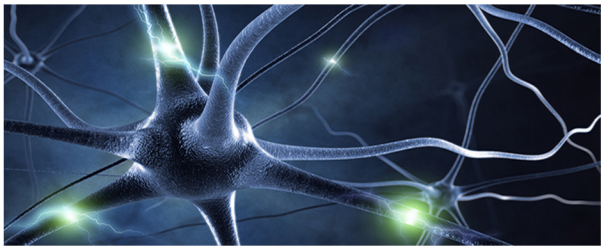
UNIVERSITY OF MIAMI
EVELYN F. MCKNIGHT BRAIN INSTITUTE
ANNUAL PROGRESS REPORT
JANUARY 1, 2017 - DECEMBER 31, 2017



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Dear Trustees,

Thank you for your continued support. Enclosed you will find 5 copies of the University of Miami Evelyn F. McKnight Brain Institute Annual Report for 2017 entailing our scientific achievements and research updates. We are looking forward to 2018 under the scientific leadership of Dr. Rundek.

Yours Sincerely,

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

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

RLS/TR/SSM/bd

cc: Susan Fox Rosellini

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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 ε4 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.

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1. Summary of Scientific and Educational Achievements Since Last Report

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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 Fernàndez McInerney, PhD and Christin Bermudez, PhD) have become Faculty members in the Department of Neurology. Dr. Fernàndez 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.

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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, Desrivières 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, Milaneschi Y, Muñoz Maniega S, Nho K, Nugent AC, Nyquist P, Loohuis LM, Oosterlaan J, Papmeyer 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, Ciccosanti 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.

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D. Basic Science Publications

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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, Veracuz, 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.

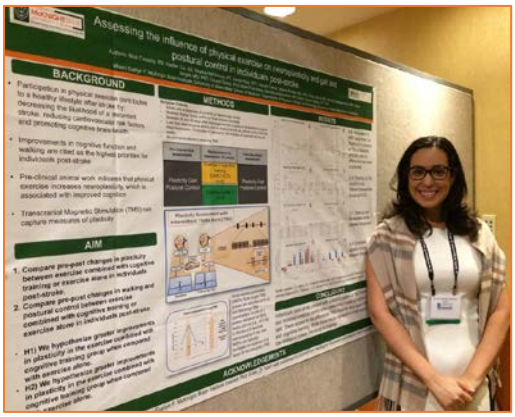
- ### Adiponectin and Components of Metabolic Syndrome are Associated with Cortical Thickness: the Northern Manhattan Study

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.**

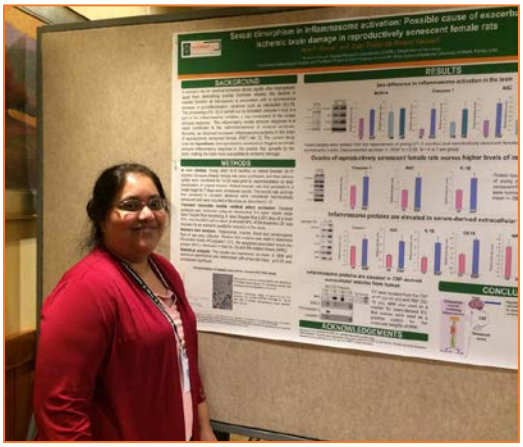
Presented by: **Joyce Gomes-Osman, PhD, PT**



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.**

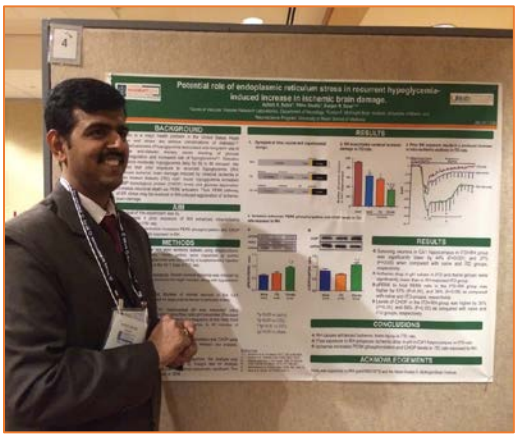
Presented by: **Ami Raval, PhD**



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-1β 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.**

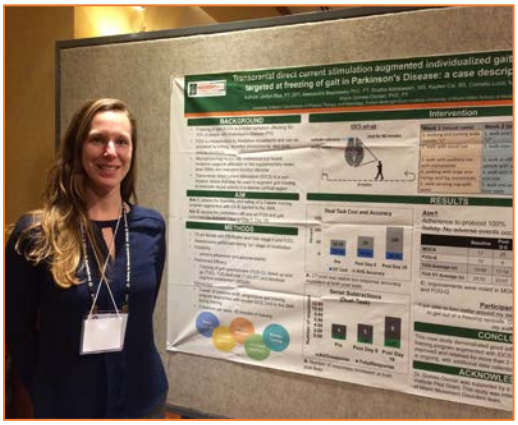
Presented by: **Ashish K. Rehni, PhD**



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**.**

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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	Biochemestry

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

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9. Clinical/Translational Programs

A. New Programs

Clinical and Population Based

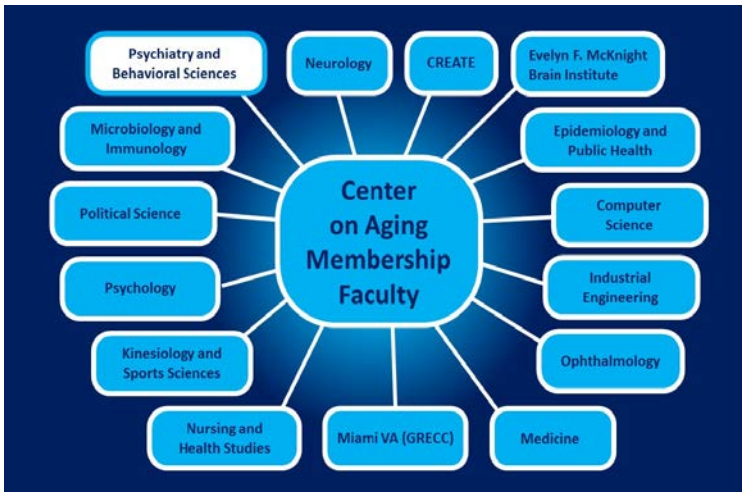
Dr. Sacco will begin his new project *The Transitions of Care Stroke Disparity Study (TCSD-S)*. It is described below on page 43. He will be focusing on the *Florida Stroke Registry* which will entail strict organization and coordination among Florida hospitals and the Florida state legislative system. 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 onthe 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 withe 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, Hungtington'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 inter-disciplinary 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. Fernàndez 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.

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 Aß42, 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 Aβ42 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 Communit*y 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 amnestic 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 amnestic 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 evaluated 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 deficiencyhas 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.**

11. Budget Update

A. Status of matching funds: Included in the Financial and Budget Sheets section below.

B. Projected budget for coming year: Included in the Financial and Budget Sheets section below.

C. Extramural Funding

Stroke Incidence and Risk Factors in a Tri-ethnic Region
Source: NIH, NINDS (R01 NS029993)
Principal Investigator: **Ralph Sacco**
2017 Budget: $1,726,580

University of Miami ASA/Bugher Foundation Center for Excellence in Stroke Collaborative Research
Source: American Heart Association Bugher Foundation
Principal Investigator: **Ralph Sacco**
2017 Budget: $604,000

Miami Clinical and Translational Science Institute
Source: NIH//NCRR/NIMHD
Principal Investigator: **Ralph Sacco**
2017 Budget: $3,405,890

Family Study of Stroke Risk and Carotid Atherosclerosis
Source: NIH/NINDS R01 NS040807
Principal Investigators: **Ralph Sacco** and **Tatjana Rundek**
2017 Budget: $347,529

Disparities in Transition of Care after Acute Stroke Hospitalization: The Transition of Care Stroke Disparity Study (TCSD-S)
Source: NIN/NIHHD MD R01MD012467
Principal Investigators: **Ralph Sacco**, **Tatjana Rundek**, and Jose Romano
2017 Budget: $800,875

Disparities in Care Delivery in Patients with Atrial Fibrillation: FLiPER-AF Study
Source: ARISTA-USA CV185-564, Pfizer/BMS
Principal Investigators: **Tatjana Rundek**
2017 Budget: $196,580

Mentor/AHA Mentee Award
Source: American Heart Association (MM26340000)
Principal Investigator: **Tatjana Rundek**
2017 Budget: $15,000

The Accreditation and Utilization of Cardiac Echo Laboratories in Medicare Beneficiaries: The VALUE-ECHO Study
Source: Intersocietal Accreditation Commission (IAC)
Principal Investigator: **Tatjana Rundek**
2017 Budget: $75,000

Protocol adc- 047-tcad: A Phase 2 Multi-center, Randomized, Double Blind, Placebo-controlled, Parallel Group Study to Evaluate the Efficacy and Safety of t-817ma in Patients with Mild to Moderate Alzheimer's Disease
Source: Toyama Chemical Co., Ltd.
Co- Investigator: **Xiaoyan Sun**
2017 Budget: $473,346

University of Miami Memory Disorder Clinic
Source: State of Florida, Division of Elder Affairs
Co-Investigator: **Xiaoyan Sun**

2017 Budget: $222,801

Novel Detection of Early Cognitive and Functional Impairment in the Elderly
Source: NIH/NIA
Co-Investigator: **Xiaoyan Sun**
2017 Budget: $498,219

The Effects of Cannabinoids on TBI
Source: Scythian Biosciences
Co-Investigator: **Bonnie Levin**
2017 Budget: $953,121

Increased Cerebral Ischemic Injury by Repeated Hypoglycemic Episodes in Diabetes
Source: NIH, NINDS (R01 NS073779)
Principal Investigator: **Kunjan Dave**
2017 Budget: $65,000

Red Blood Cell Microparticles (RMPs) to Reduce Bleeding Following Hemorrhagic Stroke
Source: NIH, NINDS (R2121 NS094896)
Principal Investigator: **Kunjan Dave**
2017 Budget: $307,000

Ischemic Preconditioning: Mechanisms of Neuroprotection
Source: NIH, NINDS (R01NS034773)
Principal Investigator: **Miguel Perez-Pinzon**
2017 Budget: $335,781

Ischemic Preconditioning: Mechanisms of Neuroprotection/Supplement for Research on Sex/Gender Differences
Source: NIH, NINDS (R01NS034773-S1)
Principal Investigator: **Miguel Perez-Pinzon**
2017 Budget: $100,000

Decellularized Extracellular Matrix Biomaterials as Therapy to Ameliorate Cerebral Ischemia Damage
Source: NIH, NINDS (R21 NS098896)
Principal Investigator: **Miguel Perez-Pinzon**
2017 Budget: $163,438

Activity-Dependent Mechanisms of White Matter Repair after Stroke
Source: Supplemental award: American Stroke Association-Bugher Foundation Centers for Excellence in Stroke Collaborative Research for Regeneration, Resilience and Secondary Prevention
Site Principal Investigator: **Miguel Perez-Pinzon**
2017 Budget: $103,611

Neuroprotective mechanisms of resveratrol pre-conditioning
Source: NIH/NINDS F31 Ruth L. Kirschstein National Research Service Award Predoctoral Fellowship # 1F31NS089356-01A1
Principal Investigator: **Kevin B. Koronowski** (PhD student in **Perez-Pinzon** lab)
2017 Budget: $37,176

Elucidating the mechanism behind the long-term cerebral ischemic tolerance mediated by resveratrol preconditioning
Source: AHA, Greater Southeast Affiliate Winter 2016 Predoctoral Fellowship (16PRE29170004)
Principal Investigator: **Nathalie Khoury** (PhD student in **Perez-Pinzon** lab)
2017 Budget: $25,950

ORCATECH Collaborative Aging (in Place) Research Using Technology CART
Source: NIH/NIA (1U2CAG054397-01)
Site PI: **Sara Czaja**
2017 Budget: $1,948,567

Augmenting Cognitive Training in Older Adults – the ACT Grant
Source: NIH/NIA
Site PI: **Sara Czaja**
2017 Budget: $1,307,013

A non-pharmacological intervention for patients with Alzheimer's disease and family caregivers
Source: NIH/NIA (1 R01 AG054009-01)
Principal Investigator: **Sara Czaja**
2017 Budget: $749,437

A Personalized Health Behavior System to Promote Health and Well-Being in Older Adults
Source: NIH (1 R01 AG053163-01)
Principal Investigator: **Sara Czaja**
2017 Budget: $834,282

Center for Research and Education for Aging and Technology Enhancement (CREATE IV)
Source: NIA/NIH (5PO1AG0172-17)
Principal Investigator: **Sara Czaja**
2017 Budget: $1,597,545

Novel Detection of Early Cognitive and Functional Impairment in the Elderly
Co-Investigator: **Sara Czaja**
Source: NIH (1R01AG047649-01A1)
2017 Budget: $582,363

A Tailored Technology Intervention for Diverse Family Caregivers of AD Patients
Source: NINR/NIH (1R01NR014434-01)
Principal Investigator: **Sara Czaja**
2017 Budget: $459,484

A Non-Pharmacological Intervention for Patients with Alzheimer's disease and Family Caregivers

Source: Florida Department of Health – (FLDOH)
Principal Investigator: **Sara Czaja**
2017 Budget: $249,095

The Role of Retinal Microvascular Impairment on Neurodegeneration
Source: National Multiple Sclerosis Society
Principal Investigator: **Hong Jiang**
2017 Budget: $148,211

Imaging of Conjunctival Microvasculature During Contact Lens Wear
Source: Johnson and Johnson contact lens study
Principal Investigator: **Hong Jiang**
2017 Budget: $23,000

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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 Mentoring a Trainee

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. 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	*Developmental Neurodiversity and Clinical Phenotypes of Dementia- A Life Course Approach*
Grace Zhai, PhD	Neuroscience	2-8-17	*Neuroprotection Against Proteinopathies: Insights From Drosophila Models*
Noam Alperin, PhD	Radiology	3-15-17	*MRI Centered Research Topics in Aging-Related Cognitive Decline*
Stephen Rao, PhD	Neuropsychology	6-28-17	*Innovations in the Cognitive Neuroscience of Aging*
David Della-Morte, MD, PhD	Neurology	7-26-17	*Novel Molecular Pathways Involved in Senescence and Neurodegeneration*
Milena Pinto, PhD	Neuroscience	8-30-17	*Mitochondrial dysfunctions in Parkinson's disease: a lesson from mouse models*
Sara Czaja, PhD	Aging and Neurology	10-4-17	*Update on the Center on Aging's Research Activities*
Joyce Gomes-Osman, PT, PhD	Physical Therapy and Neurology	11-8-17	*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.*

Jordyn Rice, PT, DPT	Physical Therapy and Neurology	11-8-17	*Transcranial direct current stimulation augmented individualized gait training targeted at freezing of gait in Parkinson's Disease: a case description*
Ashish K. Rehni, PhD	Neuroscience	11-8-17	*Potential role of endoplasmic reticulum stress in recurrent hypoglycemia-induced increase in ischemic brain damage*
Joyce Gomes-Osman, PT, PhD	Physical Therapy and Neurology	11-29-17	*An update on the work of the Neuromotor Plasticity Laboratory: in the pursuit of Exercise targeting Brain Health*
Kunjan Dave, PhD	Neuroscience	12-13-17	*Hematoma growth in ICH patients: a potential therapeutic target*

2017 Evelyn F. McKnight Brain Institute Journal Club Presentations

Speaker	Area of Expertise	Date	Title
Michelle Caunca	Neurology	1-18-17	*Age Effects on Gray Matter Volume and Attentional Performance in Zen Meditation*
Sarah Getz, PhD	Neuropsychology	2-15-17	*Decision Making in the Elderly*
Rene Hernandez-Cardenache	Neuroscience	5-17-17	*Brief Literature Review, Cognitive Effects of OSA and Brain Health*
Andrea Ruetenik	Neuroscience	6-21-17	*Huntingtin Inclusions Trigger Cellular Quiescence, Deactivate Apoptosis, and Lead to Delayed Necrosis*
Conner Haasse	Neuroscience	7-19-17	*Translational models for Vascular Cognitive Impairment: a Review Including Larger Species*

Conner Haasse	Neuroscience	7-19-17	*Considerations for the Optimization of Induced White Matter Injury Preclinical Models*
Michelle Caunca	Neurology	8-9-17	*Evaluations of Amyloid Protective Factors and Alzheimer Disease Neurodegeneration Protective Factors in Elderly Individuals*
Christian Camargo, MD	Neurology	10-18-17	*Optogenetic Stimulation of a Hippocampal Engram Activates Fear Memory Recall*

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	*Technology-Enabled Intervention for Common Mental Health Problems*
Sheila Cotton, PhD	Technology and the Aging Population	3-13-17	*Technology Use and Older Adults: Benefits, Barriers, and the Future*
Colin A. Depp, PhD	Health Technology and Psychology	5-1-17	*Mobile Technology for Serious Mental Illness and Healthy Aging*
Hans-Werner Wahl, PhD	Aging and Psychology	11-6-17	*Gero-Technology Research and Gerontology: Potential and Limits of a Growing Alliance*

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.

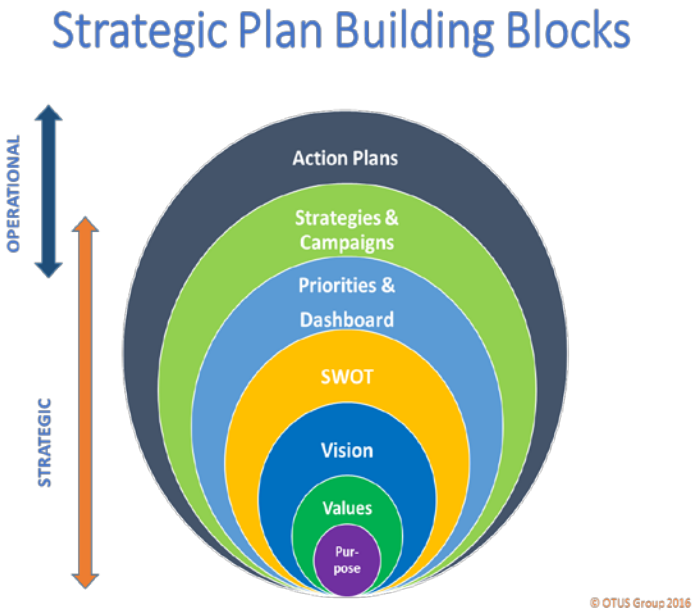
Dr. Zeki Al Hazzouri received two substantial grants on collaborations with researchers at the University of Southern California.

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

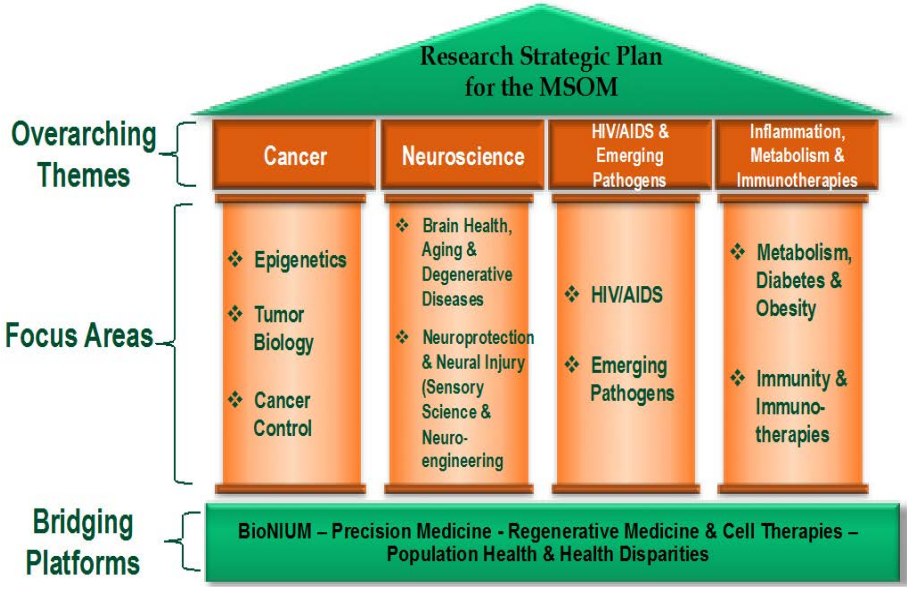
With new scientific leadership in our Institute, we will take the opportunity to re-assess, build on and re-structure some of our research and educational programs in order to advance our **mission** and accelerate *discovery of the causes, treatment and prevention of age-related memory loss and cognitive 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.



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.

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

Included in the Financial and Budget Sheets section below.

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.

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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

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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.

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

Tatjana Rundek

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

1/8/2018

Date

FINANCIAL AND BUDGET SHEETS

McKnight - FY18 Budget For Annual Report
June 1, 2017 - May 31, 2018

			Budget as submitted to McKnight	Actual as of November 30, 2017	Projected at Year End
Revenue			***738,196.08***	***366,298.53***	***732,597.06***
Personnel					
Faculty	***Role In Project***	***Effort***			
Tatjana Rundek, MD until Dec 2017	Interim Scientific Director (7 months)	10%			
Tatjana Rundek, MD starting 1/1/2018	Scientific Director (5 months)	30%			
Ralph Sacco, MD	Executive Director	5%			
Xiaoyan Sun, MD	Educational Director	25%			
Bonnie Levin, PhD	Neuropsychology	20%			
Kunjan Dave, PhD	Neurology - Basic Science	6%			
Noam Alperin, MD	Radiology	10%			
Jiang Hong, MD	Neurologist	5%			
Sara Czaja, MD	Psychiatry	5%			
David della Morte, MD	Neurology (part time)	90%			
Subtotal Faculty Salary and CFB			***306,891.40***	***103,764.40***	***333,395.10***
Staff	***Role in Project***	***Effort***			
Stacy Merritt	McKnight Project Manager	75%			
Ahmet Bagci	Radiology	40%			
Sang Lee	Radiology	25%			
Digna Cabral - Main	Neurology	7%			
Yamila Carmona until Dec 2017 - Main	Clinical Research Coordinator	65%			
Marti Flothmann replacing Yamila Carmona	Clinical Research Coordinator	80%			
Michelle Caunca	MD/PhD Student - Neuro	100%			
Isabel Saul	Research Support Specialist-Basic Science	15%			
Bure-Reyes, Annelly	Neuropsychology	25%			
Getz, Sarah J	Neuropsychology	25%			
Kaur, Sonya Sarjit	Neuropsychology	25%			
Miranda, Michelle	Neuropsychology	25%			
Sarno, Marina Lucia	Neuropsychology	25%			
Slugh, Mitchell R	Neuropsychology	100%			
Subtotal Staff and CFB			***341,947.43***	***146,156.74***	***308,392.12***
Total Personnel			***648,838.84***	***249,921.14***	***641,787.22***
Non Personnel Expenses					
Communications			2,000.00	1,126.51	2,253.02
Internal UM Services Provided/Animal purchasing/Supplies/Chemicals			17,000.00	24,623.43	28,246.43
Conference,Registration,Dues,Memberships,Travel,Postage,Freight,Printing,Publishing, etc.			29,857.24	9,434.10	25,790.15
Blood sample storage/Biorepository			3,500.00	48.00	3,548.00
Two Pilot awards			20,000.00	9,999.90	20,000.00
Other			17,000.00	972.24	10,972.24
Total Non Personnel Expenses			***89,357.24***	***46,204.18***	***90,809.84***
Grand Total Expenses			***738,196.08***	***296,125.32***	***(0.00)***

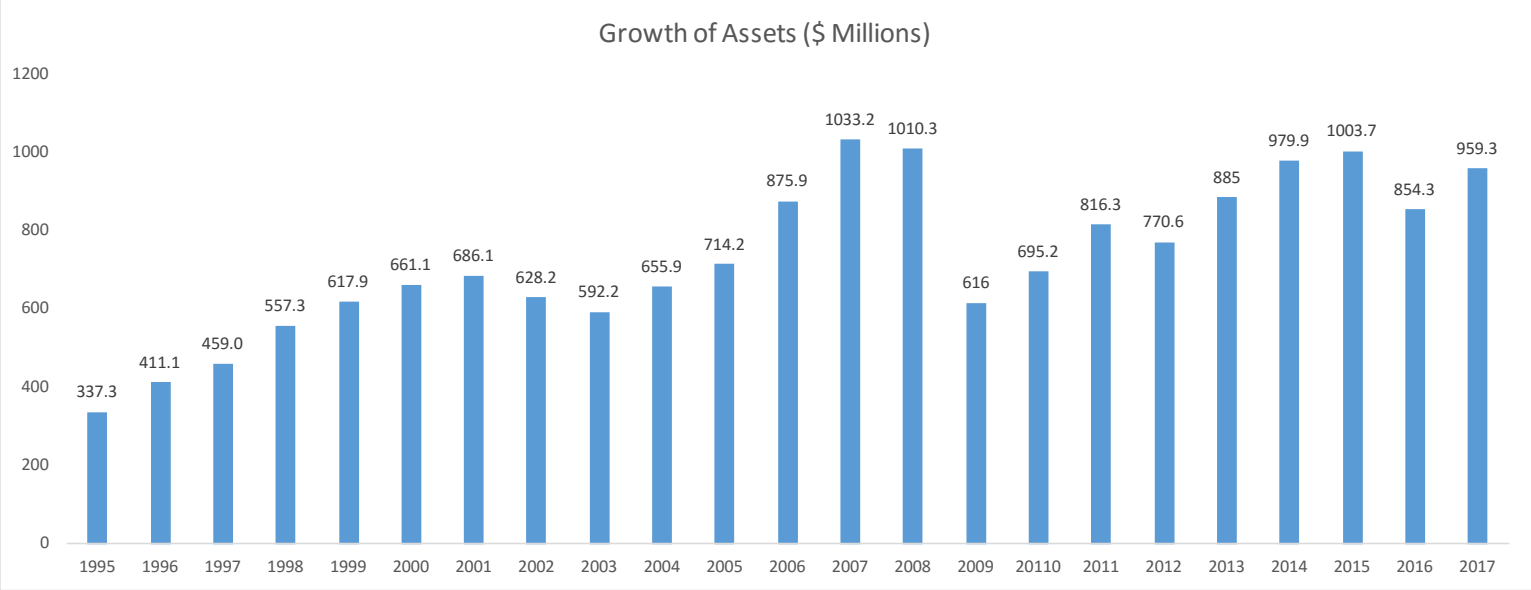
McKnight - FY19 - Budget Proposal
June 1, 2018 - May 31, 2019

			Budget Summary
Revenue (based on FY18 endowment)			**732,597.06**
Personnel			
Faculty	***Role In Project***	***Effort***	
Tatjana Rundek, MD	Scientific Director	30%	
Ralph Sacco, MD	Executive Director	5%	
Xiaoyan Sun, MD	Educational Director	10%	
TBA Cognitive chief	Research for Age-related Cognitive Disorder	20%	
Bonnie Levin, PhD	Neuropsychology	20%	
Kunjan Dave, PhD	Neurology - Basic Science	6%	
Noam Alperin, MD	Radiology	10%	
Jiang Hong, MD	Neurologist	5%	
David della Morte, MD	Neurology (part time)	90%	
Subtotal Faculty Salary and CFB			***298,266.61***
Staff	***Role in Project***	***Effort***	
Stacy Merritt	McKnight Project Manager	100%	
Sang Lee	Radiology	25%	
Digna Cabral	Neurology	7%	
Marti Flothmann	Clinical Research Coordinator	85%	
TBA	MD/PhD Student - Neuro	100%	
Isabel Saul	Research Support Specialist-Basic Science	15%	
Bure-Reyes, Annelly	Neuropsychology	25%	
Getz, Sarah J	Neuropsychology	25%	
Kaur, Sonya Sarjit	Neuropsychology	25%	
Miranda, Michelle	Neuropsychology	25%	
Sarno, Marina Lucia	Neuropsychology	25%	
Slugh, Mitchell R	Neuropsychology	100%	
Subtotal Staff and CFB			***354,389.69***
Total Personnel			***652,656.30***
Non Personnel Expenses			
Communications			2,000.00
Internal UM Services Provided/Animal purchasing/Supplies/Chemicals			17,000.00
Conference,Registration,Dues,Memberships,Travel,Postage,Freight,Printing,Publishing,Speakers,etc.			35,940.76
Two Pilot awards			20,000.00
Other			5,000.00
Total Non Personnel Expenses			***79,940.76***
Grand Total Expenses			***732,597.06***

University of Miami - All Managed Assets
Performance Periods Ending: May 31, 2017

Total Returns (Periods Greater Than 1 Year are Annualized)						
Growth Pool	**Inception**	**1 yr**	**3 yr**	**5 yr**	**7 yr**	**10 yr**
Growth Pool Total Composite	12/31/1990	13.5	3.9	8.1	7.8	3.9
Total Portfolio Benchmark[1]	12/31/1990	13.8	5.1	9.7	9.1	4.3
Value (+/-)		-0.2	-1.2	-1.5	-1.3	-0.4

15 Year Growth Pool Risk/Return as of May 31, 2017		
Growth Pool	**15 Year Return**	**15 Year Standard Deviation**
Growth Pool Total Composite	6.0	10.1
Growth Pool Market Benchmark[1]	6.1	11.1



1. A weighted average return derived by applying the target policy weights of each asset class to the performance of the asset class benchmarks

University of Miami Manager Structure - Market Values and Allocations

As of May 31, 2017

			Growth Pool
Manager	Asset Class	Market Value ($)	% of Total Fund
Vanguard Institutional Index (10/31/14)	US Large Cap Core Equity	139,191,798	14.5%
Adage Capital Mgmt (6/30/04)	US Large Cap Core Equity	74,270,650	7.7%
Columbia Dividend Income (2/2/17)	US Large Cap Core Equity	15,460,963	1.6%
Loomis Large Cap Growth (2/2/17)	US Large Cap Growth Equity	16,352,626	1.7%
MFS Large Cap Value (2/2/17)	US Large Cap Value Equity	15,333,148	1.6%
GAMCO Investors (01/01/91)	US Midcap Value Equity	21,488,800	2.2%
Janus Enterprise Mid Cap Growth (2/2/17)	US Midcap Growth Equity	14,114,523	1.5%
Vanguard Mid Cap (2/2/17)	US Midcap Core Equity	23,138,446	2.4%
Apex Capital (2/2/17)	US Small Cap Growth Equity	17,396,362	1.8%
Hillcrest (2/2/17)	US Small Cap Value Equity	16,541,194	1.7%
Vanguard Small Cap (2/2/17)	US Small Cap Equity	17,854,253	1.9%
Silchester International (6/30/05)	Non-US DM/EM Value Equity	60,361,970	6.3%
Vanguard Developed Markets (2/2/17)	Non-US DM Core Equity	57,167,536	6.0%
Schroders International Growth (2/2/17)	Non-US DM Core Equity	24,159,609	2.5%
Delaware Emerging Markets Fund (2/2/17)	Non-US EM Equity	10,143,583	1.1%
Vanguard FTSE Emerging Markets (2/2/17)	Non-US EM Equity	44,411,846	4.6%
WGI Emerging Markets (10/31/08)	Non-US EM Equity	27,172,825	2.8%
Highclere Emerging Markets SMID (7/31/14)	Non-US EM Equity	17,217,862	1.8%
Davidson Kempner (10/01/93)	Event Arbitrage	42,720,210	4.5%
Watershed Capital (1/01/08)	Event Arbitrage	1,809,422	0.2%
Regiment Capital (6/30/07)	High Yield Bonds	1,119,049	0.1%
Viking Global Equities III (11/30/10)	Equity Long/Short	38,439,709	4.0%
Glenview Capital Management (2/01/06)3	Equity Long/Short	257,293	0.0%

University of Miami Manager Structure - Market Values and Allocations

As of May 31, 2017

AQR Delta XN Offshore (1/31/17)	Multi-Strategy	17,464,641	1.8%
AQR Risk Parity (2/21/17)	Multi-Strategy	51,724,592	5.4%
AQR Style Premia (12/14/16)	Multi-Strategy	17,788,003	1.9%
TIFF Partners IV (01/31/01)2	Private Equity	2,172,552	0.2%
TIFF Partners V (04/30/04)2	Private Equity	482,069	0.1%
TIFF Partners 2006 (04/30/06)2	Private Equity	1,151,133	0.1%
TIFF Partners 2007 (01/31/07)2	Private Equity	2,604,136	0.3%
TIFF Partners 2008 (01/31/08)2	Private Equity	10,063,732	1.0%
OCM Principal Opportunities IV (12/31/06)2	Private Equity	2,224,327	0.2%
Denham Commodity Fund V (6/30/08)2	Private Equity	2,003,116	0.2%
Clayton, Dubilier & Rice Fund IX (5/31/2014)2	Private Equity	6,073,752	0.6%
Carlyle Strategic IV (11/30/16)	Private Equity	978,578	0.1%
KKR Americas XII (9/30/16)	Private Equity		
WCP Real Estate Strategies Fund (7/31/06)	Private Real Assets	110,337	0.0%
Parmenter Realty Fund III (04/30/06)	Private Real Assets	1	0.0%
WCP Real Estate Fund I (7/31/06)	Private Real Assets	1,196,933	0.1%
WCP Real Estate Fund II (11/30/08)	Private Real Assets	1,435,882	0.1%
Metropolitan Real Estate Fund (9/30/06)	Private Real Assets	651,012	0.1%
SRI Nine REIT (3/31/08)2	Private Real Assets	940,406	0.1%
LBA Realty IV (10/31/09)2	Private Real Assets	1,527,218	0.2%
Warburg Energy (5/31/14)2	Private Real Assets	3,478,608	0.4%
Vanguard Total Bond Fd (10/30/14)	Aggregate Bonds	26,280,788	2.7%
Guggenheim US Bank Loans (2/2/17)	Bank Loans	53,089,593	5.5%
Lord Abbett Limited Maturity (2/2/17)	Short Duration Bonds	17,622,086	1.8%
Prudential US High Yield (2/2/17)	High Yield Bonds	18,115,549	1.9%

University of Miami Manager Structure - Market Values and Allocations

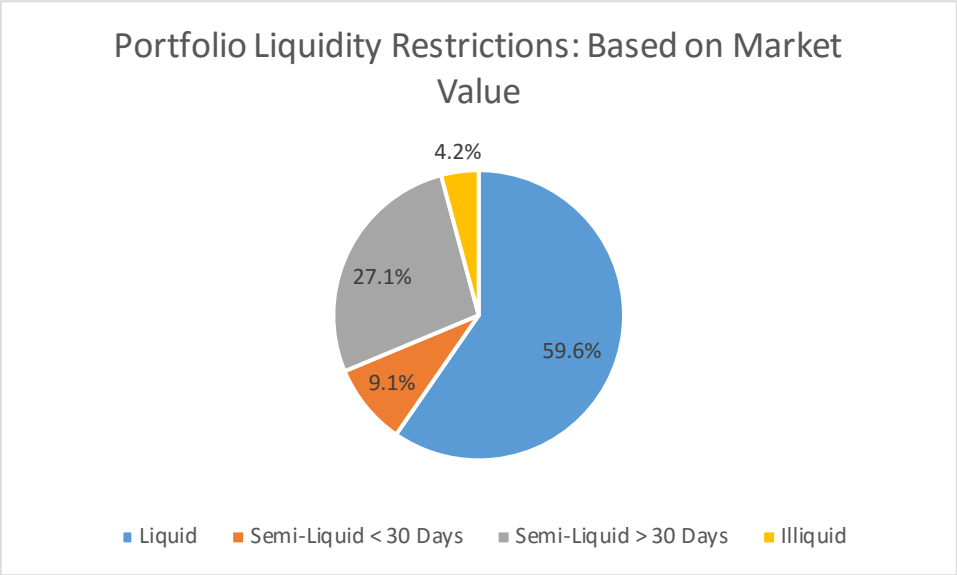
As of May 31, 2017

Cash	**23,998,635**	**2.5%**
Total Managed Assets	**959,301,356**	**100.0%**

University of Miami Manager Structure - Market Values and Allocations

As of May 31, 2017

Allocation to Index or Enhanced Index Strategies	
	Growth Pool
% of Total:	**29.4%**



University of Miami - Growth Pool

Inception to Date Performance vs. Relevant Benchmark(s)

Periods Ending - May 31, 2017

Net of Fees

Total Returns (%) - Annualized if Greater than 1 Year			
Large/Mid/All Cap Equity	**ROR**	**Value Added (+/-)**	**Years**
Vanguard Institutional Index (10/31/14)	9.14	-1.02	2.6
S&P 500	10.16		2.6
Adage Capital Mgmt (6/30/04)	11.33	2.96	12.9
S&P 500	8.37		12.9
GAMCO Investors (01/01/91)	12.61	1.92	26.4
Russell 3000 Value	10.69		26.4
Columbia Dividend Income (2/2/17)	6.18	-0.08	0.3
Russell 1000	6.26		0.3
Loomis Large Cap Growth (2/2/17)	12.82	2.51	0.3
Russell 1000 Growth	10.31		0.3
MFS Large Cap Value (2/2/17)	5.26	3	0.3
Russell 1000 Value	2.26		0.3
Janus Enterprise Mid Cap Growth (2/2/17)	8.57	1.15	0.3
Russell Midcap Growth	7.42		0.3
Vanguard Mid Cap (2/2/17)	5.17	-0.13	0.3
CRSP MidCap Index	5.30		0.3
Small Cap Equity			
Apex Capital (2/2/17)	-0.59	-5.53	0.3
Russell 2000 Growth	4.94		0.3
Hillcrest (2/2/17)	-5.48	-3.63	0.3
Russell 2000 Value	-1.85		0.3
Vanguard Small Cap (2/2/17)	2.02	0.2	0.3
CRSP US Small Cap TR Index	1.82		0.3
Developed International Equity			
Silchester International (6/30/05)	8.81	4.61	11.9
MSCI EAFE Value ND	4.20		11.9
Vanguard Developed Markets (10/31/2014)	4.63	-0.41	2.6
FTSE Dev All Cap ex US	5.04		2.6
Schroders International Growth (2/2/17)	9.82	-0.7	0.3
MSCI EAFE ND	10.52		0.3
Emerging Markets			
Delaware Emerging Markets Fund (2/2/17)	12.71	2.27	0.3
MSCI Emerging Markets ND	10.44		0.3
Vanguard FTSE Emerging Markets (2/2/17)	7.49	-2.95	0.3
MSCI Emerging Markets ND	10.44		0.3
WGI Emerging Markets (10/31/08)	12.14	9.17	8.6
MSCI Emerging Markets ND	2.97		8.6
Highclere Emerging Markets SMID (7/31/14)	-0.03	-0.79	2.8
MSCI Emerging Markets ND	0.76		2.8
Credit Strategies			
Davidson Kempner (10/01/93)	9.11	-0.3	23.7
HFR Event-Driven	9.41		23.7
Equity Long/Short			
Viking Global Equities III (11/30/10)	10.30	0.53	6.5
MSCI World Index	9.77		6.5
Multi-Strategy			
AQR Delta XN Offshore (1/31/17)	-2.80	-5.03	0.3
HFRI Fund of Funds Composite	2.23		0.3

University of Miami - Growth Pool

Inception to Date Performance vs. Relevant Benchmark(s)

Periods Ending - May 31, 2017

Net of Fees

AQR Risk Parity (2/21/17)	1.24		0.3
60 MSCI AC WORLD/40 BB Barclays U.S. Aggregate	3.65		0.3
AQR Style Premia (12/14/16)	1.65	1.4	0.4
Merrill Lynch 3M US Treasury Bill	0.25		0.4
Fixed Income			
Vanguard Total Bond Fd (10/30/14)	2.31	-0.46	2.6
BB Barclays U.S. Aggregate	2.77		2.6
Guggenheim US Bank Loans (2/2/17)	1.30	-0.13	0.3
S&P/LSTA Leveraged Loan Index	1.43		0.3
Lord Abbett Limited Maturity (2/2/17)	0.70	-0.2	0.3
BB Barclays U.S. Corporate 1-3 Year	0.90		0.3
Prudential US High Yield (2/2/17)	3.52	0.43	0.3
BB Barclays U.S. Corporate High Yield	3.09		0.3

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Summary

Evelyn F. McKnight Brain Institute's Endowments at the Miller School of Medicine Market Value Analysis 05/31/2017

2002 Gift & Match

McKnight Contribution	$5,000,000
UM Match	5,050,913
Transfers from Other University Funds	1,362,153
Investment Return	5,286,418
Distributions for Spending	(5,032,380)
05/31/17 Endowment Balance	$11,667,104
Unmatched Balance	$0

2014 Gift & Match

McKnight Contribution	$2,000,000
UM Match	2,000,000
Transfers from Other University Funds	0
Investment Return	477,260
Distributions for Spending	(191,524)
05/31/17 Endowment Balance	$4,285,736
McKnight Foundation Pledge Balance	$0

McKnight053117
Annual

University of Miami
Evelyn F. McKnight Brain Institute's Endowments
Summary Analysis at Market Value
June 1, 2016 - May 31, 2017

2002 Gift & Match

	Evelyn F. McKnight 262080	F.Peterson/ McKnight 262293	Schoninger Professorship in Neurology 262453	Schoninger Neuropsychology Clinic 262454	Other sources	Total
Beginning Balance at Market, 6/1/16	$6,592,895	$1,019,983	$926,140	$2,315,350	$0	$10,854,368
Investment Return	825,710	127,745	115,992	289,980		1,359,427
Distributions for Spending	(332,058)	(51,372)	(46,646)	(116,615)		(546,691)
Transfers from other University funds						0
Matching gifts						0
Ending Balance at Market, 05/31/17	$7,086,547	$1,096,356	$995,486	$2,488,715	$0	$11,667,104

2014 Gift & Match

	Schoninger Professor in Memory Disorders 262471	Evelyn F. McKnight Endowed Chair 262490				Total
Beginning Balance at Market, 6/1/16	$1,896,564	$1,508,628	$0	$0	$0	$3,405,192
Investment Return	237,530	238,536				476,066
Distributions for Spending	(95,522)	0				(95,522)
Transfers from other University funds						0
Matching gifts						0
McKnight Foundation gifts		500,000				500,000
Ending Balance at Market, 05/31/17	$2,038,572	$2,247,164	$0	$0	$0	$4,285,736

MEMBERS AND COLLABORATORS BIOSKETCHES

Ralph L. Sacco, M.D., M.S., FAHA, FAAN
Evelyn F. McKnight Brain Institute Executive Director
Chairman, Department of Neurology
Olemberg Family Chair in Neurological Disorders
Miller Professor of Neurology, Public Health Sciences,
Human Genetics and Neurosurgery
Chief of Neurology Service, Jackson Memorial Hospital
University of Miami, Miller School of Medicine

Tatjana Rundek, M.D., Ph.D. FANA
Evelyn F. McKnight Brain Institute Scientific Director
Professor of Neurology, Epidemiology and Public Health
Vice Chair, Clinical Research in Neurology
Director, Clinical Translational Research Division
Director, MS Degree Program in Clinical Translational Investigations
University of Miami, Miller School of Medicine

Xiaoyan Sun, M.D., Ph.D.
Evelyn F. McKnight Brain Institute Education Director
Assistant Professor
Department of Neurology
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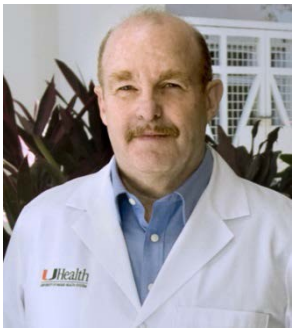
Bonnie E. Levin, Ph.D.
Evelyn F. McKnight Brain Institute Scientific Advisory Board Member
Bernard and Alexandria Schoninger Professor of Neurology
Director, Division of Neuropsychology
University of Miami, Miller School of Medicine

Noam Alperin, Ph.D.
Evelyn F. McKnight Brain Institute Member
Professor of Radiology and Biomedical Engineering
Physiologic Imaging and Modeling Lab
Advance Image Processing Lab
University of Miami, Miller School of Medicine



Sara J. Czaja, Ph.D.
Evelyn F. McKnight Brain Institute Scientific Advisory Board Member
Professor
Psychiatry and Behavioral Sciences
Industrial Engineering
Scientific Director of the Center on Aging
Director of the Center on Research and Education for Aging and Technology Enhancement
University of Miami, Miller School of Medicine

Kunjan R. Dave, Ph.D.
Evelyn F. McKnight Brain Institute Member
Research Associate Professor
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David Della Morte, M.D., Ph.D.
Evelyn F. McKnight Brain Institute Member
Associate Professor
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Joyce Gomes-Osman, PT, Ph.D.
Evelyn F. McKnight Brain Institute Member
Assistant Professor
Departments of Physical Therapy and Neurology
University of Miami, Miller School of Medicine

Hong Jiang, M.D., Ph.D.
Evelyn F. McKnight Brain Institute Member
Assistant Professor of Clinical
Neuro-ophthalmology & Neurology
Bascom Palmer Eye Institute
Department of Neurology
University of Miami, Miller School of Medicine

Miguel A. Perez-Pinzon, Ph.D.
Evelyn F. McKnight Brain Institute Scientific Advisory Board Member
Professor of Neurology & Neuroscience
Vice-Chair for Basic Science (Neurology)
Director, Cerebral Vascular Disease Research Laboratories
University of Miami, Miller School of Medicine

Stacy S. Merritt, M.A., CCRP
Evelyn F. McKnight Brain Institute Research and Administration Director
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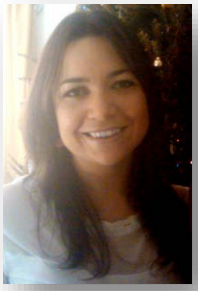

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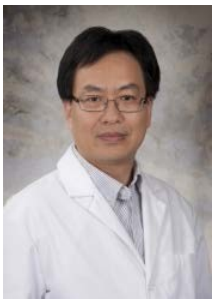

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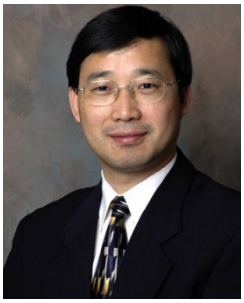

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BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Alperin, Noam

eRA COMMONS USER NAME (credential, e.g., agency login): nalperin

POSITION TITLE: Professor of Radiology and Biomedical Engineering

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Tel Aviv, Israel	B.Sc.	10/1980	Physics
Hebrew University, Jerusalem		08/1983	Medicine
University of Chicago, Chicago, IL	Ph.D	8/1992	Medical Physics
University of Chicago, Chicago, IL	Postdoctoral	10/1994	MRI

A. Personal Statement

Even before attending graduate school I was attracted to medical imaging. I started my career in imaging working as a physicist in the R&D department of a medical imaging company developing digital subtraction angiography systems. During graduate school I shifted my focus to MRI, fascinated by the ability to image blood vessels and flow without the need to inject contrast agent. One of my early publications utilized blood vessels as landmarks for registering X-ray with MR angiography data (1). During my postdoctoral training I was introduced to Chiari Malformations, a poorly understood and debilitating neurosurgical problem associated with altered cerebrospinal fluid (CSF) dynamics. I used velocity-encoding MR to image and measure CSF pulsation in the cranio-spinal system and was puzzled by the large inter-individual variability, even among healthy subjects. We were among the first to investigate the relationship between CSF and blood flow pulsations and the first to demonstrate that the cranio-spinal CSF pulsation is driven by the change in the intracranial blood volume during the cardiac cycle (2). The characterization of the driving force for the CSF pulsation has clarified what information can be derived from the CSF pulsation and to the development of a novel methodology to noninvasive measure intracranial compliance and pressure by MRI (MRICP) (3). I was fortunate to receive R21 grant to demonstrate the feasibility of the MRICP method followed by RO1 grant to apply the method in the clinical setting of Chiari Malformation (the same disorder that got me involved in CSF dynamics). This effort resulted with advancement and new insight into this disorder (4). Consistent focus on the CSF physiology and dedicated research effort helped establish our group among the leaders in this field.

