically inactive forms these
large oligomers are not seen, and instead, an increasing amount of 103Q degradation products are seen over time, supporting the hypothesis that the overexpression of these proteins confer protection through the clearance of toxic mutant huntingtin oligomers. Previously, unique 103Q degradation patterns were observed for each NAD+ salvage pathway protein. Importantly, it was observed that the same unique patterns for each protein in his preliminary studies, and furthermore observed that each catalytically inactive NAD+ salvage pathway protein displayed a visually identical degradation pattern as its wild-type counterpart. The finding that these degradation patterns are unique between proteins but identical for wild-type proteins and their catalytically inactive forms provides further evidence that the protective activities of these proteins is not disturbed by the mutations that render them catalytically inactive.

(2) NAD⁺ salvage pathway proteins display chaperone activity in vitro
To test their hypothesis that NAD⁺ salvage pathway proteins function as molecular chaperones, they performed in vitro chaperone assays of wild-type and catalytically inactive yeast NAD⁺ salvage pathway proteins purified from E. coli to determine whether these proteins have innate chaperone activity. All four wild-type yeast NAD⁺ salvage pathway proteins, as well as the catalytically inactive displayed significant chaperone activity, as seen through the ability of increasing concentrations of these proteins to inhibit the aggregation of citrate synthase, as compared to citrate synthase alone and lysozyme control.

(3) The proteasome, mitophagy, or yeast chaperone proteins Hsp42 or Ssa1 are not required for protection by NAD⁺ salvage pathway proteins
To elucidate the degradation pathways involved in degrading and clearing mutant huntingtin oligomers in cells when NAD⁺ salvage pathway proteins are overexpressed, Dr. Barrientos first tested whether protection by NAD⁺ salvage pathway proteins could be abolished or diminished by inhibiting the proteasome with MG132. While 10μM MG132 has previously been used in other studies to inhibit the proteasome in plated yeast, they further verified that the proteasome was fully inhibited by also treating cells with 50μM MG132, the concentration usually used to inhibit the proteasome in yeast cells growing in culture. Neither concentration of MG132 had any effect on the protection from 103Q toxicity by any of the NAD⁺ salvage pathway proteins, indicating that the proteasome is not required for this protection.

Dr. Barrientos further tested whether the inhibition of mitophagy could affect mutant huntingtin toxicity suppression by the NAD⁺ salvage pathway proteins through the knockout of the essential mitophagy protein Atg32. For most of the NAD⁺ salvage pathway proteins tested, the knockout of mitophagy function appears to lead to increased protection against 103Q toxicity. While this may seem counterintuitive, in research they’ve already published, they previously found that interventions that increase mitochondrial biogenesis also protects against 103Q mutant huntingtin toxicity. Thus, this data further supports their previous research and hypothesis that having elevated levels of mitochondria, even if they are only partially functional, helps protects cells against death. Furthermore, since the absence of mitophagy can further protect cells against 103Q toxicity in the presence of NAD⁺ salvage pathway proteins, they can conclude that the protection by these two mechanisms can be additive, and therefore that these two forms of protection are conferred through separate and independent mechanisms.

Furthermore, Dr. Barrientos tested whether knockout of two yeast chaperone proteins that have known interactions with mutant huntingtin proteins were essential for protection by NAD⁺
salvage pathway proteins. These proteins, Hsp42 and Ssa1 have both been found to influence the formation and clearance of mutant huntingtin aggregates. However, knockout of either Hsp42 or Ssa1 did not have a clear effect on the protection by NAD⁺ salvage pathway proteins, indicating that NAD⁺ proteins may confer protection through a pathway that does not require Hsp42 or Ssa1, or that NAD⁺ salvage pathway proteins and their catalytic mutant forms, when overexpressed, may be able to substitute for the roles that Hsp42 or Ssa1 normally play.

Dr. Milena Pinto has been expanding her knowledge and research in the study of the role of mitochondria in neurodegenerative diseases. Neuronal OXPHOS deficiency, in fact, has been associated with a variety of late-onset progressive neurodegenerative diseases. She induces 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 \textit{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.

Dr. Pinto’s manuscript describing this model was published in \textit{Molecular Neurobiology} in August of 2018. Even though her main line of research is focused on neurodegenerative disorders, her contribution has also been essential in other fields where mitochondrial dysfunctions play an important role, like aging, age-related cachexia, and mitochondrial diseases (Leber’s hereditary optic neuropathy plus dystonia), as shown in 2018 publications in \textit{Nature Medicine}.

Dr. Pinto also collaborated on a long-term project that has a strong potential to be translated into clinical practice. Mutations in the mitochondrial DNA (mtDNA) are responsible for several metabolic disorders, commonly involving the muscle and the central nervous system. Because of the critical role of mtDNA in oxidative phosphorylation, the majority of pathogenic mtDNA mutations are heteroplasmic, co-existing with wild-type molecules. Using a mouse model with a heteroplasmic mtDNA mutation, she developed a mitochondrial-targeted TALENs that can reduce the mutant mtDNA load in muscle and heart. The molecular defect, namely a decrease in transfer RNAAla levels, was restored by the treatment.
9.2. Future Research Plans

9.2.1. Upcoming Population-Based Research

During this year Dr. Noam Alperin together with Dr. Tatjana Rundek submitted an R01 application to the NIH entitled *Quantitative MRI method for mapping cerebral perfusion regulation: Application to aging*. The grant was not funded- but the plans were made for its submission in the upcoming year.

In this proposal, the effect of reduction in total blood flow to the brain on regional blood perfusion will be investigated and whether the reduced perfusion in a certain brain region correlates with the brain volume loss at the same region, due to chronic low blood perfusion due to aging. We hypothesize that more perfusion protected brain regions demonstrate a smaller rate of volume loss. In this proposal we also plan to develop and validate a novel MRI method to map the cerebral perfusion regulation at different levels of blood supply under stable conditions. We term this method *regional perfusion regulation* (RPR) as it provides a rate of regional change in perfusion (e.g. hippocampus, amygdala) with respect to changes in total cerebral blood flow. This method is expected to be reproducible in healthy adults. This novel method combines two standard MRI techniques, CBF (cerebral volumetric blood flow) that measures the volumes of blood entering the brain by velocity encoding and ASL (arterial spin labeling) that measures regional perfusion across the brain. The feasibility of this method has been established and preliminary results clearly demonstrate regional reproducible heterogeneity of perfusion regulation. If successful, the RPR will be an important and helpful brain imaging biomarker of perfusion deficits predictive of structural age-related brain changes and age-related cognitive performance and decline.

Drs. Katalina McInerney and Bonnie Levin will continue to collect data for the McKnight Frailty Project. Posters, abstracts and manuscripts will be submitted based on the array of data and will highlight novel findings from the data analysis. Currently, there are 4 manuscripts under review. The Frailty database will serve as an important resource for pilot data.

Drs. Sarah Getz and Bonnie Levin are developing innovative questionnaires that will be validated among community participants and those at especially high risk of being scammed.

Dr. Alberto Ramos has submitted a large application to the NIH/NIA titled *Sleep in Neurocognitive Aging and Alzheimer’s Research* (SANAR). The long-term goal of this research is to improve the sleep health disparities that contribute to ADRD in disparity populations, particularly in Latinos. Therefore, the study aims to quantify the contributions of sleep disorders and disturbances to silent cerebrovascular injury and brain atrophy obtained with magnetic resonance imaging. In addition, SANAR will evaluate the effect of sleep on nocturnal blood pressure using ambulatory blood pressure monitoring in a large and diverse sample of Latinos from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). The main hypothesis is that overnight hypoxemia in sleep apnea, insomnia, extreme sleep duration and/or disruption of sleep micro-architecture (arousals and reduced sleep spindles and slow wave sleep) contribute to neurocognitive deficits.
through cerebrovascular disease, effects partially mediated by elevated nocturnal blood pressure.

