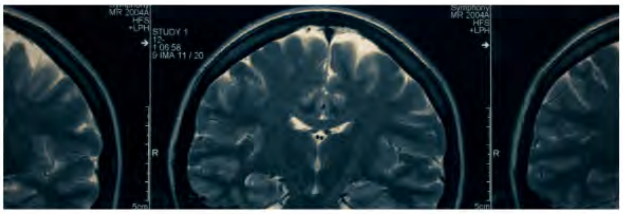
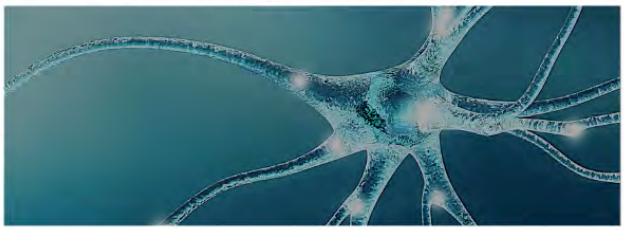
# UNIVERSITY OF MIAMI EVELYN F. MCKNIGHT BRAIN INSTITUTE
# ANNUAL PROGRESS REPORT
# JANUARY 1, 2020 - DECEMBER 31, 2020



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EVELYN F. McKNIGHT
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## JANUARY 1ST - DECEMBER 31ST, 2020

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

January 14th, 2021

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**Dear Trustees,**

This has been an unusual year, and we are all hopeful that with the vaccine the light is at the end of the tunnel. We are sad that again, we will not see you in person for the Inter-Institutional Meeting in Miami. Yet, we are excited that the virtual format will allow us all to meet and exchange some of the exciting work we continue to do.

We would like to thank you for providing the funding for the first inaugural ***Evelyn F. McKnight Neurocognitive Scholar***, the ***Precision Aging Network Pilot Grant*** and for supporting us at the McKnight Brain Institute at the University of Miami.

We are pleased to send you this report for 2020 entailing our accomplishments, achievements, awards and research updates. In addition, we have included our MBI Strategic plan as well as goals and plans for 2021.

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

cc: Susan Fox Rosellini
Stacy Merritt

## Table of Contents

# SUMMARY OF SCIENTIFIC, ACADEMIC AND EDUCATIONAL ACHIEVEMENTS SINCE LAST REPORT

## Summary of Scientific, Academic and Educational Achievements Since Last Report

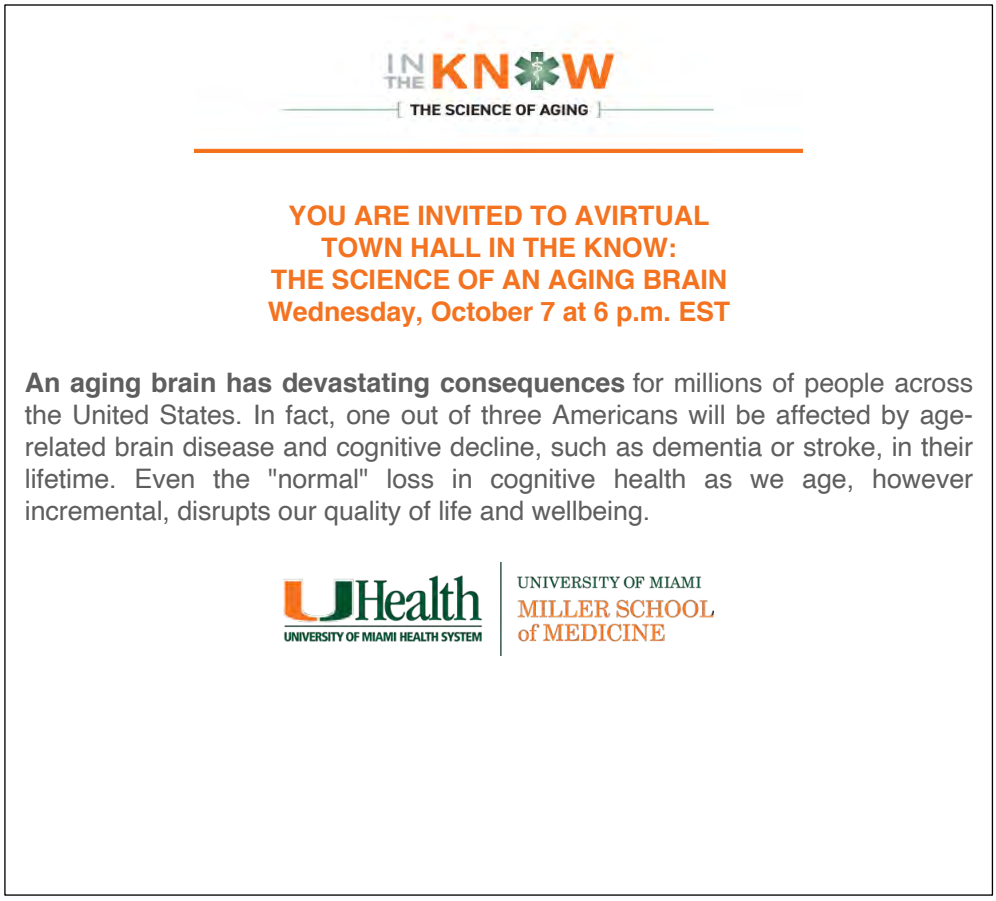
Since our last progress report and during this unprecedented COVID-19 year, we have accomplished several notable achievements. We have completed our McKnight Brain Institute (MBI) Strategic Plan, delivered several highly impactful academic and educational programs, successfully competed for several grant proposals, and received scientific and professional awards. We have highlighted some of these achievements in the sections below.

### 1. The University of Miami Evelyn F. McKnight Brain Institute Strategic Plan

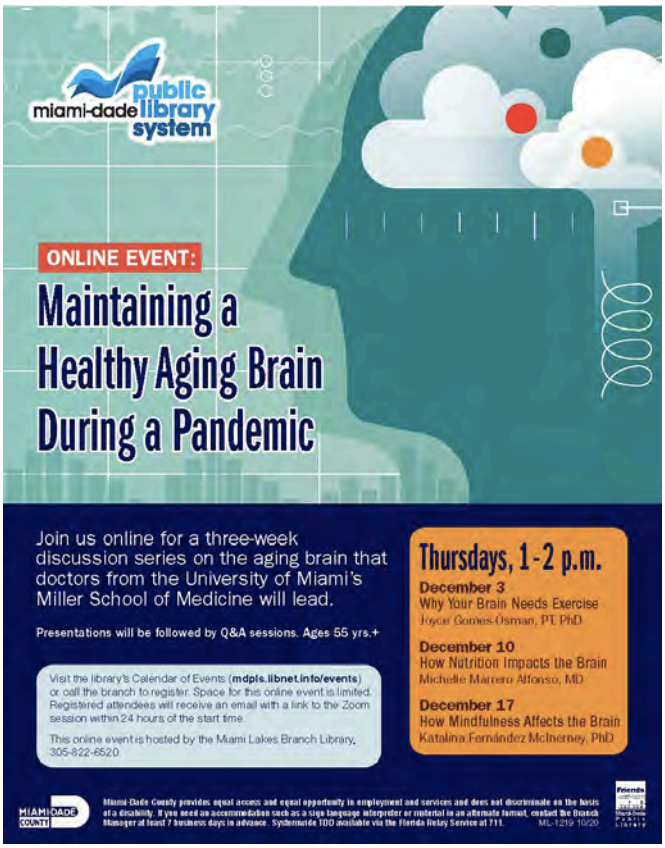
We have completed our 5-year MBI Strategic Plan in which our mission and vision led to creation of its objectives. Our 2020-2025 MBI Strategic Plan aligns with the University of Miami Miller School of Medicine (UM-MSOM) Strategic Plan that prioritizes *Brain Health and Aging* in the *Neuroscience Pillar*. Our MBI Strategic Plan defines the SMART (Specific, Measurable, Achievable, Relevant and Time-based) goals, strategies and tactics to achieve these goals in the next 5 years. We believe that a completion of the MBI Strategic Plan is a tremendous accomplishment for our MBI. Its development has been in progress for the past three years and its final version is a result of a collaborative work of our MBI leadership, Scientific Advisory Board members and other MBI members and collaborators. Our MBI Strategic Plan is included at the end of this report as **Appendix I.**

### 2. Academic and Educational Activities

In October 2020, experts and leaders in neurology, neuropsychology and neurogenetics from our MBI at the Department of Neurology held the virtual town hall "In the Know: The Science of Aging" and presented and answered questions on how the brain changes, learns, adapts and heals during aging. The panelists were **Dr. Ralph L. Sacco, Dr. Tatjana Rundek**, **Dr. Bonnie Levin** and **Dr. James E. Galvin**. It was the best attended "In the Know" series with over 400 participants and an active Q/A session that continued off-line after the town hall.




**Dr. Xiaoyan Sun** and **Stacy Merritt** coordinated a 3-part seminar series entitled *Maintaining a Healthy Aging Brain During a Pandemic* in 2020. Their goal was to reach out to aging adults to provide information and strategies that would apply to everyday brain health but would be especially important during the current COVID-19 Pandemic. The presentations were “Why Your Brain Needs Exercise,” “How Nutrition Impacts the Brain” and “How Mindfulness Affects the Brain.” The online registration for the event filled up quickly and there was a waiting list to attend. Participants were extremely interested and eager about the topics, quite engaged and keen to have discussion at the end. With such a success, we planned similar seminars in the coming year.