In the current application, we identify another CSF related clinical challenge that can benefit from the MRICP technique, the need for reliable noninvasive test to assess CSF shunt function. Incorporating the MRICP as part of a shut function test will likely yield a reliable test, which in turn, will have a significant impact on management of many pediatric and adult patients with CSF shunts. Our track record and my previous experience leading a multi-disciplinary teams will benefit the project and the likelihood for successful completion.

1. Alperin N, Levin DN, and Pelizzari CA. (1994). Retrospective registration of x-ray angiograms with MR images by using vessels as intrinsic landmarks. Journal of Magnetic Resonance Imaging, 4:139-144
2. Alperin N, Vikingstad EM, Gomez-Anson B, Levin DN. (1996). Hemodynamically-independent analysis of CSF and brain motion observed with dynamic phase-contrast MRI. Magn. Reson. in Med., 35:741-754
3. Alperin N, Lee SH, Loth F, Raksin P, Lichtor T. (2000). MR-Intracranial Pressure (ICP): A method for noninvasive measurement of intracranial pressure and elastance. Baboon and Human Study. *Radiology*, 217 (3); 877–885.
4. Alperin N, Loftus JR, Oliu CJ, Bagci AM, Lee SH, Ertl-Wagner B, Green B, Sekula R. (2014). MRI measures of Posterior Cranial Fossa Morphology and CSF Physiology in Chiari Malformation Type I. Neurosurgery 75:515–522 (Editor's Choice)

B. Positions and Honors

POSITIONS AND EMPLOYMENT

1985-1987 Physicist, Elscint Medical Imaging, Inc.
1987-1988 Product Manager, Mennen Medical, Inc.
1989-1994 Research Associate, MRI Center, University of Chicago
1994-1995 MRI Application Scientist, SMIS Inc.
1995-2001 Assistant Professor, Departments of Radiology and Bioengineering, Uni. of Illinois, Chicago
2001-2009 Associate Professor, Departments of Radiology and Bioengineering, Uni. of Illinois, Chicago
2009- Professor, Department of Radiology and Biomedical Engineering, University of Miami

Other Experience and Professional Memberships

1990-2008 Member, American Association of Medical Physicists
1994- Member, American Society of Magnetic Resonance in Medicine
2004- Ad hoc member, reviewer for several NIH study sections
2011- Member of the American Society of Neuroradiology

C. Contribution to Science

1. My early publications related to the investigations of the CSF flow dynamics aimed to characterize the origin of the cranio-spinal CSF pulsation (a-d). Effort to explain the origin of CSF pulsation started in the early 1940s where invasive measurements showed that CSF pressure pulsation is synchronous with the blood pressure pulsation. In each decade since till the late 1970s a new view of the origin of CSF pulsation was proposed, from only arterial origin through only venous origin and sometimes a complex combination of the two. In the 1990s, MRI provided new perspective into CSF pulsation, enabling quantitation of the volumes of blood and CSF entering and leaving the cranium during the cardiac cycle. Our publications adopted a system approach to describe the CSF volumetric flow rate dynamics and proposed transfer function to describe the link between CSF and blood flow, where the CSF is the output driven by the momentary difference between arterial inflow and venous outflow (the input). The CSF flow is also modulated by the mechanical properties of the intracranial compartment (i.e., compliances and resistances). This provided the first subject-specific noninvasive estimation of the lamped mechanical properties of the cranio-spinal system. This approach however, does not yield individual parameters such as the intracranial compliance, but instead, it provides measures, such as the natural frequency of the system, which is a combination of several parameters. Therefore, an alternative approach was needed to obtain a measurement of intracranial compliance from which intracranial pressure is derived.

   Alperin N, Bagci AM, Lee SH, Lam BL. Role of Cerebrospinal Fluid in Spaceflight-Induced Ocular Changes and Visual Impairment in Astronauts. Radiology (in press)

   Loewenstein D, Curiel R, Sun X, Alperin N, et al. Recovery from Proactive Semantic Interference in Mild Cognitive Impairment and Normal Aging: Relationship to Atrophy in Brain Regions Vulnerable to Alzheimer's Disease. JAD (in press)

   Obeid JP, Stoyanova R, Kwon D, Patel M, Padgett K, Slingerland J, Takita C, Alperin N, Yepes M, Zeidan YH. Multiparametric evaluation of preoperative MRI in early stage breast cancer: prognostic impact of peri-tumoral fat. Clin Transl Oncol. 2016 Jun 30. [Epub ahead of print]

   4Alperin N, Bagci AM, Lee SH, Lam B.L. Automated Quantitation of Spinal CSF Volume and Measurement of Craniospinal CSF Redistribution following Lumbar Withdrawal in Idiopathic Intracranial Hypertension. AJNR Am J Neuroradiol. 2016 Jun 9. [Epub ahead of print]

   Alperin N, Loftus JR, Bagci AM, Lee SH, Oliu CJ, Shah AH, Green BA. MRI-Based Measures Predictive of Short-Term Surgical Outcome in Chiari Malformation Type I: A Pilot Study. J Neurosurg Spine. 2016 Aug 5:1-11. [Epub ahead of print]

Alperin N, Vikingstad EM, Gomez-Anson B, Levin DN. (1996). Hemodynamically-independent analysis of CSF and brain motion observed with dynamic phase-contrast MRI. Magn. Reson. in Med., 35:741-754.

Chu D, Levin DN, and Alperin N. (1998). Assessment of the biomechanical state of intracranial tissue by dynamic MRI of Cerebrospinal fluid pulsations: a phantom study. Magn. Reson. Imag. 16:(9)1043- 48.

Alperin N, Kulkarni K, Loth F, Mafee M, Lichtor T. (2001). Analysis of MRI-Based Blood and CSF Flow Measurements in Patients with Chiari I Malformations: A System Approach. Neurosurgical Focus, 11(1):1-10.

Tain and RW, Alperin N. (2009). Noninvasive Intracranial Compliance from MRI-Based Measurements of Transcranial Blood and CSF Flows: Indirect vs. Direct Approach; IEEE Transaction in Biomedical Engineering, 56(3):544-54.

2. Following efforts were focused on developing a direct measure of intracranial compliance based on its physical definition, the change in volume for a given change in pressure (i.e., dV/dP). Our effort was motivated by the possibility to derive ICP noninvasively by MRI. Because of the mono-exponential relationship between intracranial pressure and intracranial volume, intracranial compliance is inversely related to intracranial pressure (ICP). Our initial publication demonstrated the feasibility of the MRICP

method using flow phantom, nonhuman primate model and a small number of humans (a). The volume change was derived from volumetric flow rate of blood and CSF to and from the cranium, and the pressure change was derived from the change in the pressure gradient. The following publications describe important improvements that made the MRICP method more robust. The first was the modeling of the CSF flow in the cervical canal in order to formulate the relationship between the pulse pressure and the pulse pressure gradient replacing the previous empirical relationship (b). The second important contribution was the development of a novel method for automated segmentation of lumens conducting non-steady flow for reliable quantitation of volumetric CSF and blood flow rates by MRI (c). Our lumen segmentation method incorporates temporal information in multiple images compared to available methods that are primarily based on spatial information in a single image. This method has been adopted by other investigators who utilize velocity-encoded MRI for flow quantitation (e.g., Huang et al 2004). The MRICP method is now beginning to be used independently by other groups (e.g., Muehlmann et al 2013) and by other investigators in collaboration with our group who assists with guidance and with the data analyses. For example, the MRICP methodology was very recently employed to investigate the elusive pathophysiology of *Acute Mountain Sickness*. Results published in the Annals of Neurology revealed that the severity of headaches symptoms is correlated with the change in ICP between the normal and the hypoxic conditions (d).

a. Alperin N, Lee SH, Loth F, Raksin P, Lichtor T. (2000). MR-Intracranial Pressure (ICP): A method for noninvasive measurement of intracranial pressure and elastance. Baboon and Human Study. *Radiology*, 217 (3); 877–885.

b. Loth FM, Yardimici MA, and Alperin N. (2001). Hydrodynamic modeling of Cerebrospinal Fluid Motion within the spinal cavity. Jour. of Biomechanical Engineering, 123:71-79,

c. Alperin N, Lee SH. (2003). PUBS: Pulsatility based segmentation of lumens conducting nonsteady flow, Magnetic Resonance in Medicine, 49:934–44.

d. Lawley J, Alperin N, Bagci A, Lee S, Mullins O, Oliver S, Macdonald J. (2014). Acute mountain sickness: Elevated brain volume and intracranial hypertension. Annals of Neurology. 75(6):890-8.

3. Our recently completed RO1 project focused on the potential role of the MRICP in the setting of Chiari Malformation Type I (CMI). Adult CMI affects primarily women with onset of symptoms occurring during childbearing age. Symptoms include severe headaches and motor and sensory deficits. If left untreated, patients experience poor quality of life and deficits worsen. A surgical procedure, termed decompression, where a portion of the skull base is removed, was found to provide symptomatic relief. However, due to a lack of reliable diagnostic criteria (currently diagnosis is based on an arbitrary radiologic finding of tonsilar herniation greater than 5mm), 3 to 4 out of 10 patients undergoing surgery do not improve. Therefore, there is a clear need for a fresh look at this disorder. During the award period, we collected data from CMI patients and healthy subjects. It was evident that cranial morphology, especially of the posterior cranial fossa (PCF), plays a role and should be considered together with the CSF hydrodynamics. We therefore developed an automated method for PCF parcelation (a), computed over 20 morphologic and hydrodynamic measures, and assessed differences between CMI and the control cohorts. In addition, these measures were correlated with symptomatology. The results of this work have led to a new characterization of CMI using combined morphologic-physiologic quantitative measures. We identified 10 measures that were significantly different in the CMI and were strong differentiators of CMI (b). Outcome analyses reveal that some of these new CMI markers were outside the CMI range in patients that had poor outcome following surgery. We therefore hypothesize that the combined morphologic-physiologic criterion for CMI would significantly improve diagnostic accuracy and surgical outcome. Interestingly, MRICP was among the predictive parameters and is moderately elevated in CMI. Increased ICP was proposed as a possible mechanism for CMI by the discoverer of CMI, H. Chiari, in 1891. Our latest paper on CMI addresses the different types of headaches reported in CMI (c). This work is important because neurosurgeons rely on specific symptoms for surgery consideration. We found that headaches worsen with Valsalva maneuver, which is considered a hallmark symptom of CMI, is associated with lower compliance and higher MRICP due to a smaller intracranial volume and not, as previously suggested, smaller PCF. This information has implications on utilization of symptoms in the diagnosis of CMI.

a. Bagci AM, Lee SH, Nagornaya N, Green BA, Alperin N. (2013). Automated posterior cranial fossa volumetry by MRI: applications to Chiari malformation type I. AJNR 34(9):1758-63.

b. Alperin N, Loftus JR, Oliu CJ, Bagci AM, Lee SH, Ertl-Wagner B, Green B, Sekula R. (2014*). MRI measures of Posterior Cranial Fossa Morphology and CSF Physiology in Chiari Malformation Type I*. Neurosurgery 75:515–522. (Editor's Choice)
c. Alperin N, Loftus JR, Oliu CJ, Bagci AM, Lee SH, Ertl-Wagner B, Sekula R, Lichtor T, Green AB. (2015). *Imaging-Based Features of Headaches in Chiari Malformation Type* I. Neurosurgery. Mar 23.

4. In 2010, after relocating my lab to the University of Miami I initiated collaboration with the Bascom Palmer Eye Institute focusing on another complex CSF related disorder, idiopathic intracranial hypertension (IIH). IIH is characterized by elevated ICP of unknown cause and is manifested mainly by severe headaches and often with visual impairments caused by increased CSF pressure that compresses the optic nerve and the eye globe. IIH can occur both in males and females of a wide age range, though it is most frequent in overweight women of childbearing age. Our research focused on the obesity related IIH that often presents with edema of the optic nerve (papilledema). We since published 5 important publications that were well received. Two were selected by Biomed Updater as 1st and 3rd in a list of top 20 articles in this domain published since 2013 and another article featured by AJNR news digest. Our first contribution employed our lamped parameter modeling of the cranio-spinal system to document reduced spinal canal compliance in IIH, which likely explains the associated with obesity through increased abdominal pressure (a). The following paper provided evidence for impaired CSF homeostasis and the involvement of the extra cranial venous drainage in the etiology of IIH (b). We documented increased intracranial CSF volume in the extra-ventricular spaces in IIH, consistent with the reduced ability of the spinal canal to accommodate the increased CSF volume. We made an important contribution by developing an automated method for quantitation of the eye globe deformation in IIH that provide quantitative measures of the optic nerve protrusion and posterior sclera flattening (c). Using these novel quantitative measures we found that the degree of papilledema severity is proportional to the nerve protrusion length, an observation that favors a "mechanical" over a "vascular cause of papilledema. We then correlated MRI and Optical coherence tomography (OCT) imaging of the globe and were able to translated the method to measured nerve protrusion with OCT, which is a more widely used imaging modality for the eye globes

    a. Tain RW, Bagci AM, Lam BL, Sklar EM, Ertl-Wagner B, Alperin N. (2011). Determination of cranio-spinal canal compliance distribution by MRI: Methodology and early application in idiopathic intracranial hypertension. Jour. Magn. Reson. Imag. 34:1397-404.
    b. Alperin N, Ranganathan S, Bagci AM, Adams DJ, Ertl-Wagner B, Saraf-Lavi E, Sklar E, Lam BL. (2013). MRI Evidence of Impaired CSF Homeostasis in Obesity-Associated Idiopathic Intracranial Hypertension. AJNR. 34(1):29-34.
    c. Alperin N, Bagci AM, Lam BL, Sklar E. (2013). Automated quantitation of the posterior scleral flattening and optic nerve protrusion by MRI in idiopathic intracranial hypertension. AJNR Am J Neuroradiol. 34(12):2354-9.
    d. Chang YC, Alperin N*, Bagci AM, Lee SH, Rosa PR, Giovanni G, Lam BL (2015). Relationship between Optic Nerve Protrusion Measured by OCT and MRI and Papilledema Severity. Invest Ophthalmol Vis Sci. 2015 Mar 17 (*co-first author)

5. In this section we report two recent important contributions. The first relates to another disorder of impaired CSF homeostasis that occurs in the elderly, idiopathic normal-pressure hydrocephalus (iNPH). iNPH is a reversible syndrome of gait impairment, dementia, and incontinence. Currently, the only effective treatment is surgical implantation of a shunt. The need for a pharmacologic adjunctive treatments due to high failure rates and mortality associated with shunt has been already noted at several NIH workshops. I initiated a collaboration with Weill Cornell Medical College in New York to assess the effect of acetazolamide (a drug that is effective in IIH). Results of this pilot study were recently reported in Neurology and included first radiologic evidence for the potential efficacy of pharmacologic treatment in iNPH- reversal of periventricular white matter hyperintensities in patients who had improved gait following treatment (a).

   The second contribution is related to the validity of the MRICP method. In 2005, we applied the MRICP methodology to study the effect of posture on CSF physiology in humans (b). In this publication, ICP was measured in healthy subjects noninvasively in the upright and supine positions. MRICP was lower, as

expected, in the upright posture with an average value of about 4mmHg compared to 10mmHg in the supine posture. Apparently, neurosurgeons expect mainly negative ICP values in the upright posture. We further investigated this discrepancy and found that it is related to a difference in the location of the pressure reference. We now account for the effect of the hydrostatic pressure gradient and estimate a pressure value at a more central cranial location that is compatible with invasive measurements in the upright posture (c). Mean MRICP value after adjusting for the hydrostatic pressure component is now negative, -3.4±1.7 mmHg compared to the previously unadjusted value of +4.3 ±1.8 mmHg.

a. Alperin N., Oliu CJ, Bagci AM, Lee SH, Kovanlikaya I Adams D, Katzen H, Relkin N. (2014). Low-Dose Acetazolamide Reverses Periventricular White Matter Hyperintensities in iNPH. Neurology 82:1347–1351.
b. Alperin N, Lee S, Sivaramakrishnan A, Hushek S. (2005). Quantifying the Effect of Posture on Intracranial Physiology in Humans by MRI Flow Studies, Jour. Magn. Reson. Imag. 22(5):591-596.
c. Alperin N, Lee SH, Bagci AM. (2015). MRI Measurements of Intracranial Pressure in the Upright Posture: The Effect of the Hydrostatic Pressure Gradient. J Magn Reson Imaging. Mar 9

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/pubmed/?term=Alperin+N

D. Research Support

Ongoing Research Support

NNX14AB51G Alperin (PI) 08/01/14-08/31/16
Analyses of MR Imaging of CSF flow dynamics Pre and Post Space Flights
The goal of this directive contract from NASA is to identify hydrodynamic measures that are associated with developing elevated ICP in microgravity.
Role: PI

Completed Research Support

R01 NS052122 Alperin (PI) 08/01/08-01/31/14
Development and Early Clinical Evaluation of Noninvasive MRI Measurement of ICP
The goal of the study is to implement an MRI-based measurement of intracranial compliance and pressure (MR-ICP) in the clinical setup of Chiari Malformations and evaluate the role of intracranial compliance in the pathophysiology of this relatively common but poorly understood neurological problem.
Role: PI

BIOGRAPHICAL SKETCH

Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: **BARRIENTOS, Antoni**

eRA COMMONS USER NAME (credential, e.g., agency login): **abarrientos**

POSITION TITLE: **Professor**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Univ. of Barcelona. Teachers' School. SPAIN	B.S.	1981-1984	Science Education
Univ. of Barcelona. School of Biology. SPAIN	B.S.	1986-1992	Fundamental Biology
Univ. of Barcelona. School of Medicine. SPAIN	Ph.D.	1993-1997	Mitochondrial Genetics and Biochemistry
Univ. of Miami. School of Medicine. FL. USA	Post-doctoral fellow	1997-1999	Mitochondrial Biology
Columbia University. New York. NY. USA	Post-doctoral fellow	1999-2000	Yeast mitochondrial Genetics and Biochemistry

A. Personal Statement

I have devoted my entire career to mitochondrial research in health, disease and aging. We routinely use the facultative aerobe/anaerobe yeast *Saccharomyces* cerevisiae as a model organism. Additionally, we study human cultured cells to validate and/or complement the discoveries made in yeast and generate findings that are relevant to human biology and diseases. The two main research interests in my lab are on the biogenesis of mitochondrial membrane complexes and on mitochondria-related mechanisms of neurodegenerative disease and aging. Over the last 16 years we have been extensively working on the basic mechanisms underlying the biogenesis of mitochondrial cytochrome *c* oxidase, the mitochondrial ribosomes and in mitochondrial dynamics with the support of NIH, American Heart Association and several Muscular Dystrophy Association (MDA) Research Grants. I recently obtained a MIRA (R35) award that consolidates my RO1 NIGMS grants. We have been also working on the role of mitochondrial mechanisms of neurodegeneration and aging with the support of an RC1 grant from the Florida Department of Health and more recently with the support of the Army Research Office (ARO). During my 16 years as an academic faculty I have trained 11 postdoctoral trainees; I have mentored 11 PhD students (5 currently), have been in the dissertation committee of 22 graduate students and was a mentor of 10 undergraduate students.

B. Positions and Honors

Positions:

1985-1992. Permanent position as Teacher of Sciences in Secondary Public Schools. Barcelona. SPAIN.
2000-2003. Associate Research Scientist. Dept Biological Sciences. Columbia University (New York, NY).
2003-2007. Tenure-earning track Assistant Professor. Department of Neurology. Dept of Biochemistry & Molecular Biology. University of Miami (Miami. FL)
June 2007 – June 2009. Tenure-earning track Associate Professor. Department of Neurology and Department of Biochemistry & Molecular Biology. University of Miami (Miami. FL)
June 2009 - June 2013. Tenured Associate Professor. Department of Neurology and Department of Biochemistry & Molecular Biology. University of Miami (Miami. FL)
June 2013 until present. Tenured Professor. Department of Neurology and Department of Biochemistry & Molecular Biology. University of Miami (Miami. FL)

Honors:

1993-1996. Pre-Doctoral Scholarship from the Spanish Government: Education of University' Professors.
1997-1999. Post-Doctoral Scholarship from the Spanish Government: Program for Research Profs. Abroad.
2003-2004. Selected candidate to represent the University of Miami for the Pew Award in Biomedical Sciences.
2004-2005. Selected to represent the University of Miami for the Ellison Foundation award in Aging Research.

Editorial Responsibilities:

Ad hoc reviewer for: Cell Metabolism, Nature Genetics, Journal of Biological Chemistry, Human Molecular Genetics, Molecular Biology of the Cell, Journal of Molecular Biology, Trends Mol Med, Mitochondrion,

Antioxidants and Redox Signaling, Biochemical Journal, FEBS Letters, Aging: clinical and experimental Research, Genetics in Medicine, Annals of Neurology and Neurology.

Advisory panels:

Federal Agencies

- Ad hoc reviewer for the Cellular Mechanisms of Aging and Development (CMAD) study section (NIH) and the Membrane Biology and Protein Processing (MBPP) Study Section (2011-2013).
- Ad hoc reviewer for R13 Scientific Conference Grant (NIH) since 2011.
- Stage 1 reviewer for The Fellowships ZRG1 F05-Cell Biology and Development study section (NIH) (2010)
- Stage 1 reviewer for Recovery Act RC1 (2009) and RC4 (2010) applications (NIH)
- Regular member of the Membrane Biology and Protein Processing (MBPP) Study Section since 2014.

Reviewer of research grants from:

Muscular Dystrophy Association (MDA) (*ad hoc* reviewer since 2008); Italian Telethon (*ad hoc* reviewer since 2006); The British Medical Research Council (MRC) (*ad hoc* reviewer since 2008); The Spanish National Evaluation and Foresight Agency (ANEP) from the Spanish Government Ministry of Education and Science - Secretary for Universities and Research (permanent reviewer since 2004).

C. Contribution to Science

I believe I have significantly contributed to the field of mitochondrial biogenesis in health, disease and aging. Among my most notable contributions are:

(i) Discovered a translational negative feed back regulatory system that coordinates the synthesis of mitochondrial cytochrome *c* oxidase (COX) subunit 1 with the assembly of the multimeric COX enzyme. COX, the terminal oxidase of the respiratory chain, is a hetero-oligomeric enzyme formed by subunits encoded in the nuclear and the mitochondrial DNA. Because COX contain highly reactive heme A and copper prosthetic groups, the biogenesis of this enzyme must be tightly regulated to prevent the accumulation of pro-oxidant assembly intermediates. Over the last 13 years we have discovered and characterized in yeast mitochondria the existence of a negative feedback translational regulatory system. This system coordinates the synthesis of Cox1, a mtDNA-encoded catalytic subunit containing heme A and copper centers, with its assembly into the holoenzyme. Studies during my postdoctoral training at Columbia University had shown that most COX mutants had low levels of Cox1 synthesis. Subsequently, we identified a COX1 mRNA-specific translation activator, Mss51, as the key element of the system [1]. Mss51 is a bi-functional protein that interacts with the 5'UTR of COX1 mRNA to promote translation and subsequently interacts with the newly synthesized Cox1 protein to facilitate its stability in pre-assembly complexes. Mss51 does not act alone. The mitochondrial Hsp70 chaperone Ssc1 [2] and the COX specific chaperones Cox14 [1] and Coa3 [3] dynamically interact with Mss51-containing complexes to coordinate Cox1 synthesis and assembly, and to facilitate Mss51 recycling between its two functions. Our discoveries sparked lines of investigations in several groups who have contributed to the understanding of the translational regulatory mechanism in yeast and in mammalian cells. More recently, we discovered that Mss51 binds heme [4]. This specific finding has provided a key element for a regulatory mechanism that coordinates assembly of COX, the major oxygen-consuming mitochondrial enzyme, with heme and oxygen availability for respiration and aerobic energy production. Over the last few years, researchers have found similar translational regulation mechanisms operating on the assembly of other mitochondrial OXPHOS complexes, namely the bc_1 complex or complex III and the F_oF_1 ATPase.

1 Barrientos, A.*, et al.* (2004) Mss51p and Cox14p jointly regulate mitochondrial Cox1p expression in *Saccharomyces cerevisiae*. ***EMBO J.*** 23, 3472-3482

2 Fontanesi, F.*, et al.* (2010) Mss51 and Ssc1 facilitate translational regulation of cytochrome *c* oxidase biogenesis. ***Mol. Cell. Biol.*** 30, 245-259

3 Fontanesi, F.*, et al.* (2011) Cox25 teams up with Mss51, Ssc1, and Cox14 to regulate mitochondrial COX subunit 1 expression and assembly in *Saccharomyces cerevisiae*. ***J. Biol. Chem.*** 286, 555-566

4 Soto, I.C.*, et al.* (2012) A heme-sensing mechanism in the translational regulation of mitochondrial cytochrome *c* oxidase biogenesis. ***Cell Metab.*** 16, 801-813

(ii) Discovered that mitochondrial supercomplexes or repirasomes are assembled by incorporation of individual complex subunits rather than by assembly of preexisting fully assembled complexes [5]. The structural and functional organization of the mitochondrial respiratory chain (MRC) has been a matter of debate for more than 50 years. Two models have been historically hypothesized. Following the "fluid state" model, individual MRC complexes diffuse freely in the mitochondrial inner membrane and electron transport occurs when the complexes randomly collide. Conversely, the "solid state" model proposes that OXPHOS complexes are organized in rigid higher-order assemblies known as supercomplexes or respirasomes. It is currently accepted that both organizations probably coexist, giving rise to the "dynamic aggregate" or "plasticity" model. This model suggests that OXPHOS complexes switch from freely moving to fixed structures and vice versa to adapt to changes in cellular metabolism. The mechanisms that regulate the biosynthesis of mitochondrial supercomplexes remain largely unsolved. It has been thought that supercomplexes originate by the direct association of single preassembled complexes. However, some observations had suggested that the formation of these

macromolecular assemblies does not necessarily require the preassembly of individual holocomplexes, but could also be achieved through a coordinated association of partially assembled complexes and free subunits. In collaboration with Dr. Cristina Ugalde (Spain), we reported the first human mitochondrial respirasome assembly pathway, which involves a paradigm-shifting model. Our data indicate that respirasome biogenesis involves a complex I assembly intermediate acting as a scaffold for the combined incorporation of complexes III and IV subunits, rather than originating from the association of preassembled individual holoenzymes [5]. This model allows us to explain the requirements for CI assembly, the structural interdependences among OXPHOS complexes, and why certain genetic defects affecting a single complex may lead to combined RC enzyme defects in patients. Multiple research groups are now contributing to define the proposed pathway and to identify respirasome assembly factors as facilitators the assembly process [6].

5 Moreno-Lastres, D.*, et al.* (2012) Mitochondrial Complex I Plays an Essential Role in Human Respirasome Assembly. ***Cell Metab****.* 15, 324-335

6 Barrientos, A. and Ugalde, C. (2013) I Function, Therefore I Am: Overcoming Skepticism about Mitochondrial Supercomplexes. ***Cell Metab.*** 18, 147-149

(iii) Discovered the first DEAD box RNA helicases that play roles in the assembly of the mitochondrial ribosomes in yeast and in mammals. Over the last few years we have been working on the biogenesis of the mitochondrial ribosomes. Our interest is timely because in the years of 2014-15 the structure of yeast, porcine and human mitochondrial ribosomes have been resolved by cryo-EM at a 3.4-3.9 Å resolution. The process of mitoribosome assembly is complicated by the fact that the two mitoribosomal RNAs (rRNAs) are universally mitochondrion-encoded whereas all ribosomal proteins (with a single exception in yeast) are encoded in the nuclear DNA. Even though during the last decade there have been advances on the identification mitoribosome assembly factors and the complement of mitoribosome proteins, a detailed map of the assembly pathway is yet to be determined. Several factors may have contributed to the paucity of information on this process both, in yeast and human cells. First, many assembly factors are yet to be identified. In this regard, we described MTG1 as the first conserved GTPase involved in the assembly of the large subunit (LSU) [7] and more recently we have characterized the first DEAD box helicase that plays a role in LSU assembly, called Mrh4 in yeast [8] and DDX28 in mammals [9]. For example, we have reported that Mrh4 binds to the 21S rRNA to facilitate the incorporation of three late-assembly LSU subunits [8]. Second, yeast ribosome assembly mutants tend to lose their mitochondrial DNA, therefore complicating their analyses. To bypass this challenge in yeast we have recently identified genetic suppressors that maintain mtDNA stability in the absence of mitoribosome assembly, thus allowing the study of assembly intermediates [8].

A recent breakthrough on mitoribosome assembly relates to the mitochondrial compartmentalization of this process**.** At least three distinct types of foci relevant to mtDNA expression have been identified and visualized within the mitochondrial matrix of human cells. Those are the mitochondrial nucleoids, RNA granules and the RNA degradosome. While it has been proposed that mitoribosome assembly could start near the nucleoids, our results show that the distinct compartment in the vicinity of the nucleoids are the RNA granules, where DDX28 and several other assembly factors localize [9]. Newly transcribed rRNAs and/or early mitoribosome assembly intermediates are probably transferred from nucleoids to the RNA granules, where mitoribosome assembly is completed. These RNA granules are therefore reminiscent of the nucleolus. Within the nucleus, the membrane-less nucleolus is organized around the chromosomal regions that contain the genes for the rRNAs, and is the site of rRNA transcription and processing, and of ribosome assembly. Equivalent features pertain to the mitochondrial RNA granule, which we have proposed to term “the mitochondriolus” [9].

7 Barrientos, A.*, et al.* (2003) *MTG1* codes for a conserved protein required for mitochondrial translation. ***Mol. Biol. Cell*** 14, 2292-2302.

8 De Silva, D.*, et al.* (2013) The DEAD-Box protein Mrh4 functions in the assembly of the mitochondrial large ribosomal subunit. ***Cell Metab****.* 18, 712-725

9 Tu, Y.T. and Barrientos, A. (2015) The Human Mitochondrial DEAD-Box Protein DDX28 Resides in RNA Granules and Functions in Mitoribosome Assembly. ***Cell Rep****.* 12, 00058-00053

10 De Silva D, Tu YT, Amunts A, Fontanesi F, Barrientos A. (2015) Mitochondrial ribosome assembly in health and disease. ***Cell Cycle***. Jun 1:0. [Epub ahead of print]

10 De Silva D, Poliquin S, Zeng R, Zamudio-Ochoa A, Marrero N, Perez-Martinez X, Fontanesi F, Barrientos A. (2017) The DEAD-box helicase Mss116 plays distinct roles in mitochondrial ribogenesis and mRNA-specific translation. ***Nucleic Acids Res*****.** 2017 45(11):6628-6643

(iv) Discovered that mitochondrial respiratory thresholds and ROS signaling regulate yeast chronological life span and its extension by TORC1 inhibition or caloric restriction (CR). Metabolic and mitochondrial abnormalities are a prominent feature of aging and neurodegeneration. However, the literature reports conflicting results concerning the extent and causality of the aging associated aerobic energy production decline and mitochondrial ROS-induced damage, as well as their interplay with nutritional cues. Single cell models have provided key information concerning mechanisms of aging and neurodegeneration. In collaboration with Dr. G. Shadel (Yale University, USA), we have gained insight into the mechanism by which *tor1* mutations extend yeast chronological

lifespan. We discovered that TORC1 inhibition results in increased mitochondrial respiration and enhanced ROS production, which induced an adaptive signaling that enhances stress resistance and extends chronological life span [10]. This is a clear example of mitohormesis, in which low-level of a stressor (i.e. ROS) promote adaptive changes resulting in stress resistance. Furthermore, we have characterized the role of mitochondrial respiration in regulating yeast lifespan and its extension by CR. We have shown that a 40% of wild-type respiration is enough to support regular life span and to allow the cells to benefit from CR-induced life span extension. However, while CR increases respiratory capacity and ROS production during growth, it induces shutdown of OXPHOS and ROS generation during chronological aging, thus contributing to extend life span [11]. Together, our data support a model in which ROS signaling and respiratory thresholds are complementary aging modulators that utilize two distinct mechanisms to achieve the same adaptive endpoint: increased stress resistance, efficient use of energy stores, and probably other beneficial effects in the stationary phase, all of which extend chronological life span [12].

11 Pan, Y.*, et al.* (2011) Regulation of yeast chronological life span by TORC1 via adaptive mitochondrial ROS signaling. ***Cell Metab****.* 13, 668-678.

12 Ocampo, A.*, et al.* (2012) Mitochondrial respiratory thresholds regulate yeast chronological life span and its extension by caloric restriction. ***Cell Metab****.* 16, 55-67

13 Ruetenik AL and Barrientos A. Dietary restriction, mitochondrial function and aging: from yeast to humans. ***BBA: Bioenergetics***. (2015) 1847:1434**–**1447

14 Ruetenik AL, Ocampo A, Ruan K, Zhu Y, Li C, R. Zhai GR and Barrientos A. Attenuation of polyglutamine-induced toxicity by enhancement of mitochondrial OXPHOS in yeast and fly models of aging. ***Microbial Cell***, 3 (8):338-51 (2016)

(vi) Discovered that proteotoxicities can be suppressed in yeast models by either enhancement of mitochondrial biogenesis or by increasing the levels of NAD^+ salvage biosynthetic enzymes.

Transgenic yeast expressing human neurodegenerative disease-relevant proteins recapitulate key features of neuronal proteotoxicity. They have facilitated the elucidation of basic cellular mechanisms of toxicity triggered by human neurotoxic proteins. For example, we reported that they reproduce the mitochondrial defects seen in patients [13]. More recently, we have developed novel models that screen for suppressors of proteotoxicity. We have shown that proteotoxicity can be suppressed by enhancement of mitochondrial biogenesis [14], which brought to a similar discovery in mouse models. We have also discovered that proteotoxicity can be suppressed by overexpressing several enzymes in the NAD^+ salvage biosynthetic pathway, specifically NMA1/2, QNS1, NPT1 and PNC1 [15]. Our results are consistent with those obtained in fly models for NMNAT (NMA1 homologue). We are now establishing collaborations with Dr. Grace Zhai (Molecular & Cellular Pharmacology, University of Miami) and with Dr. Lisa Ellerby (Bucks Institute, California) to test whether the four enzymes act as suppressors respectively in Drosophila and patient derived-iPSC-neuronal models of polyglutamine disorders. Results from ongoing experiments indicate that suppression is independent of sirtuins and of the catalytic activity of the enzymes. Rather, under stress, these proteins act as molecular chaperones to combat proteotoxicity [15].

13 Solans, A.*, et al* (2006) Cytotoxicity of a mutant huntingtin fragment in yeast involves early alterations in mitochondrial OXPHOS complexes II and III. ***Hum. Mol. Genet****.* 15, 3063-3081

14 Ocampo, A.*, et al.* (2010) Suppression of polyglutamine-induced cytotoxicity in *Saccharomyces cerevisiae* by enhancement of mitochondrial biogenesis. ***FASEB J****.* 24, 1431-1441

15 Ocampo, A.*, et al* (2013) NAD^+ salvage pathway proteins suppress proteotoxicity in yeast models of neuro-degeneration by promoting the clearance of misfolded/oligomerized proteins. ***Hum. Mol. Genet****.* 22, 1699-1708

Public URL for my bibliography collection in My NCBI is:
http://www.ncbi.nlm.nih.gov/sites/myncbi/antoni.barrientos.1/bibliography/41138774/public/?sort=date&direction=ascending.

D. Research Support

Ongoing Research Support

6-1-2016–5-31-2021. MIRA (R35) Grant from NIH/NIGMS (R35GM118141-01). "*Mitochondrial Biogenesis in Health and Disease".* This award consolidates 3 RO1 grants to study the biogenesis of mitochondrial respiratory chain complexes and supercomplexes and the biogenesis and function of mitochondrial ribosomes.

2-1-2016 / 1-31-2019. Research Grant from the Muscular Dystrophy Association. Research project: "*Role of cysteine rich proteins in mitochondrial cytochrome c oxidase biogenesis*". **PI**: Antoni Barrientos.

6-1-2016 / 5-31-2019. Research grant from The Army Research Office (ARO) # W911NF-16-1-0311. "*Mitochondrial Regulation of Neurodegenerative Proteotoxic Stress".* **PI**: Antoni Barrientos.

Completed Research Support over the last three years

1-1-2012 / 12-31-2015. RO1 grant from NIH (NIH # 2 R01 GM071775-06A1). "*Cytochrome c oxidase assembly in health and disease*". We use the yeast *Saccharomyces cerevisiae* and human cultured cells as models to study cytochrome *c* oxidase (COX) assembly in wild-type strains and other carrying mutations in evolutionary conserved COX assembly factors, relevant for human mitochondrial diseases. **PI:** Antoni Barrientos.

1-1-2013 / 12-31-2015. Supplement to RO1 grant from NIH (NIH # 2 R01 GM071775-06A1S3). "Macromolecular assemblies in cells". We use the human cell culture models to study COX assembly and how it is regulated at the translational level though dynamic protein-protein interactions. PI: Antoni Barrientos.

1-1-2014 / 12-31-2018. RO1 grant from NIH (NIH # R01 GM105781A). "*The biogenetic pathway of mitochondrial respirasomes*". We use the yeast *Saccharomyces cerevisiae* and human cultured cells as models to study the assembly of mitochondrial supercomplexes and respirasomes. **PI:** Antoni Barrientos. *Substituted by MIRA grant*

3-1-2015 / 2-28-2019. RO1 grant from NIH (NIH # R01 GM105781A). "*Biogenesis of the Mitochondrial Translation Machinery*". We use the yeast and human cultured cells as models to study the assembly of mitochondrial ribosomes, with a focus on the function of DEAD box proteins. **PI:** Antoni Barrientos. *Substituted by MIRA grant*

2010-2013. Research Challenge grant form the Florida Department of Health / James & Esther King Biomedical Research Program. "*Slowing degenerative processes by bolstering cellular bioenergetics*" **PI**: Antoni Barrientos, **PI**: C. T. Moraes (multiple PI grant).