**Dr. Christian Camargo** will primarily focus on the implementation of the REACTION grant once the AAN/MBRF funding is obtained and the award is executed. In addition he will work on developing a collaborative paradigm for evaluating more novel pharmacological interventions (e.g., HDAC inhibitors) for cognitive aging treatment. He will continue designing and seek funding for the study *A Role for Evaluating PET-Amyloid Status (AREPAS)* as part of the Key Hallmarks of Amyloid Tracer as an Ideal Biomarker Study (KHATIB).

**Dr. David Loewenstein** will be working on his new research project *Life Molecular Imaging – PI-2620 (TAU Imaging)*, which uses the first brain agent to be used at a Florida university for amyloid and tau imaging for at risk elders in prediction of future memory decline.

### 9.2.2. Upcoming Basic and Translational Science Research

**Drs. Kunjan Dave** and **Miguel Perez-Pinzon** will focus in 2019 on evaluating mechanisms by which physical exercise improves post-cerebral ischemic cognitive function. They will also evaluate mechanisms by which exposure of insulin-treated diabetic rats to recurrent hypoglycemia leads to cognitive impairment.

**Dr. Ami Raval** plans to investigate the effects of whole body vibration on stroke outcome in aged rats of both sexes. Secondly, she will conduct research on the effects of post-stroke physical exercise on post-stroke cognition in aged female rats.

**Dr. Antoni Barrientos** will continue working on the following research in 2019 ([Section 9.1](#))

- Catalytically inactive forms of NAD+ salvage pathway proteins retain protective activity against 103Q toxicity in yeast.

In 2017 **Dr. Milena Pinto** started 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 give them the possibility to build a “basic science” platform based on animal models at the University of Miami that can be translated clinically. 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. Pinto completed most of the experiments planned and started a new session of treatments. This research will have a strong and lasting impact on our understanding of the use of MSCs as a new neuroprotective agent. Because neurodegeneration is the cause of
several progressive diseases she also started a new project that involves the use of MSCs in the treatment of frontotemporal dementia. Using the same approach utilized for the study of Alzheimer’s Disease, she will inject two mouse models of fronto-temporal dementia (FTD) with MSCs and follow the evolvement of their pathology.

**9.2.3. Upcoming Education Program**

**Dr. Xiaoyan Sun**, our McKnight Education Director, will continue our current educational programs and will focus on enhancing the learning of cognitive neuroscience in 2019.

**We will continue:**

- Seminar series, journal clubs, joint scientific lecture series
- Community education events and programs
- Cross-disciplinary mentorship in collaboration with the MD, MD/PhD, PIBS and MS programs
- Grant and manuscript writing classes (through UM CTSI under the directorship of Dr. Sacco and MS in Clinical Translational Investigations under the directorship of Dr. Rundek)
- CTSI classes (clinical trials, study designs, biostatistics)
- Formal MS degree in Clinical Translational Investigations
- Structured Neurocognitive Training program – McKnight Fellowship in cognitive aging

We plan to focus on learning about normal brain changes in aging by strengthening our collaborative relationships to attend and learn about seminars across departments and disciplines.

**We are planning to provide diverse lectures and seminars to enhance learning of normal aging and disease process.**

- Collaborative lectures between the McKnight Brain Institute and the Department of Geriatrics
- Collaborative lectures between the McKnight Brain Institute and the Brain Endowment Bank
- Collaborative seminar series between the McKnight Brain Institute and the Department of Psychology

We aim to strengthen our community education and outreach programs by working with local community leaders to enhance relationships in the community for purposes of disseminating information on brain health in aging to include normal changes in cognition and memory. We are planning to build on our established network in the Miami area which includes assisted living facilities, community and senior centers, churches and more, by expanding outreach through lectures and presentations. Dr. Camargo and Dr. Sun together with Stacy Merritt will lead these activities.
10. Technology Transfer

N/A

11. Budget

This is included at the end of the report in the Financial and Budget Sheets Section.

12. Educational Programs Focusing on Age-Related Memory Loss

Dr. Xiaoyan Sun continues in her role as the MBI Education Director.

The Education and Training Core of the McKnight Brain Institute at the University of Miami is committed to:

- Providing education on normal cognitive aging and memory related disorders to our medical students, graduate students, neurology residents, faculty and staff;

- Fostering collaborative educational efforts between faculty and staff at the McKnight Brain Institute and Center for Cognitive Neuroscience and Aging, Departments of Psychology and Psychiatry and the Brain Endowment Bank for promoting learning and research collaboration in the studies of cognitive aging and;

- Developing community education and outreach programs focusing on the aging population and brain health.

Our McKnight Education and Training Core consists of McKnight Grand Rounds (Table 1) weekly Research Lab Meetings, monthly Research Seminars (Table 2) and Journal Clubs (Table 3) and coordination of a McKnight Brain Institute Scientific Lecture Series with other Centers, Institutes, collaborators and partners.
### Table 1. 2018 Evelyn F. McKnight Brain Institute Grand Rounds Speakers

<table>
<thead>
<tr>
<th>Speaker</th>
<th>Visiting From</th>
<th>Date</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eric M. Reiman, MD</td>
<td>Banner Alzheimer’s Institute</td>
<td>January 31st</td>
<td>Brain Imaging in the Preclinical Study and Prevention of Alzheimer’s Disease</td>
</tr>
<tr>
<td>Ron C. Petersen, MD, PhD</td>
<td>Mayo Clinic College of Medicine, Rochester, MN</td>
<td>March 9th</td>
<td>How Much Forgetfulness is Too Much?</td>
</tr>
<tr>
<td>Richard Wurtman, MD</td>
<td>MIT Department of Brain and Cognitive Sciences</td>
<td>March 16th</td>
<td>Preservation of Cognition and Memory</td>
</tr>
<tr>
<td>Howard J. Federoff, MD, PhD</td>
<td>University of California at Irvine</td>
<td>December 14th</td>
<td>The Human Peripheral Metabolome, Cognitive Function and Dementia</td>
</tr>
</tbody>
</table>