## 3. Clinical-Translational Activities and Scientific Achievements

**Dr. Bonnie Levin** with her team had two major clinical achievements:

- Dr. Levin and team developed a comprehensive neuropsychological battery for virtual-online administration to neurology patients. This virtual cognitive battery utilizes state of the art materials to evaluate cognitive and emotional well-being among those who are unable to engage in face-to-face cognitive testing. With the sudden onset of the COVID-19 Pandemic, it was an imperative measure to institute. Dr. Levin's cognitive clinic is one of the few centers in the country that has managed to rapidly build entirely fully functional online patient cognitive assessments that are feasible, reliable and valid, and adapted to English and Spanish language. This virtual cognitive program is now used in our clinics and research programs.

- Dr. Levin expanded the Schoninger Neuropsychology Program to include another arm dedicated to neurocognitive rehabilitation and cognitive interventions. The outline of this new program is included in **Appendix II**.

**Dr. Tatjana Rundek's** two grants were awarded this year.

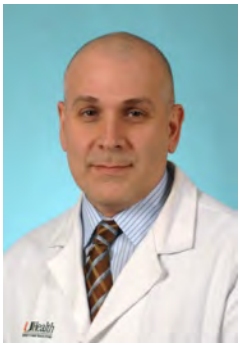
- "Carotid Ultrasound Imaging Markers of AGINg and Endothelial function in Risk of Alzheimer's Disease: The Florida IMAGINE Study of AD Risk" was awarded by the Ed and Ethel Moore Alzheimer Disease Research Program of FL DOH in December 2020. The proposed project

will examine the atherosclerotic markers of carotid artery disease as important contributors to cognitive aging, vascular brain pathology and development of a mixed vascular cognitive impairment and Alzheimer's Disease phenotype.

- As a part of the One Florida ADRC awarded in June of 2020 to UF, UM and Mt. Sinai, Research Educational Core (REC) was awarded to Dr. Rundek and Dr. Glenn Smith from UF to co-lead clinical and research education in aging and neurodegenerative disorders for junior faculty across 1FL ADRC. They have selected 3 junior faculty who already started the program.

**Dr. Bonnie Levin's** grant "Detection and reduction of scam susceptibility among Hispanic/Latinx and non-Hispanic/Latinx individuals with mild cognitive impairment and Alzheimer's disease" was awarded by the Ed and Ethel Moore Alzheimer Disease Research Program of FL DOH in December 2020. The proposed grant plans to develop an educational intervention for Hispanic and non-Hispanic elderly individuals and their caregivers/partners who are residing independently in the community but susceptible to being scammed.

**Dr. Alberto Ramos's** NIH R01 grant application "Sleep in Neurocognitive Aging and Alzheimer's Disease" received an excellent score by the NIA and will be funded in 2021.



This year, **Dr. James Galvin** joined our Department of Neurology and MBI with his clinical and research team. This was a major recruitment to our Department in 2020. Dr. Galvin brings a large NIH grant portfolio, research programs and awards to our Department (listed in the Awards section of this report). Dr. Galvin is the newest member of our MBI Scientific Advisory Board (see **Appendix V** for UM-MBI organizational chart). He is Director of the *Comprehensive Center for Brain Health (CCBH)*, a recently established Center in the Department of Neurology and approved by the UM Senate. The core mission of CCBH is brain health and prevention of cognitive disorders. Dr. Galvin's multi-disciplinary approach aims to better understand dysfunctions of the aging brain and to design treatments to prevent neurological disorders with particular focus on Lewy Body Disease and other types of dementia. Both MBI and CCBH have a different scientific focus but complementary missions to improve brain health. Therefore, the collaboration of both centers will strengthen our research, clinical and educational programs that are unified around the understanding of brain function in aging and interventions to prevent age-related memory loss and other cognitive dysfunctions, and increase quality of life through the aging process.

## 4. Basic Science Achievements by the Early-Stage Investigators

**Dr. Regina Vontell**, assistant research professor in the Department of Neurology Brain Bank (NIH NueroBioBank contract) conducted novel research that could lead to earlier intervention to improve cognition and delay later cognitive decline. She has found deviations in brain development that occur in cases of Trisomy 21 by closely investigating the complex interplay between radial glia and neuronal development. Her proposed therapies target only childhood

and early adulthood at this time, but plans are made for development of similar approaches in the older age.

**Dr. David Davis**, assistant research professor in the Department of Neurology Brain Bank **(**NIH NueroBioBank contract) received a Herbert Hoover Foundation grant this year to study "Algal Toxins and Alzheimer's Disease in Florida." The aim of this study is to investigate whether the neurotoxin BMAA, produced during harmful cyanobacterial blooms, can accelerate the deposition of pathogenic tau in individuals at risk for Alzheimer's disease. The study focuses on Floridian AD and unaffected control brain donors who have the APOE4, one of the major risk factors for AD. BMAA toxin levels in the brain will be analyzed by Braak staging, a gold standard for tau neurofibrillary tangle scoring. Automated counts of paired helical tau will be performed using QuPath software. This will be the first study to investigate the BMAA toxin and its impact on tauopathy as it relates to AD in a human sample.

**Dr. Della-Morte**, associate research professor in the Department of Neurology and MBI was stopped in Italy after visiting his primary institution in Rome (Tor Vergata University of Rome) in March of 2020 and has been actively involved in treating COVID-19 patients in Italy since. He has conducted clinical research in hospitalized patients with COVID-19. His research reported that the lower levels of plasminogen in COVID-19 patients at hospital admission had a significantly greater risk of mortality and worse outcomes in survivors in comparison to the patients with normal plasminogen levels.

## 5. Professional and Scientific Achievements and Awards

**Dr. Perez-Pinzon chaired** the 2020 International Stroke Conference Program committee.

**Dr. Rundek** received a prestigious acknowledgment in December 2020 by the University of Miami Miller School of Medicine's **Women in Academic Medicine Career Achievement Award** for her academic achievements, promotion and inspiring women and faculty for a professional and scientific career in academic medicine.

**Dr. Ralph L. Sacco** has received distinguished **recognitions** and prestigious **awards** in 2020:

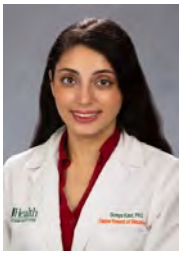
- Dr. Sacco became Editor-in-Chief of *Stroke*, an official journal of the American Heart Association/American Stroke Association (AHA/ASA), a major scientific and professional journal for neurologists and neuroscientists worldwide.
- The 2020 Highly Cited Researcher (Cross-Field) Award
- Inaugural AHA Edgar J. Kenton III Lecture Award
- Dr. Sacco is serving his first year as a member of the National Steering Committee of NCATS Clinical Translational Science Awards (CTSA) Program.
- Dr. Sacco is serving his first year as Co-Chair for the University of Miami's Health Informatics Chair Search Committee.
- The 40th TS Srinivasan Oration Award, Bengaluru, India (Dr. Sacco pictured below.)

## 6. Trainees

Our McKnight Brain Institute received funds in 2020 to support an *Evelyn F. McKnight Neurocognitive Scholar*.

After a competitive search, **Dr. Christian Agudelo, MD** was selected to be the first **Evelyn F. McKnight Neurocognitive Scholar**. He joined our MBI in July 2020. He is a trained neurologist who has completed a sleep fellowship at UM. His interest is to investigate sleep as an important and modifiable factor for sustained cognitive resilience and brain health. He has had very productive 6 months of his scholarship. One of the scientific achievements is his manuscript on sleep and cognition that was accepted for publication in the journal *Alzheimer's and Dementia* (impact factor 17). He has started to establish his national scientific and professional reputation by being invited to review manuscripts in peer-reviewed journals (he has reviewed 3 manuscripts since August 2020). He has submitted an application for the NIH Loan Repayment Program award that provides up to $50,000 per year to pay for educational debt. A separate report highlighting Dr. Agudelo's work is provided in **Appendix III**.

**Sarah Getz, PhD** was awarded an AAN McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss for her research project "Uncovering Risk Profiles of Deception and Mitigating Susceptibility to Scamming in Midlife and Older Age: A Novel Intervention Tool" in 2020.
She has started her service as a member of the *Women in Academic Medicine Scholarship Committee* at the University of Miami Miller School of Medicine.



**Sonya Kaur, PhD** had some notable achievements in 2020. She was chosen for the inaugural *Sleep Research Program for Advancing Careers Program (SOAR) of the American Academy of Sleep Medicine Foundation.* The goal of the program is to launch the research careers of sleep investigators by teaching skills and resources necessary to successfully apply for NIH grants or equivalent grants. She also submitted a grant proposal titled "The Role of Polygenic Risk in Short Sleep Duration and Cognitive Aging" for an AAN McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss in 2020. The outcome of this application is pending the AAN announcement of funded scholars. She has a manuscript accepted for publication in the journal *Alzheimer's and Dementia* entitled "Differential pathways by age and sex for the association between combined sleep disordered breathing and sleep duration with neurocognitive decline in Hispanic/Latino adults: the Hispanic Community Health Study/Study of Latinos (HCHS/SOL)."

## Most Important Scientific Achievement This Year

This year we highlight **Dr. Sacco's** nomination and selection to be the inaugural speaker at the Edward J. Kenton Lecture during the 2020 International Stroke Conference: Pre-Conference Symposium III: HEADS-UP: Health Equity and Actionable Disparities in Stroke: Understanding and Problem-Solving. (Photo below) Dr. Sacco's presentation featured multiple years of research and contributions to the improvement of stroke care disparities from the Northern Manhattan Study (NOMAS) and the Florida Stroke Registry. The important conclusion of his presentation was the need to move from "Observations to Actions" that created a movement for action to reduce health disparities.

In addition, we highlight the following:

- The interdisciplinary team science projects created through NOMAS led by Dr. Sacco: These projects have not only contributed to the scholarly literature on stroke, cognitive decline and health disparities (over 300 publications), but also have had an important influence on evidence-based prevention guidelines that directly benefit society. With current 28 years of NOMAS existence; a long list of collaborators including talented junior faculty and staff; and the most important contributors of all, the 3,497 NOMAS participants living in Northern Manhattan, continue to provide important scientific knowledge on risk of stroke and cognitive decline in an aging, urban multi-ethnic community.