2006-2011. RO1 grant from NIH (NIH # R01GM071775). Research project: "*Cytochrome c oxidase assembly in health and disease*". **PI:** Antoni Barrientos.

2009-2011. Competitive ARRA supplement NIGMS 3 R01 GM071775-04S1. Research project: "*Cytochrome c oxidase assembly in health and disease*". **PI**: Antoni Barrientos.

2011-2013. Research Grant from the Muscular Dystrophy Association. Research project: "*Characterization of novel conserved cytochrome c oxidase chaperones*". **PI**: Antoni Barrientos.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Crocco, Elizabeth A.

eRA COMMONS USER NAME (credential, e.g., agency login): CROCCO

POSITION TITLE: Associate Clinical Professor of Psychiatry and Behavioral Sciences

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Douglas College, Rutgers University, New Brunswick, NJ	B.A.	05/1989	Biology
Rutgers-Robert Wood Johnson Medical School, Piscataway, NJ	M.D.	05/1993	Medicine
Mount Sinai Medical Center, New York, NY	Residency	06/1997	General Psychiatry
Mount Sinai Medical Center, New York, NY	Admin.Chief Resident	06/1997	General Psychiatry
University of Miami/Jackson Memorial Hospital, Miami, FL	Fellowship/ Chief Fellow	06/1998	Geriatric Psychiatry

A. Personal Statement

I am currently the Director of the Memory Disorders Clinic (MDC) at the University Of Miami Miller School Of Medicine. I am Board-Certified in the sub-specialty of Geriatric Psychiatry. As the Director of the University of Miami Memory Disorder Clinic, I am an expert in conduct comprehensive memory disorder evaluations and other patient examinations and participate in multidisciplinary staffing conferences to determine patient diagnosis and treatment in neurodegenerative diseases. .I have had a significant role in both developing and testing novel neuropsychological and functional measures developed to detect Mild Cognitive Impairment (MCI) and preclinical MCI leading to Alzheimer's Dementia (AD). I also conduct several clinical trials and federally funded studies. My role in this study will consist of the facilitation of recruitment of research participants and their coordination in the study.

a. **Crocco, EA**, Sabbag, S, & Curiel, R. (2015) Bipolar Disorder in the Elderly, In: *The Bipolar Book: History, Neurobiology and Treatment,* A Yildiz, P Ruiz, CB Nemeroff, ed., Oxford University Press: NY, Chapter 40. ISBN: 978-0-199-30053-2.

b. **Crocco, EA** & Eisdorfer, C. (2014) Research in Mental Health and Caregiving, In: *The Challenges of Mental Health and Caregiving,* RC Talley, GL Fricchion, BG Druss ed., Springer, NY, 205-221. ISBN: 978-1-4614-8791-3.

c. Ownby, R.L., Hertzog, C., **Crocco, E.**, & Duara, R. (2006). Factors related to medication adherence in memory disorder clinic patients. Aging and Mental Health, 10(4), 378-385. PMCID: PMC3543157.

d. **Crocco, EA** & Sabbag, S (2017) Cholinesterase Inhibitors and Memantine, In: *The Comprehensive Textbook of Psychiatry, 10th Edition*, BJ Sadock, VA Sadock, P Ruiz ed., Lippincott Williams & Wilkins: Philadelphia, PA, Chapter 34.15. ISBN-13: 978-1451100471.

B. Positions and Honors

Positions and Employment

1998-2006	Clinical Director of Psychiatry, Wien Center for Memory Disorder, Mount Sinai Medical Center, Miami Beach, FL
1998-2015	Clinical Assistant Professor, Department of Psychiatry and Behavioral Sciences, University of Miami Miller School of Medicine, Miami, FL
2001-	Director, Geriatric Psychiatry Training Program, Jackson Memorial Hospital, Department of Psychiatry and Behavioral Sciences, Miami, FL
2001-2006	Clinical Director of Consultation-Liaison Psychiatry, Mt. Sinai Medical Center, Miami Beach, FL
2000-2006	Medical Director, Mount Sinai Medical Center Geriatric Psychiatry Inpatient Unit, Miami, FL
2006-	Medical Director, Geriatric Medical/Psychiatry Inpatient Unit, Jackson Memorial Hospital, Miami, FL
2010-	Director, Memory Disorder Center, Department of Psychiatry and Behavioral Sciences, Miller School of Medicine at University of Miami, FL
2009-	Division Chief, Geriatric Psychiatry, Department of Psychiatry and Behavioral Sciences, Miller School of Medicine at University of Miami, Miami, FL
2015-	Associate Clinical Professor, Department of Psychiatry and Behavioral Sciences, University of Miami Miller School of Medicine, Miami, FL

Other Experience and Professional Memberships

1994-2009	Member, American Psychiatric Association
1998-	Member, American Association of Geriatric Psychiatry
2003-	Florida Psychiatric Society
2009-2014	Fellow, American Psychiatric Association
2013-	Associate Member, Academy of Medical Educators, University of Miami Miller School of Medicine
2014-	Distinguished Fellow, American Psychiatric Association
2014-	Member, The American College of Psychiatrists
2014-	Member, Gerontological Society of America
2014-	Member, Anxiety and Depression Association of America

Honors

2007, 2008	Geriatric Psychiatry Training Program Teacher of the Year Award, JMH, Miami, FL
2010	University of Miami/Miller School of Medicine Faculty Citizenship Award, Miami, FL
2010	Nancy C.A. Roeske, M.D., Certificate of Recognition for Excellence in Medical Student Education, American Psychiatric Association
2011	Irma Bland Certificate of Excellence in Teaching Residents, American Psychiatric Association
2012	Geriatric Fellowship Excellence in Teaching Award, JMH, Miami, F

C. Contribution to Science

1. **Early detection of Alzheimer's disease and Mild Cognitive Impairment (MCI):** I have had a significant role in both developing and testing novel neuropsychological and functional measures developed to detect Mild Cognitive Impairment (MCI) and preclinical MCI leading to Alzheimer's Dementia (AD). The importance of early detection of AD is crucial to the current science in testing and developing disease-modifying treatment for this neurodegenerative disease. I have served as Co-PI on 1 NIA-funded grant previously (2003-2008) and am currently Co-PI on a current 5 year study predicting rates of cognitive decline in the elderly using these measures over 5 years in conjunction with other select diagnostic biomarkers and tests such as atrophy on structural Brain MRI, amyloid, tau and phosphorylated tau in CSF as well as ApoE4 genotype. I have worked closely with both Dr. David Loewenstein and Dr. Sara Czaja in this important field and have had several significant publications documenting this important work.

a. **Crocco, E.**, Curiel, R.E., Acevedo, A., Czaja, S.J., & Loewenstein, D.A. (2014). An evaluation of deficits in semantic cueing and proactive and retroactive interference as early features of Alzheimer's disease. The American Journal of Geriatric Psychiatry, 22(9), 889-897.

b. Curiel, R., **Crocco, E.,** Duara, R., Acevedo, A. & Loewenstein, D.A. (2013). A new scale for the evaluation of proactive and retroactive interference in Mild Cognitive Impairment and early Alzheimer's disease. Journal of Aging Science, 24(10): 804-813.

c. Czaja SJ, Loewenstein DA, Sabbag SA, Curiel RE, **Crocco E** & Harvey PD. (2017). A novel method for direct assessment of everyday competence among older adults. *Journal of Alzheimer's Disease*: 57: 1229-1238.

d. 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. (2017). 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*: 56(3): 1119-1126.

2) **Depression and Cognition**: The relationship between depression and cognitive impairment in the elderly is important but is not well delineated. The role of depression as risk factor, prodromal event, or symptom of dementia is not well understood. I have published several journal articles related to cognition and dementia in the elderly. This includes a widely cited meta-analysis and meta regression analysis relating early depression as a risk factor for Alzheimer's disease (AD). I have also published on the relationship of depression and other psychiatric symptoms in MCI and cognitive changes related to geriatric depression in general.

a. Ownby, R.L., **Crocco, E.**, Acevedo, A., John, V., & Loewenstein, D. (2006). Depression and risk for Alzheimer's disease: systematic review, meta-analysis and meta-regression analysis.The Archives of General Psychiatry,63(5), 530-538. PMCID: PMC3530614.

b. **Crocco, E.A.**, Castro, K., & Loewenstein, D. (2010). How late-life depression affects cognition: neural mechanisms. Current Psychiatric Reports, 12(1): 34-38.

c. **Crocco, E.** & Loewenstein, D.A. (2005). Psychiatric aspects of mild cognitive impairment. Current Psychiatric Reports, 7(1), 32-36.

d. Duara, R, Loewenstein, DA, Wright, C, **Crocco, E**, & Varon, D. (2014) Mild Cognitive Impairment, In: *Neurology in Practice: Dementia*, J Quinn ed.,Wiley-Blackwell Pub, UK, Chapter 6. ISBN: 978-0-470-67424-6

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1Pg52WCUHj95C/bibliography/47914940/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

XZ203 State of Florida Department of Elder Affairs Crocco (PI) 05/2010-Present
Alzheimer's Disease Initiative/Memory Disorder Clinic
The University of Miami Memory Disorders Clinic (MDC) is funded by an ongoing state of Florida Department of Elder Affairs contract. The role of the Principal Investigator in the clinic is to provide clinical and diagnostic services, research and training for individuals about Alzheimer's disease or related disorders, as well as to their caregivers.
Role: Principal Investigator

7AZ14 State of Florida Department of Health Curiel (PI) 2/1/2017-1/31/2020
Ed and Ethel Moore AD Research Program
A Consortium to Study Precision-based Computerized Assessment for the Detection of Mild Cognitive Impairment in Older Adults.

The role of the Co-investigator is to measure 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 amnestic mild cognitive impairment: [aMCI] and 40 Preclinical AD participants). This project is expected to provide critical data that parallels a recently submitted RO1 application to the National Institutes of Health, which will examine changes in cognitive performance using these instruments as they relate to longitudinal biological changes within the brain.
Role: Co-investigator

1 RO1AG054009-01 Czaja and Loewenstein (PI) 09/01/16-04/30/21
National Institute on Aging
A Non-pharmacological intervention for Patients with Alzheimer's Disease and Family Caregiver
The role of the Co-investigator is to develop and test the efficacy and feasibility of a dyadic-based intervention program (DT), through tablet technology and to target early stage caregiver and the recipient of care (person with Alzheimer's dementia) through the integration of an augmented evidenced-based caregiver intervention and evidenced-based cognitive/functional training for the care recipient.
Role: Co-Investigator

1R01AG047649-01A1 Loewenstein (PI) 02/01/15-01/31/20
National Institute on Aging
Novel Detection of Cognitive and Functional Impairment in the Elderly
The role of the Co-investigator is to examine 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 amnestic mild cognitive impairment (aMCI), in combination with select diagnostic biomarkers and tests such as atrophy on structural MRI, amyloid, tau and phosphorylated tau biomarkers in CSF and in predicting rate of cognitive decline.
Role: Co-Investigator

1 R01 AG047146-03 Devanand (PI) 2015-2018
National Institute on Aging
Treatment of Psychosis and Agitation in Alzheimer's Disease (Lithium Study)
I am a Co PI with a subcontract involved in the recruitment of patients in this study examining the effects of lithium on psychosis ad agitation in Alzheimer's disease.
Role: Co-Investigator

PI: Novartis. A randomized double-blind, placebo controlled, parallel group study to evaluated the efficacy and safety of CNP520 in participants at risk for the onset of clinical symptoms of Alzheimer's Disease. 2017-

PI: Novartis. 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. 2016-

PI: Avanir Pharmaceuticals. 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, 2016-

PI: Avanir Pharmaceuticals. 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. 2016-

PI: Neurim Pharmaceuticals. Randomized, Double-Blind, Parallel-Group, Placebo-Controlled, Dose-Rannfing study of Piromelatine in patients with mild dementia due to Alzheimer's disease
Sponsor. 2016-

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Sara J. Czaja, Ph.D.

eRA COMMONS USER NAME (credential, e.g., agency login): sczaja

POSITION TITLE: Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
State University of NY College at Buffalo, NY	B.S.	1975	Psychology
State University of NY at Buffalo, NY	M.S.	1976	Industrial Engineering
State University of NY at Buffalo, NY	Ph.D.	1980	Human Factors/Industrial Engineering

A. Personal Statement

Overall, I am well recognized for my expertise in aging and behavioral intervention research. Specifically I have extensive experience in interventions aimed at diverse populations of family caregivers of patients with AD as well as older adults of varying levels of cognitive and functional status. I served at these PI for the Miami site of the Resources for Enhancing Alzheimer's Caregivers Health (REACH II) program; the PI of the REACH Community Program and the VideoCare projects. Each of these projects were concerned with developing and delivering interventions to family caregivers of older adults. I am currently the PI of an NIH funded study (Caring for the Caregiver Network), which is evaluating an technology-based psychosocial interventions for diverse family caregivers of AD patients. I am also serving on an Institute of Medicine (IOM) Committee that is focusing on family caregivers of older adults and recently I served on an IOM Committee concerned with cognitive aging. I am also the PI of a project which is evaluating a functional skills training program, using computer-based simulations of everyday tasks developed at the UM Center on Aging, with Schizophrenia patients and non-impaired older adults. In addition, I have vast expertise with technology-based interventions and with the implementation of these interventions with diverse older adult populations including the oldest old. A particular focus of our work at the Center on Aging at the University of Miami Miller School of Medicine of which I am the Director, has been on aging and cognition and on strategies to enhance the functional performance of older people. Our approach to interventions is based on a person-centered design approach, which is commensurate with my background in Industrial Engineering. I am also the Director of the NIH, multi-site Center for Research on Aging and Technology Enhancement (CREATE). CREATE has been funded for the past 16 years and focuses on the interaction of older adults with technology systems in living, work and healthcare settings. We recently completed a cross-site trial, The PRISM Trial, which evaluated the efficacy of a software application in enhancing the well-being and social connectively of older adults (aged 65+) who live alone in the community and were at risk for social isolation. I have received extensive funding from the NIH in these areas and am also well published (examples provided below in the description of my scientific contributions).

B. Positions and Honors

1980-1982 Senior Research Associate, Buffalo Organization for Social and Technological Innovation, Inc
1984-1988 Assistant Professor, Department of Industrial Engineering, SUNY at Buffalo
1988-1991 Associate Professor, Tenured, Department of Industrial Engineering, SUNY at Buffalo
1989-1990 Research Associate, Professor, Department of Industrial Engineering, University of Miami

1988-1993 Research Director, Stein Gerontological Institute, Miami, FL
1991-1994 Associate Professor, Department of Industrial Engineering, University of Miami
1993-1999 Director, Center on Human Factors & Aging Research, University of Miami School of Medicine
1994-present Professor, Dept. of Psychiatry and Behavioral Sciences, University of Miami School of Medicine
1994-present Professor, Department of Industrial Engineering, University of Miami, Coral Gables, FL
1999-present Director, Center on Aging and Technology Research, University of Miami School of Medicine
2002-present Co-Director, Center on Aging, University of Miami, Miami, FL
2010-present Scientific Director, Center on Aging, University of Miami Miller School of Medicine
2016-present Director, Center on Aging, University of Miami Miller School of Medicine

Honors

Member, International Women's Forum (IWF), July 2017
United Homecare/Claude Pepper Education/Advocacy Award, May 2017
UM Research Dean's, Provost Funding Award, February 2017
APA Inaugural Recipient Prize for Interdisciplinary Team Research, CREATE Team, October 2016
M. Powell Lawton Distinguished Contribution Award for Applied Gerontology, August 2015
Panel Member, Nobel Prize Week Dialogue, Stockholm Sweden, December 2014
Jack A. Kraft Award for Innovation, Human Factors and Ergonomics Society, 2013
Social Impact Award for the Association of Computing Machinery (ACM), Special Interest Group for Human Computer Interaction (SIGCHI), 2013
The Scottish Informatics & Computer Science Alliance Distinguished Visiting Professor, School of Computing, University of Dundee, March, 2010.
IBM, University Cooperative Research Award, 2007-2009.
IBM Faculty Award, 2006
Provost's Scholarly Activity Award, 1998.
Researcher of the Year, College of Engineering, University of Miami, 1995.

C. Contribution to Science

1. A significant area of my research has been in understanding the implications of the ubiquitous diffusion of technology in all aspects of everyday life for older adults. I and my CREATE colleagues and colleagues at the Center on Aging have been focusing on three aspects of this issue: 1) the ability of older adults to successfully interact with these systems; 2) factors influencing the uptake of technology among older adults; and 3) the usability of technology/systems applications for diverse populations of older adults. I have received extensive NIH funding for work in these areas for the past 20 years. Most notable is the continuous funding for the CREATE Center which has been funded for the past 16 years and has recently received a perfect score for the IV resubmission. Examples of some of my publications in this area include:

a. Fisk, A.D., Rogers, W., Charness, N., Czaja, S.J., & Sharit, J. (2009). Designing for Older Adults: Principles and Creative Human Factors Approach (2nd. Ed). London: CRC Associates.
b. Czaja, S.J., Sharit, J., Lee, C.C., Nair, S.N., Hernandez, M., Arana, N., Fu, S.H. (2012) Factors Influencing Use of an E-health Website in a Community Sample of Older Adults. J Am Med Inform Assoc. doi: 10.1136/amiajnl-2012-000876
c. Czaja, S. J., Zarcadoolas, C., Vaughon, W., Lee, C. C., Rockoff, M., & Levy, J. (2015). The usability of electronic personal health records among an underserved patient population. Human Factors, 57, 491-506.
d. Czaja, S.J., Sharit, J., & Nair, S.N. (2008). Usability of the Medicare Health Website, JAMA, 300 (7), 790-79.

2. A second key area of my contribution relevant to this application is in behavioral intervention research. Most notably, in the use of technology to deliver interventions to diverse populations of older adults and family caregivers. I have also received extensive NIH funding and funding from foundations such as the Retirement Research Foundation and the Langeloth Foundation for this work and am widely published in this area. For example, I am currently the Principal Investigator of a study funded by the National Institute of Nursing Research (NINR) that is examining the efficacy of an evidenced-based caregiver intervention delivered via technology for minority caregivers of patients with dementia (1R01NR014434-01, Czaja, S.J., PI NINR/NIH A Tailored Technology Intervention for Diverse Family Caregivers of AD Patients".) As noted, in my personal

statement, I also recently served as PI for an NIH funded (as part of CREATE) multi-site randomized clinical trial that examined the efficacy of a software application in enhancing the well-being and social connectively of older adults (aged 65+) who live alone in the community and were at risk for social isolation (The PRISM TRIAL). Examples of relevant publications in this area include:

a. Czaja, S. J., Zarcadoolas, C., Vaughon, W., Lee, C. C., Rockoff, M., & Levy, J. (2015). The Usability of Electronic personal health records among an underserved patient population. Human Factors, 57, 491- 506.
b. Czaja, S. J., Boot, W. R., Charness, N., Rogers, W. A., Sharit, J., Fisk, A. D., Lee, C. C., & Nair, S. N. (2014).The Personalized Reminder Information and Social Management System (PRISM) Trials: Rationale, Methods, and Baseline Characteristics. Contemporary Clinical Trials 40 (2015) 35-46. November
c. Czaja, S.J., Loewenstein, D., Schulz, R., Nair, S.N., Perdomo, D. (2013) A Videophone Psychosocial Intervention for Dementia Caregivers. Nov; 21(11):1071-81. doi: 10.1016/j.jagp.2013.02.019. E pub 2013 Jul 3. Am J of Geriatr Psychiatry.
d. Taha, J., Czaja, S.J., Sharit, J., Morrow, D.G. (2013) Factors Affecting Usage of a Personal Health Record (PHR) to Manage Health. Psychology and Aging, Vol. 28, No.4, 1124-1139.

3. A third key area is related to cognition and functional assessment in diverse older populations. A central focus of this work is on understanding the implications of normative age-related changes in cognition for everyday functioning and the performance of everyday tasks. An additional focus is on understanding how conditions such as mild cognitive impairment or persistent mental illnesses such as schizophrenia impact on cognition and everyday functioning. In addition we are examining the efficacy of cognitive remediation strategies in improving functional performance. I currently am the PI (Dr. Philip Harvey and Dr. David Loewenstein are Co-PIs) of a grant from the National Institute on Aging that is focusing on these issues with older adults with Schizophrenia. (Czaja, S.J., Harvey, P., Loewenstein, D., PI's 1R21AG041740-01, NIH/NIA, Title: "Improving the Functional Outcomes in Older Adults with Schizophrenia".) Some relevant publications in this area include:

a. Crocco, E., Curiel, R.E., Acevedo, A., Czaja, S.J., Loewenstein, D.A. (2014). An Evaluation of Deficits in Semantic Cuing, Proactive and Retroactive Interferences as Early Features of Alzheimer's Disease. The American Journal of Geriatric Psychiatry, Vol. 22, Issue 9, pg. 889-897, September.
b. Harvey, P.D., Stone, L., Loewenstein, D., Czaja, S.J., Heaton, R.K., Twamley, E.W., Patterson, T.L. (2013) The convergence between self-reports and observer ratings of financial skills and direct assessments of financial capabilities in patients with schizophrenia: More detail is not always better. Schizophrenia Research 147 (2013) 86-90.
c. Harvey, Phillip D., Loewenstein, D., Czaja, S.J. (2013) Hospitalization and Psychosis: Influences on the Course of Cognition and Everyday Functioning in People with Schizophrenia. Neurobiology of Disease 53 (2013) 18-25.
d. Czaja S. J. & Loewenstein, D. (2013) Cognition and Functional Status in Adult and Older Patients with Schizophrenia. In P.D. Harvey (Ed.). Cognitive Impairment in Schizophrenia). London: Cambridge University Press (pp. 110-125).

Complete list of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/myncbi/collections/bibliography/48139033/

D. Research Support.
Ongoing research

Czaja, S.J. (PI); Harvey, Philip D (PI); Kallestrup, Peter (PI, Contact) 09/01/2017 – 05/31/2019
1 R43 AG057238-01
"A novel computer-based functional skills assessment and training program"
The objective of the proposed pilot project is to build on our prior work and expand, implement, and evaluate the acceptability, feasibility and efficacy of our 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). Our overall long-term goal 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.
I-FUNCTION, INC

Beach, S., (PI) Czaja, S.J. (Co-PI) 9/1/2017-3/31/2022
1R01AG055511 - 01
Understanding Factors Influencing Financial Exploitation among Diverse Samples of Older Adults
We propose to 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 sample of older adults. The study will be conducted at 2 sites: University of Pittsburgh and University of Miami. It will include a total of 720 adults age 60 and older.

Czaja, S.J. (PI) 9/1/16 – 8/31/2020
1U2CAG054397-01
ORATECH Collaborative Aging (in Place) Research Using Technology CART
NIH/NIA
The CART program will develop and validate an infrastructure for rapid and effective conduct of research utilizing technology to facility aging in the place. The 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 declines and transitions leading to greater dependency. The project will be focusing on the oldest-old with chronic disease, veterans living in rural communities, minorities and social isolated seniors of low income.

Czaja, S.J. (PI) 9/1/16 – 4/30/2021
1 RO1 AG0504077-01
Augmenting Cognitive Training in Older Adults – the ACT Grant
NIH/NIA
This is a randomized clinical trial 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 will also examine the influence of other clinical and demographic factors (e.g., gender) on neurocognitive, functional, and neuroimaging outcomes.

Czaja, S.J. (PI), Loewenstein, D., (Co-Investigator) 9/1/2016-4/30/2021
1 RO1 AG054009-01
NIH/NIA
A non-pharmacological intervention for patients with Alzheimer's disease and family caregivers
The proposed study is extremely relevant to public health concerns. The prevalence of individuals with AD and family caregivers is projected to increase in the upcoming decades. To address this pressing issue, the focus of the proposed study is to evaluate the acceptability and efficacy of an innovative intervention program, delivered through state-of-the art computer tablet technology that targets both ethnically/culturally diverse family caregivers of patients with Alzheimer's Disease (AD) and AD patients. The program augments an evidenced-based caregiver intervention with an evidenced-based cognitive/functional training intervention for the patient. The overall goals of the project are to improve the lives of family caregivers; the ability of caregivers to provide care to their loved ones; to improve the lives of individuals with AD; and to reduce disparities in access to needed services and support among caregiver and patient populations.

Czaja, S.J., Pirolli, P., (PI's) 9/1/2016-4/30/2021
1 RO1 AG053163-01
NIH
A Personalized Health Behavior System to Promote Health and Well-Being in Older Adults.
This proposed project is addressing a critical public concern. The population is aging and chronic conditions such as hypertension, diabetes and obesity are common among older adults especially ethnic minorities. This study will develop and evaluate a mobile technology-based intervention designed to support positive health

behavior change among diverse older adults through integrated online social support, personalized coaching and goal setting.

Czaja, S. J., PI 3/1/15-2/29/20
NIA/NIH
Center for Research and Education for Aging and Technology Enhancement (CREATE IV)
This application is a request for continued support for the Center for Research and Education on Aging and Technology Enhancement (CREATE), an established multidisciplinary, Cohesive Center that focuses on aging and technology. CREATE's goal is to ensure that older adults are able to use and realize the benefits of technology. Our objectives are to: develop a database on user preferences, needs, and problems with emerging and existing systems; assess the efficacy of design solutions; gather information on the value of technology; promote new research; support new investigators; and disseminate outcomes to a broad community

1R01NR014434-01 (Czaja, S.J.) 4/1/13-3/31/18
NINR/NIH
Title: **A Tailored Technology Intervention for Diverse Family Caregivers of AD Patients**".
The aims of this project are to evaluate the acceptability and efficacy of a culturally tailored technology-based psychosocial intervention for reducing the stress and burden and enhancing quality of life of diverse family caregivers of AD patients. The intervention is designed to address known areas of caregiver risk and to foster the ability of caregivers to leverage the type of supports they need for themselves and the AD patient. The target population is Black/African American, Hispanic, and White non-Hispanic family caregivers of AD patients.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Kunjan R. Dave

eRA COMMONS USER NAME (credential, e.g., agency login): krdave

POSITION TITLE: Research Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Gujarat University, Ahmedabad, India	B.Sc.	12 / 1993	Biochemistry
The M. S. University of Baroda, Vadodara, India	M.Sc.	12 / 1995	Biochemistry
The M. S. University of Baroda, Vadodara, India	Ph.D.	06 / 2000	Biochemistry
University of Miami School of Medicine, Miami	Post-doc	05 / 2003	Neurology

A. Personal Statement

I completed my training in the field of cerebral ischemia at the Cerebral Vascular Disease Research Center (CVDRC), University of Miami Miller School of Medicine. Since joining CVDRC I have participated in several projects studying different aspects of cerebral ischemia. Presently, my laboratory works on research projects with ultimate goal of lowering the incidence and severity of cerebral ischemia. One of the projects is focused on improving neurological health of diabetics by decreasing the severity and incidence of cerebral ischemia in diabetics as cerebral ischemia and heart disease are the most serious complications of diabetes, accounting for more than 84% of the mortality among diabetics. This project is supported by an R01 grant. Another project in my lab evaluates a strategy to lower hematoma growth following intracerebral hemorrhage.

B. Positions and Honors

Professional experience:

- Associate Director (2014 – present), Cerebral Vascular Disease Research Laboratories, Department of Neurology, University of Miami Miller School of Medicine, Miami, FL.
- Affiliate faculty Neuroscience Graduate Program (2014 – present), University of Miami Miller School of Medicine, Miami, FL.
- Research Associate Professor (2013 – present) Department of Neurology, University of Miami Miller School of Medicine, Miami, FL.
- Research Assistant Professor (2006 - 2013) Department of Neurology, University of Miami Miller School of Medicine, Miami, FL.
- Assistant Scientist (2003 - 2006) Department of Neurology, University of Miami Miller School of Medicine, Miami, FL.
- Biochemist (September, 1999 – February, 2000) Pharmacology Division, Research and Development, The Zandu Pharmaceutical works, Mumbai (Bombay), India.

Scholarship / Award:

- Stanley J. Glaser Foundation biomedical research award, University of Miami Miller School of Medicine 2007 - 2008.
- Recipient of award of Bursaries for young scientists to attend Brain'05 conference (Amsterdam, The Netherlands, June 2005) organized by the International Society for Cerebral Blood Flow and Metabolism.

- Received “Hari Ohm Ashram Prerit Shri Bhaikaka Inter-University Smarak Trust” Award, Sardar Patel University, Vallabh Vidyanagar, Gujarat, India for two research papers in year 1999-2000.
- Recipient of award of The Lady Tata Memorial Trust Research Scholarship, Mumbai (Bombay), India for years 1996-98.
- Recipient of Scholarship from Higher Education Commissioner, Government of Gujarat, India for year 1996.

Membership in Professional Societies:

- Society for Neurosciences
- International Society for Cerebral Blood Flow and Metabolism
- American Heart Association

Role as a reviewer:

- AHA Brain 5 Study section Spring 2013, Spring 2014, Spring 2015
- AHA Brain 1 study section Fall 2013
- Bando Giovani Ricercatori “Alessandro Liberati” 2013 (Italian funding agency)
- Abstract reviewer, International Stroke Conference 2014, 2015, 2016
- AHA Innovative Research Grant Study section Fall 2014, Fall 2015, Fall 2016
- Croatian Science Foundation 2014
- Abstract reviewer Brain 2015, Brain 2017 (International symposium on Cerebral blood flow, metabolism and function)
- AHA Cardiac Arrest Resuscitation Basic Study section; Spring 2015, Spring 2016
- AHA Cardiac Arrest Resus CL/Pop Merge with Basic Science Study section; Fall 2015
- AHA scientific sessions abstracts June 2016
- NIH- Acute Neural Injury and Epilepsy Study Section (ANIE) 6/2015, 10/2015, 2/2016, 6/2016, 10/2016, 2/2017
- AHA Brain 3 Study section Spring 2016, Fall 2016, Spring 2017
- Co-Chair AHA Brain 3 Study section Spring 2017

C. Contribution to Science

1. Cerebral ischemia and heart disease are the most serious complications of diabetes, accounting for more than 84% of the mortality among diabetics. Epidemiological studies of cerebral ischemia suggest that diabetes increases both the risk of incidence and exacerbates the consequences of cerebral ischemia. Hyperglycemia is one of the contributing factors. In clinical studies, intensive anti-diabetic therapy was able to delay the onset and slow the progression of secondary complications of diabetes. The major side-effect of intensive diabetic therapy is hypoglycemia. Using the streptozotocin-diabetic rat, we observed that recurrent hypoglycemia (RH) renders the insulin-treated diabetic (ITD) rat brain more sensitive to global cerebral ischemia and results in greater brain damage. Presently, we are investigating the mechanism by which RH increases ischemic damage in ITD.
   a. Dave K. R., Pileggi A., Raval A. P. Recurrent hypoglycemia increases oxygen glucose deprivation-induced damage in hippocampal organotypic slices. Neurosci Lett. 496:25-9, 2011.
   b. Dave K. R., Tamariz J, Desai KM, Brand FJ, Liu A, Saul I, Bhattacharya SK, Pileggi A. Recurrent hypoglycemia exacerbates cerebral ischemic damage in streptozotocin-induced diabetic rats. Stroke. 42:1404-11, 2011.
   c. Rehni A. K., Nautiyal N., Perez-Pinzon M. A., Dave K.R. Hyperglycemia / hypoglycemia-induced mitochondrial dysfunction and cerebral ischemic damage in diabetics. Metab Brain Dis. 2014 (In press)

2. Ischemic tolerance in brain develops when a sublethal ischemic insult occurs before a period of "lethal" cerebral ischemia. While working at Dr. Perez-Pinzon’s laboratory, I participated in studies aimed to determine mechanisms of ischemia tolerance induced by cerebral ischemia and pharmacological preconditioning.
   a. Della-Morte D., Dave K. R., Defazio R. A., Bao Y. C., Raval A. P., Perez-Pinzon M. A. Resveratrol pretreatment protects rat brain from cerebral ischemic damage via a sirtuin 1 - uncoupling protein 2 pathway. Neuroscience. 159:993-1002, 2009.
   b. Dave K. R., DeFazio R. A., Raval A. P., Torraco A., Saul I., Barrientos A., Perez-Pinzon M. A. Ischemic preconditioning targets the respiration of synaptic mitochondria via protein kinase C epsilon. J Neurosci. 28:4172-82, 2008.

c. *Raval A. P., Dave K. R., Perez-Pinzon M. A. Resveratrol mimics ischemic preconditioning in the brain, J Cereb Blood Flow Metab, 26:1141-7, 2006.
d. *Dave K. R., Lange-Asschenfeldt C., Raval A. P., Prado R., Busto R., Saul I., Perez-Pinzon M. A. Ischemic preconditioning ameliorates excitotoxicity by shifting glutamate/gamma-aminobutyric acid release and biosynthesis, J Neurosci Res., 82:665-673, 2005.

3. Cardiopulmonary arrest remains one of the leading causes of death and disability in the U.S.A. Cardiac arrest with its consequent disruption of blood flow sets in motion a cascade of cellular and systemic derangements that result in selective brain damage. I participated in project aimed to determine the mechanism of neuronal death following cardiac arrest-induced cerebral ischemia.
   a. Lin H. W., Gresia V. L., Stradecki H. M., Alekseyenko A., Dezfulian C., Neumann J. T., Dave K. R., Perez-Pinzon M. A. Protein kinase C delta modulates endothelial nitric oxide synthase after cardiac arrest. J Cereb Blood Flow Metab. 2014, 34:613-20.
   b. Dave K. R., Della-Morte D., Saul I., Prado R., Perez-Pinzon M. A. Ventricular fibrillation-induced cardiac arrest in the rat as a model of global cerebral ischemia. Transl Stroke Res. 2013, 4:571-8.
   c. Dave K. R., Bhattacharya S. K., Saul I., DeFazio R. A., Dezfulian C., Lin H. W., Raval A. P., Perez-Pinzon M. A. Activation of protein kinase C delta following cerebral ischemia leads to release of cytochrome C from the mitochondria via bad pathway. PLoS One. 6:e22057, 2011.
   d. Raval A. P., Dave K. R., Prado R., Katz L. M., Busto R., Sick T. J., Ginsberg M. D., Mochly-Rosen D., Perez-Pinzon M. A. Protein kinase C delta cleavage initiates an aberrant signal transduction pathway after cardiac arrest and oxygen glucose deprivation, J Cereb Blood Flow Metab, 25:730-741, 2005.

4. Amyotrophic lateral sclerosis (ALS) is a devastating disease, which results in degeneration of both upper and lower motor neurons of the brain, brain stem and spinal cord. The cause of most types of ALS remains uncertain, and the disease is incurable. I participated in projects aimed to determine mechanisms of cell death in mouse models of motor neuron disease.
   a. Dave K. R., Raval A. P., Purroy J., Kirkinezos I. G., Moraes C. T., Bradley W. G., Perez-Pinzon M. A. Aberrant delta PKC activation in the spinal cord of Wobbler mouse: a model of motor neuron disease. Neurobiol Dis, 18:126-133, 2005.
   b. Dave K. R., Bradley W. G., Perez-Pinzon M. A. Early mitochondrial dysfunction occurs in motor cortex and spinal cord at the onset of disease in the Wobbler mouse. Experimental Neurology, 182:412-420, 2003.
   c. Dave K. R., Prado R., Busto R., Raval A. P., Bradley W. G., Torbati D., Perez-Pinzon M. A. Hyperbaric oxygen therapy protects against mitochondrial dysfunction and delays onset of motor neuron disease in the wobbler mice. Neuroscience, 120:113-20, 2003.
   d. Xu, G-P, Dave K. R., Moraes C. T., Busto R., Sick T. J., Bradley W. G., Perez-Pinzon M. A. Dysfunctional mitochondrial respiration in the Wobbler mouse brain. Neuroscience Letters, 300:141-144, 2001.

5. Arctic ground squirrels (AGS; Spermophilus parryii) is a species of heterothermic mammals; i.e., a species that hibernates. Hibernating creatures experience fluctuating metabolic rates and body temperatures as they cycle into and out of periods of prolonged torpor. One of the main reasons for their ischemia tolerance during hibernation is hypothermia. However, during euthermia several ischemia tolerance pathways are active in AGS. In an experiment aimed to determine if AGS tolerate cerebral ischemia during euthermia, we demonstrated that AGS can be readily resuscitated from prolonged cardiac arrest (CA) without evidence of neuropathology. Tolerance to global cerebral ischemia was observed even when animals were not hibernating and when brain temperature was maintained at 37 °C. In another study we observed that epsilon PKC activation delays the collapse of ion homeostasis during ischemia in AGS but not rat.
   a. Dave K. R., Christian S. L., Perez-Pinzon M. A., Drew K. L. Neuroprotection: lessons from hibernators. Comp Biochem Physiol B Biochem Mol Biol. 162:1-9, 2012.
   b. Dave K. R., Defazio R. A, Raval A. P., Dashkin O., Saul I., Iceman K. E., Perez-Pinzon M.A., Drew K.L. Protein kinase C epsilon activation delays neuronal depolarization during cardiac arrest in the euthermic arctic ground squirrel. J Neurochem. 110:1170-9, 2009.
   c. Dave K. R., Prado R., Raval A. P., Drew K. L., Perez-Pinzon M. A. The arctic ground squirrel brain is resistant to injury from cardiac arrest during euthermia, Stroke, 37:1261-1265, 2006.

Complete List of Published Work in PubMed:

https://www.ncbi.nlm.nih.gov/sites/myncbi/kunjan.dave.1/bibliography/44169146/public/?sort=date&direction=ascending

D. Research Support

1R01NS073779 Dr. Dave, P.I. 3/1/2012 – 12/31/2017 (no cost extension)
NIH/NINDS
Increased cerebral ischemic injury by repeated hypoglycemic episodes in diabetes.
The major goal of this project is to determine the mechanism by which repeated hypoglycemic episodes increases cerebral ischemic injury in diabetics.
Role: Principal Investigator

American Stroke Association-Bugher Foundation Centers for Excellence in Stroke Collaborative Research for Regeneration, Resilience and Secondary Prevention, Ralph S. Sacco (PI): Project 2: Enriched Environment, Exercise and Neurotherapeutics to Enhance Functional Recovery Following Stroke. Project PI: Dr. Perez-Pinzon
4/1/2014 – 3/31/2018 Role: co-investigator project 2

2R01NS034773 Dr. Perez-Pinzon, P.I. 6/1/2015 – 5/31/2020
NIH/NINDS
Ischemic preconditioning: mechanisms of neuroprotection.
The major goals of this project are to define the specific molecular targets of resveratrol preconditioning that promote ischemic tolerance and to further define the molecular mechanisms of a chronic ischemic tolerant state.
Role: co-investigator

R01NS097658 Dr. Perez-Pinzon, P.I. 7/15/2017 – 4/30/2022
NIH/NINDS
Metabolic master regulators for ischemic neuroprotection.
The major goals of this project are to elucidate the mechanisms by which PKCepsilon alters NAD levels in the brain and define its downstream pathways that enhance ischemic tolerance.
Role: co-investigator

R21NS094896 (IGNITE mechanism) Dr. Dave, P.I. R21 phase: 2/1/2016 – 1/31/2017
R33 phase: 2/1/2017 – 1/31/2019
NIH/NINDS (R33 phase will depend on results of R21 phase)
Red blood cell microparticles (RMPs) to reduce bleeding following hemorrhagic stroke.
The major goal of this project is to lower hematoma growth following intracerebral hemorrhage using RMPs.
Role: Principal Investigator

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: David Della-Morte

eRA COMMONS USER NAME (credential, e.g., agency login): ddellamorte

POSITION TITLE: Associate Professor of Neurology, University of Miami Miller School of Medicine

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Medical School University of Naples, Italy	MD	1996-2002	Medicine
Medical School University of Naples, Italy	Residency	2003-2006	Internal Medicine/ Geriatrics
Medical School University of Naples, Italy	Ph.D.	2006-2010	Neuroscience
Miller School of Medicine, University of Miami, Miami, FL, U.S.A.	Fellowship	2006-2009	Neuroscience

A. Positions and Honors

Positions and Employment

2003-05	Emergency Service	Clinical Thermal Center, Fiuggi, Italy.
2003-06	Chief of Residents	Dept. of Internal Medicine, University of Naples, Italy.
2006-09	Postdoctoral Associate	Miller School of Medicine, Univ. of Miami, Miami, FL
2009-16	Assistant Professor of Neurology	Miller School of Medicine, Univ. of Miami, Miami, FL
2010-	Director of Center of Research of Physiopathology of Aging	IRCCS, San Raffaele Pisana, Rome, Italy
2013-	Assistant Professor of Internal Medicine	Dept. of Systems Medicine, University of Rome, Italy
2014-	Qualification as Associate Professor	Italian National Scientific Council
2016-	Associate Professor of Neurology	Miller School of Medicine, Univ. of Miami, Miami, FL

Honors

2003- Awarded for the best research and scientific contribute to the 48° National Congress of Italian Geriatric Society; Florence, Italy.

2007- Awarded American Heart Association (AHA identification number - 0625318B) Percentile rank: 7.53 (considered excellent).

2008- Awarded with Travel Grant for the best abstract presented at International Symposium, University of Miami, FL, USA.

2008- Ad hoc reviewer of several peer reviewed international journals such as: *Stroke, Circulation and Neurology.*

2010- Editorial Board Member of *Cardiovascular Pharmacology, International Journal of Cardiology and Research, International Journal of Diabetology & Vascular Disease Research, Cell R4, Clinical & Experimental Cardiology, Journal of Neurology and Neurophysiology, Journal of Trauma & Treatment, Alzheimer's Disease and Related Dementia, Journal of Novel Physiotherapies.*

2012- Member of Health Research Board (HRB), National Health Institute of Ireland: ad hoc reviewer for Health Research Awards.

2012- Member of American Association for the Advancement of Science (AAAS), European Association for the Study of Diabetes (EASD).

2014- US O1 VISA for Extraordinary Ability in Science.

2014- Committee Member - Thesis in Master in Diabetes and its Management, School of Medicine, University of Rome Tor Vergata, Rome, Italy.
2015- Co-Editor in Chief of Clinical Immunology, Endocrine & Metabolic Drugs.
2015- Committee Member - Test for Admission at School of Medicine, School of Medicine University of Rome Tor Vergata, Rome, Italy.
2016- Coordinator of the Internal Medicine Course, Faculty of Dentistry, School of Medicine, University of Rome Tor Vergata, Rome, Italy.