### Table 2. 2018 Evelyn F. McKnight Brain Institute Research Seminars

<table>
<thead>
<tr>
<th>Speaker</th>
<th>Area of Expertise</th>
<th>Date</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>William Hu, MD</td>
<td>Neurology</td>
<td>January 3rd</td>
<td>Biomarkers for Alzheimer’s and Related Diseases: Diagnosis, Mechanisms, and Machine Learning</td>
</tr>
<tr>
<td>Christian Camargo, MD</td>
<td>Neurology</td>
<td>January 31st</td>
<td>Defining Optimal Brain Health in Adults A Presidential Advisory From the American Heart Association/ American Stroke Association</td>
</tr>
<tr>
<td>Katalina McInerney, PhD</td>
<td>Neuropsychology</td>
<td>February 23rd</td>
<td>Cognitive, Cultural and Affective Dimensions of Frailty</td>
</tr>
<tr>
<td>Sarah Getz, PhD</td>
<td>Neuropsychology</td>
<td>February 23rd</td>
<td>The Relationship Between Fatigue and Executive Function in Aging Adults</td>
</tr>
<tr>
<td>Name</td>
<td>Field</td>
<td>Date</td>
<td>Title</td>
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</tr>
<tr>
<td>Alberto Ramos, MD</td>
<td>Neurology</td>
<td>March 14th</td>
<td>Sleep and Neurocognitive Aging in Population Based Studies</td>
</tr>
<tr>
<td>Kunjan Dave, PhD</td>
<td>Neuroscience</td>
<td>March 14th</td>
<td>Post-Stroke Physical Exercise Improves Cognitive Outcomes in Young and Elderly Animals</td>
</tr>
<tr>
<td>Bonnie Levin, PhD</td>
<td>Neuropsychology</td>
<td>March 21st</td>
<td>McKnight Brain Aging Registry I: Clinical Update</td>
</tr>
<tr>
<td>Noam Alperin, MD</td>
<td>Radiology</td>
<td>May 30th</td>
<td>Findings of Interest on MRI Cases in the McKnight Frailty Database</td>
</tr>
<tr>
<td>Christian Camargo, MD</td>
<td>Neurology</td>
<td>June 13th</td>
<td>Souvenaid: Designing Clinical Trials to Investigate the Treatment of Cognitive Decline Through the Synaptic Repair Hypothesis</td>
</tr>
<tr>
<td>Alberto Ramos, MD</td>
<td>Neurology</td>
<td>August 8th</td>
<td>Update on the Latest Findings in Sleep Research</td>
</tr>
<tr>
<td>Roger McIntosh, PhD</td>
<td>Psychology</td>
<td>August 29th</td>
<td>Update on Brain-Connectivity in fMRIs</td>
</tr>
<tr>
<td>Judith Lobo</td>
<td>Psychology</td>
<td>September 19th</td>
<td>Age-related Changes in Functional Brain Connectivity</td>
</tr>
<tr>
<td>Roger McIntosh, PhD</td>
<td>Psychology</td>
<td>October 24th</td>
<td>State Functional Brain Connectivity: A Potential Biomarker of Risk For Age-Related Cognitive Decline</td>
</tr>
<tr>
<td>Sonya Kaur, PhD</td>
<td>Neuropsychology</td>
<td>October 24th</td>
<td>Sleep Quality Mediates the Relationship Between Cognitive Dysfunction and Frailty in Non-demented Older Adults</td>
</tr>
<tr>
<td>Sarah Getz, PhD</td>
<td>Neuropsychology</td>
<td>October 24th</td>
<td>Susceptibility to Deception: Decreasing Vulnerability in Age-Related Memory Loss</td>
</tr>
<tr>
<td>Ashish K. Rehni, PhD</td>
<td>Neuroscience</td>
<td>October 24th</td>
<td>Exposure to Recurrent Hypoglycemia Modulates Endoplasmic Reticulum Stress in Hippocampus of Insulin-treated Diabetic Rats</td>
</tr>
<tr>
<td>Joyce Gomes-Osman, PT, PhD</td>
<td>Physical Therapy and Neurology</td>
<td>October 26th</td>
<td>Exercise for Brain Health: Neuroplasticity and the Pursuit of Data-driven, Dose-specific Recommendations</td>
</tr>
<tr>
<td>Nikhil Banerjee</td>
<td>Neuropsychology</td>
<td>October 26th</td>
<td>Subjective Fatigue and Cognition in Non-demented Older Adults</td>
</tr>
<tr>
<td>Speaker</td>
<td>Area of Expertise</td>
<td>Date</td>
<td>Title</td>
</tr>
<tr>
<td>-------------------------------</td>
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<tr>
<td>Christian Camargo, MD</td>
<td>Neurology</td>
<td>November 28th</td>
<td>Updates on Clinical Trials from the Clinical Trials in Alzheimer’s Disease (CTAD) Conference</td>
</tr>
<tr>
<td>Che Liu</td>
<td>Radiology</td>
<td>December 19th</td>
<td>Introduction to Resting State Functional Connectivity Data Analyses: Preliminary Results of the McKnight Brain Aging Registry Study (MBAR) Study</td>
</tr>
</tbody>
</table>

**Table 3. 2018 Evelyn F. McKnight Brain Institute Journal Clubs**

<table>
<thead>
<tr>
<th>Speaker</th>
<th>Area of Expertise</th>
<th>Date</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Christian Camargo, MD</td>
<td>Neurology</td>
<td>February 28th</td>
<td>Mechanisms, Clinical Significance, and Prevention of Cognitive Impairment in Patients With Atrial Fibrillation</td>
</tr>
<tr>
<td>Sonya Kaur, PhD</td>
<td>Neuropsychology</td>
<td>March 28th</td>
<td>Estimating Total Cerebral Microinfarct Burden From Diffusion-Weighted Imaging Part 1</td>
</tr>
<tr>
<td>Sonya Kaur, PhD</td>
<td>Neuropsychology</td>
<td>April 11th</td>
<td>Estimating Total Cerebral Microinfarct Burden From Diffusion-Weighted Imaging Part 2</td>
</tr>
<tr>
<td>Anita Seixas Dias Saporta, MD</td>
<td>Neurology &amp; Imaging</td>
<td>April 18th</td>
<td>Neuroimaging in Dementia</td>
</tr>
<tr>
<td>Anita Seixas Dias Saporta, MD</td>
<td>Neurology &amp; Imaging</td>
<td>May 23rd</td>
<td>Role of Neuroimaging as a Biomarker for Neurodegenerative Diseases</td>
</tr>
<tr>
<td>Marialaura Simonetta, MD</td>
<td>Neurology</td>
<td>May 30th</td>
<td>MD on Microinfarcts are Common and Strongly Related to Dementia in the Oldest-old: The 90+ Study</td>
</tr>
</tbody>
</table>
Structured Educational Activities at Different Levels

The McKnight Brain Institute’s goal for trainee education is to facilitate the learning of cognitive neuroscience at different levels for our students. The McKnight Brain Institute has participated in teaching at medical and graduate schools at the University of Miami. We have organized research seminars, journal clubs and 4 special McKnight Grand Rounds speakers.

Medical and Graduate Student Education

Drs. Sacco, Rundek and Sun teach a neuroscience course of MD and MD/MPH students in the spring of each year. Dr. Sun taught MD/PhD students for a neurology case review class this October. Dr. Levin taught students in the University of Miami’s Department of Psychology. Dr. Rundek organizes and teaches students in the Master Degree program through the Clinical Translational Science Institute (CTSI). Dr. Levin mentors a neuropsychology PhD student. Dr. Rundek mentors 3 MD/PhD students, 2 MD/MPH students and 2 MD students.

Post-doctoral Education

Dr. Levin has 5 Post-doctoral neuropsychology Fellows she mentors and trains. Dr. Sun has accepted students for clinical shadowing programs and is involved in mentoring the cognitive neurology Fellows in clinic. Dr. Rundek mentors KL2 and AAN research and career development awardees.

Neurology Resident Education

Our neurology residents are required to have a 2-week clinical rotation in the memory disorders clinic. The 3rd and 4th year neurology residents spend two weeks with the faculty of the memory disorders division. This rotation helps the residents understand memory-related disorders. Residents learn a systemic approach to diagnosis and treatment of patients with memory related disorders. Residents have opportunities to participate in research seminars and journal clubs at the McKnight Brain Institute. The residents have the opportunity to observe neuropsychological testing and discuss the neuropsychological test battery with our neuropsychologists. We also have an organized lecture series. Our cognitive neurology and geriatric psychiatry faculty give lectures to the neurology residents about diagnosis and management of memory related disorders during cognitive neurology month. Dr. Sun and Dr. Rundek give lectures providing an overview of dementia and cognitive decline to neurology and psychiatry residents every year.