- Our team lead by Dr. Sacco established the Florida Stroke Registry (FSR), a large collaboration of 126 Florida hospitals. The FSR is funded by the FL Department of Health and all hospitals treating stroke in Florida are mandated by law to collect and contribute data to FSR. FSR has identified numerous disparities in delivery of systems of care and currently aims to positively impact stroke systems of care. FSR is more than a registry. It has been developing intervention programs while creating actionable dashboards of hospital performance and outcomes as well as educational interventions. Our FSR may serve as a future model for health systems of care in other states.

- Of our published studies in 2020 we highlight the following findings:

  - The detrimental effect of mid-life obesity, particularly abdominal adiposity, on cognitive impairment and decline *in J Alzheimers Dis 2020;78(4):1653-60* (senior author Dr. Sacco);

  - A novel genetic finding of taste transduction pathway (TASR50 gene) in atherosclerosis and potentially in vascular cognitive impairment *in Stroke 2020;51(9):2761-9* (senior author Dr. Rundek); and

- A finding that structural brain MRI markers may be more useful for etiological than predictive modeling of cognitive decline using machine learning-based estimation of cognitive performance and regional brain MRI markers in *Brain Imaging Behav 2020 doi: 10.1007/s11682-020-00325-3* (senior author Dr. Rundek).

## Publications

See **Appendix IV**.

# PRESENTATIONS AT MEETINGS

## Presentations at Meetings

### 1. Scientific Meetings

- **Sacco RL**. Neurology "Update & Stroke Intensive, Quality Improvement in Acute Stroke Care in Florida" – The Stroke Registry, Miami, FL, January 18, 2020.

- **Wang J**, Chen Q, Hernandez J, Delgado S, **Jiang H**. "Retinal Microstructure in Patients with Multiple Sclerosis: 2-year Follow-up." ACTRIM Feb. 2020, poster.

- **Saravanan S**, Furones CF, Zhao WZ, **Dave KR**, **Perez-Pinzon MA**, **Raval AP**. "Post-stroke physical exercise improves cognition in middle-aged female rats." International Stroke Conference February 2020 at Los Angeles, Feb. 2020, refereed abstract.

- **Raval A**. "Physical Exercise and cognitive recovery in animal models: sex differences. BHT5. Cognitive Decline in Women" (a Go Red for Women Session), International Stroke Conference February 2020 at Los Angeles (Poster).

- Watanabe M, Nishimura K, Bellio M, Khan A, Hare JM, **Perez-Pinzon M, Raval A**, Yavagal "DR. Maximum Tolerated Dose of Exosomes Derived from Mesenchymal Stem Cells via Intra-Arterial Dosing in a Rat Stroke Model." International Stroke Conference 2020 (February 2020) held at Los Angeles, CA. Abstract # WP158. Abstract was refereed.

- **Rehni AK,** Cho S, Navarro Quero H, Koch S, Ahn YS, **Perez-Pinzon MA,** Jy W, **Dave KR.** "Therapeutic Window of Red Cell Microparticles in Limiting Hematoma Growth in a Rat Model of Intracerebral Hemorrhage." International Stroke Conference 2020 (February 2020) held at Los Angeles, C. Abstract # WP407. Abstract was refereed.

- **Sacco RL**. "Preventing Stroke & Maintaining Brain Health in 2020." The 40th TS Srinivasan Oration & Symposium, Bengaluru, India, February 9, 2020.

- **Rice J**, **McInerney K**, Aronova Y, Bradley J, Canton-Rodriguez A, Grajeda M, Perez A, Shack D, Van Deusen K, Cabral D, **Rundek T**, **Gomes-Osman J**. "Effect of 4-Weeks of Aerobic Exercise on Neuroplasticity and Executive Function: A Case Series." Combined Sections Meeting American Physical Therapy Association. Poster February 12-15 2020. Washington, DC.

- Asdaghi N, Wang K, Mueller-Kronast N, Gardener HE, Gutierrez CM, Lee Lau H, Saini V, Marulanda-Londoño E, Koch S, Krementz N, Dong C, Hanel R, Mehta B, Nobo U, Zevallos JC, **Rundek T,** Yavagal DR, **Sacco RL**, Romano JG. "Outcomes of Endovascular Thrombectomy in Late-presenting Patients: Findings From the Florida Stroke Registry." Poster Presentation International Stroke Conference 2020, Los Angeles, CA, February 18, 2020.

- Bustillo A, Wang K, Gardener H, Gutierrez CM, Sur N, Asdaghi N, Romano JG, **Rundek T**, **Sacco RL**, Koch S. "Race-Ethnic and Sex-Related Disparities in Subarachnoid Hemorrhage

Outcomes." Poster Presentation. International Stroke Conference 2020, Los Angeles, CA, February 18, 2020.

- Gardener H, **Sacco RL**, **Rundek T**, Mora-McLaughlin C, Cheung YK, Elkind MS. "Race, Ethnic, and Sex Disparities in Stroke Incidence in the Northern Manhattan Study." Oral Presentation International Stroke Conference 2020, Los Angeles, CA, February 18, 2020.

- Khasiyev F, Rundek T, Marquez C, Wright CB, **Sacco RL**, Elkind M, Gutierrez J. "Cervical Internal Carotid Artery Tortuosity as a Marker of Non-Atherosclerotic Aging: Results From the Northern Manhattan Study (NOMAS)." Moderated Poster International Stroke Conference 2020, Los Angeles, CA, February 18, 2020.

- Krementz NA, Landman A, Gardener HE, Rodriguez AD, Sur NB, Marulanda-Londoño E, Lee Lau H, Cannon H, Yavagal DR, Nagel S, **Sacco RL**, Yan B, Demchuk AM, Khatri P, Romano JG, Asdaghi N. "Factors Associated With Imaging and Endovascular Therapy Decisions for Mild Ischemic Stroke: An International Survey." Poster Presentation at International Stroke Conference 2020, Los Angeles, CA, February 18, 2020.

- Levine DA et al. Gross AL, Briceño EM, Tilton N, Kabeto MU, Hingtgen SM, Giordani BJ, Sussman JB, Hayward RA, Burke JF, Elkind MS, Manly JJ, Tom SE, **Sacco RL**, Wright CB, Gottesman RF, Gaskin DJ, Sidney S, Yaffe K, Galecki AT. "Sex Differences in Cognitive Decline: A Pooled Cohort Analysis of ARIC, CARDIA, CHS, FOS, NOMAS." Poster International Stroke Conference 2020, Los Angeles, CA, February 18, 2020.

- Liu Y et al, Hancock BL, Hoang T, Etherton MR, Mocking SJ, McIntosh EC, Irie RE, Bouts MJ, Broderick JP, Cole JW, Donahue KL, Giese AK, Giralt-Steinhauer E, Jimenez-Conde J, Jern C, Kittner SJ, Kleindorfer D, Lemmens R, McArdle PF, Meschia JF, Lindgren AG, Rosand J, **Rundek T**, **Sacco RL**, Schirmer MD, Schmidt R, Sharma P, Slowik A, Wasselius J, Worrall BB, Rost NS, Wu O. "Automatic Classification of Clinical MRI Stroke Datasets With a Recurrent Convolutional Neural Network." International Stroke Conference 2020, Los Angeles, CA, February 18, 2020.

- Marulanda-Londono ET, Bustillo A, Sand C, Landreth MD, Gutierrez C, Fenelon K, Asdaghi N, Dong C, Hanel RA, Mehta B, Mokim M, Mueller-Kronast N, Wang K, **Rundek T**, Romano JG, **Sacco RL**. "Variation In Acute Ischemic Stroke Metrics for Nationally Certified Versus Self-Attested Comprehensive Stroke Centers In The Florida Stroke Registry." Oral Presentation International Stroke Conference 2020, Los Angeles, CA, February 18, 2020.

- **Sacco RL**. "Stroke Disparities: From Observation to Actions." Edgar J. Kenton III Lecture, International Stroke Conference 2020, Los Angeles, CA, February 18, 2020.

- Sur NB, Koch S, Wang K, Di Tullio MR, Gutierrez C, Dong C, Gardener H, Garcia-Rivera NJ, Zevallos JC, Burgin WS, Rose DZ, Goldberger J, Romano JG, **Sacco RL**, **Rundek T**. "Factors Associated with Oral Anticoagulant Non-Use for Patients With Atrial Fibrillation-Related Stroke: The Florida Puerto Rico Atrial Fibrillation Stroke Study." Poster Presentation International Stroke Conference 2020, Los Angeles, CA, February 18, 2020.

- Sur NB, Wang K, Krementz N, Gardener H, Dong C, Yavagal DR, Saini V, Gutierrez C, **Rundek T**, **Sacco RL**, Romano JG, Asdaghi N. "The Safety and Outcomes of Endovascular Thrombectomy in Stroke Patients on Oral Anticoagulation: The Florida Stroke Registry." Poster Presentation International Stroke Conference 2020, Los Angeles, CA, February 18, 2020.

- **McIntosh, R**. "Can you feel the beat? Neurovisceral Integration in Health and Chronic Disease." Florida Atlantic University Seminar Series, Boca Raton, FL, February 18, 2020.

- **Jiang H**, Chen Q, Alba DA,Hernandez J, Delgado S, Porciatti V,**Wang J.** "Pattern Electroretinogram in patients with multiple sclerosis: 2-Year Follow-up." NANOS March, 2020, poster.

- **McIntosh R**. "Alexithymia and Cardiac Interoceptive Awareness in Women Living with HIV." at the American Psychosomatic Society, Vancouver, British Columbia, March 13, 2020.