B. Contribution to Science

1. Genetic contribution to atherosclerosis and stroke. My focus was to investigate the association between genetics and subclinical phenotypes of atherosclerosis, such as carotid plaque and carotid intima media thickness, in the risk for vascular diseases. In the past 8 years by using Northern Manhattan Study (NOMAS) and Family Study as Collaborator of Drs. Sacco and Rundek (PIs of NOMAS), I studied the interaction of genetics with vascular risk factors in determining the risk for stroke. These researches yielded novel findings regarding variation in stroke predisposition among different race-ethnicities.
   a. **Della-Morte D**, Beecham A, Rundek T, Slifer S, Boden-Albala B, McClendon MS, Blanton SH, Sacco RL. Genetic linkage of serum homocysteine in Dominican families: the Family Study of Stroke Risk and Carotid Atherosclerosis. Stroke. 2010 Jul;41(7):1356-62. PMCID: PMC2914470
   b. **Della-Morte D**, Beecham A, Rundek T, Wang L, McClendon MS, Slifer S, Blanton SH, Di Tullio MR, Sacco RL. A follow-up study for left ventricular mass on chromosome 12p11 identifies potential candidate genes. BMC Med Genet. 2011 Jul 26;12:100. PMCID: PMC3199748
   c. **Della-Morte D**, Beecham A, Dong C, Wang L, McClendon MS, Gardener H, Blanton SH, Sacco RL, Rundek T. Association between variations in coagulation system genes and carotid plaque. J Neurol Sci. 2012 Dec 15;323(1-2):93-8. PMCID: PMC3483411
   d. **Della-Morte D**, Wang L, Beecham A, Blanton SH, Zhao H, Sacco RL, Rundek T, Dong C. Novel genetic variants modify the effect of smoking on carotid plaque burden in Hispanics. J Neurol Sci. 2014 Sep 15;344(1-2):27-31. PMCID: PMC4143440

2. Epidemiology of vascular risk factors, subclinical phenotypes of atherosclerosis, and cardiovascular disease. Since the beginning of my medical and scientific career, I have started to investigate the role of vascular risk factors, including diabetes, hypertension, dyslipidemia, homocysteine in the mechanisms leading to atherosclerosis and then cardiovascular diseases, especially in aged population. We conducted several epidemiological studies where we strongly reported different prevalence of these vascular risk factors among Hispanics, blacks and white. We were also the first to suggest a revision of the AHA guideline concerning treatment for hypertension in elderly Hispanics. In this field, I maintained international collaborations, particularly with Italian research teams involved in studying cardiovascular disease and aging.
   a. **Della-Morte D**, Moussa I, Elkind MS, Sacco RL, Rundek T. The short-term effect of atorvastatin on carotid plaque morphology assessed by computer-assisted gray-scale densitometry: a pilot study. Neurol Res. 2011 Nov;33(9):991-4. PMCID: PMC3233227
   b. Testa G, **Della-Morte D**, Cacciatore F, Gargiulo G, D'Ambrosio D, Galizia G, Langellotto A, Abete P. Precipitating factors in younger and older adults with decompensated chronic heart failure: are they different? J Am Geriatr Soc. 2013 Oct;61(10):1827-8. PMID: 24117301
   c. Dong C, **Della-Morte D**, Rundek T, Wright CB, Elkind MS, Sacco RL. Evidence to Maintain the Systolic Blood Pressure Treatment Threshold at 140 mm Hg for Stroke Prevention: The Northern Manhattan Study. Hypertension. 2016 Mar;67(3):520-6. PMCID: PMC4752407
   d. Rundek T, **Della-Morte D**, Gardener H, Dong C, Markert MS, Gutierrez J, Roberts E, Elkind MSV, DeCarli C, Sacco RL, Wright CB. Relationship between carotid arterial properties and cerebral white matter hyperintensities. Neurology. 2017 May 23;88(21):2036-2042. PMCID: PMC5440241

3. Role of cerebral ischemic precondition (IPC) as endogenous mechanism of protection against cerebral and cardiac ischemia. Our studies, since 2005, were among the first demonstrating the reduction of the protective effect of IPC in aged animals and in elderly subjects compared with young control at both cardiac and cerebral levels. With research in this field, by using experimental *in vivo* and *in vitro* models, we showed novel pathways of neuroprotection IPC-mediated. We also demonstrated that IPC protection was induced by resveratrol administration and was mediated by Sirtuin-1 and Uncoupling-2 activation pathway. Through these researches I received the AHA fellowship award.

a. **Della Morte D**, Abete P, Gallucci F, Scaglione A, D'Ambrosio D, Gargiulo G, De Rosa G, Dave KR, Lin HW, Cacciatore F, Mazzella F, Uomo G, Rundek T, Perez-Pinzon MA, Rengo F. Transient ischemic attack before nonlacunar ischemic stroke in the elderly. J Stroke Cerebrovasc Dis. 2008 Sep;17(5):257-62. PMCID: PMC2676578
b. **Della-Morte D**, Dave KR, DeFazio RA, Bao YC, Raval AP, Perez-Pinzon MA. Resveratrol pretreatment protects rat brain from cerebral ischemic damage via a sirtuin 1-uncoupling protein 2 pathway. Neuroscience. 2009 Mar 31;159(3):993-1002. PMCID: PMC2668125
c. **Della-Morte D**, Raval AP, Dave KR, Lin HW, Perez-Pinzon MA. Post-ischemic activation of protein kinase C ε protects the hippocampus from cerebral ischemic injury via alterations in cerebral blood flow. Neurosci Lett. 2011 Jan 7;487(2):158-62. PMCID: PMC3004991
d. Koch S, **Della-Morte D**, Dave KR, Sacco RL, Perez-Pinzon MA. Biomarkers for ischemic preconditioning: finding the responders. J Cereb Blood Flow Metab. 2014 Jun;34(6):933-41. PMCID: PMC4050240

4. <u>Experimental studies on the effect of antioxidant proteins against vascular risk factors and atherosclerosis.</u> In the recent years, we focused our research in specific proteins such as Serum and Glucocorticoid-Inducible Kinase (SGK)-1, which have been demonstrated to have powerful antioxidant effects. By using *in vitro* models of endothelial and coronary cells we demonstrated as SGK-1, when activated is able to protect the vessel against hyperglycemia and pro-oxidant stimuli. However, more important, we were the first showing a direct effect of SGK-1 on the length of the telomeres, and therefore its capacity in delay endothelial senescence. These researches yielded a grant of $400k from Fondazione Roma (Italy). We are continuing these studies in animal models and we are investigating the association between genetic variants of SGK-1 and atherosclerosis in NOMAS with promising results.
   a. Ferrelli F, Pastore D, Capuani B, Lombardo MF, Blot-Chabaud M, Coppola A, Basello K, Galli A, Donadel G, Romano M, Caratelli S, Pacifici F, Arriga R, Di Daniele N, Sbraccia P, Sconocchia G, Bellia A, Tesauro M, Federici M, **Della-Morte D**, Lauro D. Serum glucocorticoid inducible kinase (SGK)-1 protects endothelial cells against oxidative stress and apoptosis induced by hyperglycaemia. Acta Diabetol. 2015 Feb;52(1):55-64. PMID: 24961472
   b. Basello K, Pacifici F, Capuani B, Pastore D, Lombardo M, Ferrelli F, Coppola A, Donadel G, Arriga R, Sconocchia G, Bellia A, Rogliani P, Federici M, Sbraccia P, Lauro D, **Della-Morte D**. Serum- and Glucocorticoid-Inducible Kinase (SGK)1 delay the onset of Endothelial Senescence by Directly Interacting with hTERT. Rejuvenation Res. 2016 Feb;19(1):79-89. PMID: 26230157
   c. Lauro D, Pastore D, Capuani B, Pacifici F, Palmirotta R, Abete P, Roselli M, Bellia A, Federici M, Di Daniele N, Sbraccia P, Guadagni F, Lauro R, **Della-Morte D**. Role of Serum and Glucocorticoid-Inducible Kinase (SGK)-1 in Senescence: a Novel Molecular Target against Age-Related Diseases. Curr Med Chem. 2015;22(33):3765-88. PMID: 26264924
   d. Pastore D, **Della-Morte D**, Coppola A, Capuani B, Lombardo MF, Pacifici F, Ferrelli F, Arriga R, Mammi C, Federici M, Bellia A, Di Daniele N, Tesauro M, Donadel G, Noto D, Sbraccia P, Sconocchia G, Lauro D. SGK-1 protects kidney cells against apoptosis induced by ceramide and TNF-α. Cell Death Dis. 2015 Sep 17;6:e1890. PMCID: PMC4650437

Complete List of Published Work in MyBibliography: https://www.ncbi.nlm.nih.gov/pubmed/?term=della+morte+d

C. Additional Information: Research Support and/or Scholastic Performance

<u>Ongoing Research Support</u>

NIH/NINDS R01 NS 40807 Rundek, Sacco (Multi-PI) 05/01/02-09/30/17
Family Study of Stroke Risk and Carotid Atherosclerosis
The major goal of this study is to evaluate heritability and genetic linkage of novel vascular risk factors such as carotid intima-media thickness among the families of high-risk Caribbean Hispanics.
Role: Co-I

ARISTA - USA Protocol ID# CV185--564 Rundek (PI) 01/01/17-12/31/19
Disparities in Stroke Outcomes and Care Delivery in Patients with Atrial Fibrillation: FLiPER AF Florida Puerto Rico Atrial Fibrillation Stroke Study
The major goal of this study is to evaluate the effect of Atrial Fibrillation on ischemic stroke/TIA outcomes overall, and by sex and race/ethnicity.
Role: Co-PI

Rome Foundation Pontecorvi (PI) 01/01/15-12/31/17
Diabetes and sarcopenia in the elderly; age-associated inflammation as a shared pathogenic mechanism and Potential therapeutical target
The major goal of this study is to evaluate the antioxidant protein such as Peroxiredoxin6 in the mechanism linked with diabetes and muscle mass deterioration in aging population.
Role: Co-PI

Prior Research Support

American Heart Association AHA 0625318B Della-Morte (PI) 05/07/07-05/30/09
Potential mechanism by which resveratrol mimics cerebral ischemic preconditioning
This is an study to investigate the potential role of polyphenols in neuroprotection against cerebral ischemia by the capacity to mimic the endogenous mechanism of protection called ischemic preconditioning.
Role: PI

NIH/NINDS R01 NS 40807 Rundek, Sacco (Multi-PI) 05/01/02-09/30/17
Family Study of Stroke Risk and Carotid Atherosclerosis
The major goal of this study is to evaluate heritability and genetic linkage of novel vascular risk factors such as carotid intima-media thickness among the families of high-risk Caribbean Hispanics.
Role: Co-I

NIH/NINDS R01 NS 065114 Rundek (PI) 07/01/10-06/30/16
Novel Factors for Unexplained Phenotypes of Subclinical Carotid Atherosclerosis
This is a selective genotype study of the extreme phenotypes of subclinical atherosclerosis among individuals with high burden of atherosclerosis and no risk factors (RF) and high burden of RF but no atherosclerosis.
Role: Co-I

NIH/NINDS K24 NS 062737 Rundek (PI) 09/30/09-08/31/16
Genetic Determinants of Extreme Phenotypes of Subclinical Atherosclerosis
This is an award to train young investigators in patient-oriented research, perform research on genetic factors of extreme phenotypes of subclinical atherosclerosis, and enhance career development in genetic epidemiology.
Role: Co-I

UM/SAC 2014-3R2 Pilot Award Bianchi (PI) 01/01/15-12/31/15
Role of Sirtuins in Neurodegeneration
This is an award aimed to generate preliminary data for NIH Grant on the role of Sirtuins in Neurodegeneration by using a unique model of cerebral damage in *C. elegans*.
Role: Co-PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Chuanhui Dong

eRA COMMONS USER NAME (credential, e.g., agency login): CHDONG07

POSITION TITLE: Research Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Tongji Medical University, Wuhan, China	M.D.	07/1984	Preventive Medicine
Hubei Medical University, Wuhan, China	M.A.	06/1989	Epidemiology
Shanghai Medical University, Shanghai, China	Ph.D.	07/1998	Molecular Epidemiology
Karolinska Institute, Stockholm, Sweden	Post-Doc	12/2000	Genetic Epidemiology
University of Pennsylvania, Philadelphia	Post-Doc	10/2003	Statistical Genetics

A. Personal Statement

I am a biostatistician and research associate professor in the Department of Neurology at the University of Miami. Over 10 years, my research interest has been focused on investigation of independent and interactive effects of social-demographic, environmental, behavioral, metabolic and genetic factors on the risk of complex diseases such as cognition impairment, depression, subclinical and clinical cardiovascular diseases, and efficacy of drug treatment in animal models and clinical trials. With the successful collaboration with many researchers, I have published over 100 peer-reviewed research articles.

1. Wright, C.B., **Dong, C.,** Caunca, M.R., DeRosa, J., Cheung, Y., Rundek, T., Elkind, M.S., DeCarli, C., Sacco, R.L. (2017). MRI Markers Predict Cognitive Decline Assessed by Telephone Interview: The Northern Manhattan Study. Alzheimer disease and associated disorders. 31(1):34-40.

2. Sun, X., **Dong, C.,** Levin, B., Crocco, E., Loewenstein, D., Zetterberg, H., Blennow, K., Wright, C.B. (2016). APOE ε4 carriers may undergo synaptic damage conferring risk of Alzheimer's disease. Alzheimers & Dementia 12(11):1159-1166.

3. **Dong. C.,** Della-Morte, D., Rundek, T., Wright, C.B., Elkind, M.S., Sacco, R.L. (2016) Evidence to Maintain the Systolic Blood Pressure Treatment Threshold at 140 mm Hg for Stroke Prevention: The Northern Manhattan Study. Hypertension 67(3):520-6.

4. **Dong C,** Zadeh N, Caunca MR, Cheung Y, Rundek T, Elkind MSV, DeCarli C, Sacco RL, Stern Y, Wright CB (2015). Cognitive correlates of white matter lesion load and brain atrophy: The Northern Manhattan Study. Neurology 85(5):441-9.

B. Positions

Positions and Employment

1998-2000 Research Fellow, Epidemiology, Dept. of Biosciences, Karolinska Institute, Stockholm, Sweden
2001-2003 Postdoctoral Researcher, Statistical Genetics, Dept. of Psychiatry, University of Pennsylvania, PA
2003-2006 Research Associate, Statistical Genetics, Dept. of Psychiatry, University of Pennsylvania, PA
2006-2007 Research Biostatistician, Clinical Research, American College of Radiology, PA
2007-2009 Research Assistant Professor, Dept. of Psychiatry & Behavioral Sci., University of Miami, FL
2009-2014 Research Assistant Professor, Dept. of Neurology, University of Miami, FL
2014- Research Associate Professor, Dept. of Neurology, University of Miami, FL

Professional Memberships

2012- Member, American Heart Association
2002- Member, American Association of Human Genetics
2008- Member, International Genetic Epidemiology Society
2008- Member, American Statistical Association
2002-2006 Member, International Epidemiological Association

C. Contribution to Science

1. In the collaboration with clinicians, one of my major research activities was to evaluate the cognitive correlates in population-base cohort. As a statistician, I served as the analyst in several projects.

    a. Glazer, H., **Dong, C.,** Yoshita, M., Rundek, T., Elkind, M.S.V., Sacco, R.L., DeCarli, C., Stern, Y., Wright, C.B. (2015) Subclinical cerebrovascular disease inversely associates with learning ability: The NOMAS Study. Neurology 84(23):2362-2367

    b. Wright, C.B., Gardener, H., **Dong, C.,** Yoshita, M., DeCarli, C., Sacco, R.L., Stern, Y., Elkind, M.S.V. (2015). Infectious Burden and Cognitive Decline in the Northern Manhattan Study. Journal of the American Geriatrics Society 63(8):1540-5

    c. Levin, B.E., Llabre, M.M., **Dong, C.,** Elkind, M.S., Stern, Y., Rundek, T., Sacco, R.L., and Wright, C.B. (2014). Modeling metabolic syndrome and its association with cognition: the northern Manhattan study. Journal of the International Neuropsychological Society 20, 951-960.

    d. Ramos, A.R., **Dong, C.,** Elkind, M.S., Boden-Albala, B., Sacco, R.L., Rundek, T., and Wright, C.B. (2013). Association between sleep duration and the mini-mental score: the Northern Manhattan study. Journal of Clinical Sleep Medicine 9, 669-673.

2. As a collaborator, I served as the statistician to evaluate the response of various medications in clinical studies and examined the factors influencing response of treatments.

    a. Wong ML, **Dong C,** Flores DL, Ehrhart-Bornstein M, Bornstein S, Arcos-Burgos M, and Licinio J (2014). Clinical Outcomes and Genome-Wide Association for a Brain Methylation Site in an Antidepressant Pharmacogenetics Study in Mexican Americans. The American Journal of Psychiatry 171, 1297-1309. PMID: 25220861

    b. Waldrop-Valverde, D, **Dong C,** and Ownby RL (2013). Medication-taking self-efficacy and medication adherence among HIV-infected cocaine users. The Journal of the Association of Nurses in AIDS Care 24, 198-206.

    c. Yavagal DR, Lin B, Raval AP, Garza PS, **Dong C,** Zhao W, Rangel EB, McNiece I, Rundek T, Sacco RL, et al. (2014). Efficacy and dose-dependent safety of intra-arterial delivery of mesenchymal stem cells in a rodent stroke model. PloS One 9, e93735.

d. **Dong C,** Wong ML, Licinio J (2009). Sequence variations of ABCB1, SLC6A2, SLC6A3, SLC6A4, CREB1, CRHR1 and NTRK2: association with major depression and antidepressant response in Mexican-Americans. Mol Psychiatry, 14(12):1105-1118. PMID: 19844206

3. In population-based and clinical studies, I took a lead in many data analyses to identify the factors influencing the subclinical and clinical outcomes.

   a. Wright CB, **Dong C**, Perez EJ, De Rosa J, Yoshita M, Rundek T, DeCarli C, Gutierrez J, Elkind MSV, Sacco RL. (2017) Subclinical Cerebrovascular Disease Increases the Risk of Incident Stroke and Mortality: The Northern Manhattan Study. Journal of the American Heart Association. 6(9).

   b. Rundek T, Della-Morte D, Gardener H, **Dong C**, Markert MS, Gutierrez J, Roberts E, Elkind MSV, DeCarli C, Sacco RL, Wright CB. (2017) Relationship between carotid arterial properties and cerebral white matter hyperintensities. Neurology. 88(21):2036-2042.

   c. Nirav, S., **Dong, C.,** Elkind, M.S., Sacco, R.L., Mendez, A., Barry, H., Silverberg, S., Wolf, M., Rundek, T., and Wright, C.B., (2015). Fibroblast Growth Factor 23 is associated with Carotid Plaque Presence and Area: the Northern Manhattan Study. Arteriosclerosis, Thrombosis, and Vascular Biology 35(9):2048-53

   d. **Dong C,** Rundek T, Wright CB, Anwar Z, Elkind MS, and Sacco RL (2012). Ideal cardiovascular health predicts lower risks of myocardial infarction, stroke, and vascular death across whites, blacks, and hispanics: the northern Manhattan study. Circulation 125, 2975-2984.

Complete List of Published Work in MyBibliography:

https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/42015963/?sort=date&direction=descending

D. Research Support

Ongoing Research Support

R01 MD012467 Ralph Sacco (PI) 09/17-06/22
Disparities in Transition of Care after Acute Stroke Hospitalization
To identify race-ethnic and sex disparities in hospital-to-home transition of stroke care and outcomes, social determinants of health associated with these disparities, and to develop effective hospital-initiated system level initiatives to reduce disparities and readmissions, and to improve stroke outcomes.
Role: Statistician

R01 NS 29993 Ralph Sacco (PI) 02/03-07/20
Stroke Incidence and Risk Factors in a Tri-Ethnic Region
To determine the effects of risk factors for stroke, MI, and vascular death in a prospective cohort study of 3 race-ethnic groups from Northern Manhattan.
Role: Statistician

R01MD009164, Olveen Carrasquillo (PI) 07/14-03/19
Hispanic Secondary Stroke Prevention Initiative (HISSPI)
To examine the effectiveness of a combined multilevel intervention consisting of Community Health Workers and mobile based phone technologies in lowering of systolic blood pressure which is the most important risk factor for recurrent stroke.
Role: Statistician

R33NS094896, Kunjan Dave (PI), 2016-2019

Red blood cell microparticles (RMPs) to reduce bleeding following hemorrhagic stroke

To determine the optimum therapeutic dose and time window of RMP and validate the efficacy of RMP therapy in diseased spontaneously hypertensive animals.

Role: Co-investigator/Biostatistician

Bristol-Myers Squibb Co, Tatjana Rundek (PI) 12/16-12/19

Disparities in Stroke Outcomes and Care Delivery in Patients with Atrial FibrillationFLiPER
Role: Statistician

14BFSC17690000 Ralph Sacco (PI) 04/14-03/18
American Heart Association/ASA-Bugher Foundation
To evaluate the effects of a Combined Aerobic and Resistance Exercise Training (CARET) program, a Cognitive Training Intervention (CTI), and the combination of the CARET and CTI interventions on cognitive performance in stroke patients.
Role: Co-investigator/Statistician

Completed Research Support (within the last three years):

R01 HL108623-01A1 Clinton Wright (PI) 03/12-02/16
FGF-23 and the Risk of Stroke and Cognitive Decline
To examine the relationship between FGF-23 and the risk of stroke and cognitive decline.
Role: Co-investigator/Statistician

NATL MULTIPLE SCLEROSIS SOCIETY, Melissa Ortega (PI) 12/12-11/15
(Fast-Forward) A Randomized Double-Blind Placebo-Controlled Study of Caprylic Triglyceride for Cognitive Impairment in Subjects with Multiple Sclerosis
To determine the efficacy of Caprylic Triglyceride for Cognitive Impairment in Subjects with Multiple Sclerosis
Role: Biostatistician

R01NS065114 Tatjana Rundek (PI) 07/10-06/15
Novel factors for unexplained phenotypes of subclinical carotid atherosclerosis
To identify genetic variants influencing unexplained phenotypes of subclinical carotid atherosclerosis.
Role: Co-investigator/Statistician

2KN01, Florida JEK Program, Chuanhui Dong (PI) 07/11-06/14
Gene-smoking interactions and atherosclerosis
To identify genetic moderators in the association between smoking and atherosclerosis.
Role: PI/Statistician

2KN09, Florida JEK Program, Dileep Yavagal (PI) 07/11-06/14
Intra-arterial mesenchymal stem cell delivery in a canine model of acute ischemic stroke
To evaluate safety sub-acute endovascular intra-carotid administration of MSCs in a canine stroke model.
Role: Co-investigator/Statistician

1U01NS069208 Kittner Steven (PI) 07/10-06/14
NINDS Ischemic Stroke Genetics Consortium
To assemble ischemic stroke phenotypic data and DNA samples from 11 stroke studies.
Role: Statistician

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: **Hannah Gardener, ScD**

eRA COMMONS USER NAME (credential, e.g., agency login): **HGARDENER**

POSITION TITLE: **Associate Scientist**

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Dartmouth College	AB	06/2000	Psychological and Brain Sciences
Harvard School of Public Health	ScD	08/2007	Epidemiology

A. Personal Statement

Hannah Gardener, ScD, Assistant Scientist in the Department of Neurology at the University of Miami, is an epidemiologist with a particular interest in neuroepidemiology and the epidemiology of aging. She received her doctorate in Epidemiology in 2007 from the Harvard School of Public Health. She has been conducting research on risk factors for clinical and subclinical vascular outcomes in the Northern Manhattan Study for over ten years. She is particularly interested in dietary behavior and other modifiable vascular risk factors in relation to vascular events, carotid disease, and age-related changes in brain structure and cognitive decline. She is responsible for study design, data management, design and completion of statistical analyses, interpretation of results, presentations and manuscript writing.

B. Positions and Honors

POSITIONS AND EMPLOYMENT

Traineeship

2002-04 Senior Research Assistant
Department of Society, Human Development and Health, Harvard School of Public Health
2007-09 Epidemiology Post-Doctoral Fellow
Department of Neurology, University of Miami Miller School of Medicine

Academic Appointments:

2016-present Associate Scientist Department of Neurology, University of Miami Miller School of Medicine
2009-2016 Assistant Scientist Department of Neurology, University of Miami Miller School of Medicine
2009 Research Assistant Professor Departments of Neurology and Pediatrics,
University of Miami Miller School of Medicine

Memberships:

2008- American Academy of Neurology
2007-2008 Society for Epidemiologic Research

Honors:

2006-2007 Certificate of Distinction in recognition of outstanding accomplishments and contributions in teaching: Harvard School of Public Health, Department of Epidemiology
2004-2006 National Research Service Award grant from the Training Program in Psychiatric Epidemiology and Biostatistics (T32 MH17119):
2000 Phi Beta Kappa, Dartmouth College
2000 Benner Award for Excellence in Research, Dartmouth College

C. Contribution to science

C.1. Predictors of cognitive function and decline in the population. An area of research focus is the role of novel and traditional vascular risk factors in cognitive performance and decline over time. Most notable is our finding of a role for

infectious burden in executive function as well as memory decline over time, and our studies showing relationships between sleep disturbance, physical activity, and cardiovascular health factors with decline in cognitive domains.

1. **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.
2. Wersching H, **Gardener H**, Sacco RL. Sugar-Sweetened and Artificially Sweetened Beverages in Relation to Stroke and Dementia: Are Soft Drinks Hard on the Brain? *Stroke*. 2017;48(5):1129-1131.
3. Ramos AR, **Gardener H**, Rundek T, Elkind MS, Boden-Albala B, Dong C, Cheung YK, Stern Y, Sacco RL, Wright CB. Sleep disturbances and cognitive decline in the Northern Manhattan Study. Neurology. 2016;87(14):1511-1516.
4. Willey JZ, **Gardener H***, Caunca MR, Moon YP, Dong C, Cheung YK, Sacco RL, Elkind MS, Wright CB. Leisure-time physical activity associates with cognitive decline: The Northern Manhattan Study. Neurology. 2016;86(20):1897-903.
5. **Gardener H**, Wright CB, Dong C, Cheung K, DeRosa J, Nannery M, Stern Y, Elkind MS, Sacco RL. Ideal Cardiovascular Health and Cognitive Aging in the Northern Manhattan Study. Neurology. 2016;86(20):1897-903.
6. **Gardener H**, Wright CB, Rundek T, Sacco RL. Brain health and shared risk factors for dementia and stroke. Nat Rev Neurol. 2015;11(11):651-7.
7. Wright CB, **Gardener H***, Dong C, Yoshita M, DeCarli C, Sacco RL, Stern Y, Elkind MS. Infectious burden and cognitive decline in the Northern Manhattan Study. *J Am Geriatr Soc*. 2015;63(8):1540-1545.
8. Del Brutto OH, Mera RM, Del Brutto VJ, Maestre GE, **Gardener H**, Zambrano M, Wright C. Influence of depression, anxiety and stress on cognitive performance in community-dwelling elders living in rural Ecuador. Results of the Atahualpa Project. *Geriatr Gerontol Int*. 2015;15(4):508-514.
9. Del Brutto OH, **Gardener H**, Del Brut to VJ, Maestre GE, Zambrano M, Montenegro JE, Wright CB. Edentulism Associates with Worse Cognitive Performance in Community-Dwelling Elders in Rural Ecuador: Results of the Atahualpa Project. *J Community Health*. 2014;39(6):1097-1100.
10. **Gardener H**, Wright CB, Rundek T, Sacco RL. Brain health and shared risk factors for dementia and stroke. *Nat Rev Neurol*. 2015;11(11):651-657.

C.2. MRI markers of vascular damage. A primary area of research focus has been examining the role of vascular risk factors in predicting MRI markers of vascular damage, which may be mediators in the pathways between cardiovascular health indices and both stroke and cognitive function and decline. We have shown that migraine is a risk factor for subclinical brain infarcts imaged using MRI, and that diastolic blood pressure, lipid levels, and adherence to a Mediterranean-style diet are predictive of white matter hyperintensity volume, a risk factor for both stroke and dementia. We have also examined the prevalence and risk factors for cerebral microbleeds in our urban multiethnic cohort.

1. Rundek T, Della-Morte D, **Gardener H**, Dong C, Markert MS, Gutierrez J, Roberts E, Elkind MSV, DeCarli C, Sacco RL, Wright CB. Relationship between carotid arterial properties and cerebral white matter hyperintensities. *Neurology*. 2017;88(21):2036-2042.
2. 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).
3. Monteith T, **Gardener H**, Rundek T, Dong C, Yoshita M, Elkind MSV, DeCarli C, Sacco RL, Wright CB. Migraine, White Matter Hyperintensities, and Subclinical Brain Infarction in a Diverse Community: The NOMAS Study *Stroke*. 2014;45(6):1830-1832.
4. Willey JZ, **Gardener H**, Moon MY, Sacco RL, Elkind MSV, Wright CB. Lipid profile components and subclinical cerebrovascular disease in the Northern Manhattan Study. *Cerebrovascular Diseases*. 2014;37(6):423-430.
5. Modir R, **Gardener H**, Wright C. Blood pressure and white matter hyperintensity volume – a review of the relationship and implications for stroke prediction and prevention. *European Neurological Review,* 2012;7(3):174–7.
6. **Gardener H**, Scarmeas N, Gu Y, Boden-Albala B, Elkind MSV, Sacco RL, DeCarli C, Wright CB. Mediterranean diet and white matter hyperintensity volume in the Northern Manhattan Study. *Archives of Neurology*. 2012;69(2):251-256.
7. Marcus J, **Gardener H***, Rundek T, Elkind MSV, Sacco RL, DeCarli C, Wright CB. Baseline and longitudinal increases in diastolic blood pressure are associated with greater white matter hyperintensity volume: The Northern Manhattan Study. *Stroke.* 2011;42(9):2639-2641.

C.3. Epidemiology of stroke. Over the past 8 years I have pursued research in stroke epidemiology. I have examined novel and traditional risk factors for stroke and vascular-related death in a multi-ethnic population-based study with an emphasis on understanding race/ethnic disparities. In particular, a primary research interest is the role of dietary factors in the etiology of vascular outcomes. Specifically, I have published on the role coffee and tea, soft drinks, sodium, and egg consumption as well as adherence to a Mediterranean-style diet in relation to risk of stroke, cardiovascular disease,

and vascular death. Other novel vascular risk factors that I have examined in a multiethnic population-based sample include migraine, adiponectin and HOMA insulin resistance. Most recently I have contributed to research on sex disparities in acute stroke care in Florida and Puerto Rico, and I have studied short-term outcomes in patients with mild and rapidly improving stroke symptoms using Get With The Guidelines-Stroke data.

1. Willey J, **Gardener H**, Cespedes S, Cheung YK, Sacco RL, Elkind MSV. Dietary Sodium to Potassium Ratio and Risk of Stroke in a Multiethnic Urban Population: The Northern Manhattan Study. *Stroke*. 2017;48(11):2979-2983.
2. 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.
3. Ciliberti-Vargas MA, **Gardener H**, Wang K, Dong C, Yi L, Romano JG, Robichaux M, Waddy SP, Nobo U, Diaz-Acosta S, Rundek T, Waters MF, Sacco RL. Stroke Hospital Characteristics in the Florida-Puerto Rico Collaboration to Reduce Stroke Disparities Study. *South Med J*. 2017;110(7):466-474.
4. Sacco RL, **Gardener H**, Wang K, Dong C, Ciliberti-Vargas MA, Gutierrez CM, Asdaghi N, Burgin WS, Carrasquillo O, Garcia-Rivera EJ, Nobo U, Oluwole S, Rose DZ, Waters MF, Zevallos JC, Robichaux M, Waddy SP, Romano JG, Rundek T; FL-PR CReSD Investigators and Collaborators. Racial-Ethnic Disparities in Acute Stroke Care in the Florida-Puerto Rico Collaboration to Reduce Stroke Disparities Study. *J Am Heart Assoc*. 2017;6(2).
5. 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.
6. Romano JG, Smith EE, Liang L, **Gardener H**, Campo-Bustillo I, Khatri P, Bhatt DL, Fonarow GC, Sacco RL, Schwamm LH. Distinct Short-Term Outcomes in Patients With Mild Versus Rapidly Improving Stroke Not Treated With Thrombolytics. Stroke. 2016;47(5):1278-85.
7. Monteith TS, **Gardener H**, Rundek T, Elkind MS, Sacco RL. Migraine and risk of stroke in older adults: Northern Manhattan Study. *Neurology*. 2015;85(8):715-721.
8. Romano JG, Smith EE, Liang L, **Gardener H**, Camp S, Shuey L, Cook A, Campo-Bustillo I, Khatri P, Bhatt DL, Fonarow GC, Sacco RL, Schwamm LH. Outcomes in mild acute ischemic stroke treated with intravenous thrombolysis: a retrospective analysis of the Get With the Guidelines-Stroke registry. *JAMA Neurol*. 2015;72(4):423-431.
9. Global Burden of Metabolic Risk Factors for Chronic Diseases Collaboration (BMI Mediated Effects), Lu Y, Hajifathalian K, Ezzati M, Woodward M, Rimm EB, Danaei G. Metabolic mediators of the effects of body-mass index, overweight, and obesity on coronary heart disease and stroke: a pooled analysis of 97 prospective cohorts with 1.8 million participants. *Lancet*. 2014;383(9921):970-983.
10. **Gardener H**, Rundek T, Wright CB, Elkind MSV, Sacco RL. Coffee and tea consumption are inversely associated with mortality. *J Nutr*. 2013;143(8):1299-1308.
11. **Gardener H**, Goldberg R, Mendez AJ, Wright CB, Rundek T, Elkind MSV, Sacco RL. Adiponectin and risk of vascular events in the Northern Manhattan Study. *Atherosclerosis*. 2013;226(2):483-489.
12. **Gardener H**, Rundek T, Wright CB, Elkind MSV, Sacco RL. Dietary sodium and risk of stroke in the Northern Manhattan Study. *Stroke*. 2012;43(5):1200-1205.
13. **Gardener H**, Rundek T, Markert M, Wright CB, Elkind MSV, Sacco RL. Diet soft drink consumption is associated with an increased risk of vascular events in the Northern Manhattan Study. *Journal of General Internal Medicine*. 2012;27(9):1120-1126.
14. The Global Burden of Disease Stroke Expert Group: Bennett DA, Anderson LM, Nair N, Truelsen T, Barker-Collo S, Connor M, **Gardener H**, Krishnamurthi R, Lawes CMM, Moran A, O'Donnell M, Parag V, Sacco RL, Ezzati M, Mensah G, Feigin VL. Methodology of the global and regional burden of stroke study. *Neuroepidemiology*. 2011;38(1):30-40.
15. **Gardener H**, Wright CB, Gu Y, Demmer RT, Boden-Albala B, Elkind MSV, Sacco RL, Scarmeas N. A Mediterranean-style diet and the risk of ischemic stroke, myocardial infarction, and vascular death: The Northern Manhattan Study. *American Journal of Clinical Nutrition.* 2011;94(6):1458-1464.
16. Rundek T, **Gardener H**, Xu Q, Goldberg RB, Wright CB, Boden-Albala B, Disla N, Paik MC, Elkind MSV, Sacco RL. Insulin resistance and risk of ischemic stroke among non-diabetic individuals from the Northern Manhattan Study. *Archives of Neurology*. 2010;67(10):1195-1200.
17. Sacco RL, Khatri M, Rundek T, Xu Q, **Gardener H**, Boden-Albala B, Di Tullio M, Homma S, Elkind MSV, Paik MC. Improving global vascular risk prediction with behavioral and anthropometric factors: the multi-ethnic Northern Manhattan Cohort Study. *Journal of the American College of Cardiology*. 2009;54(24):2303-2311.

C.4. Epidemiology of atherosclerosis and imaging markers of carotid disease. A primary research focus has been examining the associations of vascular risk factors with carotid atherosclerosis phenotypes to better understand their impact on clinical and subclinical vascular disease. In particular, I have studied the roles of diet (egg consumption and adherence to a Mediterranean-style diet) and genetics in the etiology of carotid atherosclerosis. I have examined the relationship between two important and distinct measures of carotid atherosclerosis measured using B-mode ultrasound – carotid intima-media thickness and carotid plaque – and have explored multiple ways to quantify plaque burden including total plaque area. In addition to diet, modifiable vascular risk factors for carotid atherosclerosis phenotypes that I have published include cigarette smoking, soluble RAGE levels, lipid levels, homocysteine, and adiponectin.

1. 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;S1052-3057(17)30537-2.
2. Tiozzo E, **Gardener H**, Hudson BI, Dong C, Della-Morte D, Crisby M, Goldberg RB, Elkind MS, Cheung YK, Wright CB, Sacco RL, Desvarieux M, Rundek T. Subfractions of High-Density Lipoprotein-Cholesterol and Carotid Intima-Media Thickness: The Northern Manhattan Study. Stroke. 2016;47(6):1508-13.
3. Haussen DC, Rose DZ, Drazin D, Newsome SD, **Gardener H**, Edgell RC, Boulos A, Bernardini G, Rundek T, Yavagal DR. Ipsilateral infarct in newly diagnosed cervical internal carotid artery atherosclerotic occlusion. *Interv Neurol*. 2015;3(3-4):142-148.
4. Yang D, Iyer S, **Gardener H**, Della-Morte D, Crisby M, Dong C, Cheung K, Mora-McLaughlin C, Wright CB, Elkind MS, Sacco RL, Rundek T. Cigarette smoking and carotid plaque echodensity in the Northern Manhattan Study. *Cerebrovasc Dis*. 2015;40(3-4):136-143.
5. Rundek T, **Gardener H**, Della-Morte D, Dong C, Cabral D, Tiozzo E, Roberts E, Crisby M, Cheung K, Demmer R, Elkind MS, Sacco RL, Desvarieux M. The relationship between carotid intima-media thickness and carotid plaque in the Northern Manhattan Study. *Atherosclerosis*. 2015;241(2):364-370.
6. Hudson BI, **Gardener H**, Liu-Mares W, Dong C, Cheung K, Elkind MS, Wright CB, Sacco RL, Rundek T. Serum soluble RAGE levels and carotid atherosclerosis: the Northern Manhattan Study. *Atherosclerosis*. 2015;240(1):17-20.
7. Tiozzo E, **Gardener H**, Hudson BI, Dong C, Della-Morte D, Crisby M, Goldberg RB, Elkind MS, Cheung YK, Wright CB, Sacco RL, Rundek T. High-density lipoprotein subfractions and carotid plaque: the Northern Manhattan Study. *Atherosclerosis*. 2014;237(1):163-168.
8. Goldberg S, **Gardener H***, Tiozzo E, Cheung YK, Elkind MSV, Sacco RL, Rundek T. Egg Consumption and Carotid Atherosclerosis in the Northern Manhattan Study*. Atherosclerosis.* 2014;235(2):273-280.
9. **Gardener H**, Wright CB, Cabral D, Scarmeas N, Gu Y, Cheung K, Elkind MS, Sacco RL, Rundek T. Mediterranean diet and carotid atherosclerosis in the Northern Manhattan Study. *Atherosclerosis*. 2014;234(2):303-310.
10. Alsulaimani S, **Gardener H**, Elkind MSV, Cheung K, Sacco RL, Rundek T. Elevated homocysteine and carotid plaque area and densitometry in the Northern Manhattan Study. *Stroke*. 2013;44(2):457-461.
11. Della-Morte D**,** Beecham A, Dong C, Wang L, McClendon MS, **Gardener H**, Blanton SH, Sacco RL, Rundek T. Association between variations in coagulation system genes and carotid plaque. *Journal of the Neurological Sciences*. 2012;323(1-2):93-98.
12. Kuo F, **Gardener H**, Dong C, Cabral D, Della-Morte D, Blanton SH, Santiago M, Elkind MSV, Sacco RL, Rundek T. Traditional cardiovascular risk factors explain only small proportion of the variation in carotid plaque. *Stroke*. 2012;43(7):1755-1760.
13. **Gardener H**, Sjoberg C, Crisby M, Goldberg R, Mendez A, Wright CB, Elkind MSV, Sacco RL, Rundek T. Adiponectin and carotid intima-media thickness in the Northern Manhattan Study. *Stroke*. 2012;43(4):1123-1125.
14. Markert MS, Della-Morte D, Cabral D, Roberts EL, **Gardener H**, Dong C, Wright CB, Elkind MS, Sacco RL, Rundek T. Ethnic differences in carotid artery diameter and stiffness: the Northern Manhattan Study. *Atherosclerosis.* 2011;219(2):827-832.
15. **Gardener H,** Beecham A, Cabral D, Yanuck D, Slifer S, Wang L, Blanton SH, Sacco RL, Juo SH, Rundek T. Carotid plaque and candidate genes related to inflammation and endothelial function in Hispanics from Northern Manhattan. *Stroke.* 2011;42(4):889-896.
16. Wang L, Yanuck D, Beecham A, **Gardener H,** Slifer S, Blanton SH, Sacco RL, Rundek T. A candidate gene study revealed sex-specific association between the ORL1 gene and carotid plaque. *Stroke.* 2011;42(3):588-592.
17. Ramos A, Wohlgemuth WK, **Gardener H**, Lorenzo D, Dib S, Wallace D, Nolan B, Boden-Albala B, Elkin MSV, Sacco RL, Rundek T. Snoring and insomnia are not associated with subclinical atherosclerosis in the Northern Manhattan Study (NOMAS). *International Journal of Stroke*. 2010;5(4):264-268.
18. Morte D, **Gardener H**, Denaro F, Boden-Albala B, Elkind MSV, Paik, MC, Sacco RL, Rundek T. Metabolic syndrome increases arterial stiffness: The Northern Manhattan Study. *International Journal of Stroke*.

2010;5(3):138-144.
19. **Gardener H**, Morte D, Elkind MSV, Sacco RL, Rundek T. Lipids and carotid plaque in the Northern Manhattan Study (NOMAS). *BMC Cardiovascular Disorders*. 2009;9:55.
20. Sacco RL, Blanton SH, Slifer S, Beecham A, Glover K, **Gardener H,** Wang L, Sabala E, Juo SH, Rundek T. Heritability and linkage analysis for carotid intima-media thickness: The family study of stroke risk and carotid atherosclerosis. *Stroke.* 2009;40(7):2307-2312.

*Shared first authorship

Link to my full list of publications:
http://www.ncbi.nlm.nih.gov/pubmed/?term=Gardener+h

D. Research Support

1. NOMAS
   R01 NS 029993 (PI: Sacco) **02/01/03-07/31/20**
   NIH/NINDS
   Stroke Incidence and Risk Factors in a Tri-Ethnic Region
   The goals of this project are to determine the effects of risk factors for stroke, MI, and vascular death, as well as evaluate predictors of cognitive impairment and the importance of subclinical MRI findings in a prospective cohort study of 3300 persons from 3 race-ethnic groups from Northern Manhattan.

