

**UNIVERSITY OF MIAMI
EVELYN F. MCKNIGHT BRAIN INSTITUTE
ANNUAL PROGRESS REPORT
JANUARY 1, 2017 - DECEMBER 31, 2017**



THE EVELYN F.

McKNIGHT BRAIN INSTITUTE®

UNIVERSITY OF MIAMI

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Introduction

In our Annual Report we first provide a summary of the McKnight Brain Institute in 2017 under the direction of Dr. Rundek as Interim Scientific Director. Next we highlight the following **new** developments: (A) New scientific leadership, (B) Pilot research award program that was initiated in 2017, and (C) Cognitive Fellowship, also initiated in 2017. The report will continue with all items, per the Annual Report template, including 2017 scientific and educational achievements of our Institute Members and Collaborators, updates on current research studies, collaborative activities with other McKnight Brain Institutes on the McKnight Brain Aging Research (MBAR) Study and the MBRF Cognitive Aging and Memory Intervention Core, and concludes with our most important scientific achievements of the year.

In the past transition year, **Dr. Rundek** successfully continued our Evelyn F. McKnight Brain Institute's research and educational program, research projects, seminar series and research meetings. The cohesiveness, structure and accomplishments of the Institute members exceeded what was achieved in 2016 and truly enriched our Institute at the University of Miami. We implemented the first Evelyn F. McKnight Small Pilot Collaborative Research Award and the first McKnight Cognitive Fellowship. Dr. Rundek challenged Members, Collaborators and Trainees across the University of Miami to collaborate between departments and disciplines on scientific ideas and research through posters, manuscripts and grant submissions. We have strengthened our collaboration with the UM Center on Aging and Dr. Czaja and Dr. David Loewenstein on numerous activities, including sharing research imaging resources, subject enrollment and educational and training activities. Moreover, we have continued our collaborations on the McKnight Brain Aging Research (MBAR) study and the MBRF Cognitive Aging and Memory Intervention Core with leaders and investigators from other McKnight Brain Institutes. Dr. Rundek's vision is one of focus and rigor that was applauded and welcomed by the McKnight researchers who expressed their respect and gratitude for her passion and leadership. Her vast experience in teamwork and collaborative approach has instilled a culture of creativity and cooperation. The McKnight team at the University of Miami is stronger than ever and forging ahead with enthusiasm.

We have accomplished all the planned goals and more since last year's progress report, including:

- Immediately after transition of our scientific leadership, we hosted the McKnight Trustees' Visit to Miami, where we presented our detailed transition plan, interim scientific leadership and plans for the search and recruitment of a new Scientific Director.
- We participated in the planning of the well-attended *NIA/McKnight Research Summit on Cognitive Reserve and Resilience* in April of 2017. Ten of our Institute members attended the Summit, which was a unique and extremely inspiring event for research ideas, collaborations and networking.
- We participated in the *2017 Society of Neuroscience meeting* in Washington, DC in November of 2017. We presented 5 posters directly sponsored by our McKnight Brain Institute.
- The McKnight Brain Aging Registry (MBAR) started and is actively enrolling study participants.

- The McKnight Registry and Biorepository enrollments have surged in collaboration with Dr. Gomes-Osman and her TMS team and with Dr. Levin's team on the frailty study.
- We have extended our research and clinical collaborations. One of these examples includes **Dr. Noam Alperin's** multidisciplinary research involving sleep apnea, brain volume loss and cognitive decline in healthy elderly individuals. Another is the new research that aims to identify race/ethnic and gender gaps in stroke care for elderly patients with Atrial Fibrillation by Dr. Sacco and Dr. Rundek. **Dr. Czaja** has continued the multi-site ACT Study and the DUAL TARGET research project.
- We have submitted 2 NIH patient-oriented grants in collaboration with **Dr. Hong Jiang** (Dr. Rundek is a co-investigator) on *retinal changes in aging and MCI* and another grant with Dr. Alperin (**Dr. Rundek** and **Dr. Alperin** are multiple PIs) on *novel MRI perfusion challenge testing for detection and evaluation of cerebral small vessel functional hemodynamic reserve*.
- Our basic science team has developed a *novel rat behavioral model* for testing of the effect of white matter stroke on cognitive outcomes. This is a new animal model in our basic science laboratory that requires a considerable amount time for validation before applying it for various interventional approaches.
- Our McKnight trainee **Michelle Caunca**, our MD/PhD Student has successfully applied for and was awarded a NINDS F30 award on the *Effects of White and Gray Matter Integrity on Cognition in a Multi-Ethnic Cohort*. Her mentors for this award are **Dr. Rundek** as the primary mentor and Dr. Clinton Wright. Michelle has successfully defended her proposed mentorship plan that included conducting research in Miami under Dr. Rundek's supervision in combination with additional MR imaging training at the NIH under Dr. Wright's supervision. Last year, Michelle spent 2 weeks at the NINDS working on MR image processing and analysis. This research will also be a part of her PhD thesis.

A. New Scientific Director of the Evelyn McKnight Brain Institute

We start our report with the news that **Dr. Tatjana Rundek, MD, PhD** was named the 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 on December 21, 2017.

After Dr. Clinton Wright ended his appointment as the Evelyn F. McKnight Scientific Director at the University of Miami on October 31 of 2016, Dr. Rundek served as the interim Scientific Director until December 21, 2017. **The Search Committee** for new Scientific Director of the Evelyn F. McKnight Brain Institute was appointed immediately after the departure of Dr. Wright in 2016. Together with **Dr. Sara Czaja, Dr. Rundek** chaired the Search Committee for a year. The Search Committee actively worked on recruiting a new Scientific Director and considered several qualified candidates. After the most recent candidate declined an offer due to personal reasons, **Dr. Rundek** stepped down from the Search Committee and was considered a candidate for the Scientific Director.

The Search Committee convened under the leadership of **Dr. Czaja** and **Dr. Ralph Sacco** and discussed Dr. Rundek's scientific qualifications and achievements. They invited Dr. Rundek to present her scientific vision for the Miami McKnight Brain Institute and answer questions from the Committee. Dr. Rundek gave a presentation that was well attended by the McKnight Brain Institute Members and Collaborators, Neurology Divisional Directors and Faculty from the

Department of Neurology and other departments of the Miller School of Medicine and the University of Miami Centers and Institutes. Immediately after her presentation, the Search Committee considered Dr. Rundek to be an extremely qualified candidate, a truly effective leader and an ideal fit for Scientific Director of the McKnight Brain Institute.

The Search Committee met on December 6 of 2017 and unanimously voted to offer Dr. Rundek the position. Under the leadership of **Dr. Sacco, the Executive Director** of the Miami McKnight Brain Institute, **Dr. Rundek was named the 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** on December 21, 2017, after discussion with Dean Edward Abraham at the Miller School of Medicine and Dr. Lee Dockery, Chair of the McKnight Foundation Board.



Tatjana Rundek, MD, PhD is a Professor of Neurology and Public Health Sciences, Executive Vice Chair of Research and Faculty Affairs in Neurology, Director of Clinical Translational Research Division in Neurology, and Director of a Master of Science degree in Clinical Translational Investigations at the University of Miami Miller School of Medicine.

Dr. Rundek was born and reared in Zagreb, Croatia. She received her medical degree and neurology training at the University of Zagreb, a PhD in Neuroscience in Germany and completed a research Fellowship at Columbia University.

Dr. Rundek is a neurologist, clinical researcher, epidemiologist and principal investigator of several NIH/NINDS funded R01 grants and foundation awards. She was a recipient of a NINDS K24 training grant and research awards from the Hazel K. Goddess for Stroke in Women and the Dr. Gilbert Baum Fund in Clinical Ultrasound for best clinical application of ultrasound in investigations of brain hemodynamics. Dr. Rundek was the first Fulbright Scholar at the Neurological Institute at Columbia University in NY. As the International Fulbright Scholar Leader in 1996-97, Dr. Rundek gave a brief presentation on the importance of the international research exchange program at the 1997 Annual UN Assembly in New York.

Dr. Rundek is a dedicated scientist with strong commitment to service to the scientific community. She serves on review study sections at the NIH, AHA, AAN and on the editorial boards of scientific journals including *Stroke* for which she is Consulting Editor, *Neurology*, *Journal of Ultrasound in Medicine*, *Frontiers in Neurology* and *Cerebrovascular Diseases*. She has published over 400 scientific publications, editorials, reviews and book chapters. She is a Fellow of the American Neurological Association and the American Heart Association, and a member of the American Academy of Neurology. She is Past President of the Neurosonology Communities of Practice of the American Institute in Ultrasound in Medicine, the largest professional medical ultrasound organization in the US. Dr. Rundek currently serves on the Intersocietal Accreditation Commission (IAC) Vascular Testing Board of Directors, a national organization that accredits clinical MRI, CT, nuclear/PET, vascular testing, echocardiography and carotid stenting programs.

Dr. Rundek's professional and scientific interests include genetic, epigenetic and environmental contributions to cerebral small vessel disease, stroke and cognitive decline with a specific focus on health disparities in women and minority populations. Her current investigations are aimed

to study the vascular mechanisms of successful aging, MCI and dementia, using MR imaging and Transcranial Doppler challenge testing in collaborations with the Einstein Aging Study in the Bronx, the Northern Manhattan Study, and with other McKnight Brain Institutes at the University of Florida, University of Arizona and University of Alabama at Birmingham. Dr. Rundek is dedicated to our **McKnight Brain Institute's Mission** to discover the causes and find effective treatments to prevent age related memory loss and cognitive decline, and to enhance brain health through translational and patient oriented research. She is also dedicated to brain health education to communities, and to training and mentoring new generations of cognitive neurologists and other professionals needed to overcome challenges of preserving and restoring brain health of the rapidly growing population of older adults in the US.

B. The Miami McKnight Brain Institute Small Pilot Collaborative Research Award Program

Under the leadership of Dr. Sacco, Interim Director, Dr. Rundek, and the Scientific Advisory Board, our Institute created a small pilot collaborative research award program in 2017. We planned for 1-2 small pilot collaborative awards per year for junior faculty or post-doctoral trainees with promising potential to become future successful investigators in age-related memory loss and cognitive decline. In addition to supporting our research talents, the goal of the **Miami McKnight Brain Institute Small Pilot Collaborative Award Program** is to advance our McKnight Brain Institute collaborative research project pipeline across our Medical School and the entire University of Miami. We have awarded one pilot award in the amount of \$10,000 in 2017.

We have announced this opportunity across our Institution similar to the NIH funding announcement and eligibility criteria to include post-doctoral trainees or young investigators according to the NIH definition. The funding announcement for the pilot program included a submission of a 3-page pilot collaborative research proposal (proposed projects need to include at least 2 different departments and/or scientific disciplines) that is aligned with the Mission of our McKnight Brain Institute, CV and a brief career development statement. Priority is given to the pilot projects that are clinical-interventional or hold promise of rapid clinical translation of proposed science to clinical interventions.



Joyce Gomes-Osman, PhD, PT is the first recipient of the Evelyn F. McKnight Small Pilot Collaborative Research Award Program (funding period: July 2017- June 2018). She is a rehabilitation scientist with expertise in clinical research that aims to harness plasticity through interventions such as non-invasive brain stimulation (NIBS) and exercise, and assesses their effects on the human nervous system during aging. She did her postdoctoral Fellowship at the Berenson-Allen Center for Noninvasive Brain Stimulation of Harvard Medical School. Her overall research aims to better understand the influence of exercise and its potential to improve function and promote neuroplasticity throughout the lifespan.

Dr. Gomes-Osman's small pilot research project is entitled *Aerobic exercise to influence mechanisms of brain plasticity and cognition in healthy aging*. The goal of this study is to compare

the effects of a moderate intensity aerobic exercise intervention (delivered at 55-64% age-predicted maximal heart rate) and high intensity aerobic exercise intervention (delivered at 65%-90% age-predicted maximal heart rate) on measures that probe cortical synaptic plasticity using transcranial magnetic stimulation (TMS) and neuropsychological tests of cognitive performance in older healthy adults at risk for developing cognitive impairments. Her primary hypothesis is that high-intensity aerobic exercise intervention is associated with a greater increase in measures that probe cortical synaptic plasticity on TMS and with greater increases in processing speed, executive function and attention. She proposed to enroll thirty participants aged 65 years or older with no cognitive impairment (Mini Mental State Exam >24), but with a family history of Alzheimer's Disease and/or $\epsilon 4$ allele carriers from the Evelyn F. McKnight Research Registry and the University of Miami Memory Clinic. The recruitment is currently ongoing (as of December, ten subjects have been enrolled in the study). The detailed study timeline is provided in *Section 9, Clinical /Translational Programs*.

C. The Miami McKnight Brain Institute Cognitive Fellowship

In July of 2017, we have started the first *McKnight Cognitive Fellowship Program*. This is the first cognitive Fellowship established in our Department of Neurology. We have created a **Mentorship Team** with expertise in clinical cognitive neurology, research and career development including **Dr. Barry Baumel**, Interim Director of the Cognitive Division in Neurology, **Dr. Xiaoyan Sun**, McKnight Brain Institute Educational Director, **Dr. Bonnie Levin**, a cognitive psychologist; and **Dr. Tatjana Rundek** as a research and career development mentor. Other potential mentors and advisors may be included depending on the interests and career objectives of the scholars. Early in the year, we selected an excellent candidate with strong interest in an academic career in cognitive neurology from our Neurology Residency Program.

We are pleased to report that **Christian Camargo, MD** is the first McKnight Brain Institute Cognitive Fellow at the University of Miami (appointment period: July 2017-June 2018). Dr. Camargo's research interests include epigenetic mechanisms of cognitive dysfunction, identification of biomarkers for prediction of cognitive decline and the therapeutic use of stem cells in primary neurodegenerative diseases.



Christian Camargo, MD did his undergraduate education at Massachusetts Institute of Technology (MIT,) where he majored in Brain and Cognitive Sciences as well as in Music, with minors in Biology and Chemistry. He conducted research on the molecular mechanisms of learning and memory, including a year under the tutelage of Nobel Laureate Dr. Susumu Tonegawa. He presented his research internationally at RIKEN-BSI in Saitama, Japan, and at several domestic conferences. For his work, he was recognized by MIT with Honorable Mention for Outstanding Research, and the Walle J.H. Nauta Award for Outstanding Research.

Dr. Camargo completed his MD degree at the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, where his major research projects included investigating the molecular mechanisms of cognitive dysfunction in disorders of abnormal myelination, and a

consecutive case series on the effectiveness of Deep Brain Stimulation (DBS) for dystonia. His thesis work investigated the use of DBS for psychiatric disorders and was performed at Harvard Medical School's Center for Nervous System Repair at Massachusetts General Hospital. He also presented an investigation of the novel use of thalamic DBS in Pelizaeus-Merzbacher Disease at the 2010 American Academy of Neurological (AAN) Surgeons meeting in Philadelphia. He completed his internship in surgery at Washington Hospital Center, where he was awarded the "Silvero Cabellon" Award by the Department of Vascular Surgery for best performance of a junior resident. In June of 2017, he completed Neurology Residency at the University of Miami.

As the McKnight Fellow, Dr. Camargo sees patients with memory and cognitive deficits and conducts research under supervision of his clinical and research mentors. He is a co-author on the recently accepted manuscript *Neurogranin as a predictor of memory and executive function decline in MCI patients* in *Neurology*. He has submitted two abstracts to the 2018 AAN Conference. He has also been spearheading our community education on Healthy Brain Aging and community outreach for the enrollment in the MBAR study and clinical trials available in our cognitive division. He is currently writing a clinical review on positive airway pressure treatment and executive dysfunction in adults with obstructive sleep apnea syndrome for *Frontiers in Neurology*.

Lastly, Dr. Camargo has helped identify our McKnight speaker for the 2018 Neurology Grand Round Series, **Dr. Richard Wurtman**, Professor Emeritus of Neuroscience at the Massachusetts Institute of Technology (MIT) Department of Brain and Cognitive Sciences. Dr. Wurtman is widely recognized for his groundbreaking research on neurotransmitters in the brain and nervous system. He is credited for discovering that melatonin is a hormone that regulates sleep and that increasing the levels of DHA, choline, and uridine in the brain can enhance the formation of synapses. Dr. Wurtman is the author and editor of 18 books, holds more than 50 patents and authored or coauthored 1,050 scientific papers. Christian will host *Dr. Wurtman* during his visit in Miami.

1. Summary of Scientific and Educational Achievements Since Last Report

We had several significant scientific achievements in 2017. Here are some highlights:

First, **Dr. Sacco** began his tenure as President of the *American Academy of Neurology (AAN)*. Next, after tremendous efforts in leading a campaign and working with the Florida Legislature, all Florida hospitals will be mandated to participate in *the Florida Stroke Registry*, led by the University of Miami. Additionally, funding will be allocated through appropriations to support the Registry.

Dr. Rundek has uncovered exciting results from the prestigious *Einstein Aging Study (EAS)*. She was also awarded a grant from the Bristol-Myers Squibb/Pfizer Alliance for *FLiPER–AF* which will research disparities in stroke outcomes and care delivery in patients with Atrial Fibrillation.

Dr. Sun's manuscript *Neurogranin as a predictor of memory and executive function decline in MCI patients* was accepted for publication in *Neurology*.

Dr. Czaja received an NIH R01 award to research a Personalized Health Behavior System to Promote Health and Well-Being in Older Adults. She also received an R01 for the research project *Understanding Factors Influencing Financial Exploitation among Diverse Samples of Older Adults*.

Two of **Dr. Levin's** Fellows (Katalina Fernández McInerney, PhD and Christin Bermudez, PhD) have become Faculty members in the Department of Neurology. Dr. Fernández McInerney has led the neurocognitive testing and training for the McKnight Brain Aging Research (MBAR) study and will continue to be involved in the MBAR study as Assistant Professor.

Our McKnight MD/PhD student **Michelle Caunca** was awarded a significant NIH research grant (F30). Two successful Faculty members (David Della-Morte, MD, PhD and Joyce Gomes-Osman, PhD, PT) have become new McKnight Brain Institute Members.

One of our McKnight Brain Institute trainees was accepted into the highly competitive University of Miami Neurology Residency program **Andres De Leon-Benedetti** in July of 2017.

Dr. Antoni Barrientos 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. He additionally made major advances on the role of NAD enzymes as neuroprotective chaperones, several new encephalocardiomyopathy mitochondrial assembly factors, and first biosynthetic pathway of mitochondrial ribosomes. Last year, Dr. Barrientos received *non-competitive renewals of the NIH-R35, MDA, ARO and VA grants.*

Dr. Perez-Pinzon and **Dr. Kunjan Dave** and their laboratory teams made tremendous progress in evaluating strategies to improve post-stroke cognitive outcomes in aged male and female rats. Additionally, they made advancement in establishing and characterizing a white matter stroke model in young and aged rats. The results using these novel models will be increasingly important in the upcoming years.

Charles Cohan, PhD a post-doctoral associate in Dr. Perez-Pinzon's laboratory received the *AHA Bugher fellow's collaborative grant* to examine the effect of exercise in improving post-stroke cognitive outcomes in reproductively senescent female rats. This project is funded by a supplement grant to the AHA Bugher Center grant.

Dr. Milena Pinto has completed a long awaited project she started several years ago. It was a tedious and intense project, which culminated in her discovering that a known protein involved in Parkinson's disease (Parkin) has a novel role in mitochondrial DNA turnover. This new discovery allowed her to publish this work, for which she obtained a fellowship from the Parkinson's disease foundation in 2014. She has submitted a K01 proposal to the NIA and received a score of

33. The final award announcement will take place in 2018. Her score indicates a high likelihood of successful competition. If not awarded, she will resubmit this proposal in 2018.