- **Vontell RT**, Davis DA, Barreda A, Blennow K. Zetterberg H. Gultekin SH, DeKosky S, **Scott WK**, **Sun X** (poster). "Reduction of neurogranin immunostaining in the hippocampus of post-mortem brain of Alzheimer's disease." AAIC. Poster/abstract 40707. July 28, 2020.

- **Sun X**, Wang Q, Blennow K, Zetterberg K, McCathy M, **Loewenstein D**, Yue Z, and Zhang B. "Selective association of neurogranin gene expression with amyloid and tau pathology in the parahippocampal gyrus in Alzheimer's disease." Poster, AAIC July 27-30.

- **Ramos AR.** "Platform Presentation. Sleep Apnea Phenotypes in Latinos." September. Association of Professional Sleep Societies meeting (virtual SLEEP) August 2020.

- **Raval AP**. "Sexual dimorphism in neuroinflammation in aged rats." At the Transformative Research in Metabolism seminar series at the University of Alaska Fairbanks, Alaska. (Virtual) August 15, 2020.

- **Agudelo C**, Tarraf W, Wu B, Wallace DM, Pate SR, Redline S, Daviglus M, Zee PC, Simonelli G, Mossavar-Rahmani Y, Sotres-Alvarez D, Zeng D, González HM, **Ramos AR**. "Actigraphy-defined Sleep and Neurocognitive Decline in Middle-age Hispanic/Latino Adults." Poster presented and abstracted accepted at the Annual Meeting of the Associated Professional Sleep Societies Virtual Meeting August 2020.

- Gei E, **Agudelo C**, Ascher K, **Sun X**, Velez-Ruiz N, **Ramos AR**. "An unusual presentation of narcolepsy in an elderly man." Annual Meeting of the Associated Professional Sleep Societies; Philadelphia, PA; Virtual Meeting; August 2020 (Refereed abstract).

- **McIntosh R**. "Keeping your Monocytes in Mind: Endothelial & Peripheral Blood Mononuclear Cells in Chronic Disease." University of Iowa, Department of Psychology, November 10, 2020.

- Cabral DLF, Koch S, **Sacco R**, **Rundek T**, Fried P, **Gomes-Osman J**. **"**Exploring the behavioral relevance of neuroplasticity assessment with iTBS in individuals post-stroke." 64th Annual Meeting of the DGKN, 7th International Conference on Non-Invasive Brain Stimulation and 4th European Conference of Brain Stimulation in Psychiatry. Poster November 10-14th, Virtual.

- Cabral DLF, Rice J, Nunez C, Abel D, Van Deusen K, Moustafi B, Kitaigorodsky M, **Loewenstein D**, Cahalin L, **Rundek T**, Pascual-Leone A, **Gomes-Osman J**. "Effects of 8-weeks of Aerobic Exercise Intervention on Fitness and Neuroplasticity in Aging Adults: Preliminary Results of an Ongoing Trial." 64th Annual Meeting of the DGKN, 7th International Conference on Non-Invasive Brain Stimulation and 4th European Conference of Brain Stimulation in Psychiatry. Poster November 10-14th, Virtual.

- Bailey M, **Saporta A**, Baumrucker C, Yen J, Rehman R, Lopez MR. "Are Psychogenic Nonepileptic Seizures in the Hispanic Population Different from Other Populations?" American Epilepsy Society 74th Annual meeting, December, 2020. Virtual.

- Lombardo M, Bellia C, Moletto C, Aulisa G, Padua E, **Della-Morte D**, Caprio M, Bellia A. "Diet rich in plant protein may prevent type 2 diabetes." The 1st International Electronic Conference on Plant Science, Dec. 2020.

- Lombardo M, Alfonso Perrone M, Guseva E, Aulisa G, Padua E, Bellia C, **Della-Morte D**, Iellamo F, Caprio M, Bellia A. "Losing weight after menopause with minimal aerobic training and Mediterranean diet." The 1st International Electronic Conference on Plant Science, Dec. 2020.

- Dueker ND, Zhao H, Dong C, **Kaur S**, Gardener H, Gutierrez C, De Fonseca Ferreira A, **Della-Morte D**, Cabral D, **Sacco RL**, **Blanton SH**, Wang L. The 2020 American Society of Human Genetics meeting, Dec. 2020.

- Coppola A, Pacifici F, Pastore D, Arriga R, Rea S, Andreadi A, Bellia A, **Della Morte D**, Lauro D. "Il trattamento con Dapagliflozin migliora la funzionalità adipocitaria nelle 3T3-L1 murine." 28th National Congress of the Italian Society of Diabetologia (SID) Rimini, Dec 2-5, 2020.

- Rea S, Pacifici F, Capuani B, Pastore D, Coppola A, Arriga R, Andreadi A, Bellia A, **Della-Morte D**, Lauro D. L'Insulina e l'Exendina riducono l'accumulo di Huntingtina mutata a livello neuronale. 28th National Congress of the Italian Society of Diabetologia (SID) Rimini, Dec 2-5, 2020.

- **McIntosh R.** "Health Neuroscience Data Hack: Exploring National Datasets. Pursuing Health Equity in the Context of COVID-19." American Psychosomatic Society, December 3, 2020.

- Kanner A, Dong Hee K, **Seixas A**, Barry J, Hamid AH, Omotola H, O'Brian T, Winawer M, Sperling M, Nadkarni S, French J. "Which of the Mood and Anxiety Disorders are the

Strongest Predictors of Suicidality in Newly Diagnosed Non-Lesional Focal Epilepsy?" American Epilepsy Society 74th Annual Meeting – December 4-8, 2020.

## 2. Professional Meetings and Invited Lectures

- **Jiang H**. "Anti-MOG antibody syndrome." Neurology Update & Stroke Intensive Review 2020, Miami, FL, Jan16, 2020.
- **Vontell RT**. "Pathological evidence of neuroinflammation in neuropsychiatric disorders" at MBI Research Seminar. Miami FL, (virtual) April 29, 2020.
- **Dave K.** Invited presenter "Recurrent hypoglycemia in diabetics and cerebral ischemia" at the Barrow Neurological Institute Neuroscience Conference Series, Phoenix, Arizona, March, 2020.
- **Sacco RL.** Brooke Army Medical Center, Grand Rounds, Stroke Prevention in 2020, San Antonio, TX, March 6, 2020.
- **Vontell RT**. "Guidelines for the Neuropathologic Assessment of Alzheimer's Disease" at MBI Research Meeting. Miami FL, April 29, 2020.
- **Raval AP**. "Interventions to improve post-stroke cognition in females." Grand Rounds, Department of Neurology, University of Miami. Virtual. May 15, 2020.
- **Gomes-Osman J. "**An Exercise Study during and (hopefully!) after the COVID-19 Pandemic" at MBI Research Seminar, Miami, FL. Virtual, July 8, 2020.
- **Sun X**, Wang Q, Blennow K, Zetterberg K, McCathy M, **Loewenstein D**, Yue Z, and Zhang B. "Selective association of neurogranin gene expression with amyloid and tau pathology in the parahippocampal gyrus in Alzheimer's disease." Poster, AAIC July 27-30, 2020.
- **Agudelo, C.** "Diffusion MRI: A biomarker of grey matter microstructure integrity in neurocognitive aging." McKnight Research Seminar. August 26, 2020.
- **Wang J**. "Age-related alterations in retinal tissue perfusion and volumetric vessel density." McKnight Research Seminar. Sept. 2, 2020.
- **Lobo J**, Hidalgo M, Andrade M, Reed M, Uddin LQ, Szeto A, Hong S, Antoni M, **McIntosh RC.** "Inflammation, Intrinsic Brain Connectivity and Depression in Post-Menopausal Women Living with HIV." International Workshop on HIV & Aging, Virtual Conference 30, September 2020- 2 October 2020.
- **Gomes-Osman J**. "Neuroplasticity: understanding the mechanisms behind cognitive benefits after exercise." 4th Annual Neural Engineering Symposium**.** Virtual, October 27, 2020.

- **Dr. Della-Morte** was an invited as Special Guest to the 1st International Conference on Longevity organized by David Sinclair. Webinar, Nov. 12, 2020.
- **Dr. Della-Morte** was an invited speaker at the International Fondazione Lorenzin Webinars. “Comorbidities and Covid-19”. Nov. 2020
- **Perez-Pinzon MA.** Invited Presenter “Consideration of Ageing in Ischemic Stroke” at the Workshop for Advancement of Victories in Experimental Stroke, organized by the Department of Neurology, Tulane University, New Orleans on Friday November 13, 2020.
- **Sacco RL**, **Rundek T**, **Levin BE, Galvin J**. University of Miami Miller School of Medicine “Virtual Town Hall: In the Know: The Science of Aging” (Virtual Webinar). October 7, 2020.

# NOTABLE AWARDS AND RECOGNITION

## Notable Awards and Recognition in 2020

### 1. Faculty

See **Appendix V** for a list of Faculty and Trainees.

- **Dr. Alperin** was awarded a follow-up grant from the Florida Department of Health (DOH) to continue studying "Lifestyle Stressors of Hippocampus and AD related brain regions: Potential for Intervention." Its focus is on the development and assessment of novel therapeutics aimed at slowing and eventually preventing the progression of AD, which remains a critically important public health goal.

- **Dr. Crocco** was awarded a grant from the State of Florida Department of Health, Ed and Ethel Moore AD Research Program for the project "Building an Advanced Cognitive and Biomarker Registry for African American Older Adults At-Risk for Alzheimer's Disease."

- **Dr. Davis** assistant research professor at the Brain Bank which **Dr. Sun** oversees, received a Herbert Hoover Foundation grant to study "Algal Toxins and Alzheimer's Disease in Florida."