2. SPIRP
   U54 NINDS SPIRP U54NS081763 (PI: Sacco) **01/01-12/31/17**
   NIH/NINDS
   Stroke Prevention/Intervention Research Program in Hispanics (& supplement FL-PR CReSD-W)
   The goal of this project is to develop high-impact stroke disparities interventions and research projects that have the ability to reduce stroke disparities in the two distinct Hispanic groups in Miami and Puerto Rico using effective and culturally appropriate methods.

3. Genentech
   Genentech (PI: Romano) **12/14/11 – 10/30/20**
   Coordinating Center: University of Miami
   Mild and Rapidly Improving Stroke Study (MaRISS) This research project encompasses two phases, a *retrospective* analysis of the existing entire Get With The Guidelines-Stroke Registry to determine prevalence and short-term outcomes among patients with mild and rapidly improving stroke symptoms and a *prospective* study in 100 select GWTG hospitals to elucidate the long-term outcomes of patients that suffered mild or rapidly improving stroke.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Joyce Gomes-Osman

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Assistant Professor, Departments of Physical Therapy and Neurology
Research Fellow, Berenson-Allen Center for Non-Invasive Brain Stimulation

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Escola Bahiana de Medicina e Saude Publica	B.S.	06/07	Physical Therapy
University of Miami Miller School of Medicine	Ph.D.	09/13	Motor Control Physiology
Harvard Medical School	Post doctoral Fellowship	09/13 - present	Non-Invasive Brain Stimulation

A. Personal Statement

I am 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 assessing their effects on the human nervous system. In my career, I have explored pertinent questions regarding the potential for NIBS (including transcranial magnetic stimulation [TMS] and transcranial direct current stimulation [tDCS]) to aid in the characterization of remaining function, and augment rehabilitation approaches aimed at restoring functional hand use after impairment due to spinal cord injury. As a result of these experiences, I have successfully carried out all aspects of research projects (subject recruitment, data analysis, data synthesis and manuscript preparation) effectively, as evidenced by my publication record. In my ongoing postdoctoral affiliation with the Berenson-Allen Center for Noninvasive Brain Stimulation of Harvard Medical School, I have had the opportunity to improve my knowledge in NIBS, advanced TMS-based plasticity measures and cognitive neurology. In my newly established Neuromotor Plasticity Laboratory, I collaborate with my investigator colleagues in the Evelyn F. McKnight Brain Institute on projects that apply my knowledge of neuroplasticity and functional performance. Our goal is to better understand the influence of exercise and its potential to improve function and promote neuroplasticity throughout the lifespan. I currently carry out projects in close collaboration with the Neurology Department, to improve functional performance through neuroplasticity and exercise in individuals post-stroke, Parkinson's disease, Memory Disorders and Apraxia of Speech.

B. Positions and Honors

Positions and Employment

2016- Collaborator, Center on Aging, University of Miami Miller School of Medicine, USA.

2014- Collaborator, Evelyn F. McKnight Brain Institute University of Miami Miller, School of Medicine, USA.

2014- Assistant Professor, Department of Physical Therapy, University of Miami Miller School of Medicine, USA.

2013- Faculty, Transcranial Magnetic Stimulation Intensive Course, Berenson-Allen Center for Non-invasive Brain Stimulation. Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA

2013- Postdoctoral Research Fellow, Berenson-Allen Center for Noninvasive Brain Stimulation, Beth Israel Deaconess Medical Center, Harvard Medical School, USA.

2010-2013 Research Support Specialist, The Miami Project to Cure Paralysis, University of Miami, Florida, USA

2007-2010 Research Associate, the Miami Project to Cure Paralysis, University of Miami, Florida, USA

Honors

2007 Humberto de Castro Lima Award by the Bahiana School of Medicine and Public Health-Salvador, Brazil as Outstanding Student in the year of 2007.

2005 Fundacao de Amparo a Pesquisa do Estado da Bahia (FAPESB) Scholarship for Young Scientists. First non-MD student to be awarded this scholarship by the State of Bahia [Brazil] Foundation for Research

Other Experience and Professional Memberships

2016 Reviewer, *Scientific Reports*
2016 Reviewer, *Topics in Spinal Cord Injury Rehabilitation*
2016- Reviewer, *Experimental Brain Research*
2015 Reviewer, *Journal of Neuroscience*
2015 Reviewer, *The Lancet Neurology*
2015- Reviewer, *Annals of Neurology*
2015 Reviewer, *Frontiers in Psychology*
2015 Reviewer, *Lancet Neurology*
2014- Reviewer, *European Journal of Neuroscience*
2010- Member, American Physical Therapy Association
2010- Member, Society for Neuroscience
2009- Reviewer, *Journal of Neurologic Physical Therapy*

C. Contribution to Science

C1. **Characterizing the influence of peripherally applied stimulation on neuroplasticity after peripheral nerve injury.** My early work measured neuroplasticity in the form of axonal sprouting in a mouse model of sciatic crush lesion. I contributed to the validation of the sciatic static index for mice, a widely used functional measure of sciatic nerve injury. These studies demonstrated that TENS and low-frequency pulsed electromagnetic fields, both clinically available stimulation devices, were associated with delayed peripheral regeneration of a crush lesion to the sciatic nerve in mice.

1. Baptista AF, Goes BT, Menezes D, Gomes FC, Zugaib J, Stipursky J, **Gomes JR**, Oliveira JT, Vannier-Santos MA, Martinez AM PEMF fails to enhance nerve regeneration after sciatic nerve crush lesion. ***J Peripher Nerv Syst***. 2009.

2. Baptista AF, **Gomes JR**, Oliveira JT, Santos SM, Vannier-Satos MA, Martinez AMB. High and low frequency transcutaneous electrical nerve stimulation delay sciatic nerve regeneration in the mouse. ***J Perypher Nerv Syst***, 2007.

3. Baptista AF, **Gomes JR**, Oliveira JT, Santos SM, Vannier-Satos MA, Martinez AMB. A new approach to assess function after sciatic nerve lesion in the mouse-Adaptation of the sciatic static index. ***J Neurosci Methods.*** 2007.

C2. **Non-invasive brain stimulation (NIBS) targeting the primary motor cortex promotes improves unimanual and bimanual fine motor performance.** My early human work focused assessing the potential for different NIBS protocols for harnessing plasticity to augment motor function, both in neurologically healthy individuals and individuals with chronic incomplete tetraplegia. In neurologically healthy individuals, I found that bi-hemispheric tDCS applied concurrently to both primary motor cortices augments fine motor hand function. In individuals with chronic incomplete tetraplegia, I found that repetitive TMS augmented the effects of neurorehabilitation exercise programs designed to improve fine motor hand function.

4. **Gomes-Osman, J**, Field-Fote EC. Bihemispheric anodal corticomotor stimulation using transcranial direct current stimulation improves bimanual typing task performance. ***J Mot Behav.*** 2013.

5. **Gomes-Osman, J**, Field-Fote EC. Improvements in Hand Function in Adults With Chronic Tetraplegia Following a Multiday 10-Hz Repetitive Transcranial Magnetic Stimulation Intervention Combined With Repetitive Task Practice. ***J Neurol Phys Ther*****.** 2015.

C3. **Exercise interventions and primed functional task practice protocols in individuals with incomplete tetraplegia.** Having learned that stimulation to the primary motor cortex could improve fine motor control of the hand, I became interested in assessing different intervention approaches in their ability to improve hand function. Consistent with the prior work of my former laboratory, primed functional task practice indirect cortical activation led to greater improvements in precision grip strength. In addition, a single-session study found that primed functional task practice with direct stimulation to the motor cortex (tDCS) was the most promising approach when compared with priming with indirect cortical activation utilizing peripherally applied stimulation using TENS and VIB in a single-session study. This body of work provides alternatives for physical therapists and patients to advance the results of their rehabilitation programs by using priming interventions. I served as primary author on these publications.

6. **Gomes-Osman J**, Tibbett JA, Poe BP, Field-Fote E. Priming for Improved Hand Strength in Persons with Chronic Tetraplegia: A Comparison of Priming-augmented Functional Task Practice, Priming Alone, and Conventional Exercise Training. ***Frontiers in Neurology***; 2017; 242.

7. **Gomes-Osman J**, Field-Fote EC. Cortical vs. afferent stimulation as an adjunct to functional task practice training: A randomized, comparative pilot study in people with cervical spinal cord injury. ***Clin Rehabil*****.** 2015.

C4. **Stability of TMS measures and guidelines to improve internal consistency in TMS studies.** In my earlier work utilizing TMS, I observed marked between-individual variability, and this led me to become interested in improving the reproducibility of this technique. I worked in a team on a study to calculate the internal consistency in different TMS measures (single-pulse TMS, paired-pulse TMS, theta-burst TMS), and the minimum number of pulses to achieve an accurate estimation of the mean, around the 95% confidence interval, for these measures. This work adds to the literature by providing guidelines to achieve reliable measurements using TMS, and has the potential to decrease the variability often seen with TMS measures across the literature.

8. Chang WH, Fried PJ, Saxena S, Jannati A, **Gomes-Osman J**, Kim YH, Pascual-Leone, A. Optimal number of pulses as outcome measures of neuronavigated transcranial magnetic stimulation. ***Clin Neurophysiol.*** 2016.

C5. **Assessing the effects of aerobic exercise on cognition and neuroplasticity in young sedentary adults.** In this work, I assessed the feasibility of evaluating the effects of a month-long exercise intervention on cognitive performance, TMS/Theta-burst measures of neuroplasticity, and brain derived neurotrophic factor (BDNF) Met carrier status in young sedentary adults. I found improvements in response inhibition following 4 weeks of regular aerobic exercise. In addition, the neuroplasticity appeared to differ according to BDNF allelic status. This work contributes to the literature by introducing an innovative neuroplasticity assessment that may be useful in further elucidating exercise-mediated improvements in cognitive performance.

9. **Gomes-Osman J**, Cabral D, Hinchman C, Jannati A, Morris TP, Pascual-Leone A. The effects of exercise on cognitive function and brain plasticity – a feasibility trial. ***Restorative Neurology and Neuroscience*****, in press,** 2017.

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/pubmed/?term=Joyce+Gomes
http://www.ncbi.nlm.nih.gov/pubmed/?term=Gomes-Osman

1. **Gomes-Osman J**, Cabral D, Hinchman C, Jannati A, Morris TP, Pascual-Leone A. The effects of exercise on cognitive function and brain plasticity – a feasibility trial. ***Restorative Neurology and Neuroscience*****, in press,** 2017.

2. **Gomes-Osman J**, Tibbett JA, Poe BP, Field-Fote E. Priming for Improved Hand Strength in Persons with Chronic Tetraplegia: A Comparison of Priming-augmented Functional Task Practice, Priming Alone, and Conventional Exercise Training. ***Frontiers in Neurology***; 2017; 242.

3. Morris T, **Gomes-Osman J**, Costa-Miserach D, Pascual-Leone A. The Role of Physical Exercise in Cognitive Recovery After Traumatic Brain Injury: A Systematic Review. ***Restorative Neurology and Neuroscience***; 2016; 977-988.

4. Neville IS, **Gomes-Osman J**, Amorim RLO, Hayashi CY, Galhardoni R, Zaninotto AL, Teixeira MJ, Paiva WS. How can transcranial magnetic stimulation change the way we treat traumatic brain injury? ***International Journal of Clinical and Experimental Medicine***; 2016; 9.

5. Chang WH, Fried PJ, Saxena S, Jannati A, **Gomes-Osman J**, Kim YH, Pascual-Leone, A. Optimal number of pulses as outcome measures of neuronavigated transcranial magnetic stimulation. ***Clin Neurophysiol***. 2016.

6. **Gomes-Osman J**, Cortes M, Guest J, Pascual-Leone A. A systematic review of experimental strategies aimed at improving motor function after acute and chronic spinal cord injury. ***J Neurotrauma.*** 2015.

7. **Gomes-Osman, J**, Field-Fote EC. Improvements in Hand Function in Adults With Chronic Tetraplegia Following a Multiday 10-Hz Repetitive Transcranial Magnetic Stimulation Intervention Combined With Repetitive Task Practice. ***J Neurol Phys Ther.*** 2015.

8. **Gomes-Osman, J**, Field-Fote EC. Cortical vs. afferent stimulation as an adjunct to functional task practice training: A randomized, comparative pilot study in people with cervical spinal cord injury. ***Clin Rehabil.*** 2015.

9. **Gomes-Osman, J**, Field-Fote EC. Bihemispheric anodal corticomotor stimulation using transcranial direct current stimulation improves bimanual typing task performance. ***J Mot Behav.*** 2013.

10. Baptista AF, Goes BT, Menezes D, Gomes FC, Zugaib J, Stipursky J, **Gomes JR**, Oliveira JT, Vannier-Santos MA, Martinez AM PEMF fails to enhance nerve regeneration after sciatic nerve crush lesion. ***J Peripher Nerv Syst.*** 2009.

11. Baptista AF, **Gomes JR**, Oliveira JT, Santos SM, Vannier-Satos MA, Martinez AMB. High and low frequency transcutaneous electrical nerve stimulation delay sciatic nerve regeneration in the mouse. ***J Perypher Nerv Syst,*** 2007.

12. Baptista AF, **Gomes JR**, Oliveira JT, Santos SM, Vannier-Satos MA, Martinez AMB. A new approach to assess function after sciatic nerve lesion in the mouse-Adaptation of the sciatic static index. ***J Neurosci Methods.*** 2007.

C. Research Support

In Progress

2017-2018 **Evelyn McKnight Brain Institute Internal Pilot Grant Drive.** Aerobic exercise to influence mechanisms of brain plasticity and cognition in healthy aging. This project consists in the assessment of a 4-week aerobic exercise intervention on neuroplasticity and cognitive performance in healthy older individuals without cognitive impairments. Role: Principal Investigator. Grant amount $10,000.

2016-2017 **Foundation to Support Research in the State of Alagoas, Brazil (Fundacao de Amparo a Pesquisa do Estado do Alagoas- FAPEAL).** The use of exercise as a potential tool for brain health in healthy older adults and individuals with MCI: a systematic review aimed at identifying dose-related exercise recommendations. This project consists in a systematic review of randomized controlled trials proposing exercise to influence cognitive performance to assess the methodological quality, describe dose parameters of exercise, and outline evidence-based dose-specific recommendations. Fellowship for Danylo Cabral. **Role: Principal Investigator**. Grant amount: $1,600.

Completed

2007-2012 **National Institutes of Health (NIH) R01 HD053854.** Improving Arm and Hand Function in Individuals with SCI. This project consisted of a comparison of different approaches to improve upper extremity function in individuals with tetraplegia using repetitive task practice and peripherally applied electrical stimulation. Principal Investigator: Edelle Field-Fote, PT, PhD. **Role: Project Coordinator**.

2010-2011 **National Institutes of Health (NIH) R01 HD053854-03S1.** Improving Arm and Hand Function in Individuals with SCI. This project consisted of a comparison of different approaches to improve upper extremity function in individuals with tetraplegia using repetitive task practice and repetitive transcranial magnetic stimulation. Principal Investigator: Edelle Field-Fote, PT, PhD. **Role: Project Coordinator**

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: **Jiang, Hong, MD PhD**

eRA COMMONS USER NAME (credential, e.g., agency login): HongJiang

POSITION TITLE: Clinical Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	START DATE MM/YYYY	END DATE MM/YYYY	FIELD OF STUDY
Zhejiang Medical University, Hangzhou, Zhejiang	MD	09/1983	07/1988	Medicine
Zhejiang Medical University, Hangzhou, Zhejiang	MS	09/1990	07/1993	Neurology
University of Hong Kong, Hong Kong	PHD	09/1998	07/2001	Neuroscience
Zhejiang Medical University, Hangzhou, Zhejiang	Other training	09/1988	07/1990	Internship (Internal Medicine)
University of Rochester, Rochester, New York	Postdoctoral Fellow	09/2001	07/2005	Neuroscience
Rochester General Hospital, Rochester, New York	Other training	09/2005	07/2006	Intership (Internal Medicine)
Jackson Memorial Hospital/University of Miami, Miami, FL	Resident	09/2007	07/2010	Neurology
Bascom Palmer Eye Institute, University of Miami, Miami, FL	Fellow	09/2010	07/2011	Neuro-Ophthalmology

A. Personal Statement

Vascular dysfunction is a possible contributor to the pathogenesis of Alzheimer's disease (AD). We propose to study the interaction between retinal microvascular changes and retinal neurodegeneration using advanced ophthalmic imaging techniques in subjects at preclinical and clinical stages of AD. The goal is to develop retinal biomarkers for monitoring disease progression and therapeutic efficacy. The preliminary data obtained with grant support from the North American Neuroophthalmology Society, McKnight brain Institute and the University of Miami revealed retinal microvascular dysfunction and retinal microstructural alterations in patients with AD and mild cognitive impairment (MCI). As a neurologically trained neuroophthalmologist, I have a broad background in both basic and clinical research. I am a member of McKnight Brain Institute at the University of Miami and have been participating in various AD clinical trials. Working with the exceptional and experienced scientists and engineering team at the Bascom Palmer Eye Institute, I have been involved in advanced structural and functional ophthalmic imaging for more than 7 years. My work has been reflected in my recent publications as the corresponding author in the field of retina and conjunctiva functional imaging. The build-up of the versatile FSLB and further development of the RFI imaging processing approach indicate that the team is well capable of conducting the proposed study. In summary, my expertise and experience make me well equipped and qualified for working in this proposed project.

1. **Jiang H**, Wei Y, Shi Y, Wright C, Sun X, Gregori G, Zheng F, Vanner EA, Lam BL, Rundek T, Wang J. Altered retinal microvasculature in mild cognitive impairment and Alzheimer's disease. Journal of neuro-ophthalmology. Epub ahead of print. PubMed PMID: 29040211.

2. Wei Y, **Jiang H**, Shi Y, Qu D, Gregori G, Zheng F, Rundek T, Wang J. Age-Related Alterations in the Retinal Microvasculature, Microcirculation, and Microstructure. Invest Ophthalmol Vis Sci. 2017 Jul 1;58(9):3804-3817. PubMed PMID: 28744554; PubMed Central PMCID: PMC5527847.

3. **Jiang H**, Delgado S, Liu C, Rammohan KW, DeBuc DC, Lam BL, Wang J. In Vivo Characterization of Retinal Microvascular Network in Multiple Sclerosis. Ophthalmology. 2016 Feb;123(2):437-8. PubMed PMID: 26299696; PubMed Central PMCID: PMC4724448.
4. **Jiang H**, Debuc DC, Rundek T, Lam BL, Wright CB, Shen M, Tao A, Wang J. Automated segmentation and fractal analysis of high-resolution non-invasive capillary perfusion maps of the human retina. Microvasc Res. 2013 Sep;89:172-5. PubMed PMID: 23806780; PubMed Central PMCID: PMC3773708.

B. Positions and Honors

Positions and Employment

1990 - 1997	Neurologist, Second Affiliated Hospital of Zhejiang Medical University, Hangzhou
2011 - 2012	Clinical Instructor, Neuro-ophthalmology and Neurology, Bascom Palmer Eye Institute, University of Miami, Miami, FL
2012 -	Clinical Assistant Professor, Neuro-ophthalmology & Neurology, Bascom Palmer Eye Institute & Dept. of Neurology, University of Miami, Miami, FL

Other Experience and Professional Memberships

2001 -	Member, American Academy Of Neurology
2010 -	Member, Association for Research in Vision and Ophthalmology
2010 -	Member, American Association of Ophthalmology
2012 -	Member, Member of American Heart Association
2012 -	Fellow, North American Neuro-Ophthalmology Society
2017 -	member, American Medical Association

Honors

1997	Lady Ivy Wu Fellowship , University of Hong Kong
1999	Travel Grant, International Federation of Parkinson's disease Foundations
2000	Young Investigator Award for Best Oral Presentation, Queen Mary Hospital
2000	Travel and Conference Award , Dr. Lo Kwee Seong Education Foundation
2008	Travel Award, Florida Society of Neurology
2011	ARVO Travel Grant, National Eye Institute

C. Contribution to Science

1. I initiated the development of automatic segmentation of the retinal microvascular network obtained using Retinal Function Imager (RFI) and Optic Coherence Tomography Angiography (OCTA) for studying retinal microvascular changes in multiple sclerosis, AD, diabetics and cerebral small vessel diseases.

    a. **Jiang H**, Wei Y, Shi Y, Wright C, Sun X, Gregori G, Zheng F, Vanner EA, Lam BL, Rundek T, Wang J. Altered retinal microvasculature in mild cognitive impairment and Alzheimer's disease. Journal of neuro-ophthalmology. Epub ahead of print. PubMed PMID: 29040211.
    b. Wei Y, **Jiang H**, Shi Y, Qu D, Gregori G, Zheng F, Rundek T, Wang J. Age-Related Alterations in the Retinal Microvasculature, Microcirculation, and Microstructure. Invest Ophthalmol Vis Sci. 2017 Jul 1;58(9):3804-3817. PubMed PMID: 28744554; PubMed Central PMCID: PMC5527847.
    c. **Jiang H**, Delgado S, Liu C, Rammohan KW, DeBuc DC, Lam BL, Wang J. In Vivo Characterization of Retinal Microvascular Network in Multiple Sclerosis. Ophthalmology. 2016 Feb;123(2):437-8. PubMed PMID: 26299696; PubMed Central PMCID: PMC4724448.
    d. **Jiang H**, Debuc DC, Rundek T, Lam BL, Wright CB, Shen M, Tao A, Wang J. Automated segmentation and fractal analysis of high-resolution non-invasive capillary perfusion maps of the human retina. Microvasc Res. 2013 Sep;89:172-5. PubMed PMID: 23806780; PubMed Central PMCID: PMC3773708.

2. To image microvasculature on the conjunctiva for studying cerebral small vessel diseases, a system called functional slit-lamp biomicroscope (FSLB) was developed. This novel system enables easily imaging the conjunctival microvascular network and small vessel blood flow velocity.

   a. Xu Z, **Jiang H**, Tao A, Wu S, Yan W, Yuan J, Liu C, DeBuc DC, Wang J. Measurement variability of the bulbar conjunctival microvasculature in healthy subjects using functional slit lamp biomicroscopy (FSLB). Microvasc Res. 2015 Sep;101:15-9. PubMed PMID: 26092682; PubMed Central PMCID: PMC4537817.
   b. Wang L, Yuan J, **Jiang H**, Yan W, Cintrón-Colón HR, Perez VL, DeBuc DC, Feuer WJ, Wang J. Vessel Sampling and Blood Flow Velocity Distribution With Vessel Diameter for Characterizing the Human Bulbar Conjunctival Microvasculature. Eye Contact Lens. 2016 Mar;42(2):135-40. PubMed PMID: 25839347; PubMed Central PMCID: PMC4591084.
   c. **Jiang H**, Zhong J, DeBuc DC, Tao A, Xu Z, Lam BL, Liu C, Wang J. Functional slit lamp biomicroscopy for imaging bulbar conjunctival microvasculature in contact lens wearers. Microvasc Res. 2014 Mar;92:62-71. PubMed PMID: 24444784; PubMed Central PMCID: PMC3960300.
   d. **Jiang H**, Ye Y, DeBuc DC, Lam BL, Rundek T, Tao A, Shao Y, Wang J. Human conjunctival microvasculature assessed with a retinal function imager (RFI). Microvasc Res. 2013 Jan;85:134-7. PubMed PMID: 23084966; PubMed Central PMCID: PMC3534915.

3. To study retinal degeneration in neurological diseases such as multiple sclerosis, I contributed to the development of slit-lamp based ultra-high resolution OCT for imaging the retina. My contribution was to run the clinical validation and report the test results. Our segmentation software can manually segment 9 retinal sub-layers. Recently adapted Orion software enables automatic segmentation of 6 maps of retinal sub-layers.

   a. **Jiang H**, Delgado S, Tan J, Liu C, Rammohan KW, DeBuc DC, Lam BL, Feuer WJ, Wang J. Impaired retinal microcirculation in multiple sclerosis. Mult Scler. 2016 Dec;22(14):1812-1820. PubMed PMID: 26903007; PubMed Central PMCID: PMC4993688.
   b. **Jiang H**, Delgado S, Liu C, Rammohan KW, DeBuc DC, Lam BL, Wang J. In Vivo Characterization of Retinal Microvascular Network in Multiple Sclerosis. Ophthalmology. 2016 Feb;123(2):437-8. PubMed PMID: 26299696; PubMed Central PMCID: PMC4724448.
   c. Wang Y, **Jiang H**, Shen M, Lam BL, DeBuc DC, Ye Y, Li M, Tao A, Shao Y, Wang J. Quantitative analysis of the intraretinal layers and optic nerve head using ultra-high resolution optical coherence tomography. J Biomed Opt. 2012 Jun;17(6):066013. PubMed PMID: 22734769; PubMed Central PMCID: PMC3381522.
   d. **Jiang H**, Abukhalil F, Shen M, Gregori G, Lam BL, Wang Y, Wang J. Slit-lamp-adapted ultra-high resolution OCT for imaging the posterior segment of the eye. Ophthalmic Surg Lasers Imaging. 2012 Jan-Feb;43(1):76-81. PubMed PMID: 22251848.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/1buofoatUF5Q8/bibliography/48052483/public/

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

NMSS, National Multiple Sclerosis Society — Jiang (PI) — 04/01/16-03/31/19
The Role of retinal microvascular impairment on Neurodegeneration in Multiple Sclerosis
The goal of this study is to determine the role of retinal microvascular impairment on neurodegeneration in MS.
Role: PI,

SUN_UM_1, Sun Yat-sen University Collaboration Award — Wang (PI) — 10/01/15-09/30/20
Clinical applications of advanced ophthalmic imaging

The goal of this study is to develop and apply advance ophthalmic imaging for clinical research in ophthalmology.
Role: Co-Investigator

US202, Toyama (pharmaceutical company) Baumel (PI) 11/21/13-05/31/18
A Phase 2 multi-center, randomized, double blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of T-817MA in patients with mild to moderate Alzheimer's Disease (US202)
Role: Co-Investigator

Daybreak, Eli Lilly (pharmaceutical company) Baumel (PI) 07/01/16-03/31/21
A Randomized, Double-Blind, Placebo-Controlled and Delayed-Start Study of LY3314814 in Mild Alzheimer's Disease Dementia
Role: Co-Investigator

Completed Research Support

NANOS Pilot 2015, North American Neuro-Ophthalmology Society Jiang (PI) 04/15/15-10/15/16
Retinal microvascular alteration as a possible biomarker in Alzheimer's disease
The purpose of this project is to characterize the retinal microvascular dysfunction and optical properties of Retinal nerve fiber layer in AD patients.
Role: PI

UM RSA 2015-41, University of Miami Jiang (PI) 12/01/14-12/31/15
Ocular microvascular biomarkers in Alzheimer's disease
This project is a clinical trial for further studying tear dynamics after treatment with Restasis in dry eye patients.
Role: PI

R01EY020607S, NIH supplemental award Cabrera DeBuc (PI) 02/01/12-01/31/14
Advanced imaging for diabetic retinopathy
This award (R01 supplement for 2 years) provides support under the Research Supplements to Promote Diversity in Health-Related Research Program to Dr. Jiang who studies retinal neurodegenerative diseases by using the unique prototype of UHR-OCT with added oximetry capability and the Retinal Function Imager (RFI).
Role: Co-Investigator

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Bonnie E. Levin, Ph.D.	Professor of Neurology and Psychology
eRA COMMONS USER NAME bonnie_levin	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Georgetown University	BS	1974	Psychology
Temple University	Ph.D.	1983	Psychology

A. Personal Statement

My role is to direct and implement all cognitive and behavioral assessments carried out in the Division of Neuropsychology, Department of Neurology at the University of Miami Miller School of Medicine. Currently, I hold the Bernard and Alexandria Schoninger Professorship in Neurology and I am the founder and Director of the Division of Neuropsychology. I direct the Neuropsychology Assessment Teaching Program and supervise the clinical activities of PhD graduate students in the Child Clinical, Adult Clinical and Behavioral Medicine tracks. I have taught the graduate level course in Foundations of Neuropsychology for over 25 years. I have had a long history of collaborations with numerous research teams in neurology, psychology and radiology, and participated in multiple projects examining cognitive, behavioral and imaging changes associated with normal aging and neurodegenerative disease. I am currently the site PI of a study examining cognitive and behavioral changes among the oldest old as funded by the Mcknight Brain Research Institute as well as the UM Mcknight Frailty Project (see presentations for 2018 below). I am also a co-investigator on the NIH-funded population based Northern Manhattan Study, in which I am a member of the neuropsychology team and the dementia adjudication consensus panel. I am also a co-investigator on the Bugher AHA grant and a recently approved study (Dept of Defense) examining brain metabolites underlying pain associated with traumatic injury. I believe I have the qualifications, expertise and administrative and leadership abilities serve as the PI or Co-I on studies of examining cognitive function over the life span.

These peer reviewed publications highlight my experience and qualifications for this project:

1. **Levin BE**, Llabre MM, Dong C, Elkind MS, Stern Y, Rundek T, Sacco RL, Wright CB. Modeling metabolic syndrome and its association with cognition: the northern Manhattan study.J Int Neuropsychol Soc. 2014 Nov;20(10):951-60.
2. Maudsley A, Govind V**, Levin B**, Saigal G, Harris LT, Sheriff S. Distributions of MR Diffusion and Spectroscopy Measures with Traumatic Brain Injury.J Neurotrauma. 2014 Oct 21. [Epub ahead of print] PMID: 25333480
3. **Levin BE**, Katzen HL, Maudsley A, Post J, Myerson C, Govind V, Nahab F, Scanlon B, Mittel A.Whole-brain proton MR spectroscopic imaging in Parkinson's disease. J Neuroimaging. 2014 Jan-Feb;24(1):39-44

Newly accepted abstracts for 2018:

Banerjee, N., McInerney, K. F., Getz, S. J., Sun-Suslow, N., Gomes-Osman, J., Bure-Reyes, A., Sarno, M., Dong, C., Sun, X., Rundek, T., Levin, B.E. (2018, March). *The Relationship between Fatigue and Executive Function in Aging Adults*. Poster accepted at the International Conference on Frailty and Sarcopenia Research, Miami, FL.

Getz, S. J., McInerney, K. F., Banerjee, N. S., Gomes-Osman, J., Sun-Suslow, S., Merritt, S. Gaztanaga, W., Bure-Reyes, A., Sarno, M., Dong, C., Sun, C., Rundek, T., Levin, B. (2018, March). *Low Emotional Reserve as a Risk Factor for the Frailty Syndrome Independent of Gender*. Poster accepted at the 8th edition of the International Conference on Frailty and Sarcopenia Research, Miami, FL.

McInerney, K. F., Gomes-Osman, J., Banerjee, N. S., Getz, S. J., Sun-Suslow, S., Bure-Reyes, A., Sarno, M., Merritt, S., Gaztanaga, W., Dong, C., Sun, X., Rundek, T., Levin, B. (2018, March). *A Comparison of Frailty Criteria in Hispanic/Latino and Non-Hispanic/Latino Older Adults in South Florida*. Poster accepted at the 8thedition of the International Conference on Frailty and Sarcopenia Research, Miami, FL.

Getz, S. J., McInerney, K. F., Sun-Suslow, S., Banerjee, N. S., Bure-Reyes, A., Sarno, M., Levin, B. (2018, February). *Low Emotional Reserve as a Risk Factor for the Frailty Syndrome*. Poster accepted at the 46th annual meeting of the International Neuropsychological Society, Washington, DC.

Sun-Suslow, S., Getz, S. J., McInerney, K. F., Banerjee, N. S., Bure-Reyes, A., Sarno, M., Levin, B. (2018, February). *The Association between Indicators of Physical Frailty Syndrome and Cognitive Function*. Poster accepted at the 46th annual meeting of the International Neuropsychological Society, Washington, DC.

Sarno, M., Bure-Reyes, A., Banerjee, N., Getz, S., McInerney, K., Sun-Suslow, N., Pinjala, M., Luca, C., Moore, H., Singer, C., & Levin, B. (2018, February). *Is Age of Onset Related to Cognition and Mood in Essential Tremor?* Poster accepted at the 46th annual meeting of the International Neuropsychological Society, Washington, DC.

Banerjee, N., Sun-Suslow, N., Getz, S. J., Sarno, M., Bure-Reyes, A., Pinjala, M., Luca, C., Levin, B.E. (2018, February). *Age-related Differences in the Association between Cardiometabolic Risk Factors and Cognition in Parkinson's Disease*. Poster accepted at the 46th annual meeting of the International Neuropsychological Society, Washington, DC.

B. Positions and Honors

POSITIONS AND EMPLOYMENT

Academic Appointments

1979-1980	Fellow in Psychology, Department of Psychiatry, Harvard Medical School, Boston, MA
1979-1980	Intern, Clinical Pediatric Neuropsychology, Children's Hospital Center, Boston, MA.
1980	Extern, Boston Veteran's Administration Hospital, Boston, MA
1981-1982	Instructor, Department of Neurology, University of Miami
1981	Director, Division of Neuropsychology, Department of Neurology, University of Miami
1986-1992	Assistant Professor, Department of Neurology, University of Miami
1992-2011	Associate Professor (with tenure), Department of Neurology, University of Miami Miller School of Medicine
2011-	Professor of Neurology, Department of Neurology, University of Miami Miller School of Medicine

Honors

Cum Laude, Georgetown University; Psi Chi Honor Society1974
Fellow, Mahoney Residential College
International Neuropsychology Society (INS) Program Chair-1997
INS Board of Governors 1998-2001
NINDS Study Section Member NSD-K, 2001-2005
NINDS AD hoc Reviewer-NSD-A 2001, 2002
NINDS Special Emphasis Panels 7/1998, 8/1999, 12/1999, 5/2000, 8/2000, 10/2000, 12/2001, 6/2001, 10/2001, 8/2002, 12/2002, 1/2004, 8/2004, 12/2004, 2/2005, 1/2006, 10/2006, 11/2006, 11/2006, 6/2007, (6/24 & 6/29) 3/2008, 4/2008.
NINDS Ad hoc reviewer, NSD-K, 2006 - 2008
Alzheimer Association Medical and Scientific Council Reviewer, 1999, 2002
Consultant: University of Miami Brain Endowment Bank, Department of Neurology; Clinical Neuroscience Unit, UM Department of Neurology
Member, National Acute Brain Injury Study: Hypothermia II: Data Safety of Monitoring Board Pediatrics; UM Sleep Center, Department of Neurology.

Professional Advisory Board: Epilepsy Foundation of South Florida
Editorial Boards: Neuropsychology, Journal of International Neuropsychology Society, Neuropsychology Review, Aging, Neuropsychology and Cognition
Alexandria and Bernard Schoninger Endowed Professorship in Neurology, 2009

C. Contributions to Science

C.1. Over the past 30 years, I have focused on cognitive and behavioral changes over the life course. My research projects are largely in the field of aging, examining age related cognitive decline and early biomarkers of behavioral and cognitive decline in normal aging and neurodegenerative disease. As the Schoninger Professor or Neurology, I oversee the Division of Neuropsychology, a major training and research site that evaluates over 300 patients a year examining age related cognitive change as well as pathological behavioral alterations associated with degenerative disease. I have published extensively on cognitive change across the lifespan.

1. Kelley, R.E., Chang, JY, Scheinman, NJ, **Levin, BE**, Duncan, RC, Shih-Chang, L: Transcranial doppler ultrasonographic assessment of cerebral artery flow velocity during cognitive activity. Stroke, 1992; 23:9-14.
2. Tomer, R**, Levin, BE**, Differential affects of aging in two verbal fluency tasks. Perceptual and Motor Skills, 1993; 76: 465-466
3. **Levin, BE**, Katzen, H.L., Klein, B., Llabre, M. Cognitive decline affects subject attrition in longitudinal research. Journal of Clinical and Experimental Neuropsychology. 2000, 22 (5), 580-586.
4. Grossman A, Levin B, Katzen H, Lechner S. PTSD symptoms and onset of neurologic disease in elderly trauma survivors. Journal of Clinical and Experimental Neuropsychology 2004: 26(5): 698-705.

C.2.Our group was among the earliest investigators to document and describe non-motor changes in Parkinson's disease. I have also examined how gait and other lateralized motor changes are linked to cognitive and behavioral symptoms and PD progression. These studies reflect my longstanding interest in gait, movement and cognition.

1. **Levin, BE**, Llabre, MM, Weiner, WJ: Cognitive impairments associated with early Parkinson's disease. Neurology, 1989, 39:557-561.
2. **Levin, BE**, Llabre, MM, Weiner, WJ, Brown, MC: Visuospatial decline in Parkinson's disease. Neurology, 1991; 41:365-369.
3. Tomer, R, **Levin, BE**, Weiner, WJ: Side of motor onset influences cognition in Parkinson's disease. Annals of Neurology, 1993; 34:579-584.
4. Katzen, H, **Levin, BE**, Llabre, M: Age of onset influences cognition in Parkinson's disease. Journal of International Neuropsychological Society, 1998, 4, 285-290.

C.3. I am currently involved in several studies examining the relationship between MRS metabolites and cognitive changes in normative aging, TBI, ALS and Parkinson's disease. These studies utlize a unique whole brain analysis that permits a study of a large fraction of the brain volume, including the cortical mantle. My role as the neuropsychologist on these projects is to identify sensitive outcome measures and to work with my collaborators linking the behavioral presentation associated a traumatic injury or neurologic illness with distributions of proton magnetic resonance spectroscopy (MRS) observed metabolites throughout the whole brain.

1. **Levin BE**, Katzen, HL, Maudsley, A, Post, J, Myerson, C, Govind, G, Nahab, F, Scanlon, B, Mittel. A Whole-brain proton MR spectroscopic imaging in Parkinson's disease. Journal of Neuroimaging, 2014, 24, 39-44
2. Maudsley, A, Govind, V, **Levin, BE**, Saigal, G, Harris, L, Sheriff, S Distributions of MR Diffusion and Spectroscopy Measures with Traumatic Brain Injury. J. Neurotrauma. 2015; 32 (14): 1056-1063
3. Widerstrom-Noga, E, Govind, VB, Adcock, J**, Levin, BE**, Maudsley, A Subacute Pain after TBI is associated with lower insular N-acetyl-aspartate concentrations. Journal of Neurotrauma (in press)

Complete List of Published Work at NCBI:
http://www.ncbi.nlm.nih.gov/pubmed/?term=(%22levin%2C%20bonnie%22%5BAll%20Fields%5D)&cmd=DetailsSearch

D. Research Support

Ongoing Research Support

Scythian Bioscience **08/01/2016-7/30/2021**
The Effects of Cannabinoids on TBI ($16,000,0000)
B. Levin, Co-Investigator, Director of Clinical Trials

This study will examine the inflammatory properties of cannabinoids and determine whether they can be used as a therapeutic intervention in traumatic brain injury

7 R01 NS 029993 (PI, Sacco) NIH/NINDS **02/01/03-03/31/21** **1.20 calendar**
Stroke Incidence and Risk Factors in a TriEthnic Region **$1,795,509**
(B. Levin, Co-Investigator)
The goals of this project are to determine the effects of risk factors for stroke, MI, and vascular death, as well as evaluate predictors of cognitive impairment and the importance of subclinical MRI findings in a prospective cohort study of 3300 persons from 3 race-ethnic groups from Northern Manhattan.

09/28/12-09/27/15 **1.20 calendar**
National Multiple Sclerosis **$169,003**
Fast Forward a Randomized Double Blind Placebo Controlled (PI: Ortega; B. Levin, Co-Investigator)
To evaluate the therapeutics effects of caprylic triglyceride administered once a day for 90 days on cognitive impairment in subjects with multiple sclerosis.

AHA/ASA 14BFSC1759000 (PI: Sacco) **04/01/14 – 03/31/18** **0.6 calendar**
AHA (B. Levin, Co-Investigator) **$234,667**
Bugher Center Foundation Center of Excellence in Stroke Award
This award will conduct two projects evaluating the effects of physical activity and cognitive training on animals and stroke survivors on cognitive recovery

DoD/CDMRP/USAMRMC (PI: Widerstrom-Noga) **11/2015-10/2018** **.84 calendar**
(B. Levin, Co-Investigator) **$977,099** (direct)
Utility of MRS Brain Biomarkers of Pain Phenotypes after TBI
Goals are to evaluate advanced metabolic imaging methods for injury assessment and prognosis following mild and moderate traumatic brain injury.

Prior Research Support
NINDS 1 UO1 NS052478-01A2 (Adelson) **7/30/07 – 6/30/2011**
Pediatric Traumatic Brain Injury Consortium: Hypothermia
This is a multicenter clinical trial to determine the efficacy of early induced moderate hypothermia after severe TBI in a pediatric sample. Subject mortality at 3 months is the primary measure of outcome. Secondary outcome measures included functional assessment and performance based neuropsychological measures. Role: Study Principal Investigator of the Outcome Center.

NIH/NINDS 2U01NS38529-07A1 (Benavente/ Romano, site PI) **02/01/2008 – 6/30/2011**
Secondary Prevention of Small, Subcortical Strokes (SPS3)

NIH/NINDS R01 NS055107 (Maudsley) **6/1/2006 – 12/31/2012**
Volumetric MRSI Evaluation of Traumatic Brain Injury
Goals are to evaluate advanced metabolic imaging methods for injury assessment and prognosis following mild and moderate traumatic brain injury.

NIH/NINDS R01 NS060874 (Govind) **1/1/2009 – 8/31/2012**
Brain Metabolic Imaging in Amyotrophic Lateral Sclerosis
The major goal of this project is to examine the efficacy of whole-brain proton MRSI and DTI methods for evaluating cerebral pathological changes in ALS.