2. Publications in Peer Reviewed Journals

The year 2017 proved to be successful with numerous manuscript submissions by UM's McKnight Members, Collaborators and Trainees being accepted into prominent journals such as *Neurology*, *Stroke*, *Journal of the American Heart Association*, *Journal of Neuroscience*, *Sleep*, *Journal of Neuroophthalmology* and others.

A. Cross-Disciplinary Collaborative Publications

Beecham A, **Dong C**, Wright CB, Dueker N, Brickman AM, Wang L, DeCarli C, **Blanton SH**, **Rundek T**, Mayeux R, **Sacco RL**. Genome-wide scan in Hispanics highlights candidate loci for brain white matter hyperintensities. *Neurology Genetics*. 2017;3(5):e185.

Crocco EA, Loewenstein DA, Curiel RE, **Alperin N**, **Czaja SJ**, Harvey PD, **Sun X**, Lenchus J, Raffo A, Penate A, Melo J, Sang L, Valdivia R, Cardenas K. A novel cognitive assessment paradigm to detect pre-mild cognitive impairment (PreMCI) and the relationship to biological markers of Alzheimer's disease. *Journal of Psychiatric Research*. 2018;96: 33-38.

Dhamoon MS, Cheung YK, **Bagci A**, **Alperin N**, **Sacco RL**, Elkind MSV, Wright CB. Periventricular White Matter Hyperintensities and Functional Decline. *J Am Geriatr Soc*. 2017. [Epub ahead of print] PMID: 29155435.

Doliner B, **Dong C**, **Blanton SH**, **Gardener H**, Elkind MSV, **Sacco RL**, Demmer RT, Desvarieux M, **Rundek T**. Apolipoprotein E Gene Polymorphism and Subclinical Carotid Atherosclerosis: The Northern Manhattan Study. *J Stroke Cerebrovasc Dis*. 2017 Nov 2. [Epub ahead of print].

Dueker ND, **Della-Morte D**, **Rundek T**, **Sacco RL**, **Blanton SH**. Sickle Cell Trait and Renal Function in Hispanics in the US: The Northern Manhattan Study. *Ethnicity & Disease*. 2017;11-14.

Gutierrez J, Kulick E, Park Moon Y, **Dong C**, Cheung K, **Ahmet B**, Stern Y, **Alperin N**, **Rundek T**, **Sacco RL**, Wright CB, Elkind MSV. Brain Arterial Diameters and Cognitive Performance: The Northern Manhattan Study. *J Int Neuropsychol Soc*. 2017 Nov 23:1-12. [Epub ahead of print] PubMed PMID: 29166955.

Hibar DP, Adams HH, Jahanshad N, Chauhan G, Stein JL, Hofer E, Renteria ME, Bis JC, Arias-Vasquez A, Ikram MK, Desrivieres S, Vernooij MW, Abramovic L, Alhusaini S, Amin N, Andersson M, Arfanakis K, Aribisala BS, Armstrong NJ, Athanasiu L, Axelsson T, Beecham AH, Beiser A, Bernard M, **Blanton SH**, Bohlken MM, Boks MP, Bralten J, Brickman AM, Carmichael O, Chakravarty MM, Chen Q, Ching CR, Chouraki V, Cuellar-Partida G, Crivello F, Den Braber A, Doan NT, Ehrlich S, Giddaluru S, Goldman AL, Gottesman RF, Grimm O, Griswold ME, Guadalupe T,

Gutman BA, Hass J, Haukvik UK, Hoehn D, Holmes AJ, Hoogman M, Janowitz D, Jia T, Jørgensen KN, Karbalai N, Kasperaviciute D, Kim S, Klein M, Kraemer B, Lee PH, Liewald DC, Lopez LM, Luciano M, Macare C, Marquand AF, Matarin M, Mather KA, Mattheisen M, McKay DR, Milanese Y, Muñoz Maniega S, Nho K, Nugent AC, Nyquist P, Loohuis LM, Oosterlaan J, Pappmeyer M, Pirpamer L, Pütz B, Ramasamy A, Richards JS, Risacher SL, Roiz-Santiañez R, Rommelse N, Ropele S, Rose EJ, Royle NA, **Rundek T**, et al. Novel genetic loci associated with hippocampal volume. *Nat Commun.* 2017;8:13624.

Jiang H, Wei Y, Shi Y, Wright C, Qu D, Gregori G, Zheng F, **Rundek T**, **Wang J**. Altered retinal microvasculature in mild cognitive impairment and Alzheimer's disease. *Journal of Neuroophthalmology (In Press)* 2017.

Jiang H, Wei Y, Shi Y, Wright C, **Sun X**, T and **Wang J**. Impaired retinal microcirculation in patients with Alzheimer's disease. *PLOS one (In Revision)* 2017.

Loewenstein DA, Curiel RE, Wright C, **Sun X**, **Alperin N**, **Crocco E**, **Czaja SJ**, Raffo A, Penate A, Melo J, Capp K, Gamez M, Duara R. Recovery from proactive semantic interference in MCI and normal aging: relationship to atrophy in brain regions vulnerable to Alzheimer's disease. *Journal of Alzheimer's Disease.* 2017;56(3):1119-1126.

Pacifici F, **Della-Morte D**, Capuani B, Piermarini F, Pastore D, Ciccocanti F, Arriga R, Coppola A, Ferlosio A, Donadel G, Sconocchia G, Fimia GM, Lauro R, Bellia A, **Rundek T**, **Barrientos A**, Orlandi A, Lauro D. Peroxiredoxin6 Modulates Senescence and Insulin Secretion Impairing Sirtuin1 and Mitochondrial Fate. *Antioxid Redox Signal.* 2017 (In Submission).

Shao Y, **Jiang H**, Wei Y, Shi Y, Shi C, Wright C, **Sun X**, Vanner E, Rodriguez A, Baumel B, Lam B, **Wang J**. Mapping focal loss of the ganglion cell-inner plexiform layer in patients with mild cognitive impairment and Alzheimer's disease. *Journal of Ophthalmology (Under Revision)* 2017.

B. Trainee (as first authors) Publications

Caunca MR, Del Brutto V, **Gardener H**, Shah N, Dequatre-Ponchelle N, Cheung YK, Elkind MS, Brown TR, Cordonnier C, **Sacco RL**, Wright CB. Cerebral Microbleeds, Vascular Risk Factors, and Magnetic Resonance Imaging Markers: The Northern Manhattan Study. *J Am Heart Assoc.* 2016; 5(9).

Cohan CH, **Stradecki-Cohan HM**, Morris-Blanco KC, **Khoury N**, **Koronowski KB**, **Youbi M**, Wright CB, **Perez-Pinzon MA**. Protein kinase C epsilon delays latency until anoxic depolarization through arc expression and GluR2 internalization. *J Cereb Blood Flow Metab (In Press)* 2017.

Gardener H, **Caunca MR***, **Dong C**, Cheung YK, Elkind MSV, **Sacco RL**, **Rundek T**, Wright CB. Ultrasound Markers of Carotid Atherosclerosis and Cognition: The Northern Manhattan Study. *Stroke.* 2017; 48(7):1855-1861. (*HG and MRC shared first authorship).

Getz S, **Levin B**. Neurocognitive and neuropsychiatric features of early Parkinson's disease. *Archives of Clinical Neuropsychology (In Press)* 2017.

Headley A, De Leon-Benedetti A, Dong C, Levin B, Loewenstein DA, Camargo C, Rundek T, Zetterberg H, Blennow K, Wright CB, Sun S, and the Alzheimer's Disease Neuroimaging Initiative. Neurogranin as a predictor of memory decline in patients with mild cognitive impairment. *Neurology* (In Press) 2017.

Lippman S, Gardener H, Rundek T, Seixas A, Elkind MS, Sacco RL, Wright CB, Ramos AR. Short sleep is associated with more depressive symptoms in a multi-ethnic cohort of older adults. *Sleep Medicine*. 2017; 40:58-62.

Oluwole SA, Wang K, Dong C, Ciliberti-Vargas MA, Gutierrez CM, Yi L, Romano JG, Perez E, Tyson BA, Ayodele M, Asdaghi N, Gardener H, Rose DZ, Garcia EJ, Zevallos JC, Foster D, Robichaux M, Waddy SP, Sacco RL, Rundek T; FL-PR Collaboration to Reduce Stroke Disparities Investigators. Disparities and Trends in Door-to-Needle Time: The FL-PR CReSD Study (Florida-Puerto Rico Collaboration to Reduce Stroke Disparities). *Stroke*. 2017;48(8):2192-2197.

Stradecki-Cohan HM, Cohan CH, Raval AP, Dave KR, Reginensi D, Gittens RA, Youbi M, Perez-Pinzon MA. Cognitive Deficits after Cerebral Ischemia and Underlying Dysfunctional Plasticity: Potential Targets for Recovery of Cognition. *J Alzheimers Dis*. 60 2017; S87-S105.

Stradecki-Cohan HM, Youbi M, Cohan CH, Saul I, Garvin AA, Perez E, Dave KR, Wright CB, Sacco RL, Perez-Pinzon MA. Physical Exercise Improves Cognitive Outcomes in 2 Models of Transient Cerebral Ischemia. *Stroke*. 48 2017; 2306-2309.

C. Clinical and Population-Based Publications

Abete P, Basile C, Bulli G, Curcio F, Liguori I, **Della-Morte D**, Gargiulo G, Langellotto A, Testa G, Galizia G, Bonaduce D, Cacciatore F. The Italian version of the "frailty index" based on deficits in health: a validation study. *Aging Clin Exp Res*. 2017;29(5):913-926.

Alperin N, Bagci AM, Oliu CJ, Lee SH, Lam BL. Role of Cerebrospinal Fluid in Spaceflight-induced Ocular Changes and Visual Impairment in Astronaut. *Radiology*. 2017;285(3):1063.

Alperin N, Bagci AM, Lee SH. Spaceflight-induced changes in white matter hyperintensity burden in astronauts. *Neurology*. 2017;89(21):2187-2191.

Alperin N, Loftus JR, Bagci AM, Lee SH, Oliu CJ, Shah AH, Green BA. Magnetic resonance imaging-based measures predictive of short-term surgical outcome in patients with Chiari malformation Type I: a pilot study. *J Neurosurg Spine*. 2017;26(1):28-38.

Asdaghi N, Romano JG, Wang K, Ciliberti-Vargas MA, Koch S, **Gardener H, Dong C, Rose DZ, Waddy SP, Robichaux M, Garcia EJ, Gonzalez-Sanchez JA, Burgin WS, Sacco RL, Rundek T.** Sex Disparities in Ischemic Stroke Care: FL-PR CReSD Study (Florida-Puerto Rico Collaboration to Reduce Stroke Disparities). *Stroke*. 2016;47(10):2618-26.

Atchaneeyasakul K, Tipirneni A, Zhang T, Khandelwal P, Ambekar S, Snelling B, Dharmadhikari S, **Dong C, Guada L, Ramdas K, Chaturvedi S, Rundek T, Yavagal DR.** Association of hypothyroidism with unruptured cerebral aneurysms: a case-control study. *Journal of neurosurgery*. 2017;1-4.

Bellia A, **Della-Morte D**, Lauro D. Suboptimal use of statins for secondary cardiovascular prevention: a "planetary" issue. *Intern Emerg Med*. 2017 Dec;12(8):1091-1092.

Bellia A, Iellamo F, De Carli E, Andreadi A, Padua E, Lombardo M, Annino G, Campoli F, Tartaglione S, D'Ottavio S, **Della-Morte D**, Lauro D. Exercise individualized by TRIMPi method reduces arterial stiffness in early onset type 2 diabetic patients: A randomized controlled trial with aerobic interval training. *Int J Cardiol*. 2017;248:314-319.

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3. Publications (Other)

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Chen W, Xu Z, **Jiang H**, et al., Altered bulbar conjunctival microcirculation in response to contact lens wear. *Eye Contact Lens*. 2017;43(2):95-99.

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4. Presentations at Scientific Meetings

A. Cross-Disciplinary Collaborative Presentations

Gutierrez J, **Dong C**, Elkind MSV, **Alperin N**, **Bagci A**, McLaughlin CM, **Sacco RL**, Wright CB, **Rundek T**. Carotid Arterial Diameters as an Effect Modifier of Pulsatile Hemodynamics and Brain Perivascular Spaces. Poster (#ATP176) 2017 International Stroke Conference, Feb 22-24, 2017, Houston, TX.

Jiang H, Wei Y, Shi Y, Wright C, **Sun X**, Gregori G, Zheng F, Lam B, **Rundek T**, **Wang J**. Retinal microvascular impairment prior to ganglion cell loss in mild cognitive impairment and Alzheimer's disease. Poster presentation at ARVO 2017, Baltimore, MD, May 6-11, 2017.

Shao Y, **Jiang H**, Wei Y, Shi Y, Wright C, **Sun X**, Lam B, **Rundek T** and **Wang J**. Hemispheric analysis for detecting intraretinal thickness in mild cognitive impairment and Alzheimer's disease. Platform presentation at ARVO 2017, Baltimore, MD, May 6-11, 2017.

B. Trainee (as first authors) Presentations

Aldraiwiesh S, Cassidy N, **Rice J**, Pastore S, Swarowsky A, Corp D, **Gomes-Osman J**. Assessing Cognitive-Motor Interference and Characterizing Task Prioritization Strategy During Dual-Task behavior in Individuals Post-Stroke. Poster Session at the University of Miami Neuroscience Day December 1st, 2017 - Poster Presentation: Miami, FL.

Cai K, **Aldraiwiesh S**, **Rice J**, **Gomes-Osman J**. Cortical reactivity and plasticity measured via transcranial magnetic stimulation in individuals post subacute stroke after exercise and cognitive training – a case series. Progress in Motor Control. Poster July 19-22, 2017. Miami, FL.

Caunca MR, **Dong C**, Marquez C, Cheung YK, **Rundek T**, **Alperin N**, **Lee SH**, **Bagci AM**, Elkind MSV, DeCarli C, **Sacco RL**, Stern Y, Wright CB. Hippocampal and white matter hyperintensity volumes are associated with domain-specific cognitive decline: the Northern Manhattan Study at American Academy of Neurology Annual Meeting. Boston, MA, April 2017.

Caunca MR, Montero D, Reyes-Iglesias Y. Moving the Neurology Clerkship to the Third Year: A Survey of Medical Students at American Academy of Neurology Annual Meeting. Boston, MA, April 2017.

Caunca MR, **Simonetto M**, **Gardener H**, Ng-Reyes M, Guerrero D, **Alperin N**, **Lee SH**, **Bagci AM**, Elkind MSV, **Sacco RL**, Wright CB, **Rundek T**. Measures of obesity and central adiposity are associated with cortical thickness: the Northern Manhattan Study (NOMAS). McKnight Brain Institute Poster Session, Society for Neuroscience, Washington, DC November 12, 2017.

Cohan C. Exercise mediated white matter injury and recovery at the International Stroke Conference. Houston TX, February 2017.

Cohan C. Exercise mediated white matter injury recovery at the Bugher Annual Symposium, Conference. Los Angeles CA, October 2017.

Cohan CH, Stradecki-Cohan HM, Morris-Blanco KC, **Khoury N, Koronowski KB, Youbi M,** Wright CB, **Perez-Pinzon MA.** Protein Kinase C epsilon activation mediates ischemic neuroprotection by activating an activity-regulated cytoskeleton associated protein dependent mechanism. International Stroke Conference, Conference held at Houston TX, February 2017. Abstract number 4223. Abstract was refereed.

Cohan CH, Stradecki-Cohan HM, Youbi M, Perez-Pinzon MA. A model of ischemic white matter injury in young and aged Fischer 344 rats. International cerebral blood flow and metabolism meeting, Brain 2017 (28th international symposium on Cerebral Blood flow, metabolism and function), Conference held at Berlin Germany, April 2017. Abstract number PS04-059. Abstract was refereed.

Marulanda-Londoño ET, Ciliberti-Vargas MA, Wang K, Asdaghi N, Ayodele M, **Dong C, Gardener H,** Gutierrez CM, Burgin WS, Foster D, Sanchez J, Mueller-Kronast N, Nobo UL, Robichaux M, Rose DZ, Sand, C, Waddy SP, **Sacco RL, Rundek T,** Romano JG. Differences in Acute Stroke Care in Primary and Comprehensive Stroke Centers in Florida: An Analysis of the Florida-Puerto Rico Collaboration to Reduce Stroke Disparities (FL-PR CReSD) Study-the NINDS Stroke Prevention Intervention Research Program at International Stroke Conference, Feb. 22-24, - Oral Presentation: Houston, TX.

McInerney K, Bermudez C, Segala L, **Sun-Suslow S,** Rooks J, Luca C, Moore H, Singer C, Jagid J, Anderson S, **Levin B.** Does Exposure to Toxins Influence Cognition in Parkinson's disease? Poster Session at the 45th Annual Meeting of the International Neuropsychological Society 2017 - Poster Presentation: New Orleans, LA.

Oluwole S, Wang K, Ciliberti-Vargas MA, Gutierrez CM, Perez-Martinez E, **Dong C, Marulanda-Londoño E,** Ayodele M, **Gardener H,** Burgin WS, Foster D, Garcia-Rivera EJ, Gonzalez- Sanchez J, Robichaux M, Rose DZ, Waddy SP, Zevallos JC, **Sacco RL, Rundek T,** for the FL-PR CReSD Investigators and Collaborators. Does Age Affect Race/Ethnic Differences in Discharge Ambulation Status? Data From the Florida Puerto Collaboration to Reduce Stroke Disparities (FL-PR CReSD) Study – The NINDS Stroke Prevention Intervention Research Program. Poster Session at the International Stroke Conference, February 2017 - Poster Presentation: Houston, TX.

Rice J, Swarowsky A, **Gomes-Osman J.** Evidence and neurophysiology-based retraining of walking in individuals with Parkinson's Disease and freezing of gait: safety and preliminary efficacy. Poster Session at Progress in Motor Control, July 10-22, 2017 - Poster Presentation: Miami, FL.

Rice J, Swarowsky A, **Cai K, Aldraiwiesh S, Gomes-Osman J.** Transcranial direct current stimulation augmented individualized gait training targeting freezing of gait in Parkinson's Disease and freezing of gait: a case description. Poster Session at Society for Neuroscience Meeting, November 11-15, 2017 - Poster Presentation: Washington DC.

Simonetto M, Gardener H, Caunca MR, Dong C, Elkind MSV, Sacco RL, Rundek T. Vertebral Artery Flow velocities and Cognition Performance in The Northern Manhattan Study at European Society of Neurosonology and Cerebral Hemodynamics Meeting. Berlin, Germany, May 2017.

Simonetto M, Gardener H, Wang K, Gutierrez CM, Ciliberti-Vargas MA, Dong C, Foster D, Waddy SP, Romano JG, Rundek T, Sacco RL. Race/Ethnicity Disparities in In-Hospital Mortality and Disability at Discharge after Acute Ischemic Stroke. Data from the Florida Puerto Rico Collaboration to Reduce Stroke Disparities (FL-PR CReSD) Study – the NINDS Stroke Prevention Intervention Research Program at American Academy of Neurology Annual Meeting. Boston, MA, April 2017.

Spengler D, Reyes D, Pattany P, Gomes-Osman J, Adams D, Luca C. Localization of Primary Progressive Apraxia of Speech Using Functional MRI- A Case Study. Poster Session at the American Academy of Neurology Annual Meeting, April 22-28th, 2017 - Poster Presentation: Boston, MA.

C. Clinical and Population-Based Presentations

Andreadi A, Capuani B, Pastore D, Rinaldi ME, Galli A, Romano M, Pozzi F, Bellia A, Cerilli M, **Della-Morte D, Lauro D.** Selenium Supplementation for Hashimoto's Thyroiditis and Subclinical Hypothyroidism. ENDO- 2017, Orlando FL, April, 1-4, 2017.