- **Dr. Galvin** received the following grants and awards:
  - "Digital Detection of Dementia ($D^3$)" - Boustani, Ben-Miled, Galvin (MPI) funded by the NIA.
  - "The LUCINDA Trial: Lupron + Cholinesterase Inhibition to Reduce Neurologic Decline in Alzheimer's Disease" - Butler, Galvin, Atwood (MPI) funded by the NIA.
  - "Reducing Disparities in Dementia and VCID Outcomes in a Multicultural Rural Population" - Funded by the NINDS.
  - "Native Alzheimer's Disease Resource Center for Minority Aging Research (NAD-RCMAR)" - Buchwald, Manson, Galvin (MPI) funded by NIA.
  - "Identifying Factors Predicting Accurately End-of-Life in Dementia with Lewy Bodies and promoting Quality End-of-Life Experiences: the PACE-DLB Study" – Co-I, funded by the NIA.

- **Dr. Gomes-Osman** was appointed and nominated as:
  - Guest Editor for the *Journal of Neurologic Physical Therapy* for a Special Issue: "Harnessing and Evaluating Neuroplasticity in Physical Therapy." This is one of the top impact journals in rehabilitation research.
  - CTSA KL2 Visiting Scholar, and matched with Harvard Medical School, where she will give Grand Rounds in Spring of 2021.

- **Dr. Jiang** received a Florida DOH Ed and Ethel Moore Alzheimer's Disease Research Program grant for her project "Retinal biomarkers for monitoring vascular contributions to Alzheimer's disease."

- **Dr. Levin** received an Ed and Ethel Moore Alzheimer Disease Research Program (DOH) Grant for "Detection and reduction of scam susceptibility among Hispanic/Latinx and non-Hispanic/Latinx individuals with mild cognitive impairment and Alzheimer's disease." The pilot study plans to develop an educational intervention for Hispanic and non-Hispanic elderly individuals and their caregivers/partners who are residing independently in the community but susceptible to being scammed.

- **Dr. McIntosh** received a Mentored Career Development Award to Promote Faculty Diversity in Biomedical Research: HIV-Related Changes in Brain Function and Hypertensive.

- **Dr. Perez-Pinzon** received two awards:
  - Discovery grant from the James and Esther King Biomedical Research Program, Florida Department of Health for the project "Mechanisms of Neuroprotection against Cardiac Arrest."
  - R01 grant from the National Institute of Neurological Disorders and Stroke (NINDS) Supplemental grant award from the NINDS to study "Strategies to ameliorate cognitive decline following cerebral ischemia in nicotine exposed rats."

- **Dr. Pinto** started her service on these advisory groups; became reviewer for Italian Ministry of Health grants, the National Biomedical 2020 Call for Grant Applications; scientific journals (reviews 4-5 papers/month); and was a judge for ESRF (Eastern Atlantic Student Research Forum) and SURF (Undergraduate Research Symposium).

- **Dr. Ramos** started his service as:
  - The Inaugural Chair for the Sleep Research Program for Advancing Careers (SOAR) of the American Academy of Sleep Medicine Foundation.
  - Leader of the Grand Rounds Committee at our Department of Neurology.

- **Dr. Raval** received a grant from the Florida DOH to study "Nicotine alters brain oxidative metabolism and exacerbates ischemic brain damage."

- **Dr. Rundek** received the following awards:
  - MBRF Award for the "Precision Aging Network Pilot Project." This work and contributions to this effort are outlined in **Appendix VII**.

- Ed and Ethel Moore Alzheimer Disease Research Program (FL DOH) grant for the research project "Carotid Ultrasound Imaging Markers of AGINg and Endothelial function in Risk of Alzheimer's Disease: The Florida IMAGINE Study."

- The University of Miami Miller School of Medicine's *Women in Academic Medicine Career Achievement Award.*

- **Dr. Sacco** received these notable awards, appointments or recognitions:

  - 2020 Highly Cited Researcher (Cross-Field).

  - The 40th TS Srinivasan Oration Award, Bengaluru, India.

  - Member of the NCATS CTSA, National Steering Committee.

  - Co-chair for the University of Miami's Health Informatics Chair Search Committee.

  - Editor-In-Chief for Stroke, the American Heart Association/American Stroke Association journal.

  - **Dr. Sacco** was awarded the inaugural AHA Edgar J. Kenton III Lecture Award. The lecture "Understanding and Problem-Solving" is published in *Stroke* (https://doi.org/10.1161/STROKEAHA.120.030428). As a primary example of the application of this process (observation to actions), he presented NOMAS work from which results have been used to develop stroke prevention recommendations, address health disparities, identify high-risk groups and specific vulnerabilities and pinpoint specific behavioral and lifestyle treatments designed to reduce vascular and cognitive risks. Another direct example of the application of observation to action is the Florida Stroke Registry. Not just a database, the Florida Stroke Registry functions as an important quality improvement resource to provide evidence-based results that impact and inform clinical guidelines; interventions addressing disparities and gaps in the quality of care; inform and create statewide policy for stroke centers and the effective transportation of stroke patients.

- **Dr. Vontell** received a National Society for Histology Scholarship.

- **Dr. Wang** was awarded a NIH NINDS R01 grant (MPI: Detre UPENN – Wang UM) to study the microvasculature in the eye and brain in healthy population and patients with small vessel diseases. **Dr. Jiang** is Co-I.

## 2. Trainees

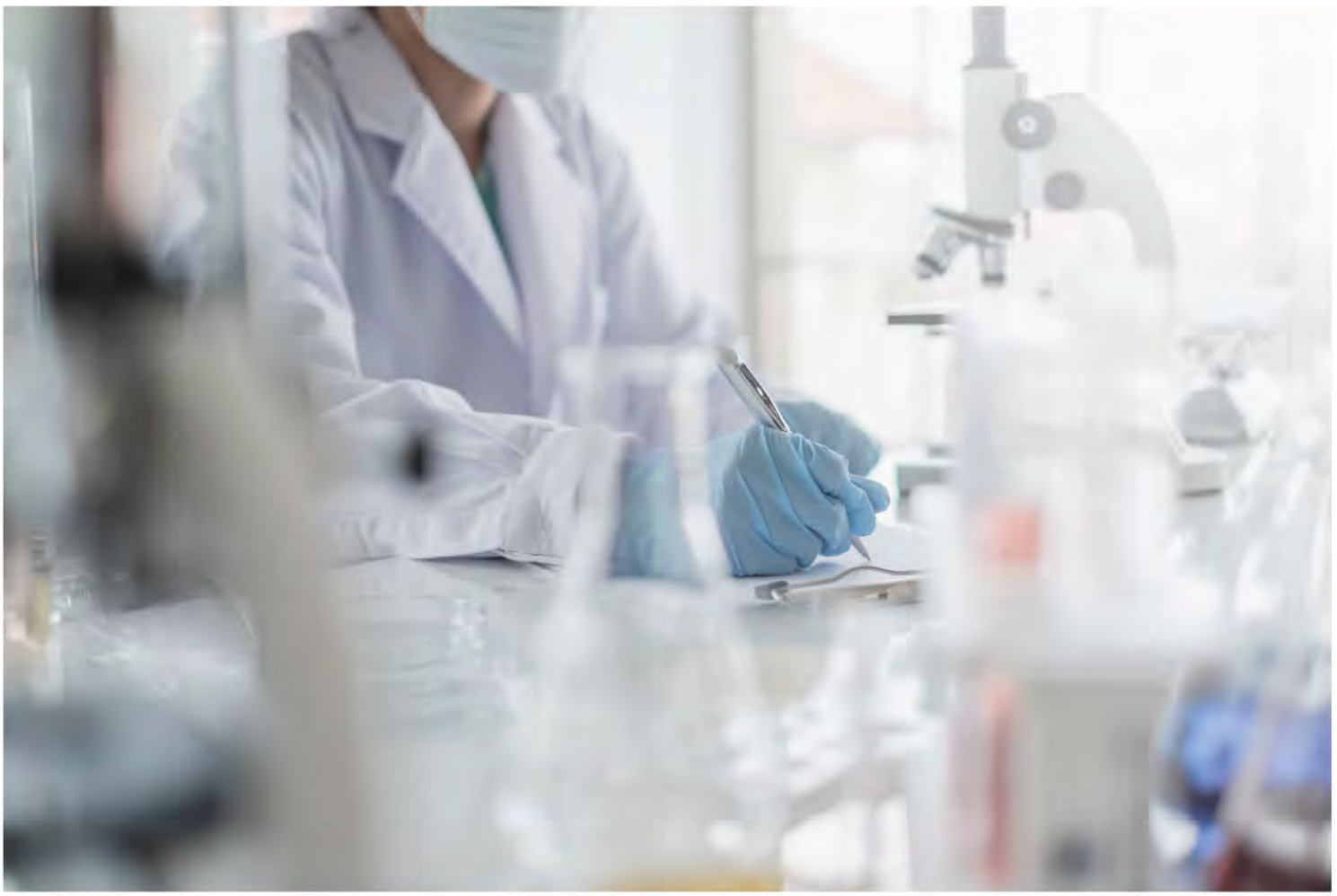
See **Appendix V** for a list of Faculty and Trainees.

- **Christian Agudelo** received the following achievements, awards and recognition: (Mentors - Drs. Rundek, Ramos, Sun)

- Selected for the *Sleep and Circadian Workshop on Indispensable Methods* hosted by the University of Pittsburgh Center for Sleep and Circadian Science.
- Joined other early career investigators that participated in the Sleep and Circadian Workshop on Indispensable Methods to Establish a Group, led by the University of Pittsburgh's Martica Hall, PhD, and Sanjay Patel, MD, that explores how to study racial disparities more effectively as they relate to sleep and health.
- Submitted an application for the NIH Loan Repayment Program award. This award provides up to $50,000 per year to pay for eligible federal educational debt.
- Submitted an application for the *American Academy of Sleep Medicine's Young Investigator Research Forum Award*.
- Reviewed manuscripts for the *British Medical Journal Open Access Journal* and *Frontiers in Aging Neuroscience*.