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Miguel A. Perez-Pinzon, PhD, FAHA	Professor
eRA COMMONS USER NAME mperezpinzon	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of Panama	B.Sc.	1983	Biology
University of Miami (RSMAS)	M.Sc.	1987	Marine Biology
University of Miami (RSMAS/Neurology)	PhD	1991	Neuroscience
New York University	Postdoc	1992	Neurophysiology
Stanford University	Postdoc	1993	Neuroscience

A. Personal Statement

Although I have been working on cerebral hypoxia/ischemia since 1987, my independent group at the University of Miami was established in 1995 and in the last two decades has been studying cerebral ischemia. I direct the Cerebral Vascular Disease Research Center at the University of Miami since 2005, which was established approximately 45 years ago by Dr. Pertiz Scheinberg (first Chair of Neurology at UM). Many seminal investigators of the field directed or were part of this center (e.g., Kyuya Kogure, Mordecai Globus, Dalton Dietrich). Dr. Myron Ginsberg led the center for 22 years until 2005. I am a Professor of Neurology and Neuroscience and I am Vice-Chairman of Basic Sciences in the Department of Neurology. My main research expertise is in the area of cerebral ischemia, which results from cardiac arrest or stroke. My research focuses on the areas of synaptic, vascular and mitochondrial dysfunction that ensue following cerebral ischemia. Over the last 20 years, my laboratory has investigated the signaling pathways that lead to neuroprotection against ischemia following ischemic preconditioning (IPC). Our goal is to develop new therapies for pre- and post-treatment in stroke and cardiac arrest patients. Our center uses a large number of techniques that include imaging, electrophysiology, behavior, stereotaxic surgeries, and molecular biology techniques.

B. Positions and Honors.

PROFESSIONAL APPOINTMENTS

1995 – 2001	Assistant Professor, Department of Neurology, University of Miami School of Medicine.
1999 – 2006	Co-Director of Cerebral Vascular Disease Center, University of Miami School of Medicine, Miami, Fl (Dr. Ginsberg, Director)
2001 – 2006	Associate Professor, Department of Neurology, University of Miami School of Medicine.
2005 – present	Director of Cerebral Vascular Disease Center, University of Miami, Miller School of Medicine, Miami, Fl
2006 – present	Professor, Department of Neurology, University of Miami Miller School of Medicine, Miami, Fl
2007 – 2010	Associate Chair for Basic Science, Department of Neurology, University of Miami Miller School of Medicine, Miami, FL
2010 – present	Vice-Chair for Basic Science, Department of Neurology, University of Miami Miller School of Medicine, Miami, Fl

AWARDS AND OTHER PROFESSIONAL ACTIVITIES:

1982, 1983	Fellowships (2), Smithsonian Tropical Research Institute (STRI). Panama
1986	Fellowship, Fishing and Conservation Trust. Miami, Fl
1989 - present	Member of Society for Neuroscience (1989), International Society on Oxygen Transport to Tissues (1996), International Society of Cerebral Blood Flow and Metabolism (1995),

	American Association for the Advancement of Science (1996) and American Heart Association (2000)
1991	Koczy Fellowship, (Graduate student of the year) for excellence in graduate research and education, Rosenstiel School of Marine and Atmospheric Science, Univ of Miami, Miami, Fl
1991	Invited speaker at the Society for Experimental Biology in Birmingham, U.K.
2000 – 03	NIH-NINDS BDCN-3 Study Section reviewer
2000	Invited speaker at the Pharmacology of Cerebral Ischemia Symposium. Marburg, Germany.
2002	Grass Traveling Scientist for the Alaska Chapter of the Society for Neuroscience. Society for Neuroscience
2004 – 08	Brain 2 American Heart Association Grant Reviewer
2006 – 10	NIH-NINDS BINP Study Section
2014	NIH-NINDS BINP Study Section Ad-hoc member
2007 – 08	International Stroke Conference Program Committee: Co-Chair–Experimental Mechanisms and Models.
2008 – 10	International Stroke Conference Program Committee: Chair–Experimental Mechanisms and Models.
2009	Associate Editor for the journal: Translational Stroke Research
2010	Assistant Editor for the journal: Stroke
2010	Elected as Fellow of the American Heart Association/American Stroke Association (FAHA)
2012-13	Co-Chair of the Program Committee for the International Society of Cerebral Blood Flow and Metabolism (Brain 13), Shanghai, China
2014	Member of the Program Committee for the International Society of Cerebral Blood Flow and Metabolism (Brain 15), Vancouver, Canada
2016-18	Vice-Chair of the Program Committee for the International Stroke Conference. I will serve in that role for 2 years before becoming Chair of the Program Committee in February 2018 for 2 more years

C. Contribution to Science

1. My group has been studying mitochondrial dysfunction for approx 20 years. In the late 1990's we carried out several studies that defined the effect of anoxia/ischemia and reperfusion on mitochondrial electron carrier hyperoxidation, including NADH. We also published simultaneously with the Pak Chan's group in 1999, the first study demonstrating cytochrome c release from mitochondria following cerebral anoxia/ischemia. For the last 15 years, my group has done seminal work on the signaling pathways that lead to mitochondrial dysfunction and apoptosis and on signaling pathways that lead to ischemic neuroprotection.

a. Morris-Blanco, K. C., Dave, K. R., Saul, I., Koronowski, K. B., Stradecki, H. M. & Perez-Pinzon, M. A. Protein Kinase C Epsilon Promotes Cerebral Ischemic Tolerance Via Modulation of Mitochondrial Sirt5. *Sci. Rep.* **20**;6:29790 (2016). PMID: 27435822
b. Morris-Blanco, K. C., Cohan, C. H., Neumann, J. T., Sick, T. J. & Perez-Pinzon, M. A. Protein kinase C epsilon regulates mitochondrial pools of Nampt and NAD following resveratrol and ischemic preconditioning in the rat cortex. *J Cereb Blood Flow Metab* **34**, 1024-1032, (2014). PMID:24667915
c. Thompson, J. W., Dave, K. R., Saul, I., Narayanan, S. V. & Perez-Pinzon, M. A. Epsilon PKC increases brain mitochondrial SIRT1 protein levels via heat shock protein 90 following ischemic preconditioning in rats. *PLoS One* **8**, e75753, (2013). PMID:24058702
d. Dave, K. R., DeFazio, R. A., Raval, A. P., Torraco, A., Saul, I., Barrientos, A. & Perez-Pinzon, M. A. Ischemic preconditioning targets the respiration of synaptic mitochondria via protein kinase C epsilon. J Neurosci 28, 4172-4182, (2008). PMID:18417696

2. My group has also been a leader in the field of ischemic preconditioning. We have been studying compounds such as resveratrol and certain PKC isoforms to pharmacologically precondition *in vivo* and *in vitro* to lessen ischemia-induced neuronal damage. We sought to identify novel preconditioning pathways to alleviate ischemia, so therapies can be developed based on this mechanistic approach.

a. Koronowski, K. B., Dave, K. R., Saul, I., Camarena, V., Thompson, J. W., Neumann, J. T., Young, J. I. & Perez-Pinzon, M. A. Resveratrol Preconditioning Induces a Novel Extended Window of Ischemic Tolerance in the Mouse Brain. *Stroke* **46**, 2293-2298, (2015). PMID:26159789
b. Neumann, J. T., Thompson, J. W., Raval, A. P., Cohan, C. H., Koronowski, K. B. & Perez-Pinzon, M. A. Increased BDNF protein expression after ischemic or PKC epsilon preconditioning promotes electrophysiologic changes that lead to neuroprotection. J Cereb Blood Flow Metab 35, 121-130, (2015). PMID:25370861
c. Narayanan, S. V., Dave, K. R., Saul, I. & Perez-Pinzon, M. A. Resveratrol Preconditioning Protects Against Cerebral Ischemic Injury via Nuclear Erythroid 2-Related Factor 2. Stroke 46, 1626-1632, (2015). PMID:25908459
d. Raval, A. P., Dave, K. R., Mochly-Rosen, D., Sick, T. J. & Perez-Pinzon, M. A. Epsilon PKC is required for the induction of tolerance by ischemic and NMDA-mediated preconditioning in the organotypic hippocampal slice. J Neurosci 23, 384-391, (2003). PMID:12533598

3. Another major area of research in my group is to define the pathological mechanisms in the brain that ensue following cardiac arrest. We have targeted multiple aspects of the pathology that include synaptic dysfunction, cognitive impairments and cerebral blood flow derangements. We have shown that PKCε activation provides neuroprotection while activation of δPKC is detrimental to the ischemic brain. Overall, my studies provide a potential pathway of ischemia-mediated neuroprotection by the regulation of cerebral blood flow from evaluating blood flow dynamics, neuroprotection, and functional neuronal outcomes/firing properties based on electrophysiological studies.

a. Cohan, C. H., Neumann, J. T., Dave, K. R., Alekseyenko, A., Binkert, M., Stransky, K., Lin, H. W., Barnes, C. A., Wright, C. B. & Perez-Pinzon, M. A. Effect of cardiac arrest on cognitive impairment and hippocampal plasticity in middle-aged rats. PLoS One 10, e0124918, (2015). PMID:25933411
b. Lin, H. W., Gresia, V. L., Stradecki, H. M., Alekseyenko, A., Dezfulian, C., Neumann, J. T., Dave, K. R. & Perez-Pinzon, M. A. Protein kinase C delta modulates endothelial nitric oxide synthase after cardiac arrest. J Cereb Blood Flow Metab 34, 613-620, (2014). PMID:24447953
c. Lin, H. W., Defazio, R. A., Della-Morte, D., Thompson, J. W., Narayanan, S. V., Raval, A. P., Saul, I., Dave, K. R. & Perez-Pinzon, M. A. Derangements of post-ischemic cerebral blood flow by protein kinase C delta. Neuroscience 171, 566-576, (2010). PMID:20813167
d. Raval, A. P., Dave, K. R., Prado, R., Katz, L. M., Busto, R., Sick, T. J., Ginsberg, M. D., Mochly-Rosen, D. & Perez-Pinzon, M. A. Protein kinase C delta cleavage initiates an aberrant signal transduction pathway after cardiac arrest and oxygen glucose deprivation. J Cereb Blood Flow Metab 25, 730-741, (2005). PMID:15716854

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/40678659/?sort=date&direction=descending

D. Research Support.

Active

R01 NS45676-08 **Perez-Pinzon (PI)** 6/1/07-5/31/17
NIH/NINDS
Mechanisms of Neuroprotection against Cardiac Arrest
The major goal of this project is to study the mechanisms of synaptic and vascular dysfunction and putative neuroprotective agents following cardiac arrest.
Non-cost extension

R01 NS34773-15 **Perez-Pinzon (PI)** 6/1/15-5/31/20
NIH/NINDS
Ischemic Preconditioning: Mechanisms of Neuroprotection

The major goal of this project is to study the signaling pathways that lead to ischemic preconditioning neuroprotection

R01 NS34773-15 **Perez-Pinzon (PI)** 6/1/17-5/31/22
NIH/NINDS
Metabolic master regulators for ischemic neuroprotection
The main goals were the elucidation of signaling pathways involved in the fate of brain mitochondria following cerebral ischemia.

American Heart Association/ASA-Bugher Foundation (14BFSC17690007). Sacco R. (PI) 4/1/14-3/31/18
Physical and Cognitive Training to Enhance Post-Stroke Outcomes. **Project 2 (PI – Perez-Pinzon)**: Enriched Environment, Exercise And Neurotherapeutics To Enhance Functional Recovery Following A Stroke

1R21NS098896-01 **Perez-Pinzon (PI)** 7/1/16-6/30/18
NIH/NINDS
Decellularized Extracellular Matrix Biomaterials As Therapy To Ameliorate Cerebral Ischemia Damage
The goals of the project are for the University of Miami to help build stroke research capabilities at INDICASAT AIP, Panama which will ultimately help foster stronger collaboration between the two institutes and to evaluate therapeutic potential of decellularized extracellular matrix biomaterials against cerebral ischemic damage.

5R01NS073779-04 **Dave, Kunjan (PI)** 3/1/12-12/1/17
Increased cerebral ischemic injury by repeated hypoglycemic episodes in diabetes.
The long-term goal of this project is to improve neurological health of diabetics by decreasing the severity and incidence of cerebral ischemia in diabetics.

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Milena Pinto	Research Assistant Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
Università degli studi di Trieste, Italy	Ms.D	2005	Medical Biotechnology
International School for Advanced Studies, Trieste, Italy	Ph.D.	2009	Neurobiology

A. Personal Statement

I have more than ten years of research experience on neurodegenerative disorders, in particular on Parkinson's and Alzheimer's disease. During my Masters and PhD studies, I extensively worked on drug-induced and genetically modified animal models of Parkinson's disease as well as on cellular models of dopaminergic neurons. When I joined Dr. Moraes lab in 2010 for my postdoctoral training, I have been involved in understanding the possible neuronal-specific role of mitochondrial dysfunctions and mitochondrial DNA deletions and depletion in mouse models of neurodegenerative disorders, in particular of Parkinson's and Alzheimer's diseases. My PhD background and my experience in Dr. Moraes' lab conferred me a specific and deep knowledge in both fields of neurology and mitochondria metabolism. Recently I was appointed with a Research Assistant Professor position at the University of Miami to study the role of mitochondria and mtDNA damage on mouse models of Alzheimer's disease.

B. Positions and Honors.

2017-Current	Research Assistant Professor at neurology department in University of Miami
2015-2017	Sr. Research Associate at neurology department in University of Miami
2010-2015	Postdoctoral associate at neurology department in University of Miami
2009	Temporary Research Fellow, International School for Advanced Studies, Trieste, Italy
Nov-2014	ISSNAF Award for young Investigators, Special Mention, Bio-Medicine and Cognitive Sciences
April-2013	UMDF, Mitochondrial Medicine 2013 Abstract Cash Award
March-2013	Medical Faculty Association Travel Award from the Margaret Whelan foundation

C. Recent Posters and Presentations.

- Miami 2016 Winter Symposium: Inflammation
  Poster presentation: Pioglitazone ameliorates the phenotype of a novel mouse model with cytochrome oxidase defect in dopaminergic neurons

- Cell Symposia: Multifaceted Mitochondria 2015 in Chicago
  Poster presentation: Pioglitazone ameliorates the phenotype of a novel mouse model with cytochrome oxidase defect in dopaminergic neurons.

- ISSNAF 2014, Washington DC
  Poster presentation: Mitochondrial TAL effector nucleases as therapy for mitochondrial diseases

- Euromit 2014 in Tampere, Finland
  Poster presentation: Lack of Parkin accelerates neurodegeneration in a mouse model of PD

- Miami 2014 Winter Symposium: The Molecular Basis of Brain disorders
  Poster presentation: Endogenous Parkin mitigates mitochondrial damage in dopaminergic neurons and ameliorates associated motor phenotypes

- NHLBI Mitochondrial Biology Symposium 2013, Bethesda
  Poster presentation: Mitochondrial DNA damage in a mouse model of Alzheimer's disease decreases Aβ plaque formation

- Miami 2013 Winter Symposium: The Molecular Basis of Metabolism and Nutrition
  Poster presentation: Induced mitochondrial DNA damage in a mouse model of Alzheimer's disease decreases A□ plaque formation

- UMDF 2013
  Oral presentation: The Role of Parkin in the Clearance of Defective Mitochondria with Deleted mtDNA. A New Mouse Model of Parkinson's Disease

- Society for Neuroscience, Neuroscience 2011
  Poster presentation: Characterization of a new mouse model to study the role of oxidative phosphorylation deficits in Parkinson's disease

D. Selected peer-reviewed publications (in chronological order).

Milena Pinto*, Alicia M. Pickrell*, Xiao Wang*, Sandra R. Bacman, Aixin Yu, Aline Hida, Lloye M. Dillon, Paul D. Morton, Thomas R. Malek, Siôn L. Williams, and Carlos T. Moraes. **(*) co-authorship**
Transient mitochondrial DNA double strand breaks in mice cause accelerated aging phenotypes in a ROS-dependent but p53/p21-independent manner.
Cell Death Differ. 2017 Feb;24(2):288-299. [PMID: 27911443]

Pinto M, Nissanka N, Peralta S, Brambilla R, Diaz F, Moraes CT.
Pioglitazone ameliorates the phenotype of a novel Parkinson's disease mouse model by reducing neuroinflammation.
Mol Neurodegener. 2016 Apr 2;11(1):25 [PMID: 27038906]

Bacman SR, Williams SL, **Pinto M**, Peralta S, Moraes CT.
Specific elimination of mutant mitochondrial genomes in patient-derived cells by mitoTALENs.
Nat Med. 2013 Sep;19(9) [PMID: 23913125]

Pinto M, Pickrell AM, Fukui H, Moraes CT.
Mitochondrial DNA damage in a mouse model of Alzheimer's disease decreases amyloid beta plaque formation.
Neurobiol Aging. 2013 Oct;34(10):2399-407 [PMID: 23702344]

Vilotti S, Codrich M, Dal Ferro M, **Pinto M**, Ferrer I, Collavin L, Gustincich S, Zucchelli S.
Parkinson's disease DJ-1 L166P alters rRNA biogenesis by exclusion of TTRAP from the nucleolus and sequestration into cytoplasmic aggregates via TRAF6.
PLoS One. 2012;7(4):e35051 [PMID: 22532838]

Milena Pinto(*), Alicia Pickrell(*), Aline Hida, Carlos Moraes **(*) co-authorship**
Striatal dysfunctions associated with mtDNA damage in dopaminergic neurons of a mouse model of PD
J Neurosci. 2011 Nov 30;31(48):17649-58 [PMID: 22131425]

Alicia Pickrell, Hirokazu Fukui, Xiao Wang, **Milena Pinto**, and Carlos Moraes
The Striatum is Highly Susceptible to Mitochondrial Oxidative Phosphorylation Dysfunctions
J Neurosci. 2011 Jul 6;31(27):9895-904 [PMID: 21734281]

Zucchelli S., Marcuzzi F., Codrich M., Agostoni E., Vilotti S., Biagioli M., **Pinto M**., Carnemolla A., Santoro C., Gustincich S. and Persichetti F.
Tumor Necrosis factor receptor associated factor 6 (TRAF6) associates with huntingtin protein and promotes its atypical ubiquitination to enhance aggregate formation
J Biol Chem. 2011 Jul 15;286(28):25108-17 [PMID: 21454471]

Zucchelli S., Codrich M, Marcuzzi F, **Pinto M**, Vilotti S., Biagioli M, Ferrer I, Gustincich S.
TRAF6 promotes atypical ubiquitination of mutant DJ-1 and alpha-synuclein and is localized to Lewy bodies in sporadic Parkinson's disease brains.
Hum Mol Genet. 2010 Jul 14 [PMID: 20634198]

Milena Pinto(*), Marta Biagioli (*), Daniela Cesselli, Marta Zaninello, Dejan Lazarevic, Roberto Simone, Christina Vlachouli, Charles Plessy, Nicolas Bertin, Antonio Beltrami, Kazuto Kobayashi, Vittorio Gallo, Isidro Ferrer, Claudio Santoro, Stefano Rivella, Carlo Alberto Beltrami, Piero Carninci, Elio Raviola and Stefano Gustincich. **(*) co-authorship**
Unexpected expression of α- and β-globin in mesencephalic dopaminergic neurons and glial cells
PNAS, 2009 Sep. vol.106 no.36 [PMID: 19717439]

Zucchelli S, Vilotti S, Calligaris R, Lavina ZS, Biagioli M, Foti R, De Maso L, **Pinto M**, Gorza M, Speretta E, Casseler C, Tell G, Del Sal G, Gustincich S.
Aggresome-forming TTRAP mediates pro-apoptotic properties of Parkinson's disease-associated DJ-1 missense mutations.
Cell Death and Differetiation 2009 Mar;16(3):428-38 [PMID 19023331]

Complete list of publications:
https://www.ncbi.nlm.nih.gov/sites/myncbi/milena.pinto.1/bibliography/50578890/public/?sort=date&direction=ascending

E. Research Support

Postdoctoral Fellowship to Milena Pinto 07/2013 – 07/2014
Parkinson's Disease Foundation
"*The role of Parkin in the clearance of defective mitochondria with deleted mtDNA. A new mouse model of Parkinson's disease*."
Role: Postdoctoral Research Fellow

Research Grant to Moraes, Carlos 09/15/2010 - 09/14/2013
Muscular Dystrophy Association
"Increased mitochondrial biogenesis as a therapy to mitochondrial disorders"
The objective of this project is to study the effect of PGC-1α in mitochondrial myopathies.
Role: Postdoctoral Research Fellow

BIOGRAPHICAL SKETCH

a) Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: **Alberto R. Ramos, MD, MSPH, FAASM**

eRA COMMONS USER NAME (credential, e.g., agency login): ARAMOS1

POSITION TITLE: Associate Professor of Neurology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	1. DEGREE *(if applicable)*	Completion Date MM/YYYY	2. FIELD OF STUDY
University of Puerto Rico, Rio Piedras, Puerto Rico	BS	05/1999	Natural Sciences
Universidad Central del Caribe, PR. **CUM LAUDE**	MD	05/2003	Medical Doctor
Jackson Memorial Hospital-U. of Miami	Residency	06/2007	Neurology
Miami VA Health Care System-U. of Miami	Fellowship	06/2008	Sleep Medicine
University of Miami, Miller School of Medicine	MSPH	08/2012	Epidemiology
University of Miami, Miller School of Medicine	MS	Expected 5/2018	Translational Research

A.

B. Personal Statement

1. I am an early stage investigator in the Department of Neurology and Sleep Medicine, at the Miller School of Medicine, University of Miami. Miami, FL. My research is aimed at the intersection between sleep disorders, cerebrovascular disease and neurocognitive aging in population based studies. My work started with the multi-ethnic cohort of the Northern Manhattan study (NOMAS). I completed a diversity supplement grant from the NIH/NINDS, aimed to determine the sleep disorders associated to stroke risk factors and cognitive decline in NOMAS. I am an investigator of the Hispanic Community Health Study/Study of Latinos (HCHS/SOL); where I serve as primary consultant for Sleep Research. I recently obtained an R21 through the National Institutes of Aging to evaluate sleep phenotypes, neurocognitive decline and incident dementia in HCHS/SOL. I am also the site-PI for the Sueño study-*Sleep as a Risk Factor for Disease in HCHS/SOL* – Field Center at the University of Miami. This NHLBI ancillary study evaluated the determinants of abnormal sleep patterns with actigraphy and their effect on cardiometabolic diseases. I am also the principal investigator of an HCHS/SOL ancillary study evaluating sleep apnea and cerebral hemodynamics as an early marker of cerebrovascular risk at the Miami field site. This study was supported by a K12 mentored award from the Clinical Translational Research Institute at the Miller School of Medicine.

C. Positions and Honors

Positions

2006-07 Administrative Chief Resident-Neurology, University of Miami/Jackson Memorial Hos., Miami, FL
2007-09 Staff Physician; Neurology Service, Miami VA Healthcare System, Miami, FL
2008-09 Instructor, Miller School of Medicine, University of Miami, Miami, FL
2009 -16 Assistant Professor of Clinical Neurology, Miller School of Medicine, Miami, FL
2010- Co-Director, Sleep Medicine Program, Miller School of Medicine, Miami, FL
2016- Associate Professor of Clinical Neurology, Miller School of Medicine, Miami, FL

Honors

2003 Alpha Omega Alpha. Universidad Central Del Caribe, School of Medicine, PR
2007 Clinical Neuroscience Prize, Neurology Residency program, U. of Miami. Miami, FL
2008 Faculty Development Award-American Neurological Association

2010-14 Who's who in America
2010-14 America's Top Physician, Consumer's Research Council of America
2011 Distinguished Judge. Department of Otolaryngology, Miller School of Medicine. Miami, FL.
2012 NIH/American Academy of Sleep Medicine Young Investigators forum award
2013 Scholar, Program to Increase Diversity among Individuals Engaged in Health-Related Research (PRIDE), NHLBI-New York University, NY
2013 Fellow, American Academy of Sleep Medicine
2015 Diversity Leadership Development Program-American Academy of Neurology, Minneapolis, MN
2015 Peer Mentor, Programs to increase Diversity among individuals Engaged in Health Related Research (PRIDE), NHLBI-New York University, NY.
2015 Award, U13 Conference Series: Sleep, Circadian Rhythms, and Aging: Supported by the National Institutes of Aging and the American Geriatric Society.

C. Contribution to Science

1. Sleep and neurocognitive aging

My research program evaluates sleep as a determinant of health disparities in neurocognitive aging and cerebrovascular risk in minority populations; particularly Hispanic/Latinos, who are at higher risk for Alzheimer's disease, cerebrovascular disease and have a large burden of sleep apnea and other sleep disorders. We published various manuscripts evaluating sleep symptoms and disorders and neurocognitive function in the Northern Manhattan study (NOMAS) and the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). We initially observed a cross-sectional association between long sleep duration and worse global cognitive function in NOMAS. This study was followed by our recent cross-sectional findings from HCHS/SOL Visit 1 ($n \approx$ 8,000). In this study, sleep apnea was associated with worse neurocognitive function, particularly among women, in the domains of memory, language and executive function. The association was stronger in younger (45-54 years), rather than older females (65-74 years). We also performed a cross-sectional evaluation of sleep duration and neurocognitive function in HCHS/SOL. We found curvilinear (inverted U-shaped) associations between self-reports of sleep duration and neurocognitive function. That is, participants with average (7.8 hours ± 1.7 hours) self-reported sleep duration had better neurocognitive scores, compared to the extremes of sleep duration. The HCHS/SOL cohort and its investigators provides the opportunity to evaluate objective and systematic measures of sleep apnea-hypoxemia and sleep habits (duration, quality and fragmentation) in a vulnerable population burdened with cerebrovascular and Alzheimer's disease.

b) **Ramos AR,** Dong C, Elkind MSV, Boden-Albala B, Sacco RL, Rundek T, Wright CB**.** Association between Sleep Duration and the Mini-Mental Score: The Northern Manhattan Study. J Clin Sleep Med 2013 15; 9:669-673. PMID: 23853560

c) **Ramos AR**, Tarraf W, Rundek T, Redline S, Wohlgemuth WK, Loredo JS, Sacco RL, Lee DJ, Arens R, Lazalde P, Choca JP, Mosely T, Gonzalez, HM. Obstructive Sleep Apnea and Neurocognitive Function among Hispanics/Latinos. Neurology 2015;84:391-398.PMID:2554030

d) **Ramos AR,** Tarraf W, Daviglus M, Davis S, Gallo LC, Mossavar-Rahmani Y, Penedo FJ, Redline S, Rundek T, Sacco RL, Sotres-Alvarez D, Wright CB, Zee PC, González HM. Sleep Duration and Neurocognitive Function in the Hispanic Community Health Study/Study of Latinos. Sleep. 2016 Jul 19. pii: sp-00405-15. [Epub ahead of print] PMID: 27450689

e) **Ramos AR**, Gardener H, Rundek T, Elkind MS, Boden-Albala B, Dong C, Cheung YK, Stern Y, Sacco RL, Wright CB. Sleep disturbances and cognitive decline in the Northern Manhattan Study. Neurology. 2016 Sep 2. [Epub ahead of print] PMID:27590286

2. **Sleep disorders and sub-clinical vascular disease**: My research in this area started while evaluating sleep symptoms and subclinical vascular disease in the Northern Manhattan study. We also evaluated subclinical vascular diseases and vascular risk factors in the Hispanic Community Health Study/Study of Latinos (N=16,415). Collectively, my body of research shows that sleep apnea symptoms and sleep duration is strongly

associated with sub-clinical vascular disease, particularly measures of cerebral small vessel disease, which are often adversely related to neurocognitive aging and neurocognitive decline.

f) **Ramos-Sepulveda A**, Wohlgemuth W, Gardener H, Lorenzo D, Dib S, Wallace DM, Nolan B, Boden-Albala B, Elkind MS, Sacco RL, Rundek T. Snoring and insomnia are not associated with subclinical atherosclerosis in the Northern Manhattan Study. Int J Stroke. 2010; 5:264-8. PMID:20636708

g) **Ramos AR**, Cabral D, Lee DJ, Sacco RL, Rundek T. Cerebrovascular Pulsatility in Patients with Sleep Disordered Breathing. Sleep Breath 2013; 17:723-6. PMID: 22773271

h) **Ramos AR,** Jin A, Rundek T, Russo C, Homma S, Elkind M, Sacco RL, Di Tullio MR. Relation between Long Sleep and Left Ventricular Mass from a Multi-Ethnic Elderly Cohort. Am J Cardiol 2013; 112:599-603. PMID: 2371181

i) **Ramos AR**, Dong C, Rundek T, Elkind ESV, Boden-Albala B, Sacco RL, Wrigth CB. Sleep Duration is associated with White Matter Hyperintensity Volume in Older Adults: The Northern Manhattan Study. J Sleep Res 2014; 23:524-30. PMID: 25040435

3. **Sleep disorders and health disparities**

The long term goal of my research program is to alleviate the sleep health disparities and improve health outcomes in minority populations. I aimed to determine the factors associated to health disparities in Hispanic/Latinos and non-Hispanic blacks. This line of research presents a unique opportunity to understand and reduce seemingly intractable stroke and cardiovascular disparity among non-Hispanic blacks and Hispanic/Latinos. There is limited awareness, knowledge and screening opportunities for sleep disorders in minorities. Our recent work showed that Hispanic/Latinos have greater frequency of sleep symptoms, compared to non-Hispanic whites; and these sleep symptoms may precede ischemic stroke diagnosis.

j) **Ramos AR**, Wohlgemuth WK, Dong C, et al. Race-ethnic differences of sleep symptoms in an elderly multi-ethnic cohort:The Northern Manhattan Study. Neuroepidemiology 2011; 37:210-5. PMID:22123526

k) Dib S, **Ramos A**, Wallace D, Rundek T.Sleep and Stroke. Periodicum Biologorum 2013;114:369-75

l) **Ramos AR**, Azizi A, Dib SI. Obstructive sleep apnea and stroke: links to health disparities. Sleep Health: Journal of the National Sleep Foundation 2015; 1: 244-248

m) **Ramos AR**, Guilliam D, Dib SI, Koch S. Race/ethnic differences in obstructive sleep apnea risk in patients with acute ischemic strokes in south Florida. Sleep Breath. 2014;18:165-8.PMID 23771345

Link to complete list of publications:
https://www.ncbi.nlm.nih.gov/sites/myncbi/alberto.ramos.1/bibliography/46171108/public/?sort=date&direction=ascending

D. RESEARCH SUPPORT (Ongoing and Completed)

Ongoing Research Support:

3. R21 : R21AG056952 NIA/NIH Ramos (PI) 08/2017-05/2019
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. 30% effort time

4. NHLBI Project number 268201300004I-0-26800004-1. Schneiderman (PI-Miami) 06/2013-06/2019
Hispanic Community Health Study/Study of Latinos.
Ongoing NHLBI-funded multicenter epidemiological longitudinal study of the health in over 16,000 U.S. Latinos designed to describe the prevalence of cardiovascular and pulmonary disease and other select chronic diseases, their protective or harmful factors, and changes in health over time, including incidence of fatal and non-fatal cardiovascular disease events, exacerbation of pulmonary disease and all-cause mortality. In addition, the role of sociocultural factors (including acculturation) on Hispanic/Latino.
Role: Co-Investigator, Miami-Site

5. Boehringer Ingelheim. Chaturvedi (PI) 05/2016-04/2018
Arrhythmia Detection In Obstructive Sleep apnea (ADIOS)
The goal of the study is to evaluate cardiac arrhythmias and use anticoagulants as a novel therapy for stroke prevention in patients with newly diagnosed obstructive sleep apnea.
Role: Co-Investigator

6. Scythian Biosciences Inc. Levin (PI) 6/2017-5/2020
The effects of cannabinoids on traumatic brain injury
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. Role: Co-Investigator

Completed Research support:

7. KL2TR000461-02 Sacco (PI) 06/2013-6/2016
Sleep apnea and cerebral hemodynamics: The Hispanic Community Health Study. The goal of this study is to evaluate the cerebral hemodynamics as an early marker of cerebrovascular risk in participants with sleep apnea and controls. National Institutes of Health, Clinical Translational Institute at the Miller School of Medicine, University of Miami, Miami, FL. Mentored Translational Research Scholars Program (K12). Role: Scholar, 75% effort time.

8. R37 (Javits Award): 2R01 (NS 29993), Sacco (PI) 06/2009-05/2012
Stroke Incidence and Risk Factors in a Tri-Ethnic Region Agency. The goal of the study was to investigate the associations between sleep symptoms and sub-clinical vascular disease in a prospective cohort of 3298 community subjects in the Northern Manhattan Study. Supplements to Promote Diversity in Health-Related Research. Role: Scholar, 50% effort time.

9. R01: HL098297 Patel (PI) 07/2011-04/2014
Sueño: Sleep patterns as a risk factor in the Hispanic Community Health Study. The goal of the study was to determine the cardiovascular consequences of abnormal sleep patterns with actigraphy in Hispanic/Latinos. Role: Site PI/Co-investigator, 10% effort time.

10. Loan Repayment Program 08/2014-07/2016
National Institutes of Health/National Institute of Minority Health and Health Disparities Amount:$40,000

11. Loan Repayment Program, one year extension 08/2013-07/2014
National Institutes of Health/National Institute of Minority Health and Health Disparities Amount: $35,000

12. Loan Repayment Program, one year extension 08/2012-07/2013
National Institutes of Health/National Institute of Minority Health and Health Disparities, Amount: $35,000

13. Loan Repayment Program 08/2010- 07/2012
National Institutes of Health/National Institute of Minority Health and Health Disparities, Amount: $75,000

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Ami P. Raval	**Research Assistant Professor**
eRA COMMONS USER NAME (credential, e.g., agency login) **ARAVAL**	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
M.S. University of Baroda, India	B. Sc	1989	Zoology, Botany, Chemistry
M.S. University of Baroda, India	M.Sc	1991	Zoology
M.S. University of Baroda, India	Ph.D	1995	Zoology (Physiology of reproduction)
University of Miami, USA	Post-doc	2000-2003	Neurophysiology
University of Miami, USA	MSPH	2010-2012	Epidemiology

A. Personal Statement

I have numerous years of experience in the field of cerebral ischemia and mitochondrial biology. My ongoing research focuses on elucidating the mechanism(s) by which the female sex hormone- estrogen - decreases the risk of cerebral ischemia in females utilizing *in* vivo and *in vitro* cerebral ischemia models in rats, and analysis of mitochondrial function. While working to earn my PhD, I studied the effects of endogenous variations of female sex hormones on non-reproductive tissues; this knowledge helped me to design studies to understand the mechanism of ischemic brain protection by estrogen. My post-doctoral training with Dr. Miguel A. Perez-Pinzon, a prominent neuroscientist and a pioneer in field of ischemic preconditioning and center PI of present application, laid a strong foundation for me in the basics essential for understanding ischemic neurodegeneration. I continued to study the mechanism of neuronal death following cerebral ischemia that is a consequence of cardiac arrest or stroke, and I am well versed in various *in vivo* and *in vitro* models of cerebral ischemia as well as in imaging, electrophysiology, and behavior and molecular biology techniques. I have also succesfully trained and supervised post-doctoral fellows, students, and technicians to perform ischemia models and the aforementioned techniques. I am also part of the University of Miami's undergraduate neuroscience program, and I am involved in education of premedical and medical students.

B. Positions and Honors:

Professional Experience:

- Lecturer: Zoology, M. S. University of Baroda, Gujarat, India. 07/1994 to 11/2000
- Assistant scientist: University of Miami, U.S.A. 9/1/2003 – 12/31/2006
- Research Assistant Professor: University of Miami, U.S.A. 2/1/2006 - Present
- American Heart Association- Innovative grant study section reviewer Fall 2014 - Present
- American Heart Association- Brain 2 study section reviewer Spring 2015 - Present
- Animal resource committee member 2009- present
- Institutional Scientific advisory committee grants Ad-hoc reviewer 2012-Present
- Facilitator for MD-MPH Problem base learning at University of Miami 2014-Present
- NIH-Neuroendocrinology, Neuroimmunology, Rhythms and Sleep Study Section Ad-hoc member 2017

Honors, Awards, and Professional Societies:

- Fellowship awarded by Gujarat Government of India for Ph.D. studies from 1991 to 1994.
- Awarded Young Scientist award on "Effect of sex hormones on Salivary gland" by ICMR, New Delhi.
- Awarded American Heart Association (Florida/Puerto Rico) Post-doctoral Fellowship 7/2002 to 6/2004. (AHA identification number- 0225227B)

- Best poster 2009 at Celebrating Excellence in Women's Health Research, University of Miami, Miami
- Member of the Society for Neuroscience.
- Member of the Society for Cerebral Blood Flow & Metabolism.

C. Contribution to Science

1. Studies form my laboratory simulating the conditions of nicotine exposure produced by cigarette smoking and the oral contraceptive (OC) regimen of women in female rats provides evidence that the severity of ischemic hippocampal damage is far greater in female rats simultaneously exposed to OC than to nicotine alone. These studies also demonstrated that the concurrent exposure of OC and nicotine reduces endogenous 17β-estradiol levels and inhibits ER-β signaling in the brains of female rats. My study demonstrated that concurrent exposure to nicotine and OC impaired ER-β-mediate mitochondrial respiration at the complex-IV level due to lower protein levels of its catalytic subunits in the hippocampus of female rats.

a. **Raval AP****, Borges-Garcia R, Diaz F, Sick TJ and Bramlett H. Oral contraceptives and nicotine synergistically exacerbate cerebral ischemic injury in the female brain. Translational Stroke Research 2013 4:402–412
b. **Raval AP****, Sick JT, Gonzalez GJ, Defazio RA, Dong C and Sick TJ. Chronic nicotine exposure inhibits estrogen-mediated synaptic functions in hippocampus of female rats. Neuroscience Letters 2012; 517(1):41-6
c. **Raval AP****,** Hirsch N, Dave KR, Yavagal DR, Bramlett H, Saul I. Nicotine and estrogen synergistically exacerbate cerebral ischemic injury. Neuroscience 2011; 181:216-25.
d. **Raval AP****. Nicotine addiction causes unique detrimental effects on female brain. Journal of Addictive Diseases. Review. 2011; 30:149–158

2. Mitochondrial dysfunction is a major factor involved in ischemic neuronal death. My early publications directly addressed the fact that protein kinase C subtype epsilon (PKCε) translocates to mitochondria following sub-lethal ischemic insult, and improved mitochondrial function and resistance to cerebral ischemic damage. My work also demonstrated that the activation of PKCε agonist phosphorylates the mitochondrial K^+_{ATP} channel subunit Kir6.2, which is involved in opening of potassium channels. The neuroprotection conferred by ischemic preconditioning was lost in the presence of K^+_{ATP} - channel antagonists. Overall, my work provided initial evidence that PKCε activation and its interaction with mitochondrial targets confer stability to mitochondrial functions during subsequent ischemic stress, thus reducing ischemic damage.

a. **Raval AP**, Dave KR, Mochly-Rosen D, Sick TJ, Perez-Pinzon MA. εPKC is required for the induction of tolerance by ischemic and NMDA – mediated preconditioning in the organotypic hippocampal slice. J Neuroscience. 2003; 23(2): 384-91.
b. **Raval AP****, Dave KR, DeFazio RA, Perez-Pinzon MA. EpsilonPKC phosphorylates the mitochondrial K(+) (ATP) channel during induction of ischemic preconditioning in the rat hippocampus. Brain Res. 2007; 1184:345-53. (PMCID: 2577914)
c. Dave KR, DeFazio RA, **Raval AP**, Torraco A, Saul I, Barrientos A, Perez-Pinzon MA. Ischemic preconditioning targets the respiration of synaptic mitochondria via protein kinase C epsilon. J Neurosci. 2008; 28(16):4172-82. (PMCID: 2678917)
d. Pérez-Pinzón MA, Dave KR, **Raval AP**. Role of reactive oxygen species and protein kinase C in ischemic tolerance in brain. Antioxidants and redox signaling 2005; Vol 7(9 & 10): 1150-57.

3. Another focus of my research is investigating the mechanism by which female sex hormone(s) provide ischemic brain protection. Studies from my lab demonstrate that either a single bolus or repetitive periodic 17β-estradiol treatments prior to ischemic episode reduces ischemic brain damage in ovariectomized rats. Periodic E_2 pretreatment protects hippocampal neurons through the activation of estrogen receptor subtype beta (ER-β) and silencing of hippocampal ER-β ameliorated 17β-estradiol-induced ischemic protection. My study also demonstrated that the activation of ER-β regulates mitochondrial function in the brain, and maintains mitochondrial function after cerebral ischemia. My research underscores that ER-β activation is a key mechanism to prevent ischemic neuronal death. My study was the first one to show that the silencing of hippocampal ER-β lowers protein levels of mitochondria-encoded complex IV subunits; it also implicates a role for ER-β in protein expression of the mitochondrial oxidative phosphorylation system.

a. **Raval AP****, Dave KR, Saul I, Gonzalez GJ, Diaz F. Synergistic inhibitory effect of nicotine plus oral contraceptive on mitochondrial complex-IV is mediated by estrogen receptor-β in female rats. J Neurochemistry 2012; 121(1):157-67.
b. **Raval AP****, Borges-Garcia R, Moreno WJ, Perez-Pinzon MA and Bramlett H.Periodic 17β-estradiol pretreatment protects rat brain from cerebral ischemic damage via estrogen receptor-β. Plos One 2013;8(4):e60716
c. **Raval AP****, Saul I, Dave KR, DeFazio1 RA, Perez-Pinzon MA, Bramlett H. Pretreatment with a single estradiol-17β bolus activates CREB and protects CA1 neurons against global cerebral ischemia. Neuroscience. 2009; 160:307–18. (PMCID: 2711690)
d. **Raval AP****, Bramlett H, Perez-Pinzon MA. Estrogen preconditioning protects the hippocampal CA1 against ischemia. Neuroscience. 2006; 141(4):1721-30.

4. It is known that cerebral ischemia activates the innate immune response, and a key component of the innate immune response is the inflammasome. Recent study from my laboratory demonstranted that the ER-β activation regulates inflammasome activation and protects the brain from global ischemic damage in reproductively senescent female rats.

a. de Rivero Vaccari JP, Patel HH, Brand III FJ, Perez-Pinzon MA, Bramlett H and **Raval AP**. Estrogen receptor beta signaling alters cellular inflammasomes activity after global cerebral ischemia in reproductively senescence female rats. J Neurochemistry 2016 Feb;136(3):492-6.