Asdaghi N, Cintra LG, Wang K, Ciliberti-Vargas MA, Koch S, **Gardener H, Dong C, Marulanda-Londono E, Rose DZ, Waddy SP, Mueller-Kronast N, Burgin WS, Robichaux M, Foste D, Garcia EJ, Rundek T, Sacco RL, Romano JG.** Disparities in Delivery of Endovascular Therapy: Who Gets it and Where? The Florida Puerto Rico Collaboration to Reduce Stroke Disparities Study. Poster Session at International Stroke Conference, Feb 22-24, 2017 - Poster Presentation: Houston, TX.

Ciliberti-Vargas MA, Wang K, **Oluwole S, Perez-Martinez E, Ayodele M, Dong C, Gutierrez CM, Marulanda-Londoño E, Burgin WS, Foster D, Garcia-Rivera EJ, Gonzalez-Sanchez J, Robichaux M, Waddy SP, Zevallos JC, Romano JG, Rundek T, Sacco RL, Koch S.** Regional, Race-Ethnic and Sex Disparities in Lifestyle Interventions: Data from the Florida Puerto Rico Collaboration to Reduce Stroke Disparities (FL-PR CReSD) Study-the NINDS Stroke Prevention Intervention Research Program. Poster Session at International Stroke Conference, Feb 22-24, 2017 – Poater Presentation: Houston, TX.

Czaja SJ. The Future of Alzheimer's Disease Family Caregiving Interventions and Support for Diverse Populations: Where Do We Go from Here? Panel member. University of California, San Diego, CA, May 2017.

Czaja SJ. The Role of Technology in Reducing Disparities Among Family Caregivers. Invited Presentation. Alzheimer's Disease Diversity and Disparities in Family Caregiving: Progress and Future Directions. University of California, San Diego, CA, May 2017.

Czaja SJ. Equal Opportunity Employment Commission (EOEC). Testimony on age discrimination in employment with a focus on the changing landscape of work and the ubiquitous use of technology in the workplace. Invited Web presentation, June 14, 2017.

Czaja SJ. Innovative Approaches to Enhance Cognitive and Emotional Functioning in At-Risk Older Adults. Symposium presentation at 2017 IAGG World Congress. San Francisco, CA, July, 2017.

Czaja SJ. Technology to Support Health, Well-being and Productivity: Perspectives from *CREATE*. Symposium presentation. 2017 IAGG World Congress, San Francisco, CA, July, 2017.

Czaja SJ. Addressing Issues Facing a Diverse Aging Population: Scientific Perspectives for Practice and Policy. Symposium Presentation. 2017 IAGG World Congress, San Francisco, CA, July 2017.

Czaja SJ. APA Prize for Interdisciplinary Team Research – Research on Aging and Technology from *CREATE*. *CREATE* Symposium. American Psychological Association Annual Meeting. Washington, DC, August 2017.

Czaja SJ. Creating Change in Caregiving: Research to Policy. Panel Presentation. National Institute of Nursing Research (NINR) Summit. Washington, DC, August 2017.

Czaja SJ. Emerging Issues and Research Findings for an Aging Workforce – The Role of Technology. Symposium. American Psychological Association Annual Meeting. Washington, DC, August 2017.

Gardener H, Leifheit-Limson EC, Lichtman J, Wang Y, Wang K, Gutierrez CM, Ciliberti-Vargas MA, **Dong C,** Robichaux M, Romano JG, **Rundek T,** **Sacco RL,** for the FL-PR CRESD Investigators and Collaborators. Race/Ethnic Disparities in Short and Long Term Mortality Among Medicare Beneficiaries in Florida and Puerto Rico: Data from the Florida Puerto Rico Collaboration to Reduce Stroke Disparities (FL-PR CRESD) Study – the NINDS Stroke Prevention Intervention Research Program. International Stroke Conference, Houston, TX, February 2017.

Gardener H, Dong C, Rundek T, McLaughlin C, Cheung K, Elkind MSV, **Sacco RL,** Wright CB. Diet Clusters in Relation to Cognitive Performance and Decline in the Northern Manhattan Study. American Academy of Neurology Annual Meeting, Boston, MA, April 2017.

Gardener H, Wang K, **Dong C,** Ciliberti M, Gutierrez C, Gandia A, Antevy P, Hodges W, Sand C, Romano J, **Rundek T, Sacco RL.** Race/ethnic Disparities in the Time from Stroke Symptom Onset to Hospital Arrival among Stroke Patients Arriving by EMS in the Florida-Puerto Rico Stroke Registry. American Academy of Neurology Annual Meeting, Boston, MA, April, 2017.

Gomes-Osman J, Ferreira D, Hinchman C, Pascual-Leone A. A 4-week aerobic exercise regimen influences transcranial magnetic stimulation-based measures of intracortical inhibitory circuits – a preliminary and ongoing pilot study. Poster Session at the (Combined Sections) Meeting American Physical Therapy Association, February 15-18, 2017 Poster Presentation: San Antonio, TX.

Gomes-Osman J, Ferreira D, Ziemba N, Saenz S; Ciparelli N, Hera Y, Andrews A, Halperin S, Gerasimovich A, Yoshimura-Rank M, Beckel S, Chambers E, Acevedo I. Exercise to promote brain health for older adults: data-driven dose-specific recommendations and educational booklet. Poster Session at the (Combined Sections) Meeting American Physical Therapy Association, February 15-18, 2017 - Poster Presentation: San Antonio, TX.

Gomes-Osman J, Cassidy N, **Rice J**, **Aldraiwiesh S**, Cabral D. The effects of a 12-week exercise and cognitive intervention on gait, posture and Transcranial Magnetic Stimulation plasticity measures individuals post stroke- an ongoing study. Poster Session at Society for Neuroscience Meeting, November 11-15, 2017 - Poster Presentation: Washington DC.

Jiang H. Application of Advanced Retinal Vascular Imaging in Neuro-ophthalmology at 43rd Annual NANOS Meeting. Washington, DC. April 1-6, 2017.

Jiang H. Advanced Ophthalmic Imaging in Neuro-ophthalmology. Vision China, Hangzhou, China, July 27-29, 2017.

Ramos AR. A Cerebral Hemodynamics in Sleep Apnea and actigraphy-determined sleep duration in a sample of the Hispanic Community Health Study/Study of Latinos. Poster Session at the World Sleep 2017 congress, October 9, 2017 - Poster Presentation: Prague, Czech Republic.

Ramos AR. Actigraphic Sleep Patterns and Hypertension in the Hispanic Community Health Study/Study of Latinos ORAL abstract presentation at World Sleep 2017 in Prague, Czech Republic. ORAL 17: Sleep Health and Other Issues. October 11, 2017.

Rundek T. Invited lecture at the American Society of Neuroimaging meeting: Ultrasound and Precision Medicine. Los Angeles, CA, January 2017.

Rundek T. Invited lecture at the NINDS PRIDE Program, New York, NY: Team Science, Collaborations and Mentoring. New York, NY, July 2017.

Rundek T. Invited lecture and Moderator of the International Cerebral Collateral Circulation Symposium. Los Angeles, CA, November 2017.

Sacco RL. Implementation of Acute Stroke Therapies Worldwide: Status, Possibilities and Obstacles (an AHA/ASA and World Stroke Organization Joint Session). Moderator, International Stroke Conference, Houston TX, February 23, 2017.

Sacco RL. Carmichael T, Traystman RJ. Clinical and Basic Perspectives on the Role of Physical and Cognitive Activity and Neural Progenitors in Stroke Recovery: the ASA-Bugher Collaborative Studies. Panel Member, International Stroke Conference. Houston, TX, February 24, 2017.

Sacco RL. Florida-Puerto Rico Collaboration to Reduce Stroke Disparities: Overview at All SPIRP 2017 Conference, NIH Campus, Bethesda MD, May 31, 2017.

Sacco RL. North American Regional Symposium, Treating and Preventing Common Neurological Conditions, XXIII World Congress of Neurology. Kyoto, Japan, September 17, 2017.

Sacco RL. Preventing Stroke and Maintaining Brain Health at World Stroke Day Congress, Moscow, Russia, October 26, 2017.

Sacco RL. Academy of Neurology Mexico, Stroke Prevention and a Healthy Brain, Veracruz, Mexico, November 2, 2017.

Sacco RL. Academy of Neurology Mexico, Current State of Cerebrovascular Disease, Veracruz, Mexico, November 2, 2017.

Segalà L, **McInerney KF**, **Rooks, J**, Anderson, S, **Sun-Suslow N**, Luca C, Moore H, Singer C, **Bermudez C**, **Levin BE**. Does Hypertension Moderate Cognition in Parkinson's Disease? Poster Session at the Pan American Parkinson's Disease and Movement Disorders Congress, 2017 - Poster Presentation: Miami, FL.

Wang J, Wei Y, **Jiang H**, Shi Y, Qu D, Gregori G and Zheng F. Age-related alterations of Retinal microcirculation, microvasculature and microstructure. Poster presentation at ARVO 2017, Baltimore, MD, May 6-11, 2017.

Zeki Al Hazzouri A. Racial/ethnic differences in the association of systolic blood pressure across midlife and late life on cognitive function: The Multi-Ethnic Study of Atherosclerosis. Oral presentation at the Alzheimer's Association International Conference (AAIC) session on Epidemiology: Social Disadvantage/Inequalities in London, England, July 16, 2017.

Ziemba N, Saenz S; Ciparelli N, Hera Y, Andrews A, Halperin S, Gerasimovich A, Yoshimura-Rank M, Beckel S, Chambers E, Acevedo I, **Gomes-Osman J**. Cortical reactivity and plasticity measured via Transcranial Magnetic Stimulation in individuals post subacute stroke after exercise and cognitive training- a case series. Combined Sections Meeting American Physical Therapy Association, February 15-18, 2017 - Poster Presentation: San Antonio, TX.

D. Basic Science Presentations

Barrientos A. Redox regulation of mitochondrial cytochrome c oxidase biogenesis at American Biophysical Society 61st Annual Meeting. New Orleans, LA, February 2017.

Capuani B, **Della-Morte D**, Pacifici F, Pastore D, Donadel G, Coppola A, Arriga R, Rea S, Caricato V, Piermarini F, Lauro D. Microarray Analysis in Insulin Receptor Knockout Mice Models Suggested Novel Biomarkers to Prevent Type 2 Diabetes Mellitus at American Diabetes Association (ADA), 77th scientific sessions. San Diego, CA, 2017.

Capuani B, Pacifici F, **Della-Morte D**, Pastore D, Donadel G, Coppola A, Arriga R, Rea S, Piermarini F, Caricato V, Sbraccia P, Lauro D. Microarray analysis in insulin receptor knockout mice identified novel biomarkers to prevent Type 2 Diabetes Mellitus at 13th International Symposium on Insulin Receptor and Insulin Action. Nice, France, April 20-22, 2017.

Capuani B, Pacifici F, Pastore D, Bellia A, Piermarini F, Donadel G, Romano M, Galli A, Arriga R, Rea S, Spallone V, Caricato V, Coppola A, **Della-Morte D**, Lauro D. miRNA 543 attiva l'infiammazione HMGB1 mediata nel diabete mellito tipo 2 at 39° Congresso Nazionale della Società Italiana di Endocrinologia (SIE). Rome, Italy, June 21-24, 2017.

Dave K. Physical exercise improves post-stroke cognitive outcomes in young and elderly animals at the International Stroke Conference. Houston TX, February 2017.

Della-Morte D, Pastore D, Capuani B, Pacifici F, Lauro D. Novel molecular pathways linking metabolic and neurological disorders by regulating vascular homeostasis at 7th Annual Scientific Meeting (ISNVD). Taormina, Italy, May 4-6, 2017.

Donadel G, Arriga R, Marchetti V, Capuani B, Pastore D, Pacifici F, Coppola A, **Della Morte D**, Lauro D. Long-term effect of human placental lactogen (hPL-A) on glucose homeostasis in mice with pancreatic islets transplantation at American Diabetes Association (ADA), 77th scientific sessions. San Diego, CA, June 9-13, 2017.

Pacifici F, Capuani B, Pastore D, Piermarini F, Coppola A, Arriga R, Rea S, Donadel G, Sbraccia P, Bellia A, **Della-Morte D**, Lauro D. Perixiredoxin6 Deletion Impairs Mitochondria Function and Insulin Secretion in Pancreatic Beta Cells at American Diabetes Association (ADA), 77th scientific sessions. San Diego, CA, June 9-13, 2017.

Pinto M. Lack of Parkin exacerbates mitochondrial DNA alterations in mouse models of PD. Poster Session at the Euromit 2017 - Poster Presentation: Cologne, Germany.

Raval AP. Sexual dimorphism in inflammasome activation: Possible cause of exacerbated ischemic brain damage in reproductively senescent (RS) female rats at Organization for the study of sex differences meeting. Montreal, Canada, May 17, 2017.

E. McKnight Brain Institute Poster Session

During the Society for Neuroscience 2017 Meeting in Washington, DC on November 12, the McKnight Brain Research Foundation held a poster reception. Trainees and junior investigators from the University of Miami presented 5 posters at the reception. These posters were directly sponsored by our McKnight Brain Institute. Although we did not win any awards for poster presentations this year, we are proud of our presenters and highlight their work in this progress report.

- **Adiponectin and Components of Metabolic Syndrome are Associated with Cortical Thickness: the Northern Manhattan Study**

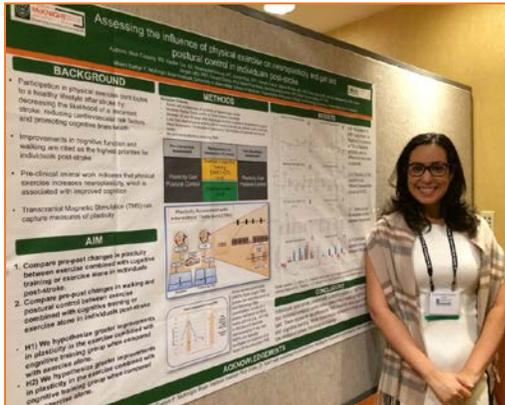
Presented by: **Michelle Caunca**



Summary: Metabolic syndrome has been associated with structural brain changes, but the relationship of adiponectin and cortical thickness is understudied. The objective of the research was to examine the association of adiponectin and metabolic syndrome components with measures of global and lobar cortical thickness. The study showed various levels of heterogeneity in the cross-sectional associations between adiponectin, metabolic syndrome components and regional cortical thickness.

- **The effects of a 12-week exercise and cognitive intervention on gait, posture and Transcranial Magnetic Stimulation plasticity measures individuals post stroke.**

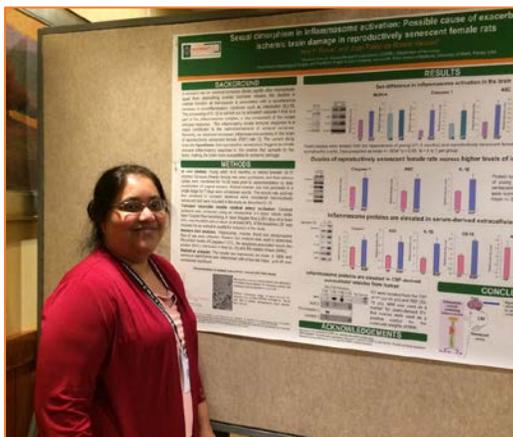
Presented by: **Joyce Gomes-Osman, PhD, PT**



Summary: Cognitive impairments greatly contribute to decreased function and disability in individuals post-stroke. The objective of the research was to compare the effects of a 12-week exercise program to a combined program of exercise and cognitive training on measures of brain plasticity, gait and postural control in individuals post-stroke. The results of this preliminary trial suggest that exercise delivered in isolation and combined with cognitive training may improve gait and postural control in persons post-stroke.

- **Sexual dimorphism in inflammasome activation: Possible cause of exacerbated ischemic brain damage in reproductively senescent female rats.**

Presented by: **Ami Raval, PhD**

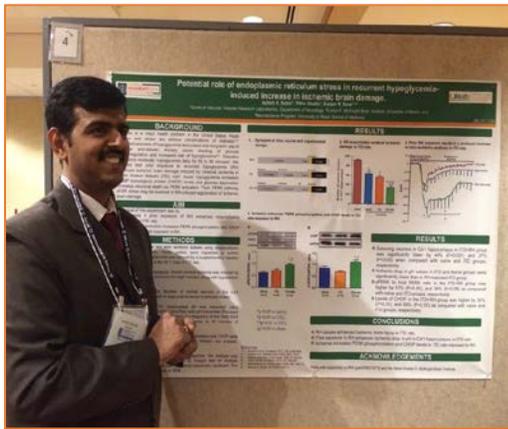


Summary: A woman's risk of a stroke increases exponentially following the onset of menopause, and underlying mechanisms remain unknown. The research study tested the hypotheses that: (1) inflammasome activation is significantly higher in the brain of RS females as compared to their young counterparts and senescent male rats, (2) RS triggers an innate immune inflammatory response in the ovaries that spreads to the brain, making the brain more susceptible to ischemic damage. Inflammasome proteins caspase-1, apoptosis-associated speck-like protein containing a caspase recruitment domain (ASC) and IL-1 β

significantly increased in the hippocampus, serum and ovaries of RSF as compared to YF ($p < 0.05$). The observed increase in ovary-derived EV containing inflammasome proteins in the brain contributes to the inflammation present in the brain of RSF, and it might exacerbate ischemic brain damage.

- **Potential role of endoplasmic reticulum stress in recurrent hypoglycemia-induced increase in ischemic brain damage.**

Presented by: **Ashish K. Rehni, PhD**



Summary: Diabetes is a serious metabolic disease and stroke among diabetics is noted to be associated with wide spread brain damage. Anti-diabetic drug therapy related episodes of hypoglycemia cause hypoglycemia associated autonomic failure and eventually lead to development of recurrent hypoglycemia (RH). The research in our lab thus far gleans that prior exposure of RH exacerbates ischemic brain injury in insulin-treated diabetic (ITD) rats. However, mechanisms known to cause this injury are least understood. This research concluded that cerebral ischemia increases ER stress in RH-exposed ITD rats and may play a role in increased

cerebral ischemic damage observed in RH exposed ITD rats. Confirming the role of ER stress in RH-induced aggravation of ischemic brain damage may help in developing new therapeutic options in diabetes.

- **Transcranial direct current stimulation augmented individualized gait training targeted at freezing of gait in Parkinson's Disease**

Presented by: **Jordyn Rice, PT, DPT**



Summary: Fifty to 70% of people with Parkinson’s Disease (PD) experience freezing of gait (FOG). Freezing episodes are significantly correlated with the risk of falling, which targeting FOG and augmented with tDCS. The results of the present study demonstrate safety and preliminary efficacy of an individualized gait training protocol augmented by tDCS. An individual in Stage II Hoehn and Yahr who experiences FOG can lead to injury, fear of falling, decreased activity levels and increased functional impairments. Current treatments for PD, such as pharmacologic agents and deep brain stimulation have a variable effect on FOG, making treatment options

limited. The objective of the research was to report on a case study assessing feasibility and preliminary efficacy of an individualized gait training.

5. Presentations at Public (Non- Scientific) Meetings and Events

Barrientos A. Mitochondria, NAD biosynthesis and Neurodegenerative disease: towards a program project. Neurology Grand Rounds. University of Miami Miller School of Medicine. Miami, FL, March 2017.

Barrientos A. Mechanisms of Protection against Polyglutamine Neurotoxicity by Moonlighting NAD⁺⁺ Biosynthetic Salvage Pathway Enzymes as Chaperones. Neurology Grand Rounds. University of Miami Miller School of Medicine. Miami, FL, May 2017.

Barrientos A. Cooperation of RNA binding proteins to promote and coordinate mtDNA gene expression. FASEB Summer Research Conference on Mitochondrial Assembly and Dynamics in Health, Disease and Aging Palm Beach, FL, May 21-26, 2017.