- **Iris Escobar** received the American Heart Association (AHA) pre-doctoral fellowship award. (Mentor - Dr. Perez-Pinzon)
- **Sarah Getz** served as a member of the *Women in Academic Medicine Scholarship Committee*, University of Miami, Miller School of Medicine. (Mentors - Drs. Levin, Rundek)
- **Charlie Jackson** received the American Heart Association (AHA) pre-doctoral fellowship award. (Mentor - Dr. Perez-Pinzon)
- **Judith Lobo** received aT32 NIH award for her Post-Doctoral appointment (Mentors - Drs. McIntosh, Heaton)
- **Amanda Neves** received a Lois Pope Fellowship Award. (Mentor - Dr. Pinto)
- **Sharnikha Saravanan** received an undergraduate fellowship. (Mentor - Dr. Raval)
- **Varun Reddy** received a Lois Pope summer fellowship. (Mentor - Dr. Raval)

# CLINICAL-TRANSLATIONAL, POPULATION BASED AND BASIC SCIENCE RESEARCH



## Clinical-Translational and Population Based Research

### 1. New Research Studies/Programs

- **Dr. Galvin** was awarded grants for these research studies/clinical trials in 2020.
  - "Digital Detection of Dementia ($D^3$)" - The major goals of $D^3$ includes two complementary studies at diverse urban, suburban and rural primary care practices within Central Indiana and South Florida that will evaluate the predictive performance, the utility and effectiveness of the Passive Digital Marker, the Quick Dementia Rating Scale (QDRS), and the combined approach (Passive + QDRS) in the early detection of Alzheimer's Disease and related dementia (ADRD). Boustani, Ben-Miled, Galvin (MPI) funded by the NIA.
  - "The LUCINDA Trial: Lupron + Cholinesterase Inhibition to Reduce Neurologic Decline in Alzheimer's Disease" - The major goal is to conduct a randomized double-blind, placebo-controlled trial of Lupron and donepezil in women with mild to moderate Alzheimer's disease to improve cognition and activities of daily living. Butler, Galvin, Atwood (MPI) funded by the NIA.
  - "Reducing Disparities in Dementia and VCID Outcomes in a Multicultural Rural Population" - The major goals of this project are to study disparities in health outcomes related to vascular contributions to cognitive impairment and dementia (VCID) in a multicultural rural community, determine rates of impairment, and provide community- based interventions to improve care and reduce costs. It is funded by the NINDS.
  - "Native Alzheimer's Disease Resource Center for Minority Aging Research (NAD-RCMAR)" - The major goals of this Center is to describe, understand, intervene on, and mitigate the Alzheimer's disease health disparities experienced by American Indians, Alaska Natives, Native Hawaiians, and Pacific Islanders by funding social and behavioral Pilot Studies that advance the field, emphasizing the recruitment and mentorship of Native junior and mid-level researchers. Buchwald, Manson, Galvin (MPI) funded by NIA.
  - "Identifying Factors Predicting Accurately End-of-Life in Dementia with Lewy Bodies and promoting Quality End-of-Life Experiences: the PACE-DLB Study" - The major goals of this project are to determine factors predicting end-of-life in dementia with Lewy bodies and improve the experience and quality of life for patients and their family caregivers. Dr. Galvin is a co-investigator. The study is funded by the NIA.

- **Dr. Getz** was awarded an AAN McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss this year for her research project "Uncovering Risk Profiles of Deception and Mitigating Susceptibility to Scamming in Midlife and Older Age: A Novel Intervention Tool." This study explores the utility of the

*Assessment of Situational Judgment* in identifying individuals who are susceptible to being scammed and understanding where faulty decision making interferes with assessing risk. She obtained IRB approval and began the planning phases of the research. The study assessments have been modified to be conducted virtually, as well as in person.

- **Dr. Levin** submitted a grant to the Ed and Ethel Moore Alzheimer Disease Research Program (FL DOH). The research project is "Detection and reduction of scam susceptibility among Hispanic/Latinx and non-Hispanic/Latinx individuals with mild cognitive impairment and Alzheimer's disease." It was funded in December.

- **Dr. Ramos** started a new project with Avadel Pharmaceutical in 2020 entitled "Open label study evaluating the effect of single dose sodium oxybate in Narcolepsy." Work was done on study set-up logistics, the budget and the IRB. Enrollment will begin next year.

- **Dr. Rundek** submitted a grant for the project "Carotid Ultrasound Imaging Markers of AGINg and Endothelial function in Risk of Alzheimer's Disease: The Florida IMAGINE Study of AD Risk" to the Ed and Ethel Moore Alzheimer Disease Research Program (FL DOH). It was funded in December.

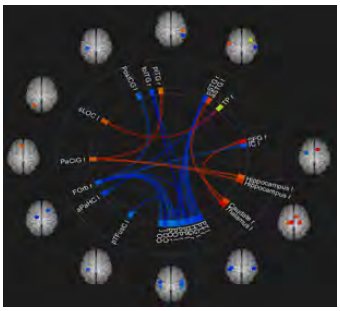
- **Dr. Rundek** is a Co-Director of the "**OneFLorida ADRC REC AlzSTARS**" program together with Dr. Glenn Smith from UF. One Florida ADRC (1FL ADC) was awarded in June 2020 to UF, UM and Mt. Sinai. The Contact PI of the 1FL ADRC is Dr. Golde at UF and the Miami PI is **Dr. Loewenstein**, our MBI Advisory Scientific Board member.

  - 1FL ADRC Research Educational Core was awarded to **Drs. Rundek** and Smith to co-lead a clinical translational educational program in aging and neurodegenerative disorders for junior faculty across 1FL ADRC. The 1FL ADRC REC program is called the *Alzheimer's Science Training to Advance Research Success (AlzSTARS)* with the primary objective to train diverse, multidisciplinary Early Stage Investigators across the 1FL ADRC consortium for leadership roles in research translation. Three selected junior faculty already started the program in October 2020.

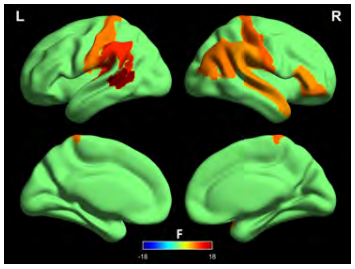
## 2. Update on Existing Research

- Update on Neuroimaging MBI Core - **Dr. Alperin** and his laboratory performed extensive analysis of the McKnight Brain Aging Registry (MBAR) MRI data. Two manuscripts pending approval from the MBAR Manuscript Approval Committee have been proposed:

- The first one is “Gender differences in brain function in the cognitively intact oldest old: resting-state fMRI findings from McKnight Brain Aging Registry (MBAR).” **Che Liu** from Dr. Alperin’s laboratory investigated gender-related differences in neural activity and brain activation patterns in the ‘resting brain’ using rest-state fMRI in a cognitively intact oldest old cohort.



- The second paper is “Gender differences in the associations between brain volumes, cerebral blood flow and cognitive performance in the cognitively intact oldest old from the McKnight Brain Aging Registry.” This manuscript addresses the link between brain tissue volume, cerebral blood flow (CBF) and cognitive performance. The paper further addresses differences related to regional brain volume and cerebral hemodynamics to enable the similar level of cognitive performance between genders. Dr. Alperin’s laboratory performed brain parcelations to test whether brain regions are uniformly smaller in women or there are differences in ratio of volumes of brain regions between men and women. The analyses revealed a strong correlation between CBF and cognitive performance in women. Total CBF was similar in men and women, but cerebral perfusion was significantly higher in women.




**Dr. Alperin’s Team**

The following clinical trials and research projects that started in 2020 were put on hold in mid-March due to the COVID-19 Pandemic, and were either halted and/or redesigned to adapt to virtual continuation:

- **Dr. Camargo's** clinical trials were halted and/or adapted and continued:

  - "Reducing the Effects of Aging on Cognition with Therapeutic Intervention of an Oral Nutrient - The REACTION Study" (funded by the AAN McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss) aims to test the effect of the formulation Souvenaid on increased synaptic plasticity and improved cognition in aging. The IRB process and clinical and cognitive assessments were modified in order to be performed via virtual clinic and virtual cognitive assessments with the help of Dr. Levin's cognitive team. This entailed multiple logistics that should be fully in place at the beginning of 2021. He has already obtained a no-cost extension from the AAN until 2022 to accommodate the delay in implementing COVID-19 Pandemic-related protocol modifications and study enrollment.

  - "A Role for Evaluating PET-Amyloid Status (AREPAS) as part of the Key Hallmarks of Amyloid Tracer as an Ideal Biomarker (KHATIB)" has proceeded despite a delay in recruitment of participants for elective Amyloid PET scans due to Pandemic-related restrictions on clinical research at UM. Research has resumed in October 2020 and enrollment of the participants is nearing completion.

  - "A Phase I, Prospective, Open-Labeled Trial to Evaluate the Safety, Tolerability and Exploratory Outcomes of Multiple Allogeneic Human Mesenchymal Stem Cell (MSC) Infusions in Patients with Mild to Moderate Alzheimer's Disease" (Co-Investigator **Dr. McInerney**) trial was able to continue during the COVID Pandemic and has almost completed the targeted enrollment.