Faculty and Staff Education

We have regular research seminars and journal clubs in which trainees, members and collaborators from the McKnight Brain Institute present their research findings and discuss the relevant papers focused on cognition in aging.
McKnight Grand Rounds

We scheduled joint Grand Rounds with the McKnight Brain Institute and the Center for Cognitive Neuroscience and with the UM Department of Psychiatry. In January, Dr. Eric M. Reiman from the Banner Alzheimer’s Institute was invited to present at Grand Rounds. The title of his presentation was “Brain Imaging in the Preclinical Study and Prevention of Alzheimer’s Disease.” In early March, Dr. Richard Wurtman from MIT, gave a talk on “Preservation of Cognition and Memory.” Also in March, Dr. Ron Petersen from the Mayo Clinic College of Medicine, Rochester, MN gave a presentation on “How Much Forgetfulness is Too Much?” In December, Dr. Howard Federoff from the University of California at Irvine gave a lecture on “The Human Peripheral Metabolome, Cognitive Function and Dementia” (See Table 1). We conducted 2-day visits with these distinguished MBI guest speakers and arranged for individual meetings with our collaborators, faculty and trainees. We also asked for their advice and suggestions regarding our MBI mission and vision and recruitment of new faculty and trainees. We may extend our Scientific Advisory Board by including some of the external members (after conducting our Phase II Strategic Plan).

McKnight Fellowship Program

Dr. Christian Camargo completed his McKnight Fellowship in cognitive neurology in June of 2018 and was recruited as faculty in the Department of Neurology. He continues to be an integral Collaborator with the McKnight Brain Institute. Dr. Anita Seixas Dias Saporta is the new McKnight Fellow beginning July of 2018. We also plan to enroll one MD/PhD student to join and formally work in our MBI on a research project and a PhD thesis. This work usually takes 3-4 years.

Mentorship Development

The mentorship development program is an important part of the McKnight Brain Institute’s education core. We are committed to helping our junior faculty and trainees develop their research and grant writing skills and their careers in cognitive aging. Dr. Rundek is a nationally recognized mentor and educator and mentors junior faculty as well as trainees in our Department, institution and nationally. Our McKnight Members and Collaborators also mentor trainees.

Community Outreach Program

Through our McKnight education program we are committed to supporting the local community by participating in community health forums via lectures, presentations and media programs. Below is a list of education and outreach done in 2018.

- January 3, 2018, Dr. Camargo was interviewed on "The Effect of Exercise on Brain Activity and Work Productivity" on The Brian Mudd Show, News Radio 610 WIOD, Miami, FL.
- Dr. Sun was interviewed by Neurology Today, the news publication for neurologists from the American Academy of Neurology on her paper published in Neurology, "Neurogranin as a Predictor of Memory and Executive Function Decline in MCI patients.”

• April 24, 2018, our Director of Research and Administration, Stacy Merritt gave a presentation at the Pine Crest Community Center on "The Aging Brain and Research" in Pine Crest, FL.

• May 11, 2018, Dr. Camargo gave a lecture at North Shore Medical Center at the Medical Education Speakers Network on "Alzheimer's Disease vs. Senile Dementia" in Miami, FL.

• June 27, 2018, Dr. Sun was on a panel at the Chamber of Commerce Alzheimer's Support Panel, Question and Answer Session: “Discerning between normal brain changes in aging and Alzheimer’s” in Coral Gables, FL.

• October 23, 2018, Dr. Camargo was interviewed for the Health News | University of Miami Hospitals and Clinics, University of Miami Health News, on “It's Not Always Dementia. Here's What to Know.”

• November 13, 2018, the article “Study Aims to Find Key to Brain Health for ‘Super’ Aging Seniors” was circulated through the University of Miami Communications network to educate the community on the importance of our research on healthy aging.

• November 27, 2018, Dr. Camargo was interviewed on the radio show Sundial airing on WLRN 91.3 FM, the local National Public Radio (NPR) affiliate. The topic was “Alzheimer's Disease Prevention through the study of 'Successful Agers.'”

• December 20, 2018, Dr. McInerney, Stacy Merritt and a study participant from the McKnight Brain Aging Registry (MBAR) study were filmed for a television segment on the local ABC television affiliate WPLG, Miami, FL. The segment title is “Why Do Some People Age Better Than Others?”

12.1. General Education Program

Dr. Ralph Sacco delivered a UHealth-sponsored lecture to about 100 community residents in Coral Gables at the Lennar Building on Treating Stroke and Preventing Cognitive Decline.

Dr. Bonnie Levin’s Post-doctoral Fellow, Dr. Annelly Buré has been providing educational information on aging and memory loss to the Spanish speaking community via a radio segment that caters to Hispanic/Latino older adults titled Para Mayores on La Poderosa 670 AM in Miami, FL. During her interview she discusses issues related to normal cognitive aging and informs the public about research studies and clinical services offered by our department.

Dr. Levin serves on the board of Circle of Friends for Human Rights Watch, with a specific focus on elder abuse.

Dr. Elizabeth Crocco has been conducting the following trainings and lectures for Community and Caregivers:

• Alzheimer’s Disease Initiative (ADI) Caregiver Training Seminars in Dementia Miami-Dade County, FL
• Alzheimer’s Disease Initiative (ADI) Caregiving Training Program in Dementia in Monroe County
• ADI Respite Care and Day Care Centers in the Florida Keys
• Development and coordination of an annual 4-hour state-mandated training to caregivers, Alzheimer’s Disease Initiative (ADI) respite and Day Care professionals and para professionals for CEUs (continuing education credits) accreditation provided in both English and Spanish in South FL
• Development and coordination of an annual 4 hour state-mandated dementia training to caregivers in Respite and Day Care Centers in Monroe County, FL
• Presentation on Memory: What Are You Going To Do? at the University of Miami-Newman Alumni Center in Coral Gables, FL
• Presentation on Focus On Caregiving at the Mount Sinai Medical Center, Wien Center for Alzheimer’s Disease & Memory Disorders in Miami Beach, FL

Dr. David Loewenstein provides education and outreach on aging and memory loss for the East Ridge Retirement Village Outreach Program and the Unidad Outreach Program in Miami, FL.

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

Dr. Ralph Sacco provides mentorship to faculty, Fellows and students listed below.

• Charles Cohan, PhD is a Fellow who receives funding from an AHA BUGHER Stroke Center of Excellence grant.
• Marialaura Simonetto, MD is a Fellow who receives funding from an AHA BUGHER Stroke Center of Excellence grant.
• Erika Marulanda-Londono, MD receives funding from StrokeNet.
• Nicole Sur, MD receives funding from StrokeNet.
• Michelle Caunca, our formal McKnight MD/PhD candidate, receives funding from an F30 grant.
• Sofia Oluwole is an MD/PhD candidate who receives funding from the research program NOMAS as well as from the Florida Department of Health (DOH).
• Brett Doliner is an MD student who graduates in 2019.

Dr. Ralph Sacco was invited to speak at the Grand Rounds Programs at Johns Hopkins and UT Southwestern Medical Center on Brain Health.

Dr. Tatjana Rundek is the formal mentor to Dr. Joyce Gomes-Osman on her research proposal for a KL2 Career Development Award. Dr. Rundek’s expertise, knowledge and mentoring skills proved instrumental in the process and to the success of Dr. Gomes-Osman being awarded the grant.