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/pubmed/?term=raval+ap

D. Active Support

NIH-NINDS 1/8/ 17 - 31/7/ 2022
Mitochondria and cerebral ischemia: Intracellular Signaling
Principal Investigator: Dr. Pérez-Pinzón
Role: Co-investigator, 15% efforts

Florida Department of Heath#7JK01 03/1/17- 2/29/2020
Whole body vibrations improves stroke outcome in nicotine-exposed rats
The major goal of this project is to study the effects whole body vibration on post-stroke frailty in nicotine exposed female rats. There is no scientific overlap with current application.
Principal Investigator: Dr. Helen Bramlett
Role: CO-PI (50% effort)

American Heart Association- Grant-in-aid
AHA # 16GRNT31300011 07/1/16- 6/30/2018
Nicotine alters brain oxidative metabolism and exacerbates ischemic brain damage
The major goal of this project is to study the effects of chronic nicotine usage on brain metabolism in adolescent and young female rats. There is no scientific overlap with current application.
Role: PI, 20% efforts

NIH/NINDS
Grant #3R01NS034773-16S1 07/1/16- 6/30/2017
Ischemic Preconditioning: Mechanisms of Neuroprotection
This project is an administrative supplement for research on sex/gender differences in ischemic preconditioning.
PI: Dr. Miguel A. Perez-Pinzon
Role: Co-investigator, 10% efforts

Department of Neurology's 2016 Pilot Research Support Program 01/1/16-6/31/17
Mechanism of neuroprotection against cerebral ischemia
Role: PI, no % efforts

Completed Research Support:

United Mitochondrial Disease Foundation 07/1/14-6/30/16
Modulation of GSK3 activity and enhancement of glycolysis to maintain neuronal survival in complex IV deficient mice
PI: Dr. Francisca Diaz
Role: Co-investigator (5% effort)

University of Florida Southeast Center for Integrated Metabolomics 07/1/14-7/30/15
Pilot and Feasibility Projects
Nicotine alters brain oxidative metabolism
Role: PI, no % efforts

Florida Department of Heath#09KN-14 07/1/11-06/30/14
Intra-arterial mesenchymal stem cell delivery in a canine model of acute ischemic stroke.
Principal Investigator: Dr. Dileep Yavagal
Role: Co-investigator (5% effort)

American Heart Association- Grant-in-aid
AHA # 11GRNT7370069 7/1/11- 6/30/2013
Nicotine inhibits estrogen-mediated synaptic plasticity after cerebral ischemia in female rat.
The major goal of this project is to study the effects of chronic nicotine usage on synaptic functions in female rats. There is no scientific/ financial overlap between NIH-R01 application under consideration and the funded AHA-grant-in-aid.
Role: Dr. Raval, PI, % efforts 25%

University of Miami Specialized Center Of Research on Addiction & Health in Women, Children & Adolescents (UM-SCOR) 10/1/2011-3/31/2013
Nicotine inhibits estrogen-mediated synaptic plasticity after cerebral ischemia in female rat
Role: PI, no % efforts

University of Miami, Stanley J. Glaser Foundation Award
UM 700852 6/1/11 - 12/31/12
Nicotine impairs hippocampal mitochondrial function in female rat.
This is a seed funding from University of Miami to generate pilot data for future federal funding. The major goal of this project is to study the effects of chronic nicotine exposure on mitochondrial function in hippocampus of female rats.
Role: Dr. Raval, PI, no % efforts

American Heart Association- Scientist Development Grant (National center)
AHA # 0730089N 1/1/11-12/31/11
Estrous cyclicity and mechanism of neuroprotection after cerebral ischemia.
The major goal of this project was to study the effects of endogenous estrogen fluctuations on neuroprotection against cerebral ischemia in normal cyclic rats.
Role: Dr. Raval, PI, % efforts 39%

Florida Department of Heath
#07KN-10 7/1/07-6/30/10
Inhibitory effects of nicotine on estrogen-induced natural hippocampal neuroprotection against ischemia
The major goal of this project was to study the effects of chronic nicotine usage and female sex hormones on cerebral ischemic outcomes.
Role: Dr. Raval, PI, % efforts 50%

NIH/NINDS

1R01NS054147-01A1 Dr. Pérez-Pinzón, P.I. 7/06/06- 5/31/10

Mitochondria and Cerebral ischemia: intracellular signaling

The major goal of this project was to study the mechanisms by which εPKC protect neuronal mitochondria whereas δPKC promotes cell death after cerebral ischemia.

Role: Dr. Raval, Co-investigator % efforts 6%

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: **Tatjana Rundek, MD PhD**

eRA COMMONS USER NAME (credential, e.g., agency login): **TR89XX**

POSITION TITLE: Professor of Neurology, Executive Vice Chair of Research and Faculty Affairs, Director of Clinical Translational Research Division, University of Miami Miller School of Medicine

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Zagreb, Croatia	B.S.	1979-1983	Applied Mathematics
Medical School University of Zagreb, Croatia	M.D.	1984-1989	Medicine
Medical School University of Zagreb, Croatia	M.S.	1989-1991	Epidemiology/Bioinformatics
Ludwig-Maximillian University, Munich, Germany	Ph.D.	1991-1995	Neuroscience
Medical School University of Zagreb, Croatia	Residency	1991-1994	Neurology
Grossharden Spital Munich, Germany	Fellowship	1994-1995	Stroke
Columbia University, New York, NY	Fellowship/MS	1998-2000	Stroke/Neuroepidemiology

A. Personal Statement

I was named Scientific Director of the Evelyn F. McKnight Brain Institute and Evelyn F. McKnight Chair for Learning and Memory in the Aging at the University of Miami on December 21, 2017. I served as an interim Scientific Director for the past year, after Dr. Wright left the University of Miami (UM). Since my relocation from Columbia University to UM in 2008, I have been dedicated to the research and education mission of our McKnight Brain Institute. As a Vice Chair and Director of the Clinical Translational Research Division in Neurology, and a PI of NIH/NINDS R01 grants and Co-I of several R01s I have been performing research on vascular factors affecting stroke and cognitive decline and providing research environment and training in neuroscience, vascular neurology and epidemiology for many graduate and post-graduate trainees and junior faculty. I am also a program Director of a Miller School of Medicine MS degree in Clinical Translational Investigations. I serve as a Training Director of the NINDS StrokeNet and NeuroNEXT (1 trainee/year) and Miami AHA Bugher Stroke Center (2 trainees/year). I was awarded a NINDS K24 training grant that provided me with the protected time for research and mentorship. In addition, I am a director of the Neurology Residents and Fellows Clinician Researcher Program, a 3-year program aimed to provide research and career development mentorship. In the past 10 years, I have mentored over 20 trainees at various stages of their career, 14 completed their MD, PhD, MS or MPH degrees during my mentorship and obtained NIH grants or other awards. I was awarded a 3-year AHA Mentor grant to mentor 3 trainees nationally for 3 years. I have been a productive investigator with over 360 publications and have extensive research collaborations with various national and international research teams, such as investigators from Columbia University on large NIH-funded population based studies (NOMAS, INVEST, CABLE, PHPT, eMERGE) and Albert Einstein in the Bronx on Einstein Aging Study. I am a collaborator and site investigator of the large international stroke genetic, MR imaging, and atherosclerosis projects and consortia (NINDS SiGN, ISGC, PROG-IMT, ELSA).

These peer-reviewed publications highlight my experience and qualifications:

1. **Rundek T**, Della-Morte D, Gardener H, Dong C, Markert MS, Gutierrez J, et al. Relationship between carotid arterial properties and cerebral white matter hyperintensities. Neurology. 2017;88(21):2036-42.
2. Wei Y, Jiang H, Shi Y, Qu D, Gregori G, **Rundek T**, Wang J. Age-Related Alterations in the Retinal Microvasculature, Microcirculation, and Microstructure. Invest Ophthalmol Vis Sci. 2017;58(9):3804-17.
3. Luca CC, **Rundek** T. Parkinsonism, small vessel disease, and white matter disease: Is there a link? Neurology. 2015;85(18):1532-3.
4. **Rundek T**, Bennett DA. Cognitive leisure activities, but not watching TV, for future brain benefits. Neurology 2006; 66(6): 794-5.

B. Positions and Honors

POSITIONS AND EMPLOYMENT

Academic Appointments:

1994-96	Assistant Professor of Neurology	Dept. of Neurology, University of Zagreb, Croatia
1996-98	Associate Professor of Neurology	Dept. of Neurology, University of Zagreb, Croatia
2002-07	Assistant Professor of Neurology	Columbia University, New York, NY
2007-11	Associate Professor of Neurology	Miller School of Medicine, U Miami, Miami, FL
2011-	Professor of Neurology (with tenure)	Miller School of Medicine, U Miami, Miami, FL
2017-	Scientific Director, McKnight Brain Institute; Evelyn F. McKnight Chair for Learning and Memory in Aging	Miller School of Medicine, U Miami, Miami, FL

Hospital Appointments:

1994-00	Stroke Attending	Department of Neurology, University of Zagreb, Croatia
2002-07	Director&Attending,Vascular Laboratory	Columbia University Medical Center, New York, NY
2007-	Director, Clinical Translational Division	Miller School of Medicine, U Miami, Miami, FL
2010-	Vice Chair, Clinical Translational	Miller School of Medicine, U Miami, Miami, FL
2014-	Director, MS Clinical Translational	Miller School of Medicine, U Miami, Miami, FL

Honors

1995	Humbolt Award, Neurosonology Laboratory, University of Ulm, Germany
1996	George Soros Scholarship, Neurology Seminars, University of Krems, Austria
1997-99	Fulbright Award and Scholarship, Neurological Institute, Columbia University, New York, NY
2006	Nassau Women Physicians Foundation Award for Stroke Research in Women; Long Island, NY
2009-14	President, the Neurosonology Community of Practice, American Institute of Ultrasound in Medicine
2012-	Member, the Board of the Directors, Intersocietal Accreditation Committee (IAC)-Vascular
2012-	Consulting Editor of *Stroke*
2013-	Editorial Board Member of *Neurology, Cerebrovascular Disease, Journal of Ultrasound in Medicine*
2014-	Member, the Clinical Standards Committee, American Institute of Ultrasound in Medicine (AIUM)
2015-	Secretary, the Executive Committee, Intersocietal Accreditation Committee (IAC)-Vascular
2015-	Reviewer, NIH section ZHL1 CT-K (C1)1 – LRP
2015	The American Heart Association Core Vitae Award for Stroke

C. Contribution to science

C.1. Neuroepidemiology. Over the past 20 years I have pursued research in neurepidemiology. The central findings from this research include the discovery of novel stroke risk factors (e.g., insulin resistance, sleep duration, homocysteine, adiponectin, oral infection). Some of these reports were among the first in the literature. We conducted the largest investigation of the role of PFO in stroke and migraine. Our group was the first to report that atorvastatin reduces the serum coenzyme Q10 levels linking it to muscle pain. More recently I have been investigating neurocognitive functions in large longitudinal studies including Einstein Aging Study, HCHS-SOL, and NOMAS. I am a strong believer in team science and many of my research products are the results of multiple collaborations with international research teams and institutions.

1. **Rundek T**, Elkind MS, Di Tullio MR, Carrera E, Jin Z, Sacco RL, Homma S. Patent Foramen Ovale and Migraine. A Cross-Sectional Study from the Northern Manhattan Study. **Circulation**. 2008;118:1419-24.
2. Fleysher R, Lipton ML, Noskin O, **Rundek T,** Lipton R, Derby CA. White Matter Structural Integrity and Trans-Cranial Doppler Blood Flow Pulsatility in Normal Aging. Magn Reson Imaging. 2017 Nov 1
3. **Rundek T**, Naini A, Sacco RL, Coates K, DiMauro S. Atorvastatin decreases the coenzyme Q10 level in the blood of patients at risk for cardiovascular disease and stroke. Arch Neurol. 2004; 61:889-92.
4. Ramos AR, Tarraf W, **Rundek T**, Redline S, Wohlgemuth WK, Loredo JS, Sacco RL, Lee DJ, Arens R, Lazalde P, Choca JP, Mosley T Jr, González HM. Obstructive sleep apnea and neurocognitive function in a Hispanic/Latino population. Neurology. 2015;84(4):391-8.

C.2. Extracranial and intracranial imaging markers of carotid disease. Vascular imaging has been my primary tool to investigate atherosclerosis. I have been in the field of ultrasound for over 25 years. I was trained in ultrasound technologies by the inventor of transcranial Doppler (TCD) Dr. Rune Aaslid in early 80's and have

been a part of an international brain hemodynamic research group since. I coauthored the first consensus document on carotid ultrasound imaging. I have been a part of large international collaborations on the progression of subclinical atherosclerosis (PROG-IMT, USE-IMT). I have applied arterial vessel wall principles to improve arterial compliance using a new technique of integrated power Doppler and changes of vessel wall diameter during cardiac cycle. In addition, I have helped advancing the field of brain circulation investigations using TCD to vascular cognitive impairment, memory loss and dementia. I have been an active member of IAC (Intersocietal Accreditation Committee) Board of Directors, the largest US accreditation body that sets the standards for performance of clinical ultrasound, CT/MRI, PET, and cardiac Echo. I have been an advocate for advancing quality and access to clinical ultrasound in medicine for vascular and cognitive disorders.

1. **Rundek T**, Blanton SH, Bartels S, Dong C, Raval A, Demmer RT, Cabral D, Elkind MS, Sacco RL, Desvarieux M. Traditional risk factors are not major contributors to the variance in carotid intima-media thickness. **Stroke**. 2013;44:2101-8.
2. **Rundek T**, Arif H, Boden-Albala B, Elkind MS, Paik MC, Sacco RLS. Carotid plaque, a subclinical precursor of vascular events: the Northern Manhattan Study. **Neurology** 2008; 70:1200-7.
3. Suemoto CK, Santos IS, Bittencourt MS, Pereira AC, Goulart AC, **Rundek T**, Passos VM, Lotufo P, Benseñor IM. Subclinical carotid artery atherosclerosis and performance on cognitive tests in middle-aged adults: Baseline results from the ELSA-Brasil. Atherosclerosis. 2015;243(2):510-5.
4. 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. Neurol Genet. 2017;3(5):e185.
5. Wei Y, Jiang H, Shi Y, Qu D, Gregori G, Zheng F, **Rundek T**, Wang J. Age-Related Alterations in the Retinal Microvasculature, Microcirculation, and Microstructure. Invest Ophthalmol Vis Sci. 2017;58(9):3804-17.

C.3. Genetic contribution to atherosclerosis and stroke. I have been investigating genetic contribution to carotid disease for the past 10 years as PI of 2 NINDS R01 grants and a NINDS K24 award, co-PI of family study of atherosclerosis and site PI of the NINDS SiGN (ischemic Stroke Genetic Network). In one of my investigations I have take the approach of extreme phenotypes by investigating genetic profile of individuals with a lot of risk factors but less atherosclerosis than expected as well as those with little to no risk factors but a lot of atherosclerosis. These investigations are now contributing novel findings on genetic and environmental determinants of atherosclerosis and stroke for targeted vascular therapies and prevention of CVD and stroke. I have also investigated family of sirtuin genes that are playing a central role in aging and caloric restriction that can be targets for anti-aging medical interventions.

1. **Rundek T**, Elkind MS, Pittman J, Boden-Albala B, Martin S, Humphries SE, Hank Juo SH, Sacco RL. Carotid Intima-Media Thickness is Associated with Allelic Variants of Stromelysin-1, Interleukin-6 and Hepatic Lipase Genes: The Northern Manhattan Prospective Cohort Study. **Stroke** 2002, 333:1420-3.
2. Dong C, Della-Morte D, Beecham A, Wang L, Cabral D, Blanton SH, Sacco RL, **Rundek T**. Genetic variants in LEKR1 and GALNT10 modulate sex-difference in carotid intima-media thickness: A genome-wide interaction study. Atherosclerosis. 2015;240(2):462-7.
3. Traylor M, Zhang CR, Adib-Samii P, Devan WJ, Parsons OE, Lanfranconi S, Gregory S, Cloonan L, Falcone GJ, Radmanesh F, Fitzpatrick K, Kanakis A, Barrick TR, Moynihan B, Lewis CM, Boncoraglio GB, Lemmens R, Thijs V, Sudlow C, Wardlaw J, Rothwell PM, Meschia JF, Worrall BB, Levi C, Bevan S, Furie KL, Dichgans M, Rosand J, Markus HS, **Rundek T**, Rost N; International Stroke Genetics Consortium. Genome-wide meta-analysis of cerebral white matter hyperintensities in patients with stroke. Neurology. 2016;86(2):146-53.
4. Della-Morte D, Ricordi C, **Rundek T**. The fountain of youth: role of sirtuins in aging and regenerative medicine. Regen Med. 2013;8(6):681-3.
5. Della-Morte D, Dong C, Beecham A, Wang L, Cabral D, Markert MS, Blanton SH, Sacco RL, **Rundek T**. Relationship between sirtuin and mitochondrial uncoupling protein genes and carotid artery stiffness. Transl Res. 2015;165(2):358-9.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/pubmed?term=rundek
https://www.ncbi.nlm.nih.gov/sites/myncbi/tatjana.rundek.1/bibliography/40707409/public/?sort=date&direction=ascending

D. Research Support
List of selected ongoing and completed research projects for the past three years:

NIH/NINDS R01 NS 40807 Rundek, Sacco (Multi-PI) 05/01/02-09/30/17
Family Study of Stroke Risk and Carotid Atherosclerosis
The major goal of this study is to evaluate heritability and genetic linkage of novel vascular risk factors such as carotid intima-media thickness among the families of high-risk Caribbean Hispanics.
Role: PI

NIN/NIHHD MR R01MD012467 Sacco/ Rundek/ Romano (Multi-PI) 09/26/17 – 06/30/22
Disparities in Transition of Care after Acute Stroke Hospitalization: The Transition of Care Disparity Study
Aims: To define race/ethnic and sex disparities in transitions of care from hospital to home after stroke, identify modifiable factors, and develop initiatives to reduce disparities and improve outcomes after stroke
Role: PI

NIH/NINDS R37 NS 029993-11 Sacco (PI) 02/01/03-01/31/20
Stroke Incidence and Risk Factors in a Tri-Ethnic Region
The major goals of this project are to determine the effect of vascular risk factors on cognitive impairment and subclinical MRI findings in a prospective cohort study from 3 race-ethnic groups from Northern Manhattan.
Role: Co-Investigator

NIH/NIDCR R01 DE 13094 Desvarieux (PI) 06/15/06-05/31/22
Oral Infections, Carotid Atherosclerosis and Stroke (INVEST)
This cohort study will examine the effect of chronic periodontal disease and inflammation as a risk factor for stroke and carotid atheroma progression.
Role: Co-Investigator

NIH/NINDS U10 NS 077423 Benatar, Sacco (PIs) 09/30/11-08/31/18
University of Miami: Network of Excellence in Neuroscience Clinical Trials (NeuroNEXT)
The goals of this proposal are to enhance quality and efficiency of NIH trial implementation at the University of Miami and to leverage existing institutional strengths to enhance NeuroNEXT consortium activities.
Role: Co-Investigator

NIH/NIA P01 AG003949 Lipton, Derby (PIs) 07/1/11-06/30/20
The Albert Einstein Study Program Project in Aging
This is a Cerebral Hemodynamics Study of Aging of the AES program project aimed to study the vascular mechanisms of normal aging, MCI and dementia using TCD challenge test.
Role: PI of TCD Core

NIH/NINDS U54 NINDS SPIRP U54NS081763 Sacco (PI) 01/01/13-12/31/17
Stroke Prevention/Intervention Research Program in Hispanics
The goal is to develop high-impact stroke disparities interventions with the ability to reduce stroke disparities in distinct Hispanic groups in Miami and Puerto Rico using effective and culturally appropriate methods
Role: PI of Core C and PI of Supplement- Stroke Outcome in Women

NIH/NINDS U10 NS086528 Romano (PI) 09/30/13-07/31/18
Miami Regional Coordinating Center for NINDS Stroke Trials Network
PI: J Romano; T. Rundek, Training Director
The major goal of this award is to function effectively as a Regional Coordinating Center for the NINDS stroke trials and to enhance quality and efficiency of NINDS stroke trial implementation at the Miami site.
Role: Training Director

NIH/NINDS R01 NS084288-01A1 Romano (PI) 04/01/14-03/31/19
Mechanisms of Early Recurrence in Intracranial Atherosclerotic Disease (MyRIAD)
The objective of this proposal is to determine the mechanisms and predictors of stroke in patients with symptomatic Intracranial Atherosclerotic Disease.
Role: Co- Investigator

NIH/NHLBI N01-HC65234 Schneiderman (PI) 06/01/14-05/31/19
Hispanic Community Health Study-Study of Latinos (HCHS-SOL) Miami Field Center
The HCHS/SOL is a multi-center epidemiologic study designed to determine the role of acculturation in disease prevalence and to identify health risk factors in Hispanics/Latinos.
Role: Adjudication Core investigator

AHA14BFSC17690000 Sacco (PI) 04/01/14-03/31/18
AHA-ASA/Bugher Foundation Center of Excellence in Stroke Collaborative Research
This initiative supports a collaboration of basic, clinical and population research and training in stroke prevention and recovery after a stroke including the areas of repair, regeneration, and rehabilitation.
Role: Training Director

AHA 15MM26340000 Rundek (PI) 07/01/15-06/30/18
NCRP Winter 2015 Mentor / AHA Mentee Award
This awards supports Dr. Rundek's mentorship activities for 2 AHA fellows (from John Hopkins & UT Huston).
Role: PI

ARISTA-USA CV185-564 Rundek (PI) 01/04/17-3/31/20
BMS
Disparities in Stroke Outcomes and Care Delivery in Patients with Atrial Fibrillation: FLiPER-AF Study
This study will examine race-ethnic and sex disparities in health care delivered to stroke patients with AF and their outcomes after acute stroke hospitalization.
Role: PI

NIH/NCATS UL1TR000460 Sacco (PI) 06/1/2012-05/30/18
UM Clinical Translation Science Institute
The Miami CTSI advances culturalized health sciences that embrace our majority racial/ethnic communities. Fundamental to accomplishing our mission is the orchestration of new and existing research, services and resources that foster excellence in translational research, promote interdisciplinarity, elevate research ethics, build research partnerships in community, and establish strong multidisciplinary graduate research programs.
Role: co-PI of Educational Core

Prior Research Support

NIH/NINDS K24 NS 062737 Rundek (PI) 09/30/09-08/31/17
Genetic Determinants of Extreme Phenotypes of Subclinical Atherosclerosis
Role: PI

NIH/NINDS R01 NS 065114 Rundek (PI) 07/01/10-06/30/17
Novel Factors for Unexplained Phenotypes of Subclinical Carotid Atherosclerosis
Role: PI

NIH/NINDS U01 U01 NS 069208 Kittner (PI) 04/01/10-3/31/16
The NINDS International Stroke Genetics Consortium Study: Ischemic Stroke Genetics
PI: S. Kittner, U Maryland; T. Rundek, Site PI
Role: Site PI

NIH/NHLBI R01 HL108623-01A1 Wright (PI) 12/01/12-11/30/16
FGF-23 and the Risk of Stroke and Cognitive Decline
Role: Co-Investigator

KN01 James & King Biomedical Research Dong (PI) 09/01/11-08/31/14
Gene-Smoking Interactions and Atherosclerosis
Role: Co-Investigator

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: **Ralph Lewis Sacco, MD MS**

eRA COMMONS USER NAME (credential, e.g., agency login): **SACCORL**

POSITION TITLE: **Chairman and Professor of Neurology, Public Health Sciences, Human Genetics, and Neurosurgery**

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Cornell University, College of Engineering	B.S. distinction	1975-79	BioElectrical Engineering
Boston University, School of Medicine	M.D. cum laude	1979-83	Medicine
Columbia University, School of Public Health	M.S.	1987-89	Epidemiology
Neurological Institute, Presbyterian Hospital	Residency	1984-87	Neurology
Columbia College of Physicians & Surgeons	Fellow	1987-89	Cerebrovascular Disease

A. Personal Statement

I serve as Executive Director for the Evelyn F. McKnight Brain Institute at the University of Miami. I am currently Professor and Chairman of Neurology at the Miller School of Medicine, Director of the UM-Clinical Translational Science Institute, and Senior Associate Dean for Clinical and Translation Science. My personal clinical translational research interests include epidemiology, diagnosis, prevention, genetic, and treatment studies of cognitive impairment, stroke, and other cardiovascular conditions. My work as Center Director for the AHA/ASA Bugher Center Foundation Center of Excellence has produced complementary studies clinical and basic Science research towards enhancing cognitive recovery and quality of life after stroke. I am also PI for several large-scale collaborative disparities research programs such as, the Northern Manhattan Study (NINDS-funded community-based, epidemiologic cohort study researching the determinants of cognitive impairment and stroke among an elderly, multi-ethnic, urban northern Manhattan population). This study has provided essential data on stroke disparities, as well as the impact of novel risk factors including inflammatory biomarkers and infectious burden. As the NOMAS study cohort ages, our focus has expanded to include the vascular contributions to cognitive aging and functional impairment. Further, my disparities related research (PI for the NINDS U54 Stroke Prevention and Intervention Research Program to support the Florida Puerto Rico Stroke Registry, and as PI in the Multi-PI Transition of Care Stroke Disparities Study), seeks to identify disparities and gaps in stroke care, which may limit cognitive recovery and severely affect quality of life after stroke. I also have an extensive record of accomplishments in clinical trials currently functioning as Co-PI for the Miami Regional Coordinating Center for NINDS; Co-chair of the Steering Committee for RE-SPECT ESUS. These experiences have collectively provided me the knowledge and motivation to carry out and direct brain health research that is translational and of clinical relevance. I have published extensively with over 600 peer-reviewed articles and over 120 invited articles in the areas of stroke prevention, treatment, epidemiology, risk factors, vascular cognitive impairment, and human genetics. Most recently, I have served on the National Academy of Medicine writing group for the book entitled, “Preventing Cognitive Decline and Dementia: A Way Forward (2017) “. I have also received numerous awards including, the Feinberg Award of Excellence in Clinical Stroke, the Wepfer Award, the Chairman’s Award from the American Heart Association, and the NINDS Javits Award in Neuroscience, and have lectured extensively at national and international conferences. I am fully committed to a clinical translational research agenda. As former president of the American Heart Association and current acting president of the American Academy of Neurology, I continue to be fully committed to advancing scientific collaborations and establish partnerships for clinical and translational brain health research.

These four peer reviewed publications highlight my experience and qualifications for this project:

1. **Sacco RL**, Boden-Albala B, Abel G, Lin IF, Elkind M, Hauser WA, Paik MC, Shea S. Race-ethnic disparities in the impact of stroke risk factors: the northern Manhattan stroke study. **Stroke**. 2001; 32:1725-31.
2. **Sacco RL**, DeRosa JT, Haley EC Jr, Levin B, Ordronneau P, Phillips SJ, Rundek T, Snipes RG, Thompson JL; Glycine Antagonist in Neuroprotection Americas Investigators. Glycine antagonist in neuroprotection for patients with acute stroke: GAIN Americas: a randomized controlled trial. **JAMA**. 2001; 285:1719-28.
3. **Sacco RL**, Adams R, Albers G, Alberts MJ, Benavente O, Furie K, Goldstein LB, Gorelick P, Halperin J, Harbaugh R, Johnston SC, Katzan I, Kelly-Hayes M, Kenton EJ, Marks M, Schwamm LH, Tomsick T; American Heart Association/American Stroke Association Council on Stroke; Council on Cardiovascular Radiology and Intervention; American Academy of Neurology. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke

Association Council on Stroke: co-sponsored by the Council on Cardiovascular Radiology and Intervention: the American Academy of Neurology affirms the value of this guideline. **Circulation**. 2006; 113:e409-49.

4. **Sacco RL**. Achieving ideal cardiovascular and brain health: opportunity amid crisis: Presidential Address at the American Heart Association 2010 Scientific Sessions. **Circulation**. 2011; 123:2653-7.

B. Positions and Honors

Academic Appointments:

89-97	Assistant Professor of Neurology & Public Health (Epidemiology) in the Sergievsky Center
97-02	Associate Professor of Neurology & Public Health (Epidemiology) (with tenure)
03-07	Professor of Neurology & Epidemiology, Columbia University, College of Physicians and Surgeons, Mailman School of Public Health, and the Sergievsky Center (with tenure)
07-	Olemberg Family Chair in Neurological Disorders, Miller Professor of Neurology, Public Health Sciences, Neurosurgery, and Human Genetics (with tenure) and Chairman of Neurology, Miller School of Medicine, University of Miami
16-	Senior Associate Dean for Clinical and Translation Science

Honors**:**

1982	Alpha Omega Alpha	1998	American Neurological Association
2001	Fellow of the American Heart Association	2004	Fellow of the American Academy of Neurology
2006	AHA/ASA William Feinberg Award	2007	AHA Chairman's Award
2008	NINDS Jacob Javits Award in the Neurosciences	2008	American Association of Physicians
2015	AHA, Gold Heart Award	2015	The Johann Jacob Wepfer Award of the ESC
2015	UM Provost's Award for Scholarly Activity	2016	World Stroke Organization, Global Leadership

Other Professional Experience

1997-03	NINDS, Performance Safety & Monitoring Committee, VISP Trial
2004-06	NINDS Neurosciences Training Grant Review Group, Member
2013-16	NINDS, National Advisory Neurological Disorders and Stroke Council
2002-03	NIH, Center for Scientific Review, EDC-3
2003-07	FDA, Peripheral and Central Nervous System Drug Advisory Panel
2005-08	AHA, National Board of Directors; ASA, Chair Stroke Advisory Committee
2010-11	AHA, President, National Board of Directors
1999-05	American Academy of Neurology, Clinical Research Subcommittee, Chair
2005-09	American Academy of Neurology, Board of Directors
2013-15	AAN, Vice President
2015-17	AAN, President-elect
2017-19	AAN, President

C. Contribution to Science

C.1. Health Disparities As Principal Investigator for both a 25-year old community-based, epidemiologic study designed to determine stroke incidence, risk factors, and prognosis in an elderly, multi-ethnic, urban population, as well as a more recent stroke registry, we have been gathering and reviewing essential data on stroke disparities. Through these studies, we have been able to document the greater incidence of stroke among Hispanics and the increased burden of hypertension and diabetes in this ethnic group. My work in the area aims to develop and implement high-impact, culturally-appropriate interventions and prevention programs aimed at minority racial/ethnic groups, as well as those who are socioeconomically disadvantaged.

1. **Sacco RL**, Boden-Albala B, Gan R, Kargman DE, Paik M, Shea S, Hauser WA, and the Northern Manhattan Stroke Study Collaborators. Stroke incidence among white, black and Hispanic residents of an urban community: the Northern Manhattan Stroke Study. **Am J Epidemiol** 1998; 147:259-268
2. **Sacco RL**, Boden-Albala B, Abel G, Lin IF, Elkind M, Hauser WA, Paik MC, Shea S. Race-ethnic disparities in the impact of stroke risk factors: The Northern Manhattan Stroke Study. **Stroke** 2001; 32:1725-1731
3. Dong C, Rundek T, Wright CB, Anwar Z, Elkind MS, **Sacco RL**. Ideal cardiovascular health predicts lower risks of myocardial infarction, stroke, and vascular death across whites, blacks, and Hispanics: the northern Manhattan study. **Circulation**. 2012; 125:2975-84.
4. **Sacco, RL**, Gardener H, Wang K, Dong C, Ciliberti-Vargas MA, Gutierrez CM, Asdaghi N, Burgin WS, Carrasquillo O, Garcia-Rivera EJ, Nobo U, Oluwole S, Rose DZ, Waters MF, Zevallos JC, Robichaux M, Waddy SP, Romano JG, Rundek T for the FL-PR CReSD Investigators and Collaborators*. Race-Ethnic Disparities in Acute Stroke Care in the Florida-Puerto Rico Collaboration to Reduce Stroke Disparities Study. **JAHA** 2017 14;6(2).

C.2. Randomized Clinical Trials – I have been involved in the design and conduct of numerous NIH and industry sponsored randomized clinical trials on stroke treatment and prevention. These include serving as PI, co-PI, co-I or on

the executive or steering committees of international multi-center trials. Some have included innovative designs and answered important evidence treatment gaps.

1. **Sacco RL**, DeRosa JT, Haley EC Jr, Levin B, Ordronneau P, Phillips SJ, Rundek T, Snipes RG, Thompson JL. Glycine Antagonist in Neuroprotection Americas Investigators. Glycine antagonist in neuroprotection for patients with acute stroke: GAIN Americas: a randomized controlled trial. **JAMA**. 2001; 285:1719-28.
2. Mohr JP, Thompson JL, Lazar RM, Levin B, **Sacco RL**, Furie KL, Kistler JP, Albers GW, Pettigrew LC, Adams HP Jr, Jackson CM, Pullicino P; Warfarin-Aspirin Recurrent Stroke Study Group. A comparison of warfarin and aspirin for the prevention of recurrent ischemic stroke. .**N Engl J Med.** 2001;15;345:1444-51.
3. Homma S, **Sacco RL**, Di Tullio MR, Sciacca RR, Mohr JP; PFO in Cryptogenic Stroke Study (PICSS) Investigators. Effect of medical treatment in stroke patients with patent foramen ovale: patent foramen ovale in Cryptogenic Stroke Study. **Circulation**. 2002; 105:2625-31.
4. **Sacco RL**, Diener HC, Yusuf S, Cotton D, Ôunpuu S, Lawton WA, Palesch Y, Martin RH, Albers GW, Bath P, Bornstein N, Chan BP, Chen ST, Cunha L, Dahlöf B, De Keyser J, Donnan GA, Estol C, Gorelick P, Gu V, Hermansson K, Hilbrich L, Kaste M, Lu C, Machnig T, Pais P, Roberts R, Skvortsova V, Teal P, Toni D, Vandermaelen C, Voigt T, Weber M, Yoon BW; PRoFESS Study Group.. Aspirin and extended-release dipyridamole versus clopidogrel for recurrent stroke. **N Engl J Med**. 2008; 359:1238-1251. PMCID: PMC2714259.

C.3. Vascular Determinants of Cognitive Aging. Through the 25-year-old Northern Manhattan Study, which maintains an aging cohort, I have led our multi-disciplinary team towards research which considers a broader definition of brain health. Some resulting studies have focused on characterizing vascular risk factors and their involvement as brain health determinants.

1. Warsch JR, Rundek T, Paik MC, Elkind MS, **Sacco RL**, Wright CB. Association between northern Manhattan study global vascular risk score and successful aging. **J Am Geriatr Soc** 2013 Apr;61(4):519-24.
2. Katan M, Moon YP, Paik MC, **Sacco RL**, Wright CB, Elkind MS. Infectious burden and cognitive function The Northern Manhattan Study. **Neurology**. 2013 Mar 26;80(13):1209-15.
3. **Sacco RL**. Evolution from Stroke Risk Factors to Brain Health Determinants. **Cerebrovascular Diseases**. 2015 Jul 18;40(3-4):102-13.
4. Gardener H, Wright CB, Dong C, Cheung K, DeRosa J, Nannery M, Stern Y, Elkind MS, **Sacco RL**. Ideal cardiovascular health and cognitive aging in the Northern Manhattan Study. **JAHA**. 2016 Mar 1;5(3):e002731.

C.4. Epidemiology of Stroke. Over the past 32 years we have pursued research in stroke epidemiology. The central findings from this research include the elucidation of novel risk stroke factors (e.g., patent foramen ovale, carotid plaque, ideal cardiovascular health, homocysteine, HDL, alcohol, inflammation and infectious burden in stroke prevention) particularly in minority populations. Some of these reports were among the first in the literature.

1. **Sacco RL**, Elkind M, Boden-Albala B, Lin I-F, Kargman DE, Hauser WA, Shea S, Paik M. The protective effect of moderate alcohol consumption on ischemic stroke. **JAMA** 1999;281:53-60
2. **Sacco RL**, Benson RT, Kargman DE, Boden-Albala B, Tuck C, Lin I-F, Cheng JF, Paik MC, Shea S, Berglund L. High-density lipoprotein cholesterol and ischemic stroke in the elderly. **JAMA** 2001;285:2729-35
3. **Sacco RL**, Anand K, Lee HS, Boden-Albala B, Stabler S, Allen R, Paik MC. Homocysteine and the Risk of Ischemic Stroke in a Triethnic Cohort. The Northern Manhattan Study. **Stroke** 2004;35:2263-9
4. **Sacco RL**, Khatri M, Rundek T, Xu Q PhD, Gardener H, Boden-Albala B, Di Tullio M, Homma S, Elkind MSV, Paik MC. Improving Global Vascular Risk Prediction with Behavioral and Anthropometric Factors: The Multi-ethnic Northern Manhattan Cohort Study. **J Am Coll Cardiol** 2009;54:2303-11

C.5. Evidence-based Treatment Recommendations, Scientific Statements and Honorary Lectures – I have participated as lead author or collaborator on numerous highly-cited evidence-based recommendations from the AHA/ASA NSA, and IOM, as well as Scientific Statements that have been important to the field of stroke and cardiovascular diseases. I have also been a collaborator on numerous consortium including the Global Burden of Disease reports, Stroke Genetics Consortia, CHARGE, and other meta-analyses.

1. **Sacco RL**, Adams R, Albers G, Alberts MJ, Benavente O, Furie K, Goldstein LB, Gorelick P, Halperin J, Harbaugh R, Johnston SC, Katzan I, Kelly-Hayes M, Kenton EJ, Marks M, Schwamm LH, Tomsick T. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke. **Stroke**. 2006 Feb 37(2):577-617 and **Circulation**. 2006 113:e409-49.
2. **Sacco RL**. The 2006 William Feinberg lecture: shifting the paradigm from stroke to global vascular risk estimation. **Stroke**. 2007 38:1980-7.
3. **Sacco RL**. Achieving ideal cardiovascular and brain health: opportunity amid crisis: Presidential Address at the American Heart Association 2010 Scientific Sessions. **Circulation**. 2011;123:2653-7.
4. **Sacco RL**, Frieden TR, Blakeman DE, Jauch EC, Mohl S. What the million hearts initiative means for stroke: a presidential advisory from the American Heart Association/American Stroke Association. **Stroke**. 2012; 43:924-8.

Complete List of Published Work in My Bibliography: http://www.ncbi.nlm.nih.gov/pubmed/?term=sacco rl

D. Current Research Support

1R01MD012467 Sacco/ Rundek/ Romano (Multi-PI) 09/26/17 – 06/30/22
Disparities in Transition of Care after Acute Stroke Hospitalization: The Transition of Care Stroke Disparity Study (TCSD-S)
Aims: To define race/ethnic and sex disparities in transitions of care from hospital to home after stroke, identify modifiable factors, and develop initiatives to reduce disparities and improve outcomes after stroke
Role: PI

R01NS 2999 Sacco (PI) 01/01/93-07/31/20
Stroke Incidence and Risk Factors in a Tri-Ethnic Region
Aims: To determine the effects of risk factors including subclinical carotid and brain disease on the risk of stroke, MI, and vascular death in a prospective cohort of 3299 stroke-free community subjects from Northern Manhattan.
Role: PI

1R01 (NS 240807) Rundek/Sacco (Multi-PI) 05/01/02-05/31/18
Family Study of Stroke Risk and Carotid Atherosclerosis
Aims: The major goals of this project are to determine the genetic determinants of carotid IMT and plaque among high-risk Caribbean Hispanic families of the NOMAS.
Role: Co-PI/PD

HHSN268200625234C Schneiderman (PI) 06/01/13-12/31/17
Hispanic Community Health Study/Study on Latinos: Miami Field Center
Aims: To determine the role of acculturation in the prevalence and development of disease, and to identify risk factors playing a protective or harmful role in Hispanics/Latinos.
Role: Co-I

U10 (NS077423) Benatar/Sacco (Multi-PI) 09/30/11-08/31/18
University of Miami: Network of Excellence in Neuroscience Clinical Trials (NEXT)
Aims: The goals of this proposal are to function effectively as a Neuro-NEXT NINDS consortium trial site
Role: PI (dual)

UL1TR000460 Sacco (PI) 06/1/2012-05/30/18
UM Clinical Translation 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 communities. Fundamental to accomplishing our mission is the orchestration of new and existing research, services and resources that foster excellence in translational research, promote interdisciplinarity, elevate research ethics, build research partnerships in community, and establish strong multidisciplinary graduate research programs.
Role: PI

U54 (NS 081763) Sacco (PI) 01/01/13-12/31/17
Hispanic Stroke Prevention Intervention Research Program
Aims: The major goals of this project are to create the Florida Puerto Rico Stroke Registry to identify and reduce stroke disparities in acute stroke and secondary prevention
Role: PI

U10 NS086528 Romano (PI) 09/01/13-08/31/18
Miami Regional Coordinating Center for NINDS Stroke-NET
Aims: The goals of the Miami RCC are to implement high-quality research clinical trials that address acute stroke treatment, prevention and recovery.
Role: Co-PI

1U01NS086872 Broderick (PI) 10/01/13-07/31/18
NSTN National Clinical Coordinating Center Stroke NET
Aims: The goals for the National Clinical Coordinating Center for the NINDS Stroke Network are to coordinate NINDS-funded trials in stroke prevention, acute therapy, and rehabilitation.
Role: Prevention, Co-chair and Co-I

R01NS083784 di Tullio (PI) 04/01/14-01/31/19
Prevalence and predictors of asymptomatic atrial fibrillation in the community
Aim: To expand knowledge of atrial fibrillation/other arrhythmias in the elderly and their relationship with stroke and other vascular events in addition to identifying high risk candidates for arrhythmia development whom might best benefit from intervention.
Role: Co-I

PROPOSALM1600980 Sacco (PI) 11/17/15-12/31/18
Boehringer-Ingelheim
Specific Services in Support of Respect-esus Trial
In addition to providing a Disparity Recruitment Support Program, Dr. Sacco serves on the Executive Committee for the Clinical Trial.
Role: PI

14BFSC17590000 Sacco (PI) 04/01/14-03/31/18
American Heart Association/ASA-Bugher Foundation
University of Miami ASA/Bugher Foundation Center of Excellence in Stroke Collaborative
The intent of this initiative is to support a collaboration of basic, clinical and population researchers from different specialties whose collective efforts will lead to new approaches, not only to improve the prevention of stroke, but to also expand upon the previous Bugher Stroke initiatives by inviting research on recovery after a stroke; including the areas of repair, regeneration, neuro-plasticity and rehabilitation.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Xiaoyan Sun	POSITION TITLE Assistant Professor at Dept. of Neurology, University of Miami Miller School of Medicine
eRA COMMONS USER NAME (credential, e.g., agency login)	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Xi'an Medical College (Present name: School of Medicine of Xi'an Jiaotong University, China)	M.D.	08/1984	Medicine
Gunma University School of Medicine (Japan)	Ph.D.	03/1996	Biochemistry/ Neuroscience

A. Personal statement

I am a board-certified neurologist with fellowship training in cognitive neurology. I started my medical career as a neurologist in China. I obtained my Ph.D in neuroscience in Japan. In 2012, I finished Neurology residency from Medical University of South Carolina in the United States. In 2014, I completed cognitive/behavioral neurology fellowship in VA Boston Healthcare System. I am a fully trained physician-scientist. Currently, I am an assistant professor in the Department of Neurology and an education director of McKnight Brain Institute, University of Miami Miller School of Medicine. My clinical and research experience have placed me on a unique position to develop a clinically relevant research project. I am an author on forty-seven peer-reviewed journal articles, seventeen of which I am the first author, and four of them I am the corresponding author.