Barrientos A. Biogenesis of the mitochondrial ribosome. Department of Biochemistry. SUNY Upstate Medical School. Syracuse, NY, December 4, 2017.

Camargo C. Community Centers Presentations on Brain health and disease across Miami Dade.

Crocco EA. Alzheimer's disease Initiative (ADI) Caregiver Training Seminars in Dementia, Miami-Dade County, FL: Develop 4 hours of state mandated training to caregivers, ADI respite and Day Care professionals and para professionals for CEU accreditation on an annual basis provided in both English and Spanish. 2009-present.

Crocco EA. ADI Caregiving Training Program in Dementia, Monroe County ADI Respite Care and Day Care Centers, Florida Keys: Develop and coordinate 4 hours of state-mandated dementia training to caregivers in Respite and Day Care Centers in Monroe County on an annual basis, 2011-present.

Crocco E. Physician Led Expertise Topic: Alzheimer's Disease & Related Dementias, Jackson Behavioral Health System, Miami, FL, April 2017.

Crocco EA. Focus On Caregiving, Mount Sinai Medical Center, Wien Center for Alzheimer's Disease & Memory Disorders, Miami Beach, FL, June 2017.

Czaja SJ. Evolving in the 21st Century. Aging in the 21st Century: Myths and Realities of the Aging Process – An Overview. Lecture. Osher Lifelong Learning Institute. April 20, 2017.

Czaja SJ. Update on the Center on Aging's Research Activities at the Evelyn F. McKnight Research Seminar. Miami, FL, October 4, 2017.

Gardener H. Invited Speeches: Cardiovascular Risk Factors in Relation to Brain and Heart Health at 6th ICCR Congress on Chronic Societal Cardiometabolic Diseases, Quebec, Canada. May 2017.

Gomes-Osman J. Exercise to promote brain health for older adults at the Florida Physical Therapy Association Spring Conference, Lake Mary, FL, March 31-April 1, 2017.

Gomes-Osman J. An update on the work of the Neuromotor Plasticity Laboratory: in the pursuit of Exercise targeting Brain Health. Monthly McKnight Research Meeting, Miami, FL, November 2017.

Jiang H. Application of Advanced Retinal Vascular Imaging in Neuro-ophthalmology at the 43rd Annual NANOS Meeting, Washington, DC. April 1-6, 2017.

Jiang H. 53rd Annual Residents' Days. Bascom Palmer Eye Institute in Miami, FL. June 16-17, 2017.

Jiang H. International Ophthalmology & Optometry Summit (Moderator) at the Vision China, Hangzhou, China, July 27-29, 2017.

Jiang H. Retinal microvascular impairment in Neurodegenerative disorders. International Retinal Conference-ZOC 2016, Guangzhou, China, November 4-7, 2017.

Pinto M. Mitochondrial dysfunctions in Parkinson's disease at the Neurological Disorder Research Group (NDRG) meeting, Miami, FL, February 27, 2017.

Pinto M. Mitochondrial dysfunctions in Parkinson's disease: a lesson from mouse models presented at the Evelyn F. McKnight Brain Institute Research Seminar, Miami, FL, August 30, 2017.

Rundek T. WHO Annual meeting on Healthy Life style and brain disorders, Vienna, Austria, June 2017.

Sacco RL. Improving Stroke Quality and Reducing Disparities, Neurology Grand Rounds, University of Michigan, Ann Arbor, MI, March 29, 2017.

Sacco RL. Tenth Annual McKnight Inter-Institutional Meeting. Birmingham, Alabama, April 5-8, 2017.

Sacco RL. Improving Stroke Quality and Reducing Disparities, Neurology Grand Rounds, Albert Einstein/Montefiore Medical Center. Bronx, NY, April 13, 2017.

Sacco RL. Diet Soft Drinks and Stroke, NBC News, April 20, 2017.

Sacco RL. Identifying and Reducing Stroke Disparities: 2017 Comprehensive Stroke Symposium, Medstar Washington Hospital Center, Washington, DC, May 19, 2017.

Sacco RL. Access to Healthcare Hypertension/Cardiac Disease, University of Miami, Miami, FL, June 9, 2017.

Sacco RL. The Balancing Act Segment on Stroke for American Heart Association, June 30, 2017.

Sacco RL. Increasing Prevalence of Vascular Risk Factors in Patients with Stroke, iHeart Radio, October 11, 2017.

Sacco RL. University of Miami Bugher Center Updates. ASA/Bugher Centers for Excellence in Stroke Research, Los Angeles, CA, October 19-20, 2017.

Sacco RL. Fifth Annual Florida Puerto Rico Collaboration to Reduce Stroke Disparities (FL-PR CReSD) Stakeholder Meeting, Miami, FL. October 23, 2017.

Sun X. Conference entitled Advances in Diagnosis, Neurobiology, and Treatment of Neurological Disorders at the University of Miami, March 2017.

Sun X. MD/MPH student lecture at the University of Miami, March 2017.

Sun X. MD student lecture at the University of Miami, May 2017.

Sun X. High school student at camp Neurocognitive disorders at the University of Miami, June 2017.

Sun X. Psychiatry resident lecture at the University of Miami, June 2017.

Sun X. Neurology resident lecture at the University of Miami, Nov 2017.

6. Awards (Other)

Michelle Caunca received the Ruth L. Kirschstein National Research Service Award (NRSA) Fellowship for Students at Institutions with (or without) NIH-Funded Institutional Predoctoral Dual-Degree Training Programs (F30) from the NINDS.

Charles Cohan, PhD a post-doctoral associate in Dr. Perez-Pinzon's laboratory received an AHA Fellow's collaborative project examining the effect of exercise in improving post-stroke cognitive outcomes in reproductively senescent female rats.

Dr. Crocco continues to receive funds from the State of Florida's Department of Elder Affairs (DOEA) Alzheimer's Disease Initiative (ADI) for our Memory Disorder Clinics. Paired with our presence in the community as an academic research institute, being one of only 11 ADIs in the state establishes us as one of excellence.

Dr. Crocco was appointed a Fellow of the Academy of Medical Educators at the University of Miami Miller School of Medicine.

Dr. Crocco received the General Psychiatry Training Program Senior Faculty Teaching Award in 2017.

Dr. Czaja was an 'Innovative Research on Aging' Award Recipient and received an Honorable Mention, from Mather lifeways, Institute on Aging in 2017. She also received a United Homecare Claude Pepper Education Advocacy Award in 2017. She also received the University of Miami Research Dean's, Provost Funding Award.

Dr. Czaja and Daniel Jimenez, PhD received a K award to study the research project *Exercise to prevent depression and anxiety in older Hispanics*. It is a pilot randomized prevention trial that compares Happy Older Latinos are Active (HOLA) prevention intervention, a community health worker led physical activity intervention with an enhanced psychoeducation condition (fotonovela) in a group of older Latinos with minor and subthreshold depression and anxiety. The funding will support trainees involved in the research

Dr. Czaja received the following recognition and appointments in 2017:

- Review Committee, American Psychological Association's conference on Technology, Mind and Society, October 2017.
- Member, International Women's Forum (IWF), July 2017.
- Member, Planning Committee, "A Systems Approach to Alleviating work-induced Stress and Improving Health, Well-Being, and Resilience of Health Professionals within and Beyond Education". National Academies of Science, Engineering and Medicine. May 2017-present.
- Academic Co-Chair, "Alzheimer's Association Research Roundtable" Innovative Trial Design with Digital Biomarkers including wearables technology, and new recruitment technology for the next generations of clinical trials. February 2017-present.
- Cross Cutting Chair, National Research Summit on Care, Services, and Supports for Persons with Dementia and their Caregivers. Health and Human Services (HHS). February 2017-present.

Dr. Czaja continued with the following appointments in 2017:

- Member, Division of Behavioral and Social Sciences and Education's Board on Human Systems Integration. National Academies of Sciences, November 2016- December 31, 2017.
- Reviewer, Veterans Administration Panel for Under Secretary's Award for Outstanding Achievement in Health Services Research, October 2016-present.
- Member, External Advisory Committee, Great Plains IDeA Center for Clinical and Translational Research. September 2016-present.
- Board Member, Executive Council of Human Factors and Ergonomics Association, August 2016-2020.
- Member, Board on Human-Systems Integration, National Research Council/National Academy of Sciences, November 2010 – 2017.
- Member, Health Working Group of the Human Factors and Ergonomics Society Government Relations Committee, October 2015 – present.
- Member, Alzheimer's & Dementia Patient/Caregiver-Powered Research Network (AD-PCPRN) Advisory Council for Communications and Outreach, October 2015 – present.
- Member, Editorial Board, NIH Director's Early Independence Award, 2015-present.

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

Dr. Gomes-Osman was selected to participate in the prestigious Training for Grantsmanship in Rehabilitation Research (TIGRR) that will take place January 9 to 13, 2018 at the Wild Dunes Resort in Charleston (Isle of Palms) South Carolina, hosted by the Medical University of South Carolina. The TIGRR Workshop is funded by NIH/NICHD grant number T15HD074546.

Dr. Gomes-Osman has won the first Evelyn F. McKnight Brain Institute at the University of Miami Pilot Grant for a project entitled *Aerobic exercise to influence mechanisms of brain plasticity and cognition in healthy aging*. Evelyn F. McKnight Brain Institute Internal Pilot Grant. Role: PI. Grant amount: \$10,000.

Dr. Gomes-Osman received her secondary appointment as Assistant Professor in the Department of Neurology and has begun formal mentorship with **Dr. Rundek**.

Dr. Jiang received Fellow status from the North American Neuro-ophthalmology Society.

Dr. Jiang resubmitted her R01 grant proposal for the study *Retinal microvascular impairment in AD* in November 2017.

Dr. Ramos received funding from the NIH/NIA R21 for the study *Exploring Sleep in Neurocognitive Aging and Alzheimer's Research (eSANAR)*. The study explores sleep phenotypes (i.e. sleep apnea) and early neurocognitive decline, mild cognitive impairment (MCI) and Alzheimer's disease (AD) in Latinos. This study addresses an important health disparity in middle-aged and older Latinos, an at-risk population for MCI/AD with a large burden of vascular disease.

Dr. Raval was awarded a grant from the Florida Department of Health (DOH) for her research project on how whole body vibrations improves stroke outcome in nicotine-exposed rats.

Andrea Ruetenik, a PhD student trainee mentored by **Dr. Barrientos** received a Fellowship from the Huntington's Disease Society of America (HDSA) as the Principal Investigator for research on the protective role of NAD salvage pathway proteins against mutant huntingtin toxicity.

Dr. Rundek received an ARISTA award (USA Protocol ID# CV185-564) to study the disparities in stroke outcomes and care delivery in patients with Atrial Fibrillation (FLiPER-AF).

Dr. Rundek together with **Dr. Blanton** and Dr. Wang has submitted an NIH/NINDS proposal to conduct a Family Study of Carotid Atherosclerosis and Stroke Risk.

Dr. Zeki Al Hazzouri was elected co-chair for the Epidemiology of Aging Interest Group (EAIG) of the Gerontological Society of America (GSA).

Dr. Zeki Al Hazzouri in collaboration with Dr. Yaffe at the University of Southern California, San Francisco was awarded a grant to study the project *Healthy Heart, Healthy Brain? A Pooled Life-course Cohort for Dementia Risk Assessment*. The goal of this study is to investigate cardiovascular risk factors over the life-course and their association with dementia risk.

Dr. Zeki Al Hazzouri in collaboration with Dr. Glymour at the University of Southern California, San Francisco received funding to study the project *A Binational Study to Understand Dementia Risk and Disparities of Mexican Americans: The Role of Migration and Social Determinants*. The goal of this study is to create a binational study of two nationally representative cohorts from the US and Mexico to study how migration influences dementia risk of Mexican Americans and factors that increase or reduce dementia risk in Mexican Americans.

7. Faculty

Our Faculty is divided by those receiving direct support from the Institute (*Members*) and those with whom the Institute is collaborating within the University of Miami (*Collaborators*). Faculty biosketches are attached at the end of the document.

Name	Center Role Members	Area of Expertise
Noam Alperin, PhD	Radiology	Physics (MRI)
Sara Czaja, PhD	Member	Aging, Psychology, Engineering
Kunjan R. Dave, PhD	Member	Neurobiology, Basic Science
David Della Morte, MD, PhD	Member	Neurology
Joyce Gomes-Osman, PhD, PT	Member	Neurology, Physical Therapy
Hong Jiang, MD, PhD	Member	Neurology, Neuroscience
Bonnie E. Levin, PhD	Member & Schoninger Professor	Neuropsychology
Tatjana Rundek, MD, PhD	Scientific Director	Epidemiology, Neurology
Ralph L. Sacco, MD, MS	Executive Director	Neurology, Epidemiology, Genetics
Xiaoyan Sun, MD, PhD	Educational Director	Neuroscience, Biochemistry

Name	Center Role Collaborators	Area of Expertise
Antoni Barrientos, PhD	Basic Science	Neuroscience, Genetics
Susan Blanton, PhD	Genetics	Genetics
Elizabeth Crocco, MD	Psychiatry	Psychiatry
Chuanhui Dong, PhD	Biostatistics	Epidemiology, Biostatistics
Hannah Gardener, ScD	Epidemiology	Epidemiology

Teshame Monteith, MD	Headache	Headache Science
Carlos Moraes, PhD	Basic Science	Neuroscience
Miguel Perez-Pinzon, PhD	Basic Science	Neuroscience
Milena Pinto, PhD	Basic Science	Neurology
Alberto Ramos, MD	Basic Science	Sleep Medicine, Neurology
Ami P. Raval, PhD	Basic Science	Neuroscience, Epidemiology
Jianhua Wang, MD, PhD	Basic Science	Neurology, Neuroscience
Juan Young, PhD	Basic Science	Genetics
Adina Zeki Al Hazzouri, PhD	Collaborator	Epidemiology

8. Trainees

Name	Center Role	Area of Expertise
Shatha Aldraiwiesh, PT	PhD Student	Physical Therapy
Kyle Andrade-Bucknor	Undergrad Student	Pre-Med
Nikhil Sebastian Banerjee	Graduate Practicum Student	Neuropsychology
Christin I. Bermudez, PhD*	Postdoctoral Fellow	Neuropsychology
Myriam Bourens, PhD	Associate Research Scientist	Neuroscience
Jabari-Ture Ghingo Brooks	Post-Bac Student	Neuroscience
Annelly Buré-Reyes, MS	Research Associate	Neuropsychology
Christian Camargo, MD	Cognitive Fellow	Neurology
Nicholas Cassidy	Undergrad Student	Neurology
Michelle Caunca, MD/PhD Student	Formal McKnight Trainee	Neurology

Austin Choi	PhD Student	Neuroscience
Charles Cohan, PhD	Postdoctoral Fellow	Neurology
Maria Diaz, MD	Research Assistant	Neurology
Katalina Fernàndez McInerney, PhD*	Fellow	Neuropsychology
Danylo Lucio Ferreira Cabral, SPT	Research Associate	Physical Therapy/Cognition
Carolina Flores	Post-Bac Student	Physical Therapy
Marti Flothmann, BE	Research Assistant	Exercise Physiology
Wendy Gaztanaga	Trainee	Neuropsychology
Sarah Getz, PhD	Postdoctoral Fellow	Neuropsychology
Alison Headley, MD	Resident	Neurology
Nathalie Khoury, BS	PhD Student	Neuroscience
Hyun-Jun Kim	PhD Student	Neuroscience
Kevin Koronowski, BS	MD/PhD Student	Neuroscience
Jonathan Landman, MD	Research Assistant	Neurology
Cril Larhssen	Undergrad Student	Physical Therapy
Diego Lasso	Undergrad Student	Biology
Suzanne Lippman	MD Student	Neurology
Priyanka Maiti, PhD	Post-Doctoral Trainee	Neuroscience
Ava Marsh	Undergrad Student	Biology
Erika Marulanda-Londono*	Fellow	Neurology and Stroke
Michelle Miranda, PhD	Postdoctoral Fellow	Neuropsychology
Qismat Bahar Niazi	Undergrad Student	Neuroscience

Eva Nyvltova, PhD	Post-Doctoral Trainee	Neuroscience
Sofia Oluwole	MD/PhD Student	Neurology
Sabrina Pastore	Undergrad Student	Physical Therapy
Pujan Patel	Undergrad Student	Neuropsychology
Maya Pinjala	Graduate Practicum Student	Neuropsychology
Ashish Rehni, PhD	Postdoctoral Fellow	Neurology
Jordyn Rice, PT, DPT	DPT, PhD Student	Physical Therapy/Cognition
Joshua D. Rooks	Graduate Practicum Student	Neuropsychology
Andrea L. Ruetenik	PhD Student	Neuroscience
Sharnikha Saravanan	Undergrad Student	Neuroscience
Kasra Sarhadi	MD/MPH Student	Physical Therapy/Cognition
Marina Sarno, PhD	Postdoctoral Fellow	Neuropsychology
Marc Schatz	MD Student	Neurology
Vibha Shukla, PhD	Postdoctoral Fellow	Neurology
Marialaura Simonetto, MD	Fellow	Neurology
Mitchell Slugh, PhD	Postdoctoral Fellow	Neuropsychology
Hesley Solano	Undergrad Student	Neuroscience
Chantel Sorochuk	Graduate Practicum Student	Neuropsychology
Courtney Sparger	Undergrad Student	Neuroscience
Holly Stradecki, MS	MD/PhD Student	Neuroscience
Ni (Sunny) Sun-Suslow	Graduate Practicum Student	Neuropsychology

Alba Timon, PhD	Postdoctoral Trainee	Neuroscience
Eduard Tiozzo, PhD*	Fellow	Exercise Physiology/Nutrition
Kristopher Wolford, MPH	Undergrad Student	Public Health
Jing Xu, BS	PhD Student	Neuroscience
Michelle Zambik	Post-Bac Student	Neuroscience
Rui Zeng	PhD Student	Neuroscience
Hui Zion	PhD Student	Biochemistry

*Became University of Miami Department of Neurology Faculty this year.

9. Clinical/Translational Programs

A. New Programs

Clinical and Population Based

Dr. Sacco will begin his new project *The Transitions of Care Stroke Disparity Study (TCSD-S)*. It is described below on page 43. He will be focusing on the *Florida Stroke Registry* which will entail strict organization and coordination among Florida hospitals and the Florida state legislative system. Additionally, he will continue working on his research projects as described below on pages 40-44.

Dr. Rundek will learn the results of the R01 application on imaging of small vessel perfusion to the NIH in Sept of 2017 and will move forward with it as a new research project if funded. It is described in this section below under Dr. Alperin on page 48. She will begin her research as Co-Investigator on the new project *The Transitions of Care Stroke Disparity Study (TCSD-S)*. It is described below on page 43. Dr. Rundek and **Dr. Zeki Al Hazzouri** submitted an R01 proposal to the NIH/NIMHD to study *Migration and Cardiovascular Health in Family Study of Dominicans and Dominican Americans*. The goal of this proposal is to compare Dominican family members living in the US and Dominican family members living in the Dominican Republic to evaluate how migration and migration-related factors influence their subclinical and clinical cardiovascular health. The grant was preferably scored but was not funded, so they will resubmit this revised proposal in 2018.