Dr. Tatjana Rundek encouraged Dr. Christian Camargo our former McKnight Cognitive Fellow, to apply for the grant award offered by the American Academy of Neurology (AAN) and McKnight Brain Research Foundation (MBRF) “AAN McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss”. Under the mentorship of Dr. Rundek they spent six months working on the submission titled Reducing the Effects of Aging on Cognition with
Therapeutic Intervention of an Oral Nutrient: The REACTION Study. She guided him along the path to further his career while fulfilling his research aspirations. Drs. Bonnie Levin and Katalina McInerney co-mentored him on the neuropsychological design of this research. The AAN/MBRF awardees have not been officially announced but Dr. Camargo has received provisional award approval (pending submission of the proposal revision according to the reviewers’ recommendation; deadline for submission of these revisions is Jan 18, 2019).

Dr. Tatjana Rundek is the Director of a Master of Science degree in Clinical Translational Investigations at the UM Miller School of Medicine. She has been teaching 2 classes: One is on team science in the fall and another is an introduction to scientific writing and grant writing course in the spring. Our McKnight trainees are encouraged to attend these classes on Tuesday and Wednesday afternoons, from 4-6 pm during the semesters. The classes are given in our Clinical Research Building.

Dr. Tatjana Rundek also leads our Neurology Resident and Fellow Research program with a number of weekly research activities and journal clubs that our McKnight trainees can attend.

Dr. Tatjana Rundek is a Training Director of our American Heart Association (AHA) Stroke Bugher Center of Excellence and Training Director of the NIH-StrokeNet and NeuroNext. Each of these programs has active research activities and career advancement on-line seminars and courses. Dr. Rundek keeps our McKnight trainees informed of these activities and provides them with the opportunities to join, participate and network with these project group members and their trainees. Her mentees have received training awards (NIH F30 and F31, AHA, ANA, KL2 and other awards).

Schoninger Neuropsychology Program

The Division of Neuropsychology directed by Dr. Bonnie Levin, has six faculty, five Post-doctoral Fellows, three students and one volunteer research assistant. Each member of the Division devotes varying degrees of effort to McKnight related clinical and research activities. The Schoninger Neuropsychology Program was first established in 2007 as a result of the Schoninger family vision and provides funding for the McKnight/Schoninger Neuropsychology Program. The program is dedicated to understanding age-related memory loss and provides extensive clinical training to graduate students and Fellows in the evaluation of patients presenting with memory complaints. In this setting, Fellows are trained in the administration, scoring and interpretation of neurocognitive measures and work directly with their supervisor to arrive at a differential diagnosis. Supervision sessions involving Schoninger clinic referrals specifically focus on the exact nature of the memory complaint as well as the etiological basis and possible interventions and treatment for memory loss. In addition, Fellows are trained to carry out an extensive interview that includes a careful history examining a wide range of factors associated with memory loss in normal cognitive aging, including sleep hygiene, nutritional/dietary patterns, activity and exercise regimens, toxic exposures, and a careful exploration of other possible neurologic contributors (e.g., cardiometabolic disorders and other vascular conditions).
All Schoninger trainees participate in the McKnight Journal Club, neuropsychology rounds, case conferences and neurology and psychiatry grand rounds. They are also involved in the training of undergraduate and graduate level neuropsychology students. Fellows receive a minimum of one hour of individual clinical supervision and 2 hours of group supervision per week. They work closely with Dr. Rundek and other disciplines in the departments (e.g., neurologists, neurosurgeons, social workers, physical therapists, neurology residents) to provide our patients with well-rounded, multidisciplinary care. Collaboration with other disciplines spans clinical and research activities, enriching the training and mentorship of our Fellows.

**Dr. Joyce Gomes-Osman** has been 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 two post-baccalaureate students who are supporting these efforts and learning about the exciting studies being carried out in her 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. Alberto Ramos** Chaired the *Young Investigator Research Program* for the American Academy of Sleep Medicine.

**Dr. Kunjan Dave** and **Dr. Miguel Perez-Pinzon** mentor and train 2 Postdoctoral Fellows and 1 MD/PhD student in their lab.

**Dr. Christian Camargo** trained neurology residents through the University of Miami, Miller School of Medicine neurology residency program.

**Dr. Loewenstein** together with Dr. Rundek co-mentors: Michelle Rae Caunca, MD/PhD candidate; and Joyce Gomes Osman, Ph.D. – KL2 Award

**Dr. Loewenstein** also mentors a PhD student and is on 2 graduate students’ dissertation committees.

**Dr. Elizabeth Crocco** led the following general education programs:

- *Geriatric Psychiatry Lecture Series*
- JMH General Psychiatry Residency Training Program
- Develop and implement comprehensive geriatric specialty lectures in all 4 years of general psychiatric residency training. Topics include: normal aging, late-life schizophrenia, late-life depression, ECT, bereavement, neurodegenerative disorders, Alzheimer’s, Vascular, Lewy body disease, caregiving issues
- *Weekly Case Conference*
- Jackson Memorial Hospital Geriatric Psychiatry Training Program
• Coordination and supervision of all geriatric psychiatry fellows’ weekly presentations of patients’ case histories, including biological, psychological and sociological data and formulates an integrated treatment plan
• *Weekly Journal Club*
• Jackson Memorial Hospital Geriatric Psychiatry Residency Training Program.
• Weekly coordination and supervision of all geriatric psychiatry fellows with the objective of critical evaluation of peer-reviewed, original research articles and application of this knowledge to the care of their geriatric patients
• *Geriatric Psychiatry Seminar*
• Jackson Memorial Hospital Geriatric Psychiatry Residency Training Program.
• Development and implementation on a weekly basis of a core curriculum-focused conference that covers knowledge and skill in 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*
• UM Miller School of Medicine Students
• Leads small groups of 20-25 medical students in diagnosis and evaluation of cognitive disorders

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

**McKnight Brain Aging Registry (MBAR)** Dr. Tatjana Rundek, the PI for the MBAR study together with other leaders at the University of Miami Dr. Bonnie Levin and Dr. Noam Alperin, collaborates with all 3 other McKnight Brain Institutes. See Section 9.1 for more information on MBAR.

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 our 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, Kristina Visscher, Virginia Bradley Grissom, Bonnie Levin and Tatjana Rundek).

The *MBRF Cognitive Aging and Memory Intervention Core* - The second call for pilot-study applications has been announced. The project must include 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.
U19 Application with the McKnight Brain Institute at the University of Arizona

A collaborative grant project is currently in progress with the University of Arizona MBI under the leadership of Dr. Carol Barnes. She leads a large U19 application to the NIA (deadline: Jan 25, 2019) to investigate main drivers of cognitive aging across the lifespan: *Precision Aging Network (PAN): Closing the Gap Between Cognitive Healthspan and Human Lifespan*. Dr. Rundek and Dr. Levin will lead the Miami Clinical Project (*In-depth Profiles of Resilience and Risk*) and serve on the PAN Executive committee.

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

**Dr. Tatjana Rundek’s** grant submission to the Florida Department of Health (DOH) through the Ed and Ethel Moore Alzheimer’s Disease Research Program was funded. This will be a collaborative program between the University of Miami, Mount Sinai Medical Center in Miami Beach, the University of Florida, Florida International University and Florida Atlantic University.