My research experience includes basic science and clinical research. I worked with world renown pathologists to study pathological changes of Alzheimer's disease (AD) in human brain early in my career. I studied biochemical properties of tau protein in the axonal transport and amyloid production in cellular and animal models of AD. My clinical research has been involved in identifying clinical biomarkers for diagnosis of AD including plasma amyloid ELISA, *APOE* 4 genotyping and neuroimaging study. I am one of the earliest scientists who developed amyloid ELISA. I continue dedicating my effort to identify clinically relevant biomarkers to improve early diagnosis and monitor of disease process in AD.

B. Positions and Honors

Positions and Employment

1983.9-1984.8 Intern, Shanxi Provincial People's Hospital, China
1984.9-1989.6 Resident Doctor, Dept. Neurology, Qinghai Provincial People's Hospital, China
1989.7-1990.9 Attending Doctor, Dept. Neurology, Qinghai Provincial People's Hospital
1990.10-1996.3 Foreign Clinical Practitioner and Ph.D. student, Dept. Neurology, Gunma University School of Medicine, Japan
1996.5-1998.3 Postdoctoral Fellow, Dept. Medicine, UCLA, Los Angeles, CA
1998.7-2002.8 Staff Scientist, Brain Science Institute of RIKEN, Japan
2002.8-2004.7 Postdoctoral Fellow, Dept. of Neurology, Center for Neurological Disease, Brigham and Women's Hospital, Harvard University School of Medicine, Boston, MA
2004.8-2008.6 ELISA Consultant , Center for Neurological Disease, Harvard University School of Medicine, Boston, MA
2004.8-2008.6 Clinical Research Fellow, Dept. of Psychiatry, New England Medical Center and School of Nutrition Science and Policy, Tufts University, Boston, MA
2008.7-2012.6 Resident, Dept. of Neurology, Medical University of South Carolina, Charleston, SC
2012.6-2014.6 Geriatric/behavioral Neurology fellow, Boston VA Medical Center, Boston, MA
2013.8-2014.6 Assistant professor in Dept of Neurology, Boston University School of Medicine, Boston, MA
2014.10-present Assistant professor in Dept of Neurology, University of Miami Miller School of Medicine, Miami, FL
2014.10-presente Education director for McKnight Brain Institute of University of Miami Miller School of Medicine, FL

Other Experience and Professional Memberships

1987.5	Psychometrics short course certificate, Macquarie University, Australia
2010-Present	Member of American Academy of Neurology since 2010
2012.9	Board Certified Neurologist #57885
2012-present	South Carolina Medical License # 30195
2012-present	Massachusetts Medical License # 251388
2014-present	Florida Medical License # ME121152

Honors

1987.2-1987.5	Clinical Fellowship,The Iodine Deficient Disorder (IDD) Project Between China And Australia
1990.10-1991.9	Clinical Fellowship of Neurology, Sasakawa Foundation, Japan
1992.4-1996.3	Japanese Government Scholarship for Ph.D. Course, Japan
1996.8	Travel Award 5th International Alzheimer's Disease Conference, Japan
1996-1997	Staff Incentive Award for Exceptional Performance and Valuable Contribution, Dept. Medicine, UCLA, USA
2002-2003	Sabbatical Program In Drug Discovery, HCNR of Harvard Medical School, USA
2010.5	Best Case Presentation Award, Dept.t of Neuroscience, Medical University of South Carolina

C. Contribution to Science

1. Development of a sensitive amyloid assay for quantifying amyloid 40 and 42 in various biological samples

Much of my effort in the research of Alzheimer's disease has been made to identify the biomarkers for the early diagnosis of Alzheimer's disease. I am one of the earliest researchers who established one of the most sensitive amyloid Sandwich ELISA in the field. By using this ELISA, my collaborators and I published more than 10 papers to address amyloid production, degradation and regulation in cellular and mouse models.

a. **Sun X.**, Cole GM, Chu T., Xia W., Galasko D., Yamaguchi H., Frautschy SA, and Takashima A. Intracellular A-beta is increased by okadic acid exposure in the transfected neuronal and non-neuronal cell lines *Neurobiol of Aging* 2002; 23:195-203
b. **Sun X.**, Sato S., Murayama O., Murayama M., Park J.-M., Yamaguchi H., and Takashima A. Lithium inhibits amyloid secretion in the cells transfected with amyloid precursor protein C100 *Neurosci Lett* 2002; 321:61-64
c. Xia X., Wang P., **Sun X,** Soriano S., Shum W.-K., Yamaguchi H., Trumbauer ME, Takashima A., Koo EH., and Zheng H. The Aspartate 257 of presenilin 1 is indispensable for mouse development and Abeta production through beta-catenin independent Mechanisms. *Proc. Natl. Acad. Sci. USA* 2002; 99:8760-8765
d. Leissring M.A., Farris W., Chang A.Y., Walsh D.M., Wu X., **Sun X.**, Frosch M.P., Selkoe D.J. Enhanced proteolysis of beta-amyloid in APP transgenic mice prevents plaque formation, secondary pathology, and premature death. *Neuron*. 2003 Dec 18; 40(6):1087-93
e. Beglopoulos V*, **Sun X*,** Saura R., Kim R., and Shen J. Reduced amyloid production and increased inflammatory responses in presenilin conditional knockout mice. *J Biol Chem*. 2004 Nov 5; 279 (45): 46907-14 (*equal contribution)
f. Qiu W.Q., *, **Sun X., ***, Selkoe D.J., Mwamburi D.M., Huang T. , Bhadela R., Bergethon P., Scott T.M., Summergrad P., Wang L., Rosenberg I., and Folstein M. . Depression is Associated with Low Plasma Ab42 Independently of Cardiovascular Disease in the Homebound Elderly. *Int J. Ger Psych*, Nov. 6, 2006 (*equal contribution)
g. **Sun X,** Steffens D.C., AU R., Folstein M., Summergrad P., Yee J., Rosenberg I., Mwamburi D.M., Qiu W.Q. Amyloid-associated depression: a prodromal depression of Alzheimer disease? *Arch Gen Psych* 2008, 65: 542-50

2. Elucidation of the mechanisms underlying cognitive impairment in AD

Elucidation of mechanisms underlying cognitive impairment in AD is critical to develop therapeutic intervention for patients with AD. My early study shows that visual spatial memory is decreased in the presenilin 1 mutation knock-in mice. Those mice had elevated amyloid 42 in the brain extract while there is no evidence of amyloid deposition in the mice brain. The finding suggests that soluble amyloid 42 might be associated with memory impairment in these mice. Another study demonstrates that the ratio of plasma amyloid 42 to amyloid 40 is correlated with memory test score in the home-bound elderly with depression. My recent study has demonstrated that synaptic function manifested by high levels of CSF synaptic protein is a strong indicator for cognitive impairment.

a. **Sun X ***, Beglopoulos V*, Mattson M, Shen J. Hippocampal Spatial Memory Impairments Caused by the Familial Alzheimer's Disease-linked Presenilin 1 M146V Mutation *Neurodegenerative Dis* 2005; 2:6-15
b. **Sun X.**, Steffens D.C., AU R., Folstein M., Summergrad P., Yee J., Rosenberg I., Mwamburi D.M., Qiu W.Q.. Amyloid-associated depression: a prodromal depression of Alzheimer disease? *Arch Gen Psych* 2008, 65: 542-50
c. **Sun X.;** Dong C. Levin B., Crocco E., Loewenstein D., Zetterberg H., Blennow K., Wright C. APOE ε4 carriers may undergo synaptic damage conferring risk of Alzheimer's disease. *Alzheimers & Dement:* 2016 Nov;12(11):1159-116

d. Headley A, De Leon-Benedetti A, Dong C, Levin B, Loewenstein D, Camargo C, Rundek T, Zetterberg H, Kaj Blennow K, Wright C**, Sun X,** and on the behalf of the Alzheimer's Disease Neuroimaging Initiative. *Neurology*, 2017 (in press)

3. Evaluation of different biomarkers in the early diagnosis of AD

Identifying a clinical relevant biomarker is my long-term research goal to improve the quality of clinical care in patients with AD. Accurate diagnosis of Alzheimer's disease at the early stage of the disease potentially benefits the treatment of patient if disease-modifying drugs become available. Besides development of amyloid Sandwich ELISA, I have investigated the application of ApoE genotyping and brain MRI in the clinical diagnosis of Alzheimer's disease. I demonstrate that ApoE genotyping is useful for the patients with early onset and atypical presentation of Alzheimer's disease.

a. **Sun X**, Bhadelia R, Liebson E, Bergethon P, Folstein M, Zhu JJ, Mwamburi DM, Patz S, Qiu WQ. The relationship between plasma amyloid-β peptides and the medial temporal lobe in the homebound elderly. *Int J Geriatr Psychiatry*. 2011 Jun; 26(6):593-601
b. **Sun X**, Nicholas J., Walker A., Wagner M., and Bachman D. APOE genotype in the diagnosis of Alzheimer's disease in the patients with cognitive impairment. *American Journal of Alzheimer's disease and other dementia*. 2012 Aug; 27 (5):315-20.
c. **Sun X**., Salat D, Upchurch K, Deason R, Kowall N, Budson A; Alzheumer's Disease Neuroimaging Initiative. Destruction of white matter integrity in patients with mild cognitive impairment and Alzheimer disease.2014 *J Investig Med*. 2014 Oct;62(7):927-33

4. Characterization of biochemical property of tau protein and amyloid protein *in vitro*

My early work was involved in understanding the biological property of tau protein and regulation of amyloid protein in cellular and animal models. After highly phosphorylated tau protein was found to be a component of neurofibrillary tangle in Alzheimer's disease, the physiological function of phosphorylated tau protein remained unclear. My work demonstrates that phosphorylated tau is physiologically present in peripheral never in rat and involved in slow axonal transport.

a. **Sun X.**, Tashiro T., Hirai S., Yamamoto H., Miyamoto E., and Komiya Y. Preparation of tau from the peripheral nerve: Presence of insoluble low molecular weight tau with high phosphorylation *Biochem. Biophy. Res. Comm*. 1995; 210:338-344
b. Tashiro T., **Sun X.**, Tusda M., Komiya Y. Differential axonal transport of soluble and insoluble tau in the rat sciatic nerve *J. Neurochem* 1996; 67(4):1566-74
c. **Sun X.**, Tashiro T., Hirai S. and Yamaguchi H. Identification of 5.8 kDa C-terminal fragments of Alzheimer amyloid generated in the lysosomal system. *Amyloid: Int.J.Exp.Clin.Invest.* 1994;1:100-106

5. Characterization of neuropathological changes of various neurological disorders

My early work was also involved in understanding of pathological characterization of neurodegenerative diseases

a. Okamoto K., Hirai S., Yamazaki T., **Sun X.,** and Nakazato Y. New ubiquitin-positive intraneuronal inclusions in the extra-motor cortices in patients with ALS. Neurosci Lett 1991, 129:233-236
b. Yamaguchi H., Yamazaki T., Kawarabayashi T., **Sun X.**, Sakai Y, Hirai S.. Localization of Alzheimer amyloid beta protein precursor and its relation to senile plaque amyloid Geronto.l 1994; 40(Suppl. 2): 36-45
c. Yamaguchi H., Ishigoro K., Sugihara S., Nakazato Y., Kawarabayashi T., **Sun X.** and Hirai S.. Presence of apolipoprotein E on extracellular neurofibrillary tangles and on meningeal blood vessels precedes the Alzheimer beta-amyloid deposition. Acta. Neurpathologica. 1994;8:413-419
d. Yang F., **Sun X.**, Beech W., Teter B., Wu S., Sigel J., Frautschy S. and Cole GM. Detection of actin cleavage at an apoptosis related site in vitro and in Alzheimer's disease. Am J Pathol 1998; 158:379-389

D. Research Support

Ongoing Research Support

R01 David Lowenstein (PI) 2015-present
Novel Detection of Early Cognitive and Functional Impairment in the Elderly 2015-present
Role: Co-Investigator
McKnight Brain Institute, University of Miami Miller School of Medicine 2014-present
FL State Dept of Elder Affairs Memory Disorder Clinics 2016-present

Completed Research Support

Boston University Alzheimer's Disease Center Pilot grant Neil Kowall (PI) 2012-2013
Hippocampal and white matter abnormalities in older veterans with post-traumatic stress disorder or dementia: a pilot imaging study
Role: Co-Investigator

FL State fund Rosa Rademakers (PI) 2015.3-2015.6
Identification of novel AD genes and disease associated pathways through FPADS: a Florida Presenile Alzheimer's Disease Subjects registry
Role: Co-Investigator

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Wang, Jianhua

eRA COMMONS USER NAME (credential, e.g., agency login): jianhuawang

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	START DATE MM/YYYY	END DATE MM/YYYY	FIELD OF STUDY
Zhejiang Medical University, Hangzhou, Zhejiang	MD	09/1983	07/1988	Medicine
University of Waterloo, Waterloo, ON	MS	04/1999	06/2000	Vision Science
University of Waterloo, Waterloo, ON	PHD	07/2000	07/2003	Vision Science

A. Personal Statement

I have a broad background in vision research and electrical engineering, especially on advanced ophthalmic imaging and human studies. As an assistant professor at the University of Rochester, I learned optics and prototyped time domain optical coherence tomography devices through joint work with OCT experts. Since moving to Miami, I have been working with other researchers to develop many other prototypes of spectral domain OCT devices. They include ultra-high resolution OCT, ultra-long scan depth OCT, dual-channel OCT, magnetomotive OCT and CMOS camera based ultra-high speed OCT. Over the past 5 years, I have worked on vascular imaging of the eye and developed the methods and hardware to image microvasculature of the conjunctiva and retina. Working with a group of clinicians, I focus on microvasculature in the retina as a window of the cerebral vasculature in multiple sclerosis and dementia. As the PI or co-Investigator on many previous industrial- and NIH-funded grants, I worked out the proposed research and published more than 100 papers in top journals. Currently, I am the co-director of scientific experimental imaging laboratory at the Bascom Palmer Eye Institute and manage my own lab. In summary, I have a good record of successful research projects in the area of ophthalmic imaging. My expertise and experience make me well equipped and qualified for working in this proposed project.

1. **Jiang H**, Wei Y, Shi Y, Wright C, Sun X, Gregori G, Zheng F, Vanner EA, Lam BL, Rundek T, **Wang J**. Altered retinal microvasculature in mild cognitive impairment and Alzheimer's disease. Journal of neuro-ophthalmology. Epub ahead of print. PubMed PMID: 29040211.

2. Wei Y, **Jiang H**, Shi Y, Qu D, Gregori G, Zheng F, Rundek T, **Wang J**. Age-Related Alterations in the Retinal Microvasculature, Microcirculation, and Microstructure. Invest Ophthalmol Vis Sci. 2017 Jul 1;58(9):3804-3817. PubMed PMID: 28744554; PubMed Central PMCID: PMC5527847.
3. **Jiang H**, Delgado S, Tan J, Liu C, Rammohan KW, DeBuc DC, Lam BL, Feuer WJ, **Wang J**. Impaired retinal microcirculation in multiple sclerosis. Mult Scler. 2016 Dec;22(14):1812-1820. PubMed PMID: 26903007; PubMed Central PMCID: PMC4993688.
4. **Jiang H**, Delgado S, Liu C, Rammohan KW, DeBuc DC, Lam BL, **Wang J**. In Vivo Characterization of Retinal Microvascular Network in Multiple Sclerosis. Ophthalmology. 2016 Feb;123(2):437-8. PubMed PMID: 26299696; PubMed Central PMCID: PMC4724448.

B. Positions and Honors

Positions and Employment

1988 - 1990 Resident, Department of Ophthalmology, Hangzhou First Hospital, Hangzhou
1991 - 1995 Ophthalmologist, Department of Ophthalmology, Hangzhou First Hospital, Hangzhou
1996 - 1999 Professional Affairs Manager, Johnson & Johnson Vision Products, China, Shanghai
2001 - 2001 Research Associate, University of Waterloo, Waterloo, ON

2003 - 2006	Research Assistant Professor, University of Rochester, Department of Ophthalmology, Rochester, NY
2006 - 2010	Assistant Professor, Bascom Plamer Eye Institute, University of Miami, Miami, FL
2008 -	Assistant Professor, Department of Electrical and Computer Engineering, University of Miami, Miami, FL
2009 -	Scientific Co-director of Experimental Imaging Laboratory, Bascom Plamer Eye Institute, University of Miami, Miami, FL
2010 - 2012	Associate Professor, Bascom Plamer Eye Institute, University of Miami, Miami, FL
2012 -	Associate Professor (Tenured), Bascom Plamer Eye Institute, University of Miami, Miami, FL

Other Experience and Professional Memberships

1999 -	Member, Association for Research in Vision and Ophthalmology (ARVO)
2001 -	Fellow, American Association of Optometry (FAAO)
2001 -	Member, American Association of Ophthalmology (AAO)
2002 -	Member, Contact Lens Association of Ophthalmologists (CLAO)
2003 -	Fellow, International Association of Contact Lens Research (IACLE)
2005 -	Member, International Society of Contact Lens Research (ISCLR)

Honors

2000	Irvin M. & Beatrice Borish Student Travel Fellowship Award, American Academy of Optometry
2001	Travel award, International Society of Contact Lens Research
2003	Best Paper in Session, American Society of Cataract & Refractive Surgery
2003	Travel award, International Society of Contact Lens Research
2004	Pearson Medal for Creative Research, University of Waterloo

C. Contribution to Science

1. Through my more than 15 years of career development, I have significantly contributed to the development of optical coherence tomography prototypes for clinical research, especially in the field of anterior segment imaging. Working with OCT experts, high speed time-domain OCT was developed for imaging tear film and tear dynamics in contact lens wearers and patients with dry eye syndrome. I collaborated with clinicians and engineers to develop ultra-high resolution OCT devices for imaging the anterior segments and for imaging the tear film, epithelium and ocular tumors in clinical research.

    a. Shao Y, Tao A, Jiang H, Mao X, Zhong J, Shen M, Lu F, Xu Z, Karp CL, **Wang J**. Age-related changes in the anterior segment biometry during accommodation. Invest Ophthalmol Vis Sci. 2015 Jun;56(6):3522-30. PubMed PMID: 26030106; PubMed Central PMCID: PMC4464043.

    b. Zhu D, Shen M, Jiang H, Li M, Wang MR, Wang Y, Ge L, Qu J, **Wang J**. Broadband superluminescent diode-based ultrahigh resolution optical coherence tomography for ophthalmic imaging. J Biomed Opt. 2011 Dec;16(12):126006. PubMed PMID: 22191923; PubMed Central PMCID: PMC3247935.

    c. Chen Q, **Wang J**, Shen M, Cui L, Cai C, Li M, Li K, Lu F. Tear menisci and ocular discomfort during daily contact lens wear in symptomatic wearers. Invest Ophthalmol Vis Sci. 2011 Apr 6;52(5):2175-80. PubMed PMID: 21051728.

    d. Palakuru JR, **Wang J**, Aquavella JV. Effect of blinking on tear dynamics. Invest Ophthalmol Vis Sci. 2007 Jul;48(7):3032-7. PubMed PMID: 17591869.

2. Working with optics experts, I contributed significantly in developing long scan depth OCT for imaging full eyes for studying accommodation and full eye biometry. We developed a unique system consisting of two spectral domain OCT devices equipped with wavefront sensor.

    a. Du C, Shen M, Li M, Zhu D, Wang MR, **Wang J**. Anterior segment biometry during accommodation imaged with ultralong scan depth optical coherence tomography. Ophthalmology. 2012 Dec;119(12):2479-85. PubMed PMID: 22902211; PubMed Central PMCID: PMC3505244.

b. He JC, **Wang J**. Measurement of wavefront aberrations and lens deformation in the accommodated eye with optical coherence tomography-equipped wavefront system. Opt Express. 2014 Apr 21;22(8):9764-73. PubMed PMID: 24787861; PubMed Central PMCID: PMC4083049.

c. Shao Y, Tao A, Jiang H, Mao X, Zhong J, Shen M, Lu F, Xu Z, Karp CL, **Wang J**. Age-related changes in the anterior segment biometry during accommodation. Invest Ophthalmol Vis Sci. 2015 Jun;56(6):3522-30. PubMed PMID: 26030106; PubMed Central PMCID: PMC4464043.

3. I contributed significantly to imaging microvasculature on the ocular surface and retina. A system called functional slit-lamp biomicroscope (FSLB) was developed for generating conjunctival microvascular network maps. This novel system enables easy imaging of the conjunctival microvascular network and small vessel blood flow velocity, which can be used to study microvascular response to contact lens wear and changes in dry eye. Working with vascular experts in neuro-ophthalmology, we developed automatic segmentation of the retinal microvascular network using a Retinal Function Imager (RFI) for studying retinal microvascular changes in multiple sclerosis, AD, diabetes and cerebral small vessel diseases. In addition, we developed ultra-high resolution OCT for imaging the retina and our segmentation software can segment 9 retinal sub-layers. Recent developments in segmentation software enable automatic segmentation of 6 maps of retinal sub-layers. Furthermore, by designing an optical adapter, I modified RFI for the first time imaging of the conjunctiva.

   a. Jiang H, Delgado S, Tan J, Liu C, Rammohan KW, DeBuc DC, Lam BL, Feuer WJ, **Wang J**. Impaired retinal microcirculation in multiple sclerosis. Mult Scler. 2016 Dec;22(14):1812-1820. PubMed PMID: 26903007; PubMed Central PMCID: PMC4993688.

   b. Xu Z, Jiang H, Tao A, Wu S, Yan W, Yuan J, Liu C, DeBuc DC, **Wang J**. Measurement variability of the bulbar conjunctival microvasculature in healthy subjects using functional slit lamp biomicroscopy (FSLB). Microvasc Res. 2015 Sep;101:15-9. PubMed PMID: 26092682; PubMed Central PMCID: PMC4537817.

   c. Jiang H, Zhong J, DeBuc DC, Tao A, Xu Z, Lam BL, Liu C, **Wang J**. Functional slit lamp biomicroscopy for imaging bulbar conjunctival microvasculature in contact lens wearers. Microvasc Res. 2014 Mar;92:62-71. PubMed PMID: 24444784; PubMed Central PMCID: PMC3960300.

   d. Jiang H, Debuc DC, Rundek T, Lam BL, Wright CB, Shen M, Tao A, **Wang J**. Automated segmentation and fractal analysis of high-resolution non-invasive capillary perfusion maps of the human retina. Microvasc Res. 2013 Sep;89:172-5. PubMed PMID: 23806780; PubMed Central PMCID: PMC3773708.

4. I am also the first person who applied molecular imaging in ophthalmic research by using multimodal imaging modalities. Working with biologists, I developed a strategy to use novel spectroscopic and magnetomotive OCT approaches for in vivo detection of cochlin (a protein) in glaucomatous mice. This approach significantly improved our ability to detect and quantify proteins that are predictors of susceptibility (and/or progression or efficacy of treatments) in specific local tissue prior to clinical detection. The breakthrough will be immensely helpful to control various disease states.

   a. **Wang J**, Wang MR, Jiang H, Shen M, Cui L, Bhattacharya SK. Detection of magnetic particles in live DBA/2J mouse eyes using magnetomotive optical coherence tomography. Eye Contact Lens. 2010 Nov;36(6):346-51. PubMed PMID: 21060257; PubMed Central PMCID: PMC3401487.

   b. Goel M, Sienkiewicz AE, Picciani R, **Wang J**, Lee RK, Bhattacharya SK. Cochlin, intraocular pressure regulation and mechanosensing. PLoS One. 2012;7(4):e34309. PubMed PMID: 22496787; PubMed Central PMCID: PMC3319572.

   c. **Wang J**, Aljohani A, Carreon T, Gregori G, Bhattacharya SK. In vivo quantification of cochlin in glaucomatous DBA/2J mice using optical coherence tomography. Sci Rep. 2015 Jun 5;5:11092. PubMed PMID: 26047051; PubMed Central PMCID: PMC4457137.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/jianhua.wang.1/bibliography/48035987/public/?sort=date&direction=descending

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

Sun_UM_1, Sun Yat-sen University collaboration award Wang, Jianhua (PI) 10/01/15-09/30/20
Clinical applications of advanced ophthalmic imaging
The goal of this study is to develop and apply advance ophthalmic imaging for clinical research in ophthalmology.
Role: PI

NMSS, National Multiple Sclerosis Society Hong Jiang (PI) 04/01/16-03/31/19
The Role of retinal microvascular impairment on Neurodegeneration in Multiple Sclerosis
The goal of this study is to determine the role of retinal microvascular impairment on neurodegeneration in MS.
Role: Co-Investigator

Imaging Research, Bausch & Lomb, CooperVision and Allergan Jianhua Wang (PI) 01/01/06-12/31/20
Advanced ophthalmic imaging research
Unrestricted grants from Bausch & Lomb, CooperVision and Allergan for developing advanced ophthalmology imaging lab and clinical research.
Role: PI

Food UM 01, Global Healthcare Focus LLC Wang, Jianhua (PI) 01/01/17-12/31/17
Food supplement Ocufolin on retinal blood flow velocity in patients with vascular retinopathy
The goal of this study is to determine retinal blood flow velocity in patient with vascular retinopathy after taking food supplement Ocufolin for 6 months.
Role: PI

Completed Research Support

JJVC, Johnson & Johnson Vision Product Hong Jiang (PI) 12/01/14-12/31/16
Conjunctival microvascular characterization of contact lens wear
The purpose is to characterize conjunctiva microvascular in contact lens wearer
Role: Co-Investigator

UM SAC 2015-27R1, University of Miami Jianhua Wang (PI) 01/01/15-06/30/16
Conjunctival Microvasculature and its association with tear protein biomarkers in dry eye syndrome
The purpose is to characterize conjunctival microvasculature in dry eye
Role: PI

NANOS, North American Neuro-Ophthalmology Society Hong Jiang (PI) 04/15/15-10/15/16
Retinal microvascular alteration as a possible biomarker in Alzheimer's disease
The purpose of this project is to characterize the retinal microvascular dysfunction and optical properties of Retinal nerve fiber layer in AD patients.
Role: Co-Investigator

R21 EY021012-01 National Eye Institute (NEI) WANG, JIANHUA (PI) 08/05/10-07/31/12
Magnetomotive optical coherence tomography for molecular imaging of the eye
The purpose of this project is to develop magnetomotive OCT for molecular imaging of the eye.
Role: PI

R03 EY016420-02 National Eye Institute (NEI) WANG, JIANHUA (PI) 09/30/05-08/31/08
Characterization of Tear Dynamics
The purpose of this project is to characterize human tear dynamics using custom built optical coherence tomography
Role: PI

Allergan UM Contract, Allergan Jianhua Wang (PI) 07/25/11-12/31/15
Tear dynamics after Restasis treatment in dry eye patients
This project is a clinical trial for further studying tear dynamics after treatment with Restasis in dry eye patients.
Role: PI

R21EY021336-01A1, National Eye Institute (NEI) He, Jichang (PI) 12/01/11-12/01/14
Optical coherence tomography equipped wavefront system for studying accommodation
The purpose of this project is to develop optical coherence tomography equipped wavefront system for studying accommodation
Role: Co-Investigator

1R21 EY019742-01A2, National Eye Institute (NEI) Wang, Michael (PI) 08/01/10-07/31/12
Optical reflectometry for tear film measurement
The purpose of this project is to develop a novel method called optical reflectometry for measuring human tear film in a nanometer scale.
Role: Co-Investigator

R03 EY016420-03 National Eye Institute (NEI) WANG, JIANHUA (PI) 09/30/05-08/31/08
Characterization of Tear Dynamics
The purpose of this project is to characterize human tear dynamics using custom built optical coherence tomography
Role: PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Zeki Al Hazzouri, Adina

eRA COMMONS USER NAME (credential, e.g., agency login): ahazzouri

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
American University of Beirut, Lebanon	B.S.	06/04	Biology
American University of Beirut, Faculty of Health Sciences, Lebanon	MSc	06/06	Epidemiology
University of Michigan School of Public Health, Department of Epidemiology	PhD	06/11	Epidemiology
University of California San Francisco, Department of Epidemiology and Biostatistics		10/13	Post-doctoral fellow (AHA/ASA/AAN Fellow)

A. Personal Statement

I am an Assistant Professor of Epidemiology in the Department of Public Health Sciences at the University of Miami. I am a social epidemiologist and my primary research focus pertains to how social and cardiovascular factors experienced across the life-course influence cognitive aging, stroke and other related health outcomes in minority populations, Latinos in particular. In my work, I also focus on social and economic disparities. My ultimate research goal is to employ lifecourse models to better understand how modification of social and cardiovascular factors or their timing may reduce the burden of cognitive aging, stroke and dementia disparities.

Examples of publications especially relevant to the current proposal:

a. **Zeki Al Hazzouri A**, Mayeda ER, Elfassy T, Lee A, Odden MC, Thekkethala D, Wright CB, Glymour MM, Haan MN. Perceived Walking Speed, Measured Tandem Walk, Incident Stroke and Mortality in Older Latino Adults: A Prospective Cohort Study. Journal of Gerontology: Medical Sciences 2017; 72(5): 676-682.

b. Thekkethala DW, Longstreth Jr. WT, Arnold AM, Varadhan R, **Zeki Al Hazzouri A**, Cushman M, Newman AB, Odden MC. Factors associated with ischemic stroke survival and recovery in older adults. Stroke, 48(7):1818-1826, 2017.

c. **Zeki Al Hazzouri A**, Elfassy T, Sidney S, Jacobs D, Perez-Stable EJ, Yaffe K. Sustained Economic Hardship and Cognitive Function: The Coronary Artery Risk Development in Young Adults Study. Am Journal of Preventive Medicine, 2017; 52(1): 1-9.

d. Kaiser P, Arnold AM, Benkeser D, **Zeki Al Hazzouri A**, Hirsch CH, Psaty BM, Odden MC. Comparing methods to address bias in observational data: Statin use and cardiovascular events in a US cohort. International Journal of Epidemiology. Forthcoming.

B. Positions and Honors

Positions and Employment

11/2013 – 9/2014	Assistant Professor of Epidemiology, Department of Epidemiology and Biostatistics, University of California San Francisco.
9/2014 – Present	Assistant Professor of Epidemiology, Department of Public Health Sciences, University of Miami.

Honors

2009	Student Dissertation Workshop Award on Epidemiological Methods. 42nd Annual Society for Epidemiologic Research (SER) meeting, June 23, 2009 Anaheim, CA.
2010 – 2011	The Barbour Scholarship for women from the 'Orient' region and who are of high academic and professional caliber. Rackham Graduate School. University of Michigan.
2010	The Harburg Student Award for Excellence in Social Epidemiology. Center for Social Epidemiology and Population Health, School of Public Health. University of Michigan.
2011	RAND Summer Institute award to attend the Mini-Med workshop and the workshop on Aging. RAND Institute, Santa Monica, CA.
2012	Award for "Excellence in Research on Alzheimer's and Related Disorders" from the Alzheimers' Association in Northern California and Northern Nevada.
2012	American Heart Association/American Stroke Association/ American Brain Foundation (AHA/ASA/ABF) Lawrence M. Brass, M.D. Stroke Research Postdoctoral Fellowship.

C. Contributions to Science

1. Early Life and cumulative Social and Psychosocial Determinants of Cognitive Aging and Dementia

Dr. Zeki Al Hazzouri's dissertation research challenged the life-course framework of cognitive aging and dementia in minority populations. Using data from the Sacramento Area Latino Study on Aging, she was among the first to examine life-course socioeconomic determinants of cognitive aging and dementia in Latinos. She evaluated the role of a childhood socioeconomic construct, determined by variables such as sibling mortality and parental education and occupation, along with adult and late-life socioeconomic constructs on cognitive function and dementia incidence. She also evaluated how socioeconomic mobility across the life course (upward or downward mobility) shaped these older age outcomes. Her findings suggested that greater cumulative socioeconomic disadvantage and all-time low or downward socioeconomic mobility were associated with faster cognitive decline and greater dementia incidence, compared with more advantageous life-course socioeconomic trajectories. She also investigated the influence of the neighborhood's social context on trajectories of cognitive decline and the role of individual-level socioeconomic factors in mediating these contextual effects. For her work in this area of research, she received the Harburg Award by the University of Michigan School of Public Health as recognition for outstanding study of psychosocial and biological correlates of health. More recently, she examined how cumulative depressive symptoms over 20 years influenced cognition and dementia risk in very old white women. In her work she continues to focus on long-term and cumulative psychosocial and socioeconomic burden. For example, she has recently examined how cumulative exposure to economic hardship over 25 years, as determined by the federal poverty level, is associated with cognitive function in young and middle-aged adults of the CARDIA (Coronary Artery Risk Development in Young Adults) study. These findings have been recently published in the American Journal of Preventive Medicine. Dr. Zeki Al Hazzouri conducts this work with the goal of better understanding how social and psychosocial exposures from across the life-course influence cognitive health of minority and vulnerable populations.

a. **Zeki Al Hazzouri A**, Haan MN, Kalbfleisch J, Galea S, Lisabeth L, Aiello A. Life course socioeconomic position and incidence of dementia and cognitive impairment without dementia in older Mexican Americans: Results from the Sacramento Area Latino Study on Aging. Am J Epidemiol 2011; 173(10):1148-58.

b. Haan MN, **Zeki Al Hazzouri A**, Aiello AE. Life course socioeconomic trajectory, nativity and cognitive aging in Mexican Americans: the Sacramento Area Latino Study on Aging. J Gerontol B Psychol Sci Soc Sci, 2011; 66 Suppl 1: i102-i110.

c. **Zeki Al Hazzouri A**, Vittinghoff E, Byers AL, Covinsky K, Blazer D, Diem S, Ensrud K, Yaffe K. Long term depressive symptom burden and risk of cognitive decline and dementia among very old women. The Journals of Gerontology, Series A, Biological Sciences and Medical Sciences, 2014;69(5):595-601.

d. **Zeki Al Hazzouri A**, Elfassy T, Sidney S, Jacobs D, Perez-Stable EJ, Yaffe K. Sustained Economic Hardship and Cognitive Function: The Coronary Artery Risk Development in Young Adults Study. American Journal of Preventive Medicine, 2017; 52(1): 1-9.

2. Determinants of cardiovascular Disease And Risk Factors, Nativity, and Acculturation

Because of the cultural characteristics of the Latino population and the modifiable nature of cardiovascular disease risk factors, Dr. Zeki Al Hazzouri has been interested in how nativity and acculturation, among other determinants, shape cardiovascular health and consequently cognitive aging. She has led or contributed to research evaluating the association of intergenerational education and acculturation on metabolic syndrome and cardiovascular disease risk factors in Latinos. In addition, using data from the Sacramento Area Latino Study on Aging, she created a cardiovascular risk score that predicted the 10-year risk of cardiovascular disease in Mexican Americans, and evaluated its association with dementia incidence. Her findings suggested that higher 10-year cardiovascular risk score was associated with higher dementia risk, only in individuals with low education level, a marker of low cognitive reserve. Dr. Zeki Al Hazzouri is also leading work on determinants of stroke outcomes in minority populations. For example, she has recently examined whether measures of walking speed are associated with risk of stroke among Mexican Americans, independent of cognitive and physical functions. These findings have been recently published in the Journals of Gerontology: Medical Sciences.

a. **Zeki Al Hazzouri A,** Haan MN, Neuhaus JM, Pletcher M, Peralta CA, Lopez L, Perez Stable EJ. Cardiovascular risk score, cognitive decline, and dementia in older Mexican Americans: The role of sex and education. J Am Heart Assoc, 2013; 2(2): e004978.

b. **Zeki Al Hazzouri A**, Haan MN, Robinson W, Gordon-Larsen P, Clayton E, Aiello A. Associations of intergenerational education with waist circumference, metabolic syndrome, and type-2 diabetes in US Latinos. Obesity, 2015; 23(5): 1097-1104.

c. **Zeki Al Hazzouri A**, Mayeda ER, Elfassy T, Lee A, Odden MC, Thekkethala D, Wright CB, Glymour MM, Haan MN. Perceived Walking Speed, Measured Tandem Walk, Incident Stroke and Mortality in Older Latino Adults: A Prospective Cohort Study. Journal of Gerontology: Medical Sciences, 2017; 72(5): 676-682.

d. Elfassy T, Glymour M, Kershaw K, Carnethon M, Lewis CE, **Zeki Al Hazzouri A**. Sustained poverty and increases in body mass index over time: Sex and race differences in the CARDIA study. American Journal of Epidemiology. Forthcoming.

3. Subclinical and Clinical Cardiovascular Risk Factors of Cognitive Function and Dementia

Dr. Zeki Al Hazzouri leads ongoing work on how subclinical and clinical cardiovascular risk factors contribute to cognitive aging, Alzheimer disease and other dementias. She has led research, jointly funded by the American Heart Association, American Stroke Association and American Brain Foundation, evaluating the associations of biological biomarkers and subclinical cardiovascular disease with cognitive aging in diverse populations. For example, she showed that obesity and leptin, a biomarker of body fat, interacted in their influence on cognitive decline and development of dementia in older adult Hispanics and non-Hispanic whites – and for this work she was granted an award for “Excellence in Research on Alzheimer’s and Related Disorders” from the Bay Area Alzheimers’ Association. Furthermore, she showed that pulse wave velocity and heart rate variability were associated with measures of cognitive function. Recently, using data from the Coronary Artery Risk Development in Young Adults Study, she showed that intima-media thickness, a measure of subclinical vascular disease, was strongly associated with worse cognitive performance at a mean age of 50 years old. In addition, Dr. Zeki Al Hazzouri has recently contributed, as a member of the writing group, to the American Heart Association/American Stroke Association scientific statement on the impact of hypertension on cognitive function. As part of her K01 and R01 grants from the National Institute on Aging, Dr. Zeki Al Hazzouri continues to examine subclinical and clinical cardiovascular risk factors in relation to older age outcomes.

a. **Zeki Al Hazzouri A**, Newman AB, Simonsick E, Sink KM, Tyrrell KS, Watson N, Satterfield S, Harris T, Yaffe K, for the Health ABC study. Pulse Wave Velocity and Cognitive Decline in Elders: The Health, Aging, and Body Composition Study. Stroke 2013; 44(2):388-93.

b. **Zeki Al Hazzouri A**, Haan MN, Deng Y, Yaffe K. Reduced heart rate variability is associated with worse cognitive performance in elderly Mexican Americans. Hypertension 2014; 63(1):181-7.
c. **Zeki Al Hazzouri A**, Vittinghoff E, Sidney S, Reis J, Jacobs D, Yaffe K. Intima-Media Thickness and Cognitive Function in Stroke-Free Middle-Aged Adults: Findings From The Coronary Artery Risk Development in Young Adults Study. Stroke, 46(8): 2190-2196, 2015.
d. Iadecola C, Yaffe K, Biller J, Bratzke LC, Faraci FM, Gorelick PB, Gulati M, Kamel H, Knopman DS, Launer LJ, Saczynski JS, Seshadri S, **Zeki Al Hazzouri A**. The Impact of Hypertension on Cognitive Function. American Heart Association Scientific Statement. A Scientific Statement for Health Care Professionals from the American Heart Association/American Stroke Association. Hypertension 2016; 68(6): e67-e94.
e. Z**eki Al Hazzouri A**, Elfassy T, Carnethon MR, Lloyd-Jones DM, Yaffe K. Heart Rate Variability and Cognitive Function In Middle-Age Adults: The Coronary Artery Risk Development In Young Adults. American Journal of Hypertension. Forthcoming.

Complete List of Published Work in My Bibliography:

http://www.ncbi.nlm.nih.gov/sites/myncbi/1-OQdGSK0wU5Q/bibliograpahy/46032250/public/?sort=date&direction=descending

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

K01AG047273 Zeki Al Hazzouri (PI) 04/14 – 03/19
NIH/NIA
Lifecourse cardiovascular risk, depression and cognition in black & white adults.
The goal of this study is to address the associations between cardiovascular risk factors and outcomes of cognitive function and depressive symptoms. This project will conduct separate analyses in a cohort of young adults and another of older adults.
Role: PI.

1RF1AG054443 Yaffe/ Zeki AL Hazzouri (Multiple PIs) 05/17 – 04/21
NIH/NIA
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.
Role: Multiple PI.

1RF1AG055486 Zeki Al Hazzouri/ Glymour (Multiple PIs) 04/17 – 03/21
NIH/NIA
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.
Role: Multiple PI.

Completed Research Support

University of California San Francisco 09/13 – 06/14
Center for Aging in Diverse Communities- Pilot Grant
Race/ethnicity, life course socioeconomic factors, and cognitive performance among non-Hispanic white and African American young to middle-aged adults: findings from the Coronary Artery Risk Development in Young Adults (CARDIA) study.
The goal of this grant was to examine the role of life course socioeconomic factors on cognitive performance among black and white middle-aged adults.
Role: PI.

University of California San Francisco 8 KL2 TR000143-08 10/13 – 04/14
(Johnston)
NCATS
Clinical and Translational Science Institute (CTSI)
Effects of race and lifecourse cardiovascular risk on neuropsychiatric outcomes.
The goal of the CTSI KL2 career development award is to increase the number and quality of clinical and translational investigators skilled at leading multidisciplinary research teams. My role was as a KL2 Scholar, for which I receive salary support for 9 calendar months, plus research funds. The goal of my project was to evaluate the associations of cardiovascular risk factors with the risk of neuropsychiatric outcomes.
Role: KL2 scholar.

Lawrence M. Brass, MD Stroke Research Fellowship 01/12 – 10/13
American Heart Association, American Stroke Association, and American Brain Foundation
Cardiovascular risk factors for stroke and consequences of stroke among three racial/ethnic groups.
The goal of this Postdoctoral research fellowship grant was to examine subclinical measures of disease and risk factors for stroke (such as arterial stiffness and heart rate variability) in relation to cognitive function among three racial/ethnic older adult populations: Mexican Americans, African Americans and Non-Hispanic Whites.
Role: PI.

University of California San Francisco 10/11– 06/13
Center for Aging in Diverse Communities- Pilot Grant
Socioeconomic factors, metabolic and inflammatory biomarkers in relation to cognitive status in older Mexican Americans.
The goal of this grant was to examine the interplay between socioeconomic factors, inflammatory and metabolic biomarkers in predicting cognitive outcomes among older adult U.S. Hispanics.
Role: PI.

University of California San Francisco Department of 01/12 – 12/12
Psychiatry- Pilot Grant
Arterial stiffness and depressive symptoms among white and black older adults.
The goal of this grant was to examine whether arterial stiffness was associated with change in depressive symptoms and whether this association was different for whites and blacks.
Role: PI.

Pending Research Support
NIH/NIMHD R01 Rundek/ Zeki AL Hazzouri (Multiple PIs)
Migration and Cardiovascular Health in Family Study of Dominicans and Dominican Americans.
The goal of this grant 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.
Role: Multiple PI.