Dr. Sun and **Dr. Camargo** will develop several projects in 2018. Their preliminary data were submitted as abstracts to the 2018 American Academy of Neurology (AAN) conference, as following: (1) Biomarkers of Alzheimer's Disease in Cognitively Intact Patients – Can Neurogranin

Serve as a Preclinical Marker? (Authors: **Christian Camargo** and **Xiaoyan Sun**) with the objective to investigate the potential role of Neurogranin in cognitive decline in cognitively intact individuals; and (2) CSF Neurogranin Levels Predict Cognitive Decline in MCI Patients (Authors: **Alison J. Headley, Andrés De León, Chuanhui Dong, Bonnie E. Levin, David Loewenstein, Christian Camargo, Tatjana Rundek, Henrik Zetterberg, Kaj Blennow, Clinton Wright, Xiaoyan Sun**) to examine the relationship between cerebral spinal fluid levels of Neurogranin (Ng)- a post synaptic protein – and longitudinal performance on memory and executive functioning tests in individuals with mild cognitive impairment (MCI) and cognitively normal elderly (NC).

Dr. Czaja has had numerous achievements and successes as Director of the Center on Aging and Director for Research and Education on Aging. Her experience and knowledge of aging research is a natural complement to the McKnight Brain Institute’s goals. She has worked to improve quality of life for the aging population for decades and her collaboration with the Institute has enhanced our research and strengthened our ties to the community. Dr. Czaja has mastered the important concept of multi-disciplinary research. This picture portrays her extensive collaborative research model. Research she will be working on next year is described below.



Dr. Czaja has recently received an NIH R01 award to research *a Personalized Health Behavior System to Promote Health and Well-Being in Older Adults beginning* in 2018. The study objectives are to examine the usability and efficacy for diverse older adults of a new tablet-based dynamic system: the Fittle Senior System (FSS) that will provide: (1) personalized behavior-change programs for improved diet and increased physical activity and (2) online social interaction and support from small teams pursuing similar goals. The duration of the intervention phase will involve an active 12-week intervention phase followed by a 12-week maintenance phase. She will also examine factors such as diet and exercise self-efficacy that mediate the relationship between the FSS and paper-based psycho-education (BPE) interventions, health outcomes, and the influence of potential moderating variables such as education, health literacy, ethnicity, gender and SES status on these relationships (interactions).

Dr. Czaja received an SBIR award entitled: *A novel computer-based functional skills assessment and training program, I-FUNCTION, INC.* The objective of the proposed pilot project is to build on her prior work and expand, implement and evaluate the acceptability, feasibility and efficacy of the novel computer-based functional skills assessment/training (FST) program, which provides individually tailored training on everyday tasks critical to independent living (e.g., financial and medication management). The overall long-term goal of this proposal is to develop a commercially available integrated technology-based functional skills training and assessment

program that can be deployed on a variety of technology platforms (e.g., clinical settings, home environments) with diverse populations.

Dr. Czaja also received an R01 award entitled: *Understanding Factors Influencing Financial Exploitation among Diverse Samples of Older Adults*. This project will examine both direct and indirect effects of socio-demographic factors, social integration/isolation, general cognitive abilities, financial skills/advice and support and psychosocial factors on susceptibility to financial scams (exposure and vulnerability) and financial exploitation in diverse samples of older adults. The study will be conducted at 2 sites, the University of Pittsburgh and the University of Miami. It will include a total of 720 adults age 60 and older.

Dr. Czaja will serve as the Principal Investigator of the University of Miami project entitled *ORCATECH Collaborative Aging (in Place) Research Using Technology CART*, funded by the NIA. The CART program will develop and validate an infrastructure for rapid and effective conduct of research utilizing technology to facilitate aging in place. This demonstration project is designed as a feasibility study of the technology system, testing whether the CART system measures and detects maintenance of independence and/or functional decline leading to greater dependency. The project will be focusing on the oldest-old with chronic disease, veterans living in rural communities, minorities and socially isolated seniors of low income.

Dr. Alperin together with **Dr. Rundek** (multiple PIs) submitted a proposal to the NINDS to develop and validate *Novel quantitative method for mapping small vessel regulation of cerebral perfusion*. The objective of this research is to establish normative values of a MR regional perfusion regulation index (ratio of regional perfusion change per change in global blood flow, over a wide range of blood flow levels) in healthy participants across different age groups, and in patients with diabetes with a various degree of small vessel disease. This novel MRI-based perfusion regulation method may hold a promise to provide valid imaging biomarker for testing small vessel function and compensatory capacity in pre-clinical stage of small vessel disease, and for monitoring of the progression (or effects of therapies) of small vessel disease in a wide range of related metabolic and neurodegenerative disorders.

Dr. Levin is collaborating on the joint multicenter proposal (under consideration) with McKnight collaborators at the University of Florida and University of Arizona examining risk factors contributing to increased susceptibility to deception in aging. This project addresses a growing public health concern pertaining to the expanding number (1 in 5 over the age of 65 years) of older Americans who fall victim to some form of financial abuse. This proposed study will determine specific processes associated with susceptibility to scamming and proposed effective interventions to increase deception detection.

Dr. Jiang's research will continue to uncover the role of retinal microvascular dysfunction in pre-MCI, MCI and AD patients to identify the sensitive ocular biomarkers in predicting cognitive function decline and monitoring therapeutic efficacies. Together with **Dr. Rundek**, she submitted an R01 to the NIA in September of 2017 in order to determine the association of retinal microvascular network, microcirculation and microstructure with cerebral hemodynamics in aging, MCI and AD. The objective is to characterize the early retinal changes in microvascular network, microcirculation and microstructure in cognitive decline, and to develop these

measures as retinal biomarkers to aid in better identification of patients at risk of cognitive decline and AD.

Basic Science

Drs. Dave and Perez-Pinzon will be evaluating synergistic effects of physical exercise and resveratrol treatment on post-stroke cognitive function in middle aged rats. The goal is to determine if increasing the duration of exercise in reproductively senescent female rats is able to improve post-stroke cognitive function. **Charles Cohan, PhD**, post-doctoral associate in Dr. Perez-Pinzon's laboratory will be examining the effect of exercise on post-stroke cognitive outcomes in reproductively senescent female rats. This project is funded by a supplement grant to the Bugher center grant.

Dr. Della-Morte's plan for the near future is to continue his research on the mechanisms able to help in slowing down typical phenotypes of aging brain, such as memory loss, and/or even to treat related diseases like cerebral ischemia and dementia. He will pursue research on Peroxiredoxin 6 (PRDX6) and aging, particularly by translating all results on neuronal models to confirm in the brain the results obtained in muscle and pancreatic cells. He will investigate the association between Serum Glucocorticoid Inducible Kinase (SGK-1), a stressor response kinase able to significantly delay the onset of senescence, with the reduction of the huntingtin protein accumulation in neurons. The accumulation of misfolded huntingtin has been demonstrated to be among most important causes of memory loss. Moreover, by using the Northern Manhattan Study (NOMAS) data he will explore the association between genetic variants of these antioxidant proteins and age-related diseases, including phenotypes of atherosclerosis, cognitive decline and metabolic diseases. Also through NOMAS, he will continue epidemiological research on the interaction between phenotype of atherosclerosis, such as carotid intima media thickens and white matter hyperintensities.

Dr. Barrientos will continue working on his project to characterize the role of NAD⁺ salvage pathway proteins in cellular aging and PROTECTION against proteotoxicity. He created a full set of the strains needed in 2017. In 2018, he will begin researching chronological life span assays. He aims to continue work to determine whether the neuroprotective activity of NMA1/NMNAT and other NAD⁺ salvage pathway proteins protect against protein misfolding-induced proteotoxicity in neuronal cells derived from HD-patient fibroblasts. While working in the Bucks Institute in California he learned how to manipulate iPSC cells and obtained as a gift several cell lines derived from HD patients. These cell lines, differentiated into neuronal stem cells, are now being cultured in the laboratory. Therefore, all the constructs needed for the expression of NMNAT, NADS, NDase and NMPRT are already available in the lab.

Dr. Pinto will continue her work with Dr. Baumel into 2018. The long-term goal of her project is to characterize the neuroprotective function of MSCs in a mouse model of Alzheimer's disease. The achievement of this goal will provide the possibility to build a "basic science" platform based on animal models at the University of Miami that can be translated directly into clinic. To achieve the goals of this study the following approach will be used: they will extract and expand MSCs from a healthy mouse donor, inject the cells into a mouse model of AD and follow the progression

of the pathology in presence or absence of MSCs. This research will make a strong and lasting impact on our understanding of the use of MSCs as a new neuroprotective agent. The results of this project will provide insight into a mechanism of neuroprotection that can be exploited as new therapeutic options for Alzheimer's disease. Moreover, because neurodegeneration is the cause of several progressive diseases (Parkinson's, Huntington's, Amyotrophic lateral sclerosis), we expect that the information derived from this project will likely impact not only Alzheimer's disease but also other progressive neurological diseases.

Dr. Raval was recently awarded a grant from the Florida Department of Health (DOH) for her research project on how whole body vibrations improves stroke outcome in nicotine-exposed rats. She will be delving into this research in 2018. The major goal of the project is to study the effects whole body vibrations have on post-stroke frailty in nicotine exposed female rats.

B. Update on Existing Clinical Trials and Research

Clinical or Population Based

Dr. Sacco (Executive Director) has had a number of achievements since our last progress report. He has recently become a multi-PI and a Contact PI of the *Disparities in Transition of Care after Acute Stroke Hospitalization: Transition of Care Stroke Disparities Study (TCSD-S)* that was awarded by the NIH in October of 2017. **Dr. Rundek** and Dr. Jose Romano (Stroke Division Director) are also multi-PIs on this project. Dr. Sacco has also recently received funding to lead *the Florida Stroke Registry*, which is a statewide initiative, funded through state appropriations, and accompanied by law stating that all Florida Stroke Hospitals will participate in the registry overseen by the University of Miami. This is a grand achievement for improving quality of care for stroke patients, their families and communities by engaging over 80 Florida hospitals in a collaborative network to improve quality of care, education and research. Dr. Sacco is also a PI of three recent proposals submitted to the NIH, including competitive renewal of the Miami CTSA, StrokeNet and NeuroNext.

Dr. Sacco has been a leader of the *UM Clinical Translational Science Institute (UM CTSI)*. Our CTSI is dedicated to accelerate and transform culturalized clinical and translational (C/T) science at UM. Serving as an indispensable resource for C/T researchers and stakeholders, the CTSI is equipped to be the Miami Hub of the nation-wide NIH Clinical and Translational Science Award (CTSA) research network, which aims to advance scientific discoveries into improved health care. The institution is funded through NCATS (\$3 million in direct costs per year) and institutional matching funds. Reinforcing the success of the UM CTSI's mission is the partnership with the UM UHealth System, which consists of hospitals, medical centers and non-profits dedicated to health services, patients and health policy. As a first line of action towards actualizing effective culturalized C/T science, the UM CTSI provides training to enhance the careers of a diverse research workforce (Dr. Rundek is the CTSI Educational co-Director). A proficient C/T research workforce is fostered through UM CTSI programs such as "Translation Workforce Development", "Team Science", "Biostatistics, Epidemiology and Research Design", among others.

The Northern Manhattan Study (NOMAS) - Stroke Incidence and Risk Factors in a Tri-Ethnic Region is in its third year of funding of the fifth NOMAS cycle. Although originally designed as a stroke study, the aging of the NOMAS cohort has presented an opportunity to study aging and cognitive decline with a specific focus on vascular and inflammatory determinants of aging, cognitive trajectories and functional outcomes such as disability and quality of life. As a result, the current NOMAS cycle aims to address important gaps in knowledge on the risks and determinants of cognitive impairment and dementia. Through the ongoing 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.

This year, research to determine the relationship between cognitive trajectories and novel neuro-immune and inflammatory biomarkers has advanced with the completion of the third neuropsychological assessments among the 240 NOMAS participants (from MRI subcohort of 1290 subjects). Additionally, all plasma samples from this same cohort have been processed with the neuro-immune biomarker panel. These data will enable us to conduct analysis to define the relationship between soluble and MRI biomarkers and cognition.

Completed studies this year have resulted in over 19 manuscripts to date. Our published results include the association between brain imaging biomarkers and trajectories in specific cognitive domains. These studies describe a non-linear relationship between brain arterial diameters and cognitive performance (PMID: 29166955), and an association between global and region MRI metrics and domain-specific cognitive decline (PMC5272913). We have also reported on the relationship between the AHA-defined target levels for 7 cardiovascular health factors and a decrease in cognitive performance. Among those with better cognitive performance at initial assessment, the associations were observed between the number of ideal cardiovascular health factors and less decline in the domains of executive function and episodic memory (PMC4943249). In a separate study, we found that greater hippocampal volumes were associated with less decline in executive function and episodic memory, while greater white matter hyperintensity volume was associated with greater decline in semantic memory (**Michelle Caunca**, MD/PhD student, 2017 AAN Annual Meeting; manuscript in progress).

We have also reported on cerebral microbleeds (CMBs) and other brain MRI metrics in the NOMAS. We found that greater age and the presence of subclinical brain infarcts were associated with greater odds of CMB presence, while taking diabetes medications was associated with lower odds of CMB presence (PMC5079015). Our other MRI studies indicated that participants with greater white matter lesion load burden exhibited greater cognitive decline compared to those with the least white matter lesion load burden, and that those with larger cerebral volumes exhibited greater decline when compared to those with the smallest cerebral volumes (PMC5272913).

Findings on the relationship between white matter hyperintensity volumes (WMHV) and longitudinal trajectories of functional status were also reported this year. We have found that periventricular brain WMHV is associated with accelerated long-term functional decline (PMID: 29155435) and that left-right asymmetry of regional WMHV may disrupt brain network efficiency (PMC5609109). We have explored differences in associations between subclinical brain infarcts (SBI) and WMHV hypothesizing that SBI and WMHV moderated relationships between cognitive performance and education, and functional trajectories. Education did not modify associations between cognition and functional trajectories. In another analysis, MRI measurements included SBI, and size and number of perivascular spaces (PVS). In this study we found that SBI but not PVS were associated with doubling of the rate of functional decline over time, independently of risk factors and vascular events. This highlights the strong and independent association between “subclinical” markers of cerebrovascular injury and important clinical, patient-centered functional trajectories (manuscript in review).

NOMAS has also entered into multiple external collaborations and maintained collaborations with other large, longstanding cohorts such as WHICAP. In this collaboration, we have published novel candidate gene loci for WMHV in *Neurology Genetics* in Sept 2017 (PMC5619914). NOMAS’s productivity and “team science” approach continues to reinforce the value of our data, increasing the potential to inform designs of interventions to prevent stroke and cognitive decline in diverse populations.

Dr. Sacco has been successfully leading the UM American Heart Association/Bugher Center of Excellence, which is in its fourth year of funding. The Centers’ research focus is on recovery after stroke, resilience and rehabilitation, and involves a multidisciplinary approach combining basic science, clinical translational research, and population science with a strong emphasis on interdisciplinary and multi-institutional training and collaborations. The Center aims to enhance cognitive recovery and quality of life after stroke through complementary studies in Clinical and Basic Science research. The Clinical Research Bugher Project (led by Dr. Koch who replaced Dr. Wright as PI on the Bugher project) investigates the effects of a combined aerobic and resistance exercise training (CARET) program and a Cognitive Training Intervention (CTI) on cognitive performance, physical fitness and quality of life among stroke survivors with mild to moderate physical disability. Currently, the study is close to completion of enrollment of 120 subjects. Preliminary study observations indicate successful project feasibility with minimal withdrawal from the study and upon completion the subjects express a wish to continue the activities beyond the study period. Anticipated results will offer insight towards behavioral/environmental modifications to decrease sedentary behavior; which when not addressed, exacerbate a cascade of physical, emotional, and cognitive deterioration after stroke.

The Basic Science Bugher Project led by **Dr. Miguel Perez-Pinzon** compliments the Clinical Research project, in order to provide insights into cellular mechanisms underlying stroke-mediated damage and repair in an animal model. This year, studies were completed on both young and aged rats to determine how exercise intensity affects 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. Results also revealed differences in the benefits of exercise in post-stroke rats by age. In young post-stroke rats, moderate exercise ameliorated cognitive deficits, while in aged rats exercise reduced

cognitive deficits following stroke. Overall, exercise improved plasticity following stroke in both young and aged rats. Another basic science study initiated this year in **Dr. Perez-Pinzon's laboratory** includes testing of pharmacological approaches as potential therapies for improving stroke outcomes. Data collected for various *resveratrol* doses in aged rats is currently being analyzed. These initial studies will lead to studies to explore pharmacological agents that increase BDNF (brain-derived neurotrophic factor) to further enhance the effects of enhanced exercise to ameliorate the detrimental effects of stroke.

Dr. Sacco has been successfully leading the *UM Stroke Prevention Intervention Research Program, Florida-Puerto Rico Collaboration to Reduce Stroke Disparities (FL-PR CReSD)* in its final year of NIH funding. The study results have identified a number of race-ethnic and sex disparities in acute stroke care and have involved implementing novel hospital quality improvement programs. The FL-PR CReSD stroke registry is the first comprehensive stroke registry in Florida and Puerto Rico created to monitor longitudinal trends in disparities in acute stroke care. Currently, the FL-PR CReSD Stroke Registry is comprised of 78 Florida hospitals and 14 Puerto Rico hospitals, and to date we have compiled 162,633 stroke cases from both regions. With this valuable data, the registry has served as an important tool for monitoring and tracking disparities and improving performance. We have reported on regional disparities in overall stroke care between Florida and Puerto Rico (PMC5642916; PMC5523741). We have also revealed persistent disparities for both Florida blacks and Puerto Ricans, showing that they less likely receive the clot-busting drug, tissue plasminogen activator (PMC5523741), as well as rapid stroke care (PMC5639478) compared to Florida whites and Florida Hispanics. In a separate study, our finding revealed that women are still less likely to receive thrombolysis, especially in Puerto Rico (PMC5039084).

We have also reported on the steady improvement over time in overall stroke care among Florida blacks and Hispanics (PMC5523741). Through self-monitoring tools, hospitals may track and measure their performance annually, identify gaps in quality of care and define where to implement best practices for improvement. The state of Florida has recognized the impact and value of this stroke registry as a quality improvement tool for addressing disparities in quality stroke care. In 2017, Florida passed a state law to fiscally and legally support the use of a Florida Stroke Registry and to be run and managed by the University of Miami under the leadership of **Dr. Sacco**. The state policy enables the stroke registry, originally developed in the FL-PR CReSD project, to continue to function beyond the completion of the current NIH funded award.

The Transitions of Care Stroke Disparity Study (TCSD-S) is a new project awarded in October of 2017 (MPI: **Drs. Sacco, Rundek, Romano**) to identify disparities in transitions of stroke care and key factors associated with effective transitions of care. In its first year of funding, the project will address its aims through structured telephone interviews to evaluate medication adherence, healthy lifestyle, utilization of rehabilitation interventions and medical follow-up 30 days after hospital discharge to home in 2,400 participants across 6 comprehensive stroke centers in Florida. A novel Transitions of Stroke Care Performance Index (TOSC PI) will be derived and validated. The primary outcomes are the TOSC PI and 90-day hospital readmissions. Based on identified predictors of disparities in TOSC, we will develop and demonstrate feasibility of initiatives for interventions to reduce disparities in TOSC that target systems of care with a TOSC

disparities dashboard, and health care providers with a training module for enhanced education to support successful transition of care after discharge to home.

Dr. Rundek (Scientific Director) has had a number of achievements since the last progress report. She has joined Dr. Sacco in the research effort in the NOMAS as an investigator for 20 years. She is a Training Director of the AHA Bugher Stroke Center of Excellence, Core Director of the Stroke Prevention Intervention Research Program, Florida-Puerto Rico Collaboration to Reduce Stroke Disparities (FL-PR CReSD) and PI of the Transitions of Care Stroke Disparity Study (TCSD-S). Dr. Rundek also joins Dr. Sacco in his CTSI leadership. Dr. Rundek serves as a co-Director of the Miami CTSI Translational Workforce Development and KL2 research Program. Dr. Rundek is also Director of a Master of Science degree in Clinical Translational Investigations that is funded through the Miami CTSI. Last year, Dr. Rundek was awarded a grant Disparities in Stroke Outcomes and Care Delivery in Patients with Atrial Fibrillation: FLiPER-AF Study by Bristol-Myers Squibb/Pfizer Alliance. The project is addressing race/ethnic and gender gaps in stroke care for patients with atrial fibrillation using online surveys and the new AHA 'Get With The Guidelines' AFib data collection on-line tool. The ongoing study is planned for 3 years.