The overarching goal of this proposal is to determine the impact of novel brain vascular imaging phenotypes (VIPs) and modifiable vascular comorbidities on cognitive and neurodegenerative profile typical of the Alzheimer’s Disease (AD) phenotype. Brain small vessel disease is the most prevalent cause of progressive cognitive impairment in the elderly. MRI studies have shown the high prevalence of covert small-vessel disease in the elderly and population-autopsy series have verified the high frequency of the coexistence of vascular pathology with AD pathology. The need for quantitative evaluations of the impact of brain vascular phenotypes on cognitive and neurodegenerative changes related to AD pathology is evident. To achieve our goal we would leverage reach and in-depth brain magnetic resonance (MR) imaging, clinical and neurocognitive data from the NIH-funded 1*Florida Alzheimer Disease Research Center* (1FL ADRC), which enrolled a diverse population of South Florida with a large representation of Hispanics/Latinos.

Our proposed research is of particular importance for the Hispanic/Latino population of South Florida, which is the largest and fastest growing ethnic minority in the US. Hispanics/Latinos have a disproportionately high burden of vascular risk factors and comorbidities and they are largely underrepresented in AD research. Moreover, vascular comorbidities are modifiable and preventable. The results from the proposed investigations will uniquely position our team to start closing the gap in our understanding of the mechanisms by which vascular phenotype contributes to AD pathology and to inform future strategies to reduce AD risk specifically tailored to high vascular-AD risk populations.

**Dr. Ralph Sacco** and **Dr. Tatjana Rundek** have active research programs with the NOMAS team at Columbia University in NY. They also 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.
**Dr. Ralph Sacco** and **Dr. 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 NHLBI.

**Dr. Tajana Rundek** actively participates in research on brain hemodynamics in aging with the Einstein Aging Study (EAS) in the Bronx.

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

We are excited to execute and implement our future plans for the UM Evelyn F. McKnight Brain Institute in 2019. Here is an overview of what we plan to focus on:

**Dr. Rundek and Dr. Sacco together with the MBI Scientific Advisory Board** will move forward with **Phase II of the McKnight Brain Institute Strategic Plan** in 2019 to further the mission of our McKnight Brain Institute.

The next phase of Strategic Planning will include the development of our strategic goals along with tactics, measurable outcomes and timelines. We will build upon the team vision to develop a unified framework of cognitive aging and brain health utilizing our wealth of inter-disciplinary and multi-departmental knowledge and resources. We will prepare the MBI Strategic Plan document, share it with our team members, collaborators and broader community to present its goals and start its implementation. We plan for these activities to take significant time and effort in the next progress year. The conclusion of our Strategic Plan will also determine most of our activities in 2019.

**Dr. Rundek and Dr. Loewenstein** will begin 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)**. A description of the project can be found in **Section 14**.

**Dr. Rundek and Dr. Loewenstein** will collaborate on the competitive renewal of the 1FL ADRC (newly named ADC) with the University of Florida (PI: Todd Golde). They will participate in the 1FL ADC Clinical Core, Recruitment Core and co-direct Educational/Training Core in conjunction.
Dr. Rundek and Dr. Levin will collaborate on the submission of the U19 Application with the McKnight Brain Institute at the University of Arizona (PI: Carol Barnes). A description of the project can be found in Section 13.

Within our population-based prospective cohort, NOMAS (Section 9.1.1), upcoming work in 2019 will focus on expanding recent studies on the role of the immune mechanisms in vascular cognitive impairment and dementia. Through the use of a highly multiplexed method for profiling innate and adaptive immunity pathways, we will enhance our efforts to explore inflammation networks in cerebrovascular disease as determinants of cognitive trajectories and functional decline.

We will expand our collaborative relationship with the University of Miami’s newly established Center for Cognitive Neuroscience and Aging under the leadership of Dr. David Loewenstein. This will include partnering with his team of scientists on grant and research opportunities and creating a joint seminar series of prestigious speakers on topics relevant to our mission on aging and brain health.

Dr. Bonnie Levin, together with her neuropsychology team will continue leading the McKnight Frailty Project. Along with Dr. Sarah Getz, Dr. Levin will validate newly developed innovative questionnaires for scamming among community participants and those at especially high risk of being scammed. Posters, abstracts and manuscripts will be submitted based on their data and will highlight novel findings from the data analysis.

Dr. Sarah Getz under the mentorship of Dr. Levin is planning to apply for a CTSI pilot grant to examine scam detection and prevention among the vulnerable elderly. Without an effective ‘primary elder financial fraud and scams intervention’, the magnitude of this burgeoning public health crisis will likely increase twofold in the next 20 to 30 years in line with the ever growing elderly population. Minorities and those with lower SES and education are at the greatest risk. The proposed research will be highly innovative because it represents a substantive departure from the status quo by specifically targeting vulnerable minority populations with a behavioral science based primary intervention, and by assessing scam detection abilities pre and post intervention.

Dr. Bonnie Levin will continue working in collaboration with faculty in other Departments at UM including Ophthalmology, Medicine and Otolaryngology on NIH grants examining topics related to early biomarkers of cognitive change in normal aging and those presenting with memory complaints.

Dr. Christian Camargo will work on developing a collaborative paradigm for evaluating more novel pharmacological interventions (e.g., HDAC inhibitors) for cognitive aging treatment. He will be implementing the study A Role for Evaluating PET-Amyloid Status (AREPAS) as part of the Key Hallmarks of Amyloid Tracer as an Ideal Biomarker Study (KHATIB).

The UM McKnight Brain Institute MBI is one of the organizers and sponsor of the 13th International Conference on Cerebral Vascular Biology, Miami, June 2019.
**Dr. Sacco** will be one of the keynote speakers and **Dr. Rundek** will moderate a session on the aging brain and age-related memory loss. 
Dr. Vladimir Hachinski, MD, a renowned cognitive neurologist from London, Ontario, Canada, will be our MBI guest speaker at the conference.

Dr. Sun will lead the plans for our Educational Program in 2019 for our neurology residents, faculty and staff as well as our McKnight Brain Institute trainees, members and collaborators.

Dr. Sun will begin the process of implementing a **brain cutting class**, which will be instrumental to our neurology residents and McKnight Brain Institute trainees, members and collaborators in identifying the characteristics of normal aging brains versus those with pathological, and especially neurodegenerative conditions.

The Educational Program will also seek to enhance our community education and outreach via a structured lecture series. We want to reach more aging communities to teach about the significance of maintaining brain health through the aging process. We also plan to identify and collaborate with other partners with already strong community outreach and education programs (e.g., Center for Cognitive Neuroscience and Aging, All of Us, and others).

In June of 2019, **Dr. Ron Lazar**, the Director of the University of Alabama at Birmingham Evelyn F. McKnight Brain Institute, will be our MBI special Grand Rounds invited guest speaker.
Additional research endeavors for next year include:

**Dr. Alberto Ramos** will delve into the NIH/NIA funded project titled *Sleep in Neurocognitive Aging and Alzheimer’s Research* (SANAR). The long-term goal of this research is to improve the sleep health disparities that contribute to ADRD in disparity populations, particularly in Latinos.

**Dr. David Della-Morte** will work on the newly awarded project *Diabetes Mellitus, Regenerative and Reparative Processes, and Improvement of Pancreatic Beta Cell Function: Role of Bone Marrow-Mesenchymal Stem Cells, MicroRNAs, M2 Macrophages and Myeloid Derived Suppressor Cells*.

**Dr. Kunjan Dave** and **Dr. Miguel Perez-Pinzon** will focus in 2019 on evaluating mechanisms by which physical exercise improves post-cerebral ischemic cognitive function. They will also evaluate mechanisms by which exposure of insulin-treated diabetic rats to recurrent hypoglycemia leads to cognitive impairment.