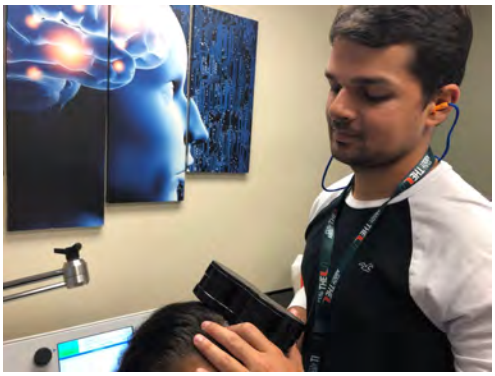
- "McKnight Brain Aging Registry (MBAR)"
  In the final year of study recruitment, the UM site led by **Drs. Rundek and Levin** with participation of **Drs. Alperin**, **McInerney, Kaur**, along with **Stacy Merritt**, **Marti Flothmann** and **Sang Lee,** was close to meeting the enrollment goal when the COVID-19 Pandemic began. With 58 subjects enrolled at our MBI, there was one Baseline visit to be completed and 10 MRI visits to reach the ultimate goal of 50 participants with full and detailed clinical, cognitive and multi-modality neuroimaging assessments. Since March all sites have continued bi-weekly calls and have been double scoring, cleaning and organizing collected data. Additionally, questionnaires pertaining to COVID-19 were added and approved by the IRB to administer to the study subjects. These are being done by telephone with most subjects agreeing to participate. We have called our MBAR participants at the UM site to offer help during COVID. All, except one who died (death unrelated to COVID-19) seem to be coping reasonably well with the lockdown and environmental changes. They have adopted virtual technology and have been using Zoom to stay socially engaged with family, friends, and with clubs organized by various organizations. They are staying physically active by taking regular walks in the

neighborhood. They are utilizing grocery delivery services and continue their daily activities as much as possible while socially distancing. They are participating in our MBI virtual webinars and engaging in activities (e.g., virtual cooking classes).

- Dr. Gomes-Osman's Transcranial Magnetic Stimulation Lab
  - **Dr. Gomes-Osman** continues to make progress on the project that is part of her Career Development Award (KL2) by the Miami Clinical and Translational Science Institute. For this project, aging adults are participating in a 2-month exercise intervention, and she is examining neuroplasticity, neurocognitive performance, exercise capacity and genetic modification of response. Currently, 40 participants have been enrolled and 20 have completed the program. **Dr. Rundek** is her primary mentor, and **Dr. Loewenstein** and Dr. Alvaro Pascual-Leone (from Harvard) serve on her mentoring team.

  - As a result of the COVID-19 Pandemic, **Dr. Gomes-Osman** converted her KL2 in-person exercise study to a fully remote intervention, consisting of home-based assessments of cognition and exercise capacity, and a 2-month home-based exercise. Currently, 16 participants have completed the study remotely, and she is on target to complete 32 participants by the end of the grant in spring 2021. As the exercise program is virtually supervised and performed at home, most participants would like to continue after completion. There is a possibility that this program may be commercialized if public demand continues to increase.

Brain stimulation for neuroplasticity testing in Dr. Gomes-Osman's Lab



- Drs. Jiang and Wang's Neuro Ophthalmology Laboratory

  **Dr. Jiang** and **Dr. Wang** worked on their pilot study on artificial intelligence (AI) and intraretinal thickness mapping to differentiate diseased eyes from those of the normal population. They also continued their FL DOH-funded prospective study of retinal biomarkers for monitoring vascular contributions to cognitive decline and AD.

- MBI Frailty Project

  **Drs. Levin** and **McInerney** oversee the Frailty project, **Stacy Merritt** coordinates the database logistics and **Dr. Seixas-Saporta** analyzes the aging brain MRI images. Data collected includes demographic, medical/clinical, neuropsychological, neuroimaging, psychosocial and frailty data. Dr. Levin and team successfully launched their virtual neuropsychological testing, which is the data source for the project. There are 517 subject records in the study. With all working from home, this year's data has not been entered. Data analysis has continued on MRI brain image analyses.

  - Over the past year, all high quality structural images (n=128) have been processed. **Dr. Seixas-Saporta**, our MBI fellow has been exploring volumetric differences in hippocampal volumes as well as in other structures early affected in those at AD risk. She is also exploring the brain aging process in normal aging and in pathological conditions through the study of the cerebellum. She focuses on this brain structure because the cortical contributions to age-related declines in motor and cognitive performance are well-known but potential contributions of the cerebellum are less clear. The diverse functions of the cerebellum go beyond motor function and include emotion, language and cognition which make it an important structure to investigate in aging. Dr. Seixas-Saporta is currently working on the analysis of the data and plans to publish the results in 2021.

- **Dr. Levin** is Co-Investigator on the "Role of Gut Microbiota on the Brain Metabolism, Cognition, Immune Function and Inflammation in Alzheimer's disease: Novel Biomarkers and Understanding Mechanisms" research project funded by FL DOH. The goal of this study is to test the associations between dysbiosis of the gut microbiome and intestinal permeability and microbial translocation markers with brain GABA, brain inflammation markers, peripheral amyloids and lipopolysaccharides, peripheral inflammation markers and cognitive function in patients at the early stage of cognitive impairment and age-matched healthy controls.

**Dr. Levin's Team**

- **Dr. Ramos** continued to work on his projects:

  - "Atrophy and Neurocognition in Treated Obstructive sleep apnea (MAGNETO)" This (NIH) study was able to enroll subjects despite the COVID-19 Pandemic by transitioning parts of it to take place virtually. This investigator initiated study evaluates the neuroimaging and neurocognitive substrates of residual daytime sleepiness in patients with treated obstructive sleep apnea. Sleep apnea can affect cognition.

  - "Sleep Apnea Phenotypes in Latinos (SLEPT)" (NIH) will continue in 2021. This study will help develop risk-stratification strategies for sleep apnea and inform future intervention studies in cardiovascular risk and sleep apnea; providing a step towards personalized medicine in sleep. This study would contribute to reducing health disparities among diverse Latinos, who are burdened by increased risk for cardiovascular disease and a high prevalence of sleep apnea. Both of these can contribute to cognitive decline in aging.

- **Dr. Rundek** has made progress on the following studies:

  - "The Brain Vascular Imaging Phenotypes, Vascular Comorbidities and the Risk for Alzheimer's Study (VIP Study)" - Under **Dr. Rundek's** leadership, **Dr. Seixas-Saporta** and VIP study team conducted visual and automated MRI analysis to quantify silent cerebrovascular disease-related lesions, such as white matter hyperintensities. In addition, the analyses of cerebral microbleeds, silent brain infarcts and enlarged perivascular spaces were visually analyzed, while automated methods are in development. There are 299 cases with MR images available for analyses. The study includes 5 different MRI processing techniques: 2 visual (Fazekas; MARS/BOMBS); and 3 semi-automated (one for each type of the following lesions: white matter hyperintensities; lacunes; enlarged perivascular spaces). Currently, 83% and 23% of the 299 cases were completed for visual and semi-automated analysis, respectively, and the results are entered in the REDCap database.

  - "Family Study of Cognitive Decline Risk" research was extended this year to study cognitive assessments in collaboration with Dr. Ron Lazar, MBI Director at UAB. The study is a NIH supplement to a currently ongoing NINDS-Family study of genetic risk for subclinical atherosclerosis. Over 30% of the targeted population has received cognitive assessments by phone. This NIH supplement will investigate genetic and epigenetic markers of vascular cognitive impairment (PI: Rundek).

  - "Disparities in Stroke Outcomes and Care Delivery in Patients with Atrial Fibrillation: FLiPER-AF" has been completed this year. Several manuscripts were published using the data of this study and show a disparity in stroke outcome in patients with Atrial Fibrillation (AF). Women with AF have poor outcome after stroke (increased in-hospital mortality and discharge disability) in comparison to men. Women were also less likely discharged on anticoagulation then men.

- "Transcranial Doppler Ultrasound (TCD) Core of The Albert Einstein Study (AES) Program Project in Aging" This NIA-funded study has been completed this year and its competitive renewal is currently under review. The study has had several major publications, showing impaired cerebral flow velocities on TCD with aging process, association of increased cerebral blood flow pulsatility with impaired cognition and with global and regional structural and functional white matter integrity on MRI.

- "Oral Infections, Carotid Atherosclerosis and Stroke (INVEST)" This NIH-funded study with Columbia University has been completed this year and its competitive renewal is currently under review. This study has several major publications showing that chronic periodontal disease and related inflammation are associated with increased risk of subclinical and clinical atherosclerosis, vascular cognitive decline and dementia.

- "Hispanic Community Health Study - Study of Latinos (HCHS-SOL)" at the Miami Field Center (Dr. Rundek is a study investigator, mentor, and stroke adjudicator). The HCHS/SOL (NIH contract) 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. The stroke adjudicators have created an adjudication protocol with definitions of stroke types and ischemic stroke subtypes and Manual of Operations on the process and details on data collection needed to extract from the clinical charts. About 200 events were adjudicated so far.

- "OneFlorida Alzheimer's Disease Research Center (ADRC)" This is a collaborative NIA project between the University of Florida (Dr. Todd Golde, Contact PI), Mt. Sinai Medical Center in Miami Beach (Dr. Ranjan Duara, PI), University of Miami (Dr. Loewenstein, PI), Florida International University and Florida Atlantic University. The UM Clinical site investigators include **Dr. Rundek** (she is also a Co-Director of Research Education Core AlzSTARS), and **Dr. Sun**. The overall goal of the 1FL ADRC is to advance the understanding of Alzheimer's Disease and Related Dementia, especially in underrepresented minority groups. Work on this project this year included preparation of a complex IRB and on the clinical, multi-modal neuroimaging MRI and PET imaging, biomarkers and cognitive protocols.