Dr. Rundek has had a number of publications in 2017. She authored or co-authored 32 publications in 2017, among which 7 were related to the NOMAS, 7 to genetics of subclinical vascular disease and 12 are collaborations with large genetic and imaging consortia and other population studies such as the Einstein Aging Study (EAS) in the Bronx and the Hispanics Community Health Study-Study of Latinos.

Specifically, we highlight the results from the Einstein Aging Study (EAS), a population based study of aging that has been funded by the NIA for over 25 years (PI, Dr. Richard Lipton). Together with Dr. Carol Derby from the EAS, Dr. Rundek is a leader of Einstein Cerebral Hemodynamics Study of Aging and PI of the Ultrasound Imaging Core in Miami. The study is aimed to investigate the vascular mechanisms of normal aging, MCI and dementia using TCD challenge test. In the recent publication (Magn Reson Imaging), we have reported on significant and specific regional relationships between the brain hemodynamic pulsatility index (PI) and white matter microstructural changes. We have identified spatial clusters of significant correlations between elevated PI and reduced FA (fractional anisotropy on MR diffusion imaging) that were not limited to the vascular territories. Our results suggest that the linkage between PI and FA is less likely a function of perfusion, but is more consistent with injury caused by mechanical wave emanating from pulsating vessel walls. If validated, this observation may be of important relevance contributing to our understanding of the brain hemodynamic effects on cerebral white matter disease leading to cognitive decline, the mechanism that is amenable to prevention and therapeutic modifications.

In another collaboration with the EAS, **Dr. Rundek** has recently published on brain hemodynamic changes in relation to lower extremity function (J Am Geriatr Soc.). In this publication, low blood flow velocities in the anterior and posterior cerebral circulation were associated with worse lower extremity function and balance in older adults. This observation indicates the importance of age-related changes in cerebral hemodynamics of brain regions involved in specific aspects of individual function and physical performance.

In the past year, **Dr. Rundek** has extended some of the findings in the EAS using the NOMAS cohort. For instance, in the manuscript on *the Relationship between carotid arterial properties and cerebral white matter hyperintensities* (recently published in *Neurology*), we reported on the association of increased carotid artery diameters and decreased STRAIN (local pulsation of the carotid artery within a cardiac cycle) with greater WMH burden. These associations suggest an important pathophysiologic role of extracranial large artery remodeling and arterial hemodynamic response to arterial remodeling in the burden of WMH.

In collaboration with **Dr. Sun**, **Dr. Rundek** has published *an editorial* on the association between increased arterial stiffness and cognitive impairment (recently published in *Stroke*) as a commentary on the results from the Framingham Offspring Study that reported an association of arterial stiffness with an increased risk of MCI and incident dementia. These results have focused on the investigation of vascular mechanisms of MCI and dementia and on the search for valid and early vascular biomarkers of cognitive decline. Interventions that modify vascular risk factors and arterial stiffness may have enormous potential for prevention of cognitive impairment and dementia. Dr. Rundek also co-authored Dr. Sun's paper on *Neurogranin as a predictor of memory and executive function decline in MCI patients*, recently accepted for publication in *Neurology*.

McKnight Brain Aging Registry (MBAR)

Dr. Rundek has made a significant effort to enroll participants for the collaborative MBAR study. Our site has been contacted by 59 potential study participants in 2017. Of these 59, 9 were eligible and enrolled in the study. They are at varying points in the study (one didn't meet criteria to complete the study; two have completed) and are expected to complete the required visits in early 2018. Most were excluded because of contraindications to having an MRI. There has been an overwhelmingly positive response to this innovative research on healthy aging adults as opposed to those with dementia, which seem to dominate the research climate.

Three MBAR study participant visits were scheduled during Hurricane Irma and could not take place. Rescheduling those and continuation of already enrolled participant's study visits have been delayed as well, due to the aftermath conditions of South Florida. Bi-weekly calls with all McKnight Brain Institutes continue so all McKnight Institutes can provide updates on study progress, discuss concerns or issues, share best practices and brainstorm on increasing enrollment. These are productive calls in which the study design and its protocol are examined for accuracy and consistency. Bi-weekly calls also take place between the Principal Investigators at each site in which future pilot studies, grant submissions and multi-disciplinary projects are being planned that will build and expand on the vital MBAR research data. Through these efforts led by **Dr. Rundek** at our site, a collaborative inter-institutional team has blossomed into a fruitful partnership that promises to achieve much success in 2018.

Dr. Sun (Education Director) has worked on discovering the role of synaptic protein neurogranin in cognitive impairment in patients with mild cognitive impairment (MCI). Using the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset, she found that neurogranin can predict memory and executive function decline in a period of 8 years. After three successful rounds of revisions, Dr. Sun's manuscript *Neurogranin as a predictor of memory decline in patients with mild cognitive impairment* was accepted for publication in *Neurology*. She has also

been collaborating with the Center on Aging to write a grant proposal for an NIH R01 proposal on biomarkers and cognitive function. The aim of the research submitted is to study the relationship of biomarkers using a sensitive memory test battery.

Dr. Levin began working on the Scythian Biosciences Inc. study on *the effects of cannabinoids on traumatic brain injury* in 2017. The research goal is to evaluate the effects of cannabinoids on patients with mild to moderate traumatic brain injury, including the effect of cannabinoids on sleep duration, sleep continuity, insomnia symptoms – and daytime sleepiness.

Dr. Levin initiated the frailty project, a multi-tiered investigation of frailty and cognitive aging. This project involves numerous collaborations with McKnight members, and will address multiple components of the frailty syndrome including comorbid cognitive status, emotional well-being, life style risk factors, sleep dysregulation, cardiometabolic health, polypharmacy, imaging parameters and inflammatory biomarkers. Three abstracts have been accepted for the 2018 Frailty and Sarcopenia Conference in March of 2018.

This year a community outreach program, which involves McKnight post-doctoral Fellows working with undergraduate and graduate students, has been created to build a database of fully independent older adults not experiencing subjective cognitive complaints. This database is the control group for the frailty project as well as other McKnight endeavors.



Dr. Levin's Team

Dr. Rundek, Dr. Levin, Dr. Fernández McInerney and Stacy Merritt have worked to improve and strengthen the McKnight Registry database. *The UM McKnight Registry was developed with the goal of building a comprehensive longitudinal database for patients with age-related memory complaints and determine longitudinal cognitive changes and development of dementia.* This entailed vigorous research and continuous team discussions and meetings. The goal is to guarantee that (1) novel, relevant and important patient information is obtained; (2) the REDCap database is designed using appropriate variables; and (3) data entry and overall research integrity is maintained. Participants receive a neurologic evaluation, MRI and labs (and DNA collection), functional testing and Neuropsychological Testing, frailty assessment, functional activities and mood/emotional screening. These measures will result in scientifically rigorous data collection that will build the data resources for analysis, presentations at scientific meetings, manuscripts in peer-reviewed journals as well as translate into clinical care models.

Currently our registry consists of 399 subjects, 286 with MMSE 27 or greater ('normal') and about 50 MCI subjects. The mean age of the participants is 72 years, 57% are women, 46% Hispanic-Latinos, 20% living alone. Mean education is 14 years of school, 22% completed high school. Among vascular risk factors, 55% have hypertension, 50% dyslipidemia, and 20% diabetes. Majority of participants fulfill criteria for frailty (59%), and 14% are pre-frail. Our goal is to complete data entry for all of these subjects and prepare a grant application focused on emotional frailty and cognition in elderly.

Dr. Czaja's research mission can be exemplified in the picture below. It is a model used for the array of research projects and collaborations she's been working on in 2017.

Dr. Czaja - Augmenting Cognitive Training in Older Adults (ACT)

This randomized clinical trial is a collaboration with the McKnight Brain Institutes in Gainesville and Arizona. The research is designed to test whether transcranial direct current stimulation (tDCS) of frontal cortices enhances neurocognitive and functional outcomes achieved from cognitive training in older adults experiencing age-related cognitive declines. The study examines the influence of other clinical and demographic factors (e.g., gender) on neurocognitive, functional, and neuroimaging outcomes. Recruitment efforts have begun. Weekly calls are setup to discuss the progress of the study and subject participation of the study. Issues are discussed and efforts are made to resolve these issues.

Successful Aging



Dr. Czaja - DUAL TARGET

This project is an integration of an *augmented* evidenced-based caregiver intervention and evidenced-based cognitive/functional training for the care recipient. The program will be tailored for the caregiver and emphasize issues important to caregivers, not only in the earlier stages of caregiving, but will also target issues across the caregiving trajectory to help prepare the caregiver for changes in their role. The cognitive/functional training will be targeted to the needs of the care recipient. The program is highly innovative given the focus on a dyadic approach, the use of state-of-the-art technology for intervention delivery, a community-based and stage-model approach to intervention development, the inclusion of the caregiver as a therapy extender and cultural tailoring of the program. This project is active and will continue into 2018.

Dr. Czaja - PARC

The study involves a unique industry-university collaboration between the Palo Alto Research Center (PARC) and UM, which brings together a multidisciplinary team of behavioral, neural, cognitive and computer scientists, engineers and clinicians. The Fittle Senior System (FSS) builds on two technology-based systems developed by the investigative team: (1) the computer-based PRISM system, designed for older populations to support social connectivity and well-being, and (2) the Fittle+ mobile platform (PARC) designed to support positive health behavior change through integrated online social support and personalized coaching based on artificial intelligence (AI). Meetings with UM and PARC reps are established to discuss project objectives and goals. Computer tablets are sent out for testing the systems to be used in the project. Study start-up work has been done so far and recruitment will begin in 2018.

Dr. Czaja - CREATE IV

This is an NIA/NIH funded research center involving Georgia Institute of Technology, Florida State University, and the University of Miami. The focus of the center is on ensuring that older adults are able to use and realize the benefits of technology. A collaborative project, involving all 3 universities, is evaluating the impact of an innovative easy to use computer-based Personalized Reminder Information and Social Management System (PRISM 2.0) software application,

especially designed for older adults, on the degree of social isolation and support, well-being, quality of life and functional ability among a diverse sample of older adults who live alone and are at risk for social isolation. The study will be examining the impact of PRISM 2.0 on social connectivity, engagement, social support and loneliness. Research associates are assigned for recruitment and participant assessments for the PRISM 2 project. Findings thus far are that the participants have all been successfully trained to use the PRISM. Reported benefits of using PRISM are better communication with family members, they are able to reconnect with the past and renew friendships. They are happy to have opportunities to learn new things and are also simply enjoying PRISM for fun, games and entertainment.

Dr. Czaja - NINR – A Tailored Technology Intervention for Diverse Family Caregivers of AD Patients

This innovative project has an intervention that is (1) tailored to the individual needs of the caregiver using a risk appraisal approach – distinguishing from the “one size fits all” intervention approach; (2) culturally tailored to diverse population of caregivers varying in terms of ethnicity, cultural and other socio-demographic characteristics (e.g., education, SES); (3) employing state-of-the-art computer technology to facilitate the delivery of the intervention program; and (4) based on a multi-disciplinary approach including social/behavioral scientists, clinicians and engineers. Research associates are assigned in the field for recruitment and participant assessments. The study enrolled 244 participants. It is no longer recruiting. Some of the outcomes are that caregivers adapt easily to the technology and like using tablets. They were benefitting from the video support group sessions.

In 2017, **Dr. Alperin** implemented and successfully optimized the MRI protocol for the MBAR project on the UM clinical scanner and successfully scanned 2 subjects age 85+. Other scheduled scans later in the year were cancelled due to scanner unavailability. MBAR is an important project aligned with our McKnight Brain Institute’s mission to work in collaborations with other McKnight Brain Institutes.

Dr. Alperin together with **Dr. Rundek** submitted an R01 application on imaging of small vessel perfusion to the NIH in Sept of 2017. In addition, Dr. Alperin submitted another grant on the role of sleep on dementia to the state of Florida in 2017. Dr. Alperin has also worked on preliminary data for these grants submissions. Specifically for the small vessel disease proposal, the preliminary data was very important as cerebral small vessels cannot be imaged with current conventional imaging modalities and thus our ability to detect their morphological and functional changes is very limited. The NIH has identified a need for “noninvasive imaging techniques to study human brain vasculature in different CNS gray and white matter regions” and the proposed project was submitted in the response to the NIH FOA. The main objective is to develop a novel imaging technique to reliably and non-invasively measure the small vessel function to regulate regional perfusion. Currently, the cerebral vascular reactivity test is one of the few techniques that provide information about changes in blood flow in response to manipulations of the breathing levels of CO₂. This technique is mostly used to detect a steno-occlusive disease. However, its limitations such as a lack of reproducibility and standardized protocols restrict the use of this technique. We proposed to develop and validate a novel method that provides measures of the small vessel regulation of regional perfusion. We term this method *regional perfusion regulation*. The proposed method combines 2 independent MRI techniques, one that measures total volume of the blood entering the brain, and the other that measures regional

perfusion rates. In contrast to reactivity test, measurements from our proposed method are obtained under tight controlled levels of PaCO₂, assuring more reproducible results. *Our aim* is to establish normative values of regional perfusion regulation indices (ratio of regional perfusion change per change in global blood flow, over a wide range of regional blood flow levels) in healthy participants across different age groups, and in patients with diabetes with a various degree of small vessel disease and cognitive decline. The regional degree of perfusion regulation may also elucidate the role of small vessels in age-related brain volume loss. This novel MRI-based perfusion regulation method may provide a perfusion imaging biomarker of cerebral small vessel function and compensatory capacity in pre-clinical stage of small vessel disease, and for monitoring of the progression (or effects of therapies) of small vessel disease in a wide range of small vessel related metabolic and neurodegenerative disorders.

Dr. Alperin has also worked on the project assessing cardiovascular and lifestyle stressors of hippocampus and AD related brain regions. The pathology associated with AD starts years before manifestation of signs of cognitive decline. AD is a multi-factorial disease with multiple stressors contributing to its progression. This research focuses on two stressors that can be modified and treated if detected early thereby reducing the risk for progression to AD. These are sleep quality and cerebral hemodynamics (i.e., cerebral blood volume pulsatility). In collaboration with Dr. David Loewenstein, Dr. Alperin has been working on an R01 project that leverages the existing cohorts of normal and pre MCI and MCI subjects and has been performing the brain hemodynamics measurements using advanced brain parcelation techniques.

Dr. Gomes-Osman a new Member of the McKnight Brain Institute, has been primarily involved in research of her McKnight Small Pilot Collaborative Research Award. She has also started another related study that will recruit sixty participants with normal cognition and sixty participants with MCI. Clinical assessment and sensitive memory stress tests will be performed on all participants. The levels of pre-synaptic and post-proteins in cerebrospinal fluid (CSF) will be determined. Transcranial magnetic stimulation (TMS) will be used to assess cortical synaptic plasticity. Cortical thickness, hippocampus volume and resting state functional brain activity will be measured. Finally, association of synaptic function with memory performance in relation to A β 42, tau protein brain volumetric measurement will be analyzed. A two-year follow-up with neuropsychological testing and TMS will be performed. This cross-sectional and longitudinal study of *in vivo* synaptic function associated with memory performance in patients with MCI will greatly improve our understanding of mechanisms underlying cognitive impairment. Understanding of synaptic function in relation to other AD biomarkers such as A β 42 and tau protein will potentially provide insight into development of novel therapeutic measures in AD. In addition, she has completed a large-scale quantitative systematic review on Exercise Guidelines for Brain Health, which manuscript is currently undergoing peer review.

Dr. Gomes-Osman has written a review 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 (this manuscript is also under peer review).

Dr. Gomes-Osman has completed and published the feasibility trial (*Restor Neurol Neurosci.*), in which she evaluated the effects of short-term regular exercise on cognitive performance. She has showed that acute exercise interventions in sedentary adults can be meaningfully conducted

along with cognitive and neurophysiologic measures to assess behavioral and neurobiological effects. TMS measures of plasticity were shown to be useful in the evaluation of the effects of exercise on brain plasticity, and related to neuropsychological measures of cognition in this feasibility pilot trial.

Dr. Gomes-Osman continues to work on different projects related to brain plasticity, cognitive health and walking function. In addition to her published work, she submitted several manuscripts for publication this year. She has completed the large-scale quantitative systematic review on Exercise Guidelines for Brain Health, which is currently undergoing peer review. In addition, she has written a review 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 (this manuscript is under peer review). Furthermore, she has developed a cognitively challenging walking protocol and demonstrated its feasibility and preliminary efficacy in improving mobility and functional walking in individuals with Parkinson’s disease (paper in submission). This protocol will be adapted for individuals with age-related memory decline and individuals post-stroke, who often present with functional walking deficits.



Dr. Gomes-Osman’s Research Team

Following Dr. Gomes-Osman’s publication on the feasibility of assessing changes in brain plasticity and cognitive performance after exercise in healthy sedentary adults, she has begun planning studies to translate these results to older adults undergoing cognitive aging. Her Institute pilot grant will compare two different exercise intensities (moderate vs. high) on brain plasticity and cognitive performance in older adults. In this project, she is collaborating with Drs. Rundek, Levin and McInerney. The project timeline is included in this Table.

Timeline for Pilot Grant awarded to Dr. Gomes-Osman by the UM McKnight Brain Institute		
Stage	Procedure	Timeline
I	Study Design	Jan 2017 (completed)
II	Institutional Review Board Approval	March 2017 (completed)
III	Grant funds approved	July 2017
IV	Training of research personnel	Aug - Oct 2017 (completed)
V	Recruitment (ongoing)	Dec 2017 - July 2018
VI	Data Analysis	Aug - Oct 2018
VII	Manuscript Preparation	Nov - Dec 2018

Furthermore, in the fall of 2017, Dr. Gomes-Osman has conducted a smaller scale study (that has completed recruitment and is now in the data analysis stage) assessing the reliability of brain plasticity measurements with transcranial magnetic stimulation.

In addition to the studies above, **Dr. Gomes-Osman** has been collaborating with **Dr. Rundek** and the remainder of the UM Bugher team on a project where she is studying brain plasticity changes in individuals post-stroke who are undergoing combined exercise and cognitive training, exercise in isolation or stretching exercises. She has also continued making progress on a project that is aimed at acquiring brain plasticity data on individuals who participate in the McKnight Registry.

Furthermore, **Dr. Gomes-Osman** is supervising a project to assess the influence of repetitive transcranial magnetic stimulation (rTMS) for individuals with primary progressive apraxia of speech with a Movement Disorders Fellow **Danielle Spengler**.

Dr. Gomes-Osman has been actively involved on an NIH-funded project by **Dr. Czaja** that consists of proposing app-based intervention study for older individuals, and **Dr. Gomes-Osman** has been involved in creating the content. Finally, **Dr. Gomes-Osman** is collaborating with the Alagoas State University for Health Sciences, in Brazil, and is conducting a study to evaluate the influence of an exercise literacy workshop to improve engagement in physical activity and cognitive performance in older adults.

Dr. Jiang and **Dr. Wang** and their team have been studying the retina and its role in vascular dysfunction in the pathophysiology of cognitive functional decline. Thus far, it has been revealed that there are decreased retinal microvascular blood flow velocities and microvascular network in elderly individuals and patients with MCI and AD. The retinal ganglion cell layer thickness remains within normal ranges which indicates that the vascular dysfunction may precede and contribute to the neuronal loss. Two papers on these important findings were published and two others are under revision. While working with AD and MCI patients, they have set up the normality lines of age related retinal microvascular changes by studying the population age ranged from 18 to 85 years old. They found there is age related decline of retinal microvascular network densities and blood flow velocities. The proposal to extend these retinal findings on brain hemodynamics has been submitted to the NIH in Sept of 2017 (Dr. Rundek is co-I).