**Dr. Ami Raval** plans to investigate the effects of whole body vibration on stroke outcomes in aged rats of both sexes. Secondly, she will conduct research on the effects of post-stroke physical exercise on post-stroke cognition in aged female rats.

**Dr. Antoni Barrientos** will continue working on the following research in 2019: (1) Catalytically inactive forms of NAD+ salvage pathway proteins retain protective activity against 103Q toxicity in yeast; and (2) NAD+ salvage pathway proteins display chaperone activity in vitro.

**Dr. Milena Pinto** will continue her collaboration with Dr. Barry Baumel on the use of mesenchymal stem cells (MSCs) in the treatment of Alzheimer’s disease.

And finally, **Susan Fox-Rosellini** will increase her role at the UM MBI, starting in February of 2019. She will be responsible for managing and updating the MBI marketing, communications and social media platforms to include our website, collateral and social media serving as the MBI representative to the McKnight Communications Working Group. She will help with our Phase II Strategic Planning and the preparation of our Strategic Plan Document. She will also oversee the financials and operations, including the planning of the 11th Annual Inter-institutional Meeting in 2020, and annual reporting to the MBRF.

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

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This is included at the end of the report in the *Financial and Budget Sheets* Section.
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
22. **What do you consider your most important scientific achievements this year?**

We are pleased with the UM MBI’s grant awards, accomplishments and achievements in 2018. Our most important attainments are listed below.

We are most excited about our trainees’ success and accomplishments:

**Dr. Joyce Gomes-Osman’s KL2 award** is an important accomplishment that will further the mission of our McKnight Brain Institute. McKnight leadership at the University of Miami is proud that a McKnight Brain Institute Member has secured a Career Development Award. The successful completion of the research and training that comprise this grant will allow her to approach her long-term goal of developing exercise interventions that can be individually tailored to promote cognitive brain health in aging adults, which will be the focus of a future R proposal.

**Dr. Christian Camargo has been provisionally awarded the AAN McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss**, for the project *Reducing the Effects of Aging on Cognition with Therapeutic Intervention of an Oral Nutrient: The REACTION Study*. Pending the result of his submission to the reviewers’ responses by January 18th, he will receive 2 years of funding. This will allow him dedicated research time and a tremendous opportunity to advance his career in cognition and memory in aging.

The appointment of the **Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging** to **Dr. Tatjana Rundek** is a truly honorable achievement. The University of Miami is grateful to the McKnight Brain Aging Foundation for the Chair award and the opportunity to fulfill the mission of learning about the role of aging in memory.

**Dr. Rundek’s Florida Department of Health (DOH) Ed and Ethel Moore Alzheimer’s Disease Research Program** grant received funding.

The work and effort of **Dr. Levin’s team on MBAR and McKnight Frailty Registry; her post-doctoral Fellows and graduate students working together with Stacy Merritt, Research and Administration Director**, has populated and expanded REDCap to include a large demographic and medical data base of almost 400 subjects. This provided the framework for seven conference presentations or posters. Currently, there are 4 manuscripts based on this database under review.

The award for the research project collaboration with the McKnight Brain Institutes at the Universities of Florida and Arizona *Uncovering Risk Profiles of Deception and Mitigating Susceptibility to Scamming in Midlife and Older Age: A Novel Intervention Tool* was awarded by the **McKnight Brain Research Foundation** through its Inter-Institutional Cognitive Aging and Memory Interventional Core.
Lastly, a truly significant scientific achievement to report in 2018 is Dr. Ralph Sacco’s nomination to the prestigious National Academy of Medicine (NAM).

The National Academy of Medicine, established in 1970 as the Institute of Medicine, is an independent organization of eminent professionals from diverse fields including health and medicine; the natural, social and behavioral sciences; and beyond. It serves alongside the National Academy of Sciences and the National Academy of Engineering as an adviser to the nation and the international community. Through its domestic and global initiatives, the NAM works to address critical issues in health, medicine and related policy and inspires positive action across sectors.

The NAM announced Dr. Ralph Sacco as one of the 75 new members and 10 international members at its annual meeting on October 15, 2018. Membership in the NAM is considered one of the highest honors in the fields of health and medicine and recognizes individuals who have demonstrated outstanding professional achievements and commitment to service. The Academy nominated him as a result of his “instrumental involvement in policies promoting ideal cardiovascular health, brain health, stroke prevention, and non-communicable disease targets”. He is humbled and proud to know that his clinical research has had an impact on the practice of medicine nationwide. The award encourages him to fortify his dedication towards new discoveries that advance the field and to disseminate those findings. It is an honor and privilege for him to join past honorees from UM and serve on the NAM recommendation panels that have had a tremendous impact on health care, education and public health. He is proud to share the extraordinary honor with the entire University of Miami community. Particularly, he shares this great honor with the incredibly talented people he’s had the great fortune to work with in the past as well as today. This achievement recognizes the success of team-based research which has been a cornerstone of our McKnight Institute. He is motivated and energized by this important scientific achievement, and looks forward to another successful and productive year for the McKnight Institute. The press release is included below.

PRESS RELEASE
Top UM Neurologist Dr. Ralph Sacco Elected to Prestigious National Academy of Medicine

A luminary stroke neurologist and researcher, Ralph L. Sacco, M.D., MS, professor and chair of neurology and the Olemberg Family Chair of Neurological Disorders at the University of Miami Miller School of Medicine, has been elected to the prestigious National Academy of Medicine (NAM).

This extraordinary honor reflects the height of professional achievement and commitment to service in health and medicine. Dr. Sacco received the honor “for his instrumental involvement in policies promoting ideal cardiovascular health, brain health, stroke prevention, and non-communicable disease targets,” according to the Academy.

University of Miami President Julio Frenk, himself a member of the National Academy of Medicine, said, “This is an extraordinary honor, not only for Dr. Sacco, but our entire University community. It speaks to the excellence of Ralph’s clinical research and its impact on the practice of medicine nationwide. His dedication to making new discoveries that advance the field and disseminating those findings in a meaningful way are the hallmark of his stellar career.” Membership in the NAM is considered one of the highest honors in the fields of health and medicine and
The National Academy of Medicine, established in 1970 as the Institute of Medicine, is an independent organization of eminent professionals from diverse fields including health and medicine; the natural, social, and behavioral sciences; and beyond. It serves alongside the National Academy of Sciences and the National Academy of Engineering as an adviser to the nation and the international community. Through its domestic and global initiatives, the NAM works to address critical issues in health, medicine, and related policy and inspire positive action across sectors. The NAM collaborates closely with its peer academies and other divisions within the National Academies of Sciences, Engineering, and Medicine.
23. **Signature, date, and title of person submitting the report**

![Signature Image]