Michelle Caunca, the University of Miami and McKnight Brain Institute MD/PhD student has successfully competed for the NIH F30 award under the primary mentorship of Dr. Rundek. This year Michelle has received the *Ruth L. Kirschstein National Research Service Award (NRSA) Fellowship for Students at Institutions with NIH-Funded Institutional Predoctoral Dual-Degree Training Programs (F30)*. This is a remarkable accolade as these awards are very competitive. Her project, *Effects of White and Gray Matter Integrity on Cognition in a Multi-Ethnic Cohort* is related to brain MRI regional markers of cognitive decline.

Dr. Ramos worked on tabulating and reporting the results for the *Hispanic Community Health Study/Study of Latinos (HCHS-SOL) Sleep as a risk factor of disease (Sueño) in the Hispanic Community study*. Over 2,200 participants were enrolled and his 5 manuscripts were accepted for publication in 2017. Dr. Ramos received NIH R21 funding for analysis of sleep in HCHS-SOL.

In 2017, **Dr. Ramos** and **Dr. Alperin** resubmitted the study *Sleep and MRI markers of Brain Health* to the Scientific Advisory Committee internal pilot grants program at the University of Miami. They will find out if it was accepted in 2018.

Dr. Crocco - Novel Detection of Cognitive and Functional Impairment in the Elderly

As Co-investigator on this study, she examines the utility of a unique set of neuropsychological and daily-functioning tests in individuals ranging from cognitively normal (NC) to those with preclinical mild cognitive impairment (preMCI) and those with amnesic mild cognitive impairment (aMCI). The study looks at a combination with select diagnostic biomarkers and tests such as atrophy on structural MRI, amyloid, tau and phosphorylated tau biomarkers in CSF in predicting the rate of cognitive decline. The planned enrollment is 285 subjects and the study has now enrolled its 445th subject. It is still actively recruiting. Cross-sectional data has yielded promising results, which has been published across many peer reviewed journals in the field. Longitudinal data is now being analyzed.

Dr. Crocco - A Consortium to Study Precision-based Computerized Assessment for the Detection of Mild Cognitive Impairment in Older Adults

This study is a result of a Florida Department of Health, Ed and Ethel Moore AD Research Program grant. This study measures for early detection of cognitive impairment of Hispanic and non-Hispanic elderly persons by administering three novel computerized tests to 120 older adults (40 normal elderly, 40 amnesic mild cognitive impairment: [aMCI] and 40 Preclinical AD participants). This project is expected to provide critical data that parallels a recently submitted R01 application to the National Institutes of Health (NIH), which will examine changes in cognitive performance using these instruments as they relate to longitudinal biological changes within the brain. Investigators are actively recruiting and no results have been generated yet.

Dr. Crocco - A randomized double-blind, placebo controlled, parallel group study to evaluate the efficacy and safety of CNP520 in participants at risk for the onset of clinical symptoms of Alzheimer's Disease

This clinical trial is completed and the data obtained from the study procedures and assessments is being analyzed.

Dr. Crocco - Randomized, Double-Blind, Parallel-Group, Placebo-Controlled, Dose-Ranging study of Piromelatine in patients with mild dementia due to Alzheimer's disease

This clinical trial is 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. It has 3 participants enrolled and will continue to actively enroll into 2018.

Dr. Crocco - A Phase 3, Multicenter, Long-term, Extension Study of the Safety and Efficacy 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

The year 2017 was spent on the necessary study start-up preparations. Upon obtaining IRB approval, it will begin recruitment and enrollment in 2018.

Dr. Crocco - 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.

This clinical trial is currently active and has successfully enrolled 5 research participants. Enrollment will continue into 2018.

Dr. Zeki Al Hazzouri actively investigates the Lifecourse of cardiovascular risk, depression and cognition in black and white adults (NIH-funded). The goal of this grant is to address the life course nature of the associations of cardiovascular risk factors with cognitive function and depressive symptoms, and the role of structural brain changes. This project will use data from the CARDIA (Coronary Artery Risk Development in Young Adults) study and the Health ABC (Health, Aging and Body Composition) study.

Basic Science



McKnight Basic Science Lab Team

Dr. Dave and **Dr. Perez-Pinzon** along with their team of exemplary trainees are performing team science research from *the bench to the bed* by studying post-stroke efficacious treatment to decrease mortality rates and improving survival and functional recovery. This is extremely relevant work pertaining to normal aging through the life-span and to stroke, which is the fifth leading cause of death in the US. The majority of stroke patients suffer long-term disability impacting both motor and cognitive function.

Physical exercise has been shown to improve functional recovery following focal cerebral ischemia by facilitating brain plasticity. However, the exercise intensity that promotes optimal cognitive recovery needs to be examined. In a prior study, they showed that focal cerebral ischemia impaired cognitive function and moderate intensity physical exercise provided a beneficial impact on cognitive recovery in *young* male rats. In a follow up study conducted in

2017, they observed that exercise was also able to improve post-stroke cognitive function in *middle-aged male rats*. Additionally, they observed that moderate exercise intensity that showed beneficial effects on post-stroke cognitive function in middle-aged male rats, was not effective in reproductively senescent female rats. This is a new and potentially relevant study for clinical follow up, as it indicates sex disparity in the effect of physical exercise post stroke.

Cardiac arrest affects over half a million people in the US annually. Currently, no treatment exists to eradicate cognitive impairments afflicting survivors. Physical exercise can reduce cognitive deficits after cerebral ischemia by augmenting brain plasticity. **Holly Stradecki** an MD/PhD student in **Dr. Perez-Pinzon's** laboratory examined how forced treadmill exercise improves performance of Sprague Dawley rats on spatial memory tests (Barnes Maze & contextual fear conditioning) and reduces hippocampal long-term potentiation deficits. This research has been recently published in *Stroke* in 2017.

The goal of another animal research project conducted in the lab of **Drs. Dave and Perez-Pinzon** was to characterize a model of white matter injury (WMI) in young (3 months) and aged rats (12–18 months), using microinjections of the nitric oxide synthase inhibitor N5-(1-iminoethyl)-L-ornithine, dihydrochloride (L-NIO). L-NIO microinjections in to the corpus callosum (CC) were completed using the neurostar automated stereotaxic system. Twenty-four hour survival, immunofluorescence characterization of glial fibrillary acid protein (GFAP), apoptosis inducing factor (AIF), rotarod injury preinjury, and four days post injury were assessed. A 24-hour survival rate following L-NIO injection was 100% in young rats and 80% in aged rats ($n = 13/13$, $n = 8/10$). AIF intensity increased 2.92 ± 0.18 fold in young animals and 1.78 ± 0.11 fold in aged animals ($n = 3$, $p < 0.05$, ANOVA). GFAP intensity was increased $1.31 + 0.06$ fold in young animals ($n = 3$ $p < 0.05$, ANOVA) but was not significantly different in aged animals, likely due to increased baseline fluorescence. Rotarod performance decreased to 63.8 ± 5.92 % ($n = 7$, $p < 0.05$, t-test) in young animals, however the decrease in aged animals was not significant, again most likely due to low baseline performance. L-NIO CC injections resulted in a consistent injury in young and aged animals that presented with differences in injury characterization and behavioral outcomes.

Dr. Della-Morte, a new Member of the McKnight Brain Institute conducted several lines of research in the field of aging. His studies have focused on exploring the role of antioxidant proteins that may delay the progress of the aging brain when activated. His most important discoveries are with the regard of Sirtuin and Peroxiredoxin proteins in a model of *Caenorhabditis elegans*. His research team found that knock-out of mitochondrial sirtuin sir-2.3, homologous to mammalian SIRT4, was protective in both chemical ischemia model and hyperactive channel induced necrosis. This work has suggested a deleterious role of SIRT4 during cerebral ischemic processes in mammals and revealed a novel pathway that can be targeted for therapies aimed at protecting neurons from death in ischemic and neurodegenerative conditions.

In another study, Dr. Della-Morte has demonstrated that knockout mice and knockdown cells for peroxiredoxin 6 (PRDX6) are more prone to develop aging phenotypes, like short telomeres, increase in oxidative stress and mitochondrial dysfunction. For the first time, he has demonstrated that PRDX6 may be a therapeutic target for age-related diseases, including memory loss.

Dr. Barrientos - Characterization of the role of NAD⁺ salvage pathway proteins in cellular aging

and PROTECTION against proteotoxicity

With the objective of determining whether NMA1 and other NAD⁺ salvage pathway proteins protect against polyQ-induced toxicity in chronologically aged yeast, Dr. Barrientos had to engineer yeast strains to allow for constitutive expression of NAD⁺ salvage pathway proteins in yeast expressing non-toxic 25Q and toxic 103Q polyglutamine domains. He has now created a full set of the strains needed. Those include strains expressing wild-type versions of NMA1, NPT1, QNS1 and PNC1. His lab is starting the chronological life span assays. His next step will be to determine the neuroprotective activity of NMA1/NMNAT and other NAD⁺ salvage pathway proteins against protein misfolding-induced proteotoxicity in neuronal cells derived from HD-patient fibroblasts with the human cell lines obtained.

Dr. Barrientos - Defining the enzyme-independent MECHANISM of protection against proteotoxicity by NAD⁺ salvage pathway proteins

In 2017, **Dr. Barrientos** aimed to determine the chaperone activity of Nma1/NMNAT and other NAD⁺ salvage pathway proteins. His lab purified recombinant proteins, either WT or carrying catalytically inactive mutations. At least four repetitions of *the in-vitro* chaperone assay with each protein had already been done. They concluded that NMA1, NPT1, QNS1 and PNC1 have chaperone activity that is independent of their catalytic activity. This data has shown that the yeast NAD⁺ salvage pathway proteins and their catalytically inactive forms equally protect against the growth deficit of 103Q-expressing cells, and display basically identical 103Q oligomer degradation timelines and patterns.

Dr. Barrientos - Establishing whether the efficacy of protection against proteotoxicity by NAD⁺ salvage pathway proteins is affected by MODULATION of mitochondrial functions

In order to examine the crosstalk between the protection against proteotoxicity exerted by overexpression of NAD⁺ salvage pathway proteins and by enhancement of mitochondrial biogenesis in yeast and HD-iPSCs, he started generating the necessary constructs. They involve constructs to overexpress transcription factors that regulate mitochondrial biogenesis. They have obtained (and previously used) yeast vectors to overexpress HAP4, the master regulator of mitochondrial biogenesis in yeast. His lab has now created constructs to overexpress PGC1-alpha, the master regulator of mitochondrial biogenesis in human cells.

Dr. Pinto is expanding her knowledge and research in the study of the role of mitochondria in neurodegenerative diseases. Neuronal OXPHOS deficiency has been associated with a variety of late-onset progressive neurodegenerative diseases, including Parkinson's disease and Alzheimer's disease. Most animal models of PD are created by knocking out or knocking in mutated forms of the genes involved in the rare genetic forms of PD. In order to create a model resembling the more common sporadic forms of PD, she induces mitochondrial defects in different neuronal subpopulations, mimicking the mitochondrial functional decline that occurs naturally with aging. She induced OXPHOS deficiency in neurons by inducing mitochondrial DNA depletion, or by knocking out mitochondrial Complex IV, one of the complexes that is deficient in PD patients. By inducing mtDNA depletion in neurons she discovered that the striatum is particularly sensitive to defects in OXPHOS and these results helped explain how mitochondrial dysfunctions alone can lead to a preferential elimination of certain neuronal populations *in vivo*. In the past, she created and compared two different mouse models of PD, one mimicking the

pathology slow progression that occurs in sporadic PD cases, the other more similar to late stages of the disease.

In 2017, she completed a project started three years ago and created a mouse model that combines what are considered genetic and environmental causes (the related paper has been accepted for publication in *Journal of Neuroscience*). Because mitochondrial dysfunctions have been closely associated with PD, the creation of these new mouse models provides important clues to the pathophysiology of the disease. The PD mouse models have been widely received and accepted in the scientific field and can provide a valuable tool to test new mitochondrial therapies in the treatment of this disease.

This year **Dr. Pinto** also started a collaboration with Dr. Baumel on the use of mesenchymal stem cells 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. This project is ongoing.

10. Technology Transfer

Dr. Czaja is working on a technology transfer for the **SBIR/i-Function**.

12. Educational Programs Focusing on Age-Related Memory Loss

Dr. Sun (Educational Director) directed the McKnight Brain Institute Educational Program, which has been constructed to fulfill the mission of promoting cognitive neuroscience. This educational content was geared toward medical students, neurology residents, students and trainees, faculty and staff. She was involved in bringing education and awareness on brain well-being to the community. To fulfill the education mission of the educational core of the McKnight Brain Institute she organized an annual McKnight Ground Rounds presentation as well as monthly Research Seminars and Journal Clubs. **Dr. Steven T. DeKosky** was our invited presenter for the McKnight Brain Institute Ground Rounds in March 31, 2017. His presentation on *Aging, Brain Trauma and Neurodegenerative Disease* was a great success resulting in critical dialogue about the aging brain. The monthly Research Seminar presenters were researchers who are McKnight Members and Collaborators and represent cross-disciplinary topics. The Research Seminar promoted an array of academic activities and fostered collaboration among laboratories. The monthly Journal Clubs provided updates on the progress of cognitive neuroscience.

A. Scientific Education

Dr. Sun led the medical student education curriculum. She designed two annual neuroscience lecture series specifically for MD and MD/MPH student courses. She provides education on cognitive neuroscience for the neurology Residents. She also coordinated the 2-week mandatory clinical rotation curriculum for neurology Residents. The third and fourth year neurology Residents spent two weeks with the Faculty of the Cognitive Division. This curriculum provided real-life training on the diagnosis and management of memory related disorders by using clinical assessment, neuropsychological testing and neuro-imaging methods. These Residents had the opportunity to observe neuropsychological testing and discuss neuropsychological batteries with neuropsychologists. Our Faculty members who teach cognitive neurology, geriatric psychiatry, neuroradiology and neuropsychology gave lectures to the neurology Residents about diagnosis and management of cognitive and memory related disorders.

Dr. Sun together with Dr. Rundek created a structured training curriculum for **Dr. Camargo**, the McKnight Cognitive Fellow. He spends 50% of his time clinically and 50% on research. For clinical training, he works with Dr. Baumel and **Dr. Sun** at the UM Memory Disorder Clinic. His main research project under the guidance of Dr. Baumel was to work on obtaining an IND to propose stem cell treatment in neurodegenerative disorders. His other research projects under mentorship of Drs. Sun and Rundek are highlighted in the Introduction section of this report.

Dr. Sun leads the McKnight Education and Training Core which consists of weekly Research Lab Meetings, monthly Research Seminars, monthly Journal Clubs and quarterly McKnight Brain Institute/Center on Aging Scientific Lecture Series. These activities in past year are listed in the tables on pages 64-66.

Dr. Rundek is Director of a Master Degree in Clinical Translational Investigations at the UM Millers School of Medicine. She also teaches 2 classes: on team science in the fall and 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. 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. Rundek is a Training Director of our AHA Stroke Bugher Center of Excellence and Training Director of the NIH-StrokeNet and NeuroNext. Each of these programs have 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.

Dr. Czaja oversees the Certificate in Gerontology Program at the University of Miami's Center on Aging. The Certificate Program provides education and training on the science of aging with the aim to increase the number of qualified providers to work with and study the growing aging population.

Dr. Czaja coordinates and hosts the University of Miami Center on Aging/ Evelyn F. McKnight Brain Institute Scientific Lecture Series, held at the Center on Aging. The educational presentations are used as a forum to learn about on-going research related to aging/memory loss both within and outside of the University for exchange of ideas, and to hopefully foster new collaborations.

Dr. Czaja serves as Director for the Evaluation Component of CTSI from NCATS, entitled *Miami Clinical and Translational Science Institute*. To propel scientific discovery and its translation into evidence-based practice and community health, the Miami CTSI advances culturalized health sciences that embrace our majority racial/ethnic community. Fundamental to accomplishing our mission is the orchestration of new and existing research, services and resources that foster excellence in translational research, promote Interdisciplinary interaction, elevate research ethics, build research partnerships in the community and to establish strong multidisciplinary graduate research programs.

Dr. Czaja has planned the upcoming Aging and Work Scientific Conference on January 18-19, 2018.

Dr. Levin has an extensive training program with 6 post-doctoral Fellows, 3 graduate PhD students and 2 undergraduates. All trainees are closely supervised in the assessment of cognition and emotion. In addition, the trainees spend a minimum of one day a week testing referrals from the Memory Disorders Clinic and receive ongoing supervision as part of the Schoninger Training Program.

Dr. Levin teaches a 3 credit upper level graduate class (Psychology 615) for advanced PhD students examining foundations of clinical neuroscience and neuropsychology. This 12 week course focuses on age related memory loss and other changes across the lifespan and neural circuitry underlying cognition and behavior.

Dr. Levin also leads a bi-weekly neuropsychology rounds for practicum students, interns and post-doctoral Fellows that include clinical case conferences, assessment, scoring and interpretation of data and group supervision. Case discussions include all patients seen in the Memory Disorders Clinic where students are trained in the evaluation and assessment of age related and non-age related memory loss. She also holds weekly teaching and case supervision meetings with McKnight post-doctoral Fellows.



Dr. Levin Mentoring a Trainee

Dr. Gomes-Osman taught a 3-credit graduate level class Neuroscience II 641, to physical therapy students. In this class, students learned about clinical neurophysiology and functional performance in the healthy nervous system and in neurologic conditions. She also mentored two PhD Students from the Department of Physical Therapy at the University of Miami, **Jordyn Rice** and **Shatha Aldraiwiesh**. They have 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 (Nicholas Cassidy and Michelle Zambik), and four undergraduate students (Sabrina Pastore, Cril Larhssen and Carolina

Flores), who are supporting these efforts and learning about the exciting studies being carried out in **Dr. Gomes-Osman's** lab. Fortunately, two new PhD students will be joining her lab in 2018 (Sulaiman Alanazi, PT and Danylo Cabral, PT).

Dr. Crocco leads Doctoring II: Dementia Small Groups Miller/UM SOM for small groups of 20-25 medical students in diagnosis and evaluation of cognitive disorders and aging. She also leads Doctoring II: Neuroscience and Behavioral Science, mood and anxiety disorders and addiction for small groups Miller/UM for small groups of 20-25 medical students in evaluation and management of common psychiatric disorders in aging and the Geriatric Psychiatry Lecture Series Miller/UM SOM 3rd year psychiatry clerkship.

Dr. Crocco also develops and implements comprehensive geriatric psychiatry lectures in psychiatric clerkship to all 3rd year medical students. This includes topics including: aging and normal aging, late-life depression and anxiety, ECT, bereavement, neurodegenerative disorders, Alzheimer's, vascular and Lewy body disease.

Dr. Crocco is also involved with the Jackson Memorial Hospital (JMH) General Psychiatry Residency Training Program: (1) Psychiatry Lecture Series. She develops and implements 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 and caregiving issues; (2) Geriatric Psychiatry Seminar – She also develops and implements on a weekly basis the core curriculum-focused conference that covers knowledge and skill areas that are necessary for the successful completion of the geriatric psychiatry training program and commonly seen diagnoses in geriatric psychiatry.

As part of the JMH Geriatric Psychiatry Training Program, **Dr. Crocco** has a weekly case conference. She coordinates and supervises all geriatric psychiatry Fellows' weekly presentations of patient case history, including biological, psychological and sociological data and formulates an integrated treatment plan with special emphasis on aging. She holds a weekly journal club overseeing the coordination and supervision of all geriatric psychiatry Fellows with the objective of critical evaluation of peer-reviewed, original research articles and applies this knowledge to the care of their geriatric patients and aging issues.