January 15, 2019

Tatjana Rundek, M.D., Ph.D.
Scientific Director
Evelyn F. McKnight Brain Institute
<table>
<thead>
<tr>
<th>Name</th>
<th>Center Role</th>
<th>Area of Expertise</th>
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<tbody>
<tr>
<td>Noam Alperin, PhD</td>
<td>Member</td>
<td>Radiology, Physics (MRI)</td>
</tr>
<tr>
<td>Kunjan R. Dave, PhD</td>
<td>Member</td>
<td>Neurobiology, Basic Science</td>
</tr>
<tr>
<td>David Della Morte, MD, PhD</td>
<td>Member</td>
<td>Neurology</td>
</tr>
<tr>
<td>Joyce Gomes-Osman, PhD, PT</td>
<td>Member</td>
<td>Physical Therapy, Neurology</td>
</tr>
<tr>
<td>Hong Jiang, MD, PhD</td>
<td>Member</td>
<td>Neuro-opthalmology, Neurology</td>
</tr>
<tr>
<td>Bonnie Levin, PhD</td>
<td>Cognitive Core Director, Scientific Advisory Board Member</td>
<td>Neuropsychology</td>
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<tr>
<td>Tatjana Rundek, MD, PhD</td>
<td>Scientific Director, Scientific Advisory Board Member</td>
<td>Neurology, Epidemiology</td>
</tr>
<tr>
<td>Ralph L. Sacco, MD, MS</td>
<td>Executive Director, Scientific Advisory Board Member</td>
<td>Neurology, Epidemiology, Genetics</td>
</tr>
<tr>
<td>Xiaoyan Sun, MD, PhD</td>
<td>Educational Director, Scientific Advisory Board Member</td>
<td>Neuroscience, Biochemistry</td>
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</table>
**Faculty (Collaborators)**

<table>
<thead>
<tr>
<th>Name</th>
<th>Center Role</th>
<th>Area of Expertise</th>
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<tbody>
<tr>
<td>Antoni Barrientos, PhD</td>
<td>Collaborator</td>
<td>Neuroscience, Genetics</td>
</tr>
<tr>
<td>Susan Blanton, PhD</td>
<td>Collaborator</td>
<td>Genetics</td>
</tr>
<tr>
<td>Scott Brown, PhD</td>
<td>Collaborator</td>
<td>Public Health</td>
</tr>
<tr>
<td>Christian Camargo, MD</td>
<td>Collaborator</td>
<td>Neurology</td>
</tr>
<tr>
<td>Elizabeth Crocco, MD</td>
<td>Collaborator</td>
<td>Psychiatry</td>
</tr>
<tr>
<td>Chuanhui Dong, PhD</td>
<td>Collaborator</td>
<td>Epidemiology, Biostatistics</td>
</tr>
<tr>
<td>Hannah Gardener, ScD</td>
<td>Collaborator</td>
<td>Epidemiology</td>
</tr>
<tr>
<td>David Loewenstein, PhD</td>
<td>Collaborator, Scientific Advisory Board Member</td>
<td>Neuropsychology</td>
</tr>
<tr>
<td>Katalina McInerney, PhD</td>
<td>Collaborator</td>
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</tr>
<tr>
<td>Roger McIntosh, PhD</td>
<td>Collaborator</td>
<td>Psychology</td>
</tr>
<tr>
<td>Teshame Monteith, MD</td>
<td>Collaborator</td>
<td>Headache Science</td>
</tr>
<tr>
<td>Carlos Moraes, PhD</td>
<td>Collaborator</td>
<td>Neuroscience</td>
</tr>
<tr>
<td>Miguel Perez-Pinzon, PhD</td>
<td>Collaborator, Scientific Advisory Board Member</td>
<td>Neuroscience</td>
</tr>
<tr>
<td>Milena Pinto, PhD</td>
<td>Collaborator</td>
<td>Neuroscience</td>
</tr>
<tr>
<td>Alberto Ramos, MD</td>
<td>Collaborator</td>
<td>Neurology, Sleep Medicine</td>
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<tr>
<td>Ami P. Raval, PhD</td>
<td>Collaborator</td>
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</tr>
<tr>
<td>Jianhua Wang, MD, PhD</td>
<td>Collaborator</td>
<td>Neuro-ophthalmology, Neurology</td>
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# Trainees

<table>
<thead>
<tr>
<th>Name</th>
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<tbody>
<tr>
<td>Shatha Aldraiwiesh, PT</td>
<td>PhD Student</td>
<td>Physical Therapy</td>
</tr>
<tr>
<td>Nikhil Sebastian Banerjee</td>
<td>Graduate Practicum Student</td>
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</tr>
<tr>
<td>Myriam Bourens, PhD</td>
<td>Associate Research Scientist</td>
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<tr>
<td>Jabari-Ture Ghingo Brooks</td>
<td>Post-Bac Student</td>
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<tr>
<td>Kyle Andrade-Bucknor</td>
<td>Undergrad Student</td>
<td>Pre-Med</td>
</tr>
<tr>
<td>Annelly Buré-Reyes, PhD*</td>
<td>Postdoctoral Fellow</td>
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<tr>
<td>Danylo Cabral, BS, PT</td>
<td>PhD Student</td>
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<tr>
<td>Nicholas Cassidy</td>
<td>Undergrad Student</td>
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<tr>
<td>Michelle Caunca, MD/PhD Student</td>
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<tr>
<td>Austin Choi</td>
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<tr>
<td>Charles Cohan, PhD</td>
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<tr>
<td>Crizia Crespo, PhD</td>
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<tr>
<td>Samuel Del'Olio, BS</td>
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<tr>
<td>Brett Doliner</td>
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<td>Carolina Flores</td>
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<tr>
<td>Wendy Gaztanaga</td>
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<td>Sarah Getz, PhD*</td>
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<td>Alison Headley, MD</td>
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<td>Jason Hokenson</td>
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<td>Sonya Kaur, PhD</td>
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<td>Nathalie Khoury, BS</td>
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<td>Hyun-Jun Kim</td>
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<td>Kevin Koronowski, BS</td>
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<td>Jonathan Landman, MD</td>
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<td>Hui Zhong, BS</td>
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</tbody>
</table>

*Became University of Miami Department of Neurology Faculty this year.*
Ralph L. Sacco, M.D., M.S., FAHA, FAAN
Evelyn F. McKnight Brain Institute Executive Director and Scientific Advisory Board Member
Professor and Olekemberg 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
Director, Master of Science in Clinical Translational Investigations
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Clinical Director, Brain Endowment Bank
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Bernard and Alexandria Schoninger Professor of Neurology
Director, Division of Neuropsychology
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Vice-Chair for Basic Science (Neurology)  
Director, Cerebral Vascular Disease Research Laboratories  
University of Miami, Miller School of Medicine

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Neurology and Public Health Sciences
Vice Chair for Education and Training
John P. Hussman Institute for Human Genomics
Dr. John T. Macdonald Department of Human Genetics
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Associate Professor of Human Genetics and Neurology
Dr. John T. Macdonald Department of Human Genetics
Associate Director of Communications and Compliance
Hussman Institute for Human Genomics

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Research Associate Professor
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University of Miami, Miller School of Medicine
Geriatric Psychiatry Training Director
Jackson Memorial Hospital
Chuanhui Dong, Ph.D.
Evelyn F. McKnight Brain Institute Collaborator
Biostatistician
Research Associate Professor
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Assistant Scientist
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University of Miami, Miller School of Medicine

Sarah Getz, Ph.D.
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Esther Lichtenstein Professor in Neurology
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Milena Pinto, Ph.D.
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Research Assistant Professor
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University of Miami, Miller School of Medicine
Alberto Ramos, M.D., MSPH, FAASM
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Associate Professor of Clinical Neurology
Co-Director of the Sleep Disorders Program
University of Miami, Miller School of Medicine

Ami Pravinkant Raval, Ph.D.
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Research Associate Professor
Basic Science Division
Department of Neurology
University of Miami, Miller School of Medicine

Jianhua Wang, M.D., Ph.D.
Evelyn F. McKnight Brain Institute Collaborator
Associate Professor
Department of Ophthalmology Bascom Palmer Eye Institute
University of Miami, Miller School of Medicine