Dr. Dave and **Dr. Perez-Pinzon** mentor and train 2 Postdoctoral Fellows, 3 MD/PhD students and 2 PhD students in their labs.

Dr. Raval has been teaching the following undergraduate courses: (1) *Cellular and molecular neuroscience*; (2) *Neural Mechanisms of Disease*; and (3) *Faculty overview of research and undergraduate mentoring*. She is also the facilitator for the MD-MPH Problem based learning for first and second year medical students.

B. Public Education

Under Dr. Sun, our community education program involved reaching out to senior community and retirement centers in the greater Miami area. Our McKnight Cognitive Neurology Fellow, **Dr.**

Camargo, and McKnight Director of Research and Administration, **Stacy Merritt**, provided community education lectures about normal aging and memory disorders. Under **Dr. Sun's** and **Dr. Rundek's** direction, we made valuable contacts and relationships in the community which we will build upon. By collaborating with the activity venues frequented by the aging population, many in the community have learned about maintaining healthy cognition, improving brain well-being and preventative risk factors, which may lead to memory and cognitive decline through the aging process.

Dr. Crocco through the Miami Area Geriatric Education Center (MAGEC) contributes to the planning, development and implementation of educational programs to diverse health care professionals who provide services to older adults in a variety of settings in the South Florida area. Select lectures provided include intensive psychiatric courses in agitation in dementia, geriatric depression and other aging issues.

Dr. Crocco as part of the Florida Department of Elder Affairs Alzheimer's Disease Initiative (ADI), provides caregiver training seminars on Dementia in Miami-Dade County. She also leads the ADI Caregiving Training Program on Dementia to ADI Respite Care and Day-Care Centers in Monroe County. She developed a 4-hour state-mandated training for caregivers, ADI Respite, Day-Care professionals and para-professionals for CEU accreditation on an annual basis in both English and Spanish. She also developed and coordinates 4 hours of state-mandated dementia training to caregivers in Respite and Day Care Centers in Monroe County.

2017 Evelyn F. McKnight Brain Institute Research Seminar Series

Speaker	Area of Expertise	Date	Title
Alon Seifan, MD, MS	Dementia	1-11-17	<i>Developmental Neurodiversity and Clinical Phenotypes of Dementia- A Life Course Approach</i>
Grace Zhai, PhD	Neuroscience	2-8-17	<i>Neuroprotection Against Proteinopathies: Insights From Drosophila Models</i>
Noam Alperin, PhD	Radiology	3-15-17	<i>MRI Centered Research Topics in Aging-Related Cognitive Decline</i>
Stephen Rao, PhD	Neuropsychology	6-28-17	<i>Innovations in the Cognitive Neuroscience of Aging</i>
David Della-Morte, MD, PhD	Neurology	7-26-17	<i>Novel Molecular Pathways Involved in Senescence and Neurodegeneration</i>

Milena Pinto, PhD	Neuroscience	8-30-17	<i>Mitochondrial dysfunctions in Parkinson's disease: a lesson from mouse models</i>
Sara Czaja, PhD	Aging and Neurology	10-4-17	<i>Update on the Center on Aging's Research Activities</i>
Joyce Gomes-Osman, PT, PhD	Physical Therapy and Neurology	11-8-17	<i>The effects of a 12-week exercise and cognitive intervention on gait, posture and Transcranial Magnetic Stimulation plasticity measures individuals post stroke- an ongoing study.</i>
Jordyn Rice, PT, DPT	Physical Therapy and Neurology	11-8-17	<i>Transcranial direct current stimulation augmented individualized gait training targeted at freezing of gait in Parkinson's Disease: a case description</i>
Ashish K. Rehni, PhD	Neuroscience	11-8-17	<i>Potential role of endoplasmic reticulum stress in recurrent hypoglycemia-induced increase in ischemic brain damage</i>
Joyce Gomes-Osman, PT, PhD	Physical Therapy and Neurology	11-29-17	<i>An update on the work of the Neuromotor Plasticity Laboratory: in the pursuit of Exercise targeting Brain Health</i>
Kunjan Dave, PhD	Neuroscience	12-13-17	<i>Hematoma growth in ICH patients: a potential therapeutic target</i>

2017 Evelyn F. McKnight Brain Institute **Journal Club Presentations**

Speaker	Area of Expertise	Date	Title
Michelle Caunca	Neurology	1-18-17	<i>Age Effects on Gray Matter Volume and Attentional Performance in Zen Meditation</i>
Sarah Getz, PhD	Neuropsychology	2-15-17	<i>Decision Making in the Elderly</i>

Rene Hernandez-Cardenache	Neuroscience	5-17-17	<i>Brief Literature Review, Cognitive Effects of OSA and Brain Health</i>
Andrea Ruetenik	Neuroscience	6-21-17	<i>Huntingtin Inclusions Trigger Cellular Quiescence, Deactivate Apoptosis, and Lead to Delayed Necrosis</i>
Conner Haasse	Neuroscience	7-19-17	<i>Translational models for Vascular Cognitive Impairment: a Review Including Larger Species</i>
Conner Haasse	Neuroscience	7-19-17	<i>Considerations for the Optimization of Induced White Matter Injury Preclinical Models</i>
Michelle Caunca	Neurology	8-9-17	<i>Evaluations of Amyloid Protective Factors and Alzheimer Disease Neurodegeneration Protective Factors in Elderly Individuals</i>
Christian Camargo, MD	Neurology	10-18-17	<i>Optogenetic Stimulation of a Hippocampal Engram Activates Fear Memory Recall</i>

2017 Evelyn F. McKnight Brain Institute/Center on Aging **Scientific Lecture Series**

Speaker	Area of Expertise	Date	Title
David Mohr, PhD	Behavioral Intervention Technologies	2-6-17	<i>Technology-Enabled Intervention for Common Mental Health Problems</i>
Sheila Cotton, PhD	Technology and the Aging Population	3-13-17	<i>Technology Use and Older Adults: Benefits, Barriers, and the Future</i>
Colin A. Depp, PhD	Health Technology and Psychology	5-1-17	<i>Mobile Technology for Serious Mental Illness and Healthy Aging</i>
Hans-Werner Wahl, PhD	Aging and Psychology	11-6-17	<i>Gero-Technology Research and Gerontology: Potential and Limits of a Growing Alliance</i>

13. Collaborative Programs with other McKnight Institutes, Institutions and Research Programs

The MBRF Inter-institute initiatives continue to be on track with considerable progress made on all fronts. The MBAR study of successful cognitive aging in people over the age of 85 is also now fully active at the four MBI sites, with approximately 35 participants assessed so far. We are planning on submitting a R01 grant proposal to the NIA in the spring with Site leaders as MPIs.

In Miami, under the direction of **Dr. Rundek** and **Stacy Merritt**, enrollment began for the **McKnight Brain Aging Registry (MBAR)** in 2017. A recruitment campaign consisting of meeting with community center directors, senior recreational groups, libraries, senior exercise venues, lifetime learning programs and the independent sectors of assisted living facilities was instituted. They attended senior fairs to discuss the study while providing education on the healthy aging brain, gave presentations to older adult audiences about normal vs. pathological brain changes and the importance of research participation. Stacy Merritt wrote an article that was published in a senior community newspaper. Our MBAR study information is printed in many community newsletters. Thus far, these efforts resulted in a total of 59 people contacting us with interest in the research. There are still many outlets to pursue for further recruitment in 2018.

The MBRF Cognitive Aging and Memory Intervention Core has also been very active with core faculty from the four McKnight Brain Institutes exerting considerable effort towards developing this Core. A plan for the pilot project program was created and approval to move forward obtained from the MBRF Trustees. Initially we obtained letters of intent to submit proposals from 12 investigators. These pre-proposals were reviewed by the Core faculty of the Intervention Core (Rundek-UM, Cohen-UF, Alexander-UA, Grissom-Bradley-UAB, and Woods-UF). Full applications were then requested for seven of the proposals. We have received 3 full applications for review. We reached agreement across the four sites on external reviewers. Pilot proposals are in the process of undergoing external review. Based on these reviews, the Core's faculty will be making recommendations to the MBRF Trustees in January 2018 regarding collaborative projects considered to be of high merit and worthy of consideration for funding. We have been providing regular updates on the Cognitive Aging and Memory Intervention Core activities, the MBRF Leadership Council.

Dr. Czaja is conducting the ACT study in collaboration with the University of Florida and Arizona Institutes. The study needed substantial time to prepare and harmonize the appropriate imaging and behavioral testing protocols before its start. Currently subjects are being enrolled.

Dr. Rundek led the MBRF Cognitive Aging and Memory Intervention Core at UM and has been putting forth considerable effort directed at developing this core with the other McKnight Brain Institutes. Collaborative Pilot Proposals were submitted to this Interventional Core and are in the process of undergoing external review.

Dr. Rundek, the PI for the MBAR study together with other leaders **Dr. Levin** and **Dr. Alperin**, collaborates with all 3 other McKnight Institutes.

Dr. Rundek is collaborating on Inter-institute initiatives including submitting an R01 submission grant proposal to the NIA in the spring with other site leaders.

14. Collaborative Programs with Non-McKnight Institutes, Institutions and Research Programs

Dr. Sacco and **Dr. Rundek** have active research programs with the NOMAS team at Columbia University in NY (as detailed in earlier sections).

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

Dr. Sacco and **Dr. Rundek** also participate and collaborate with the Hispanic Community Health Study- Study of Latinos with the Miami Site PI, Dr. Neil Schneiderman. They are also involved with Dr. Schneiderman T32, one of the longest standing T32 training programs on cardiovascular risk funded by the NHLBI.

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

Dr. Gomes-Osman is collaborating with the Alagoas State University for Health Sciences, in Brazil, and is conducting a study to evaluate the influence of an exercise literacy workshop to improve engagement in physical activity and cognitive performance in older adults.

Dr. Zeki Al Hazzouri received two substantial grants on collaborations with researchers at the University of Southern California.

15. Briefly describe plans for future research and/or clinical Initiatives

With new scientific leadership in our Institute, we will take the opportunity to re-assess, build on and re-structure some of our research and educational programs in order to advance our **mission**

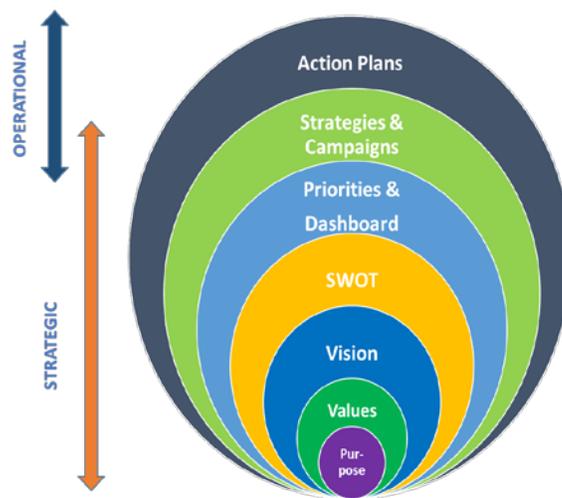
and accelerate *discovery of the causes, treatment and prevention of age-related memory loss and cognitive decline and enhance brain health*. This will require a strategic action plan that will effectively and strategically advance translational and patient oriented research in our Evelyn F. McKnight Brain Institute.



In the recent presentation, **Dr. Rundek** discussed her SWOT analyses of our McKnight Brain Institute and listed numerous strengths of our Institute, identified some weaknesses that may be turned into strengths and clearly emphasized internal and external threats that also may provide great opportunities to advance our Institute’s mission and vision. In order to re-assess our Institution’s future directions, our major goal in the next year is to hold a one-day **UM McKnight**

Brain Institute Strategic Planning Retreat, which will set 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 assess and adjust the Institute's direction in response to a changing research and funding environment. We plan to perform a group SWOT analysis, establish yearly SMART (Specific, Measurable, Achievable, Realistic, and Time-based) objectives for the next 3-5 years and create a detailed action plan defining how these objectives will be achieved following a realistic timeline.

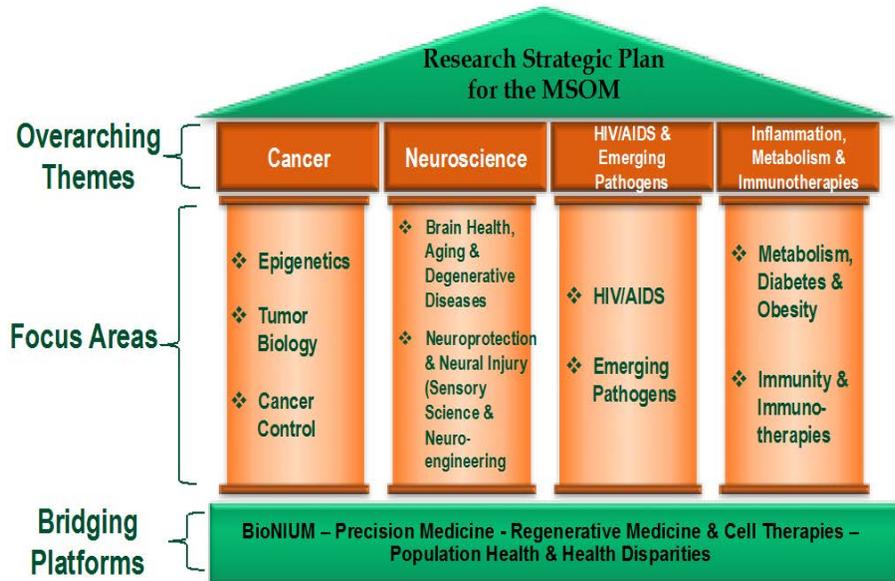
Strategic Plan Building Blocks



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In order to organize and conduct our strategic planning retreat we need to expand our *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 of the University of Miami, particularly with the Schools of Nursing and Health Studies, Engineering, and Education and Human Development. This broad representation of our *Scientific Advisory Board members* will present a large network of

stakeholders that will energize our research and educational activities, advance our mission and help create a successful strategic plan for our McKnight Brain Institute. We plan to align our *McKnight Brain Institute Strategic Plan* with the recently completed **Miller School of Medicine Research Strategic Plan**. In November of 2017, Dean Edward Abraham charged our



Research Deans and Leadership to execute the plan. Under this plan, *Brain Health, Aging, and Degenerative Diseases* are *focused areas* under the *Neuroscience* pillar, one of the strategically focused areas of the Research Strategic Plan. This will create new opportunities for the Miami McKnight Brain Institute to advance its goals and mission through strategically

targeted collaborations and partnerships and by leveraging institutional infrastructure, resources and research support.

The majority of our McKnight Brain Institute future activities will be focused towards priorities determined by the strategic plan. In the meantime, we plan to continue current research and education projects and plan future grant applications through collaborations, team science and partnerships across our institution and with other McKnight Brain Institutes. Several new collaborative grants are already in a planning stage with specific focus on the oldest old, frailty, sleep and small vessel disease. In addition, we will start planning a *T32 training grant in aging and brain health* in partnership with our Center on Aging in the next year.

We plan to expand our *McKnight Brain Institute Cognitive Disorders Clinical and Biorepository Registry* in the collaboration with Dr. Gomes-Osman’s TMS research team and with Dr. Levin’s frailty research team. This registry has been and will continue to provide valuable resources for hypotheses testing and generating preliminary data for grant applications. Recently two grants have been submitted to the NIH using preliminary data from the Registry (Dr. Jiang’s retinal and brain hemodynamic proposal, and Drs. Alperin/Rundek’s proposal on MR imaging of cerebral small vessel perfusion).

Our current clinical projects that are fully or partially sponsored by our McKnight Brain Institute will continue until successful completion. These include our Institutional projects (*Biomarkers for Early Diagnosis of Cognitive Impairment in the Elderly; Frailty as a Preventive Measure in Maintaining Quality of Life in Aging; Retinal Microvascular Dysfunction in Pre-MCI, MCI and Late MCI Patients; Imaging of small vessel perfusion reserve, Sleep and cognitive decline in aging, CARET- Cognitive and Exercise training post stroke, and Pharmacological ischemic pre-conditioning to reduce cognitive decline*) and collaborative projects with other McKnight

Institutes (*MBAR-McKnight Brain Aging Registry study, and ACT- Augmenting Cognitive Training in older adults*) and other funding agencies, including the NIH (*Age-Related Cognitive trajectories in the NOMAS; Hemodynamic study in Einstein Aging Study in the Bronx*).

Our basic science projects will focus on treatments for improving cognitive outcomes using a novel white matter stroke behavioral model in rats. We will continue 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.

As our McKnight trainee Michelle Caunca, MD/PhD Student successfully obtained a F30 NIH award we have availability to accept another MD/PhD student to our McKnight cognitive graduate training program. Dr. Rundek serves on the MD/PhD admission committee and will have an opportunity to select the best candidate for our next McKnight cognitive graduate training program from a pool of highly selected students to our MD/PhD program.

We plan to advance Dr. Christian Camargo to instructor/faculty position in Cognitive Neurology after completion of his McKnight fellowship in July of 2018. He will continue his research as a McKnight collaborator. We plan for another cognitive fellowship position in 2018/19.

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.

At the end of December of 2017, our clinical research coordinator Yamila Carmona, has accepted another position and left the University of Miami. We have already made plans to transition another extremely skillful coordinator Marti Flothmann, BE (exercise physiologist) to our McKnight team in April of 2018. Marti is currently a critical team member of the AHA Bugher Stroke Clinical project that recruits research patients for exercise and cognitive training to improve cognitive outcomes after stroke. She is already known to our McKnight Brain Institute research team as a serious, hard working and terrific coordinator who is equipped with important research skills needed for successful continuation of our clinical projects including our Registry, the MBAR study and community outreach programs. Yamila has trained Marti on the specifics of our McKnight project protocols and recruitment procedures before her departure. Marti has already started to be involved in the MBAR study under Stacy Merritt's supervision. Stacy will increase her efforts and dedicate time to patient enrollment until Marti fully joins our McKnight research team in April.

Research space and availability of MR imaging for research studies continue to be our major challenges for a successful patient oriented research mission of the Institute. In our Institutional negotiations with the new Dean of the UM Miller School of Medicine, we have requested more research exam rooms and support for clinical research space in the proximity of our clinics. We also need some dedicated administrative McKnight research space that our Executive Director Dr. Sacco is currently working on with the new Dean and Vice Dean for Research in our medical school.

Availability of research time on MRI scanner continues to be an issue for our studies. We have to compete with the MR scanner's clinical slots and our study participants often get bumped or delayed. In addition, we do not have enough dedicated scanner slots and MR personnel dedicated to our research studies. This also has been an issue for other Centers and Institutes in our medical school. There is currently a school wide initiative to improve research neuroimaging facilities and Dr. Sacco participates in this initiative. We hope that some of our McKnight Institute's immediate and critical needs for research space and MR imaging availability will be fulfilled in the next year.

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

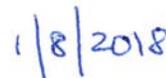
22. What do you consider your most important scientific achievement this year?

We consider our grant applications to the NIH on retinal structural and microcirculatory changes in aging and cognitive decline (**Dr. Jiang, Dr. Rundek**) and on novel MR perfusion methods for testing of cerebral small vessel function (**Dr. Alperin, Dr. Rundek**) to be the most important scientific achievements this year. These investigators have prepared and published scientific preliminary data needed for these grant applications. In addition, **Dr. Sun's** manuscript on neurogranin as a predictor of memory and executive function decline in MCI that was accepted for publication in a prestigious journal, *Neurology*, is also among major achievements this year. Our MD/PhD student star Michelle Caunca has received her NIH F30 award, despite losing her primary mentor Dr. Wright in the midst of her grant submission. She successfully transitioned her primary mentorship to Dr. Rundek and obtained funding.

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



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



Date