- **Dr. Sacco** leads several large collaborative research programs:

  - "The Northern Manhattan Study (NOMAS)" - The longitudinal study, Risk Factors for Stroke and Cognitive Decline in a Tri-Ethnic Region, is currently in its 5$^{th}$ cycle and has achieved 28 years of continuous NIH funding. The study aims overall are to understand the relationship of novel and traditional vascular risk factors of stroke to cognitive decline, MCI, and dementia among whites, blacks and Hispanics living in the same community.
    a. In the final year of cycle 5, **Dr. Sacco** and his vast team has conducted ongoing annual follow-up calls, a standardized neuropsychological battery, and the NOMAS Dementia Adjudication process on the MRI cohort. To determine the risk and vascular contributors to dementia in the multiethnic, population-based MRI

cohort, they used their "Visit 2" adjudications ("Visit 3" reviews are underway). The NOMAS Dementia Adjudication process incudes a previously created algorithm which classifies cases as probable dementia, mild cognitive impairment (MCI) or normal categories. Cases identified to require manual review are distributed to the Dementia Adjudication reviewers who utilized the online database to remotely access participant data. They submitted a manuscript on recent results that demonstrated significantly increased prevalence of MCI and dementia among Blacks and Hispanics compared to whites with sociodemographic and brain imaging factors explaining the most variance in the race/ethnicity associations. White matter hyperintensity (WMHI) burden explained much of the disparity between Black and White, but not between Hispanic and White. Other publications on vascular determinants of cognitive performance and decline including AHA-defined ideal cardiovascular health, their NOMAS-derived Global Vascular Risk Score, physical activity, sleep and carotid atherosclerosis. Most recently, they found that people who were socially isolated and reported loneliness had an increased risk of dementia or MCI, and that people who frequently spoke to friends and family on the phone had a decreased risk of dementia or MCI. The results from this study are currently under review for publication.

b. NOMAS investigators also advanced their work towards understanding the role of infection and inflammation in cognitive trajectories and dementia. This year, they published the finding that a novel Infectious Burden index, a composite measure of past exposure to five common infections, is associated with cognitive decline on neuropsychological battery over 5 years, particularly for memory performance. Additionally, using the 60-plex immune profiling panel of inflammatory markers, they have found significant associations of specific sets of immune markers with cognition overall and white matter hyperintensity burden. They have plans to further explore preliminary findings indicating that past infection and inflammation-related vascular injury may contribute to cognitive impairment.

c. In another set of studies, NOMAS investigators reviewed WMH, SBI and brain volumes, and subclinical MRI biomarkers, to explore the relationship between cognitive performance and stroke risk factors. This year, they published findings on cholinergic tract WMHI and associations with worse processing speed and AD-region cortical thickness. They also reported the association of WMHI with a regional pattern of gray matter atrophy that was mitigated by BP control, exacerbated by aging and associated with cognitive performance.

d. They also began to explore pilot data regarding the gut-microbiome-brain axis. Forty cases were selected with high levels of activation of specific immune molecules (IL-1, IL-17 and TNF) and evaluated plasma levels of two gut-permeability markers, LPS and sCD14 in these samples. They hypothesized that gut microbial dysbiosis and increased gut permeability would be associated with cognitive decline, specifically in a subset of subjects whose cognitive decline

appears to be driven by inflammation. They observed elevated levels of sCD14 only in samples that had higher levels of IL-1, suggesting that sCD14 may have a role in the IL-1 inflammatory pathway. Furthermore, preliminary analyses among these 40 cases found that higher values of sCD14 and LPS were associated with greater cognitive decline and higher risk of MCI and dementia. These results are pending publication.

- "The Florida Stroke Registry" led by **Dr. Sacco** - Funded by state appropriations through the FL Department of Health, the University of Miami, Department of Neurology, was awarded its fourth round of annual funds for 2019-2020 to manage and maintain the Florida Stroke Registry (the Registry). The Registry now consists of 76% of all stroke centers (~165) in Florida and maintains over 300 stakeholders statewide. Because of its wide reach, the Florida Stroke Registry is well positioned as a platform for communication between stakeholders. During this year centered around the COVID-19 Pandemic, the Registry's communication platform was refocused and quickly mobilized as an informational resource to its 126 participating Florida stroke centers needing news on the virus and its relation to their stroke patients. Through the Registry's various communication modes and access to its multidisciplinary health professional network, the Florida Stroke Registry compiled, documented and developed informational resources specifically related to COVID-19, tackling uncharted clinical territory. Among the multiple Registry media forums utilized during the past year (website, listserv, newsletter, twitter, and webinars), the "FSR at the Front Lines" is a featured initiative focused on COVID-19, local stroke health care practices, and informal, "boots on-the-ground" information. The initiative consists of short 10min Zoom recorded conversations between 2-3 Registry member clinicians/researchers informally discussing their COVID-19/stroke related experiences, practices, latest findings and ongoing questions. Various topics have been discussed such as (i.e., availability of PPE; protocol for stroke patients diagnosed with COVID-19; the marked drop in stroke admissions shortly after the Pandemic escalated; patients' reluctance to utilize hospital services due to fears of risks of COVID-19 transmission; the use of stroke treatments on COVID-19 positive stroke patients, etc.) The videos are archived at the publicly available website. Though viewership and initiative impact have not yet been formally reviewed, an indication of the initiatives value may be derived from the ongoing requests from Registry members to participate in the recordings.

  Despite the Pandemic, the Registry continued to develop and establish new relationships among a multidisciplinary group of potential stakeholders. Throughout this past year, the Florida Stroke Registry has not only increased the number of participating stroke centers, but has also facilitated the engagement of non-hospital agencies (i.e., EMS, pharmacy, government, academia, etc.), many of which organized to create regional stroke coalitions. Uniting and attracting the various Florida Stroke Registry stakeholders is the Registry's ongoing collection of data; to date having collected over 300,000 Florida stroke cases representing years 2010 to current.

Among other research related endeavors, the Registry uses the collected data to provide evidence-based reports. The annual and quarterly reports function as self-monitoring tools for hospitals to improve performance and the outcomes of their patients, goals that directly and indirectly impact the entire stroke system of care. These powerful performance monitoring tools are actively being used in south and west Florida as the Registry continues to identify and engage local Registry members in the east, north and pan handle Florida regions to lead the initiatives within their respective areas. This year, EMS agencies have approached the Florida Stroke Registry to develop similar tools to address their "pre-hospital" needs, and the Registry has initiated internal discussions to develop reports applicable to a "post-hospital" phase of care. In December of this year, the Registry was approved access to statewide data further enhancing the applicability of Florida Stroke Registry self-monitoring tools and increasing the impact of the Registry at all phases of stroke care. Along with the Registry's communication initiatives, ongoing self-monitoring reports, research (on quality improvement, clinical treatments for stroke, transitions of care, disparities, etc.), and its growing statewide network, this year's approval to access state data has squarely positioned the Registry to establish its place as a central axis and resource that impacts the organizational landscape of Florida's stroke system of care.

- "Transitions of Care Stroke Disparity Study (TCSD-S)" (PI: **Dr. Sacco**) This NIH study aims to identify disparities in transitions of stroke care and key factors associated with effective transitions of care. Programmatically, the study is an example of creativity and persistence as it continues to struggle to accomplish desired enrollment numbers; further impacted this year by the COVID-19 Pandemic and hospital restrictions. Along with multiple online enrollment enhancements including virtual consenting, this year, the study successfully added 5 more study sites. A remaining 3 are pending full onboarding after which a total of 14 statewide stroke centers will be activated as study site collaborators. By the end of 2020, 512 patients were enrolled.

  The ongoing Pandemic continues to slow study progress regarding enrollment numbers. Therefore, to successfully proceed with study aims despite the current low study enrollment numbers, he has identified other accessible data sources through the state of Florida. Recently, the application to access data from the Agency for Health Care Administration (AHCA), a large Florida statewide dataset was approved. They are currently organizing the new data set which will become part of an "Inception Cohort" and which will be utilized to develop and validate the proposed Transitions of Care Performance Index. Through the "Inception Cohort" a prediction model for transition of care may be derived which will then be tested on a "Validation Cohort" consisting of the smaller, more detailed, selective, and data-rich TCSD-S enrolled cases. They are enthusiastic to apply the strategy as it supports the project aims to identify disparities in transitions of stroke care, and key factors associated with effective transitions of care after hospital discharge.

  Finally, and in parallel to the application of enrollment enhancement efforts, the study team continues to identify patient/caregivers and health care professionals to

nominate to the Intervention Advisory Committee. The committee which is patient-centered, is even more relevant in light of the Pandemic likely new barriers to accomplish successful transition of care from hospital to home. They have recently initiated the involvement of a pharmacy director from one of the participating study sites. Within that hospital system, a unique and successful model of transitions of care that incorporates pharmacist follow-up of stroke patient after discharge. They will continue to seek and engage other health care professionals representing and applying various other models of transition of care (i.e., physical therapists, community paramedics, and community health workers) to develop a wide ranging and experienced committee that will help inform initiatives that may be applied statewide or regionally.

- **Dr. Sacco** is the Director of The University of Miami Clinical Translational Science Institute (UM CTSI), a university-wide institute dedicated to accelerating and transforming culturalized clinical and translational science. Created to be an indispensable resource for researchers and stakeholders, the Miami CTSI serves as the Miami Hub of the national Clinical and Translational Science Award consortium, which works to advance scientific discoveries into improved health care for diverse communities and stakeholders. Together with hub partners that include the entire University of Miami/University of Miami Health System, Jackson Health System, Miami VA Healthcare System, OneFlorida Clinical Research Consortium, Health Choice Network, and Health Council of South Florida, the Miami CTSI focuses on culturalizing health sciences, building and improving clinical and translational research infrastructure and processes, developing the translational research workforce, and community and stakeholder engagement.

  Over the past year, the Miami CTSI was highly engaged in the CTSA Consortium, working with nine CTSA institutions across the country on innovative projects, including the development of a lay-friendly clinical research portal and expansion of the I-Corps Entrepreneurship Training Program. In addition, the Miami CTSI supported six mentored career scholars and 16 pilot and collaborative projects. The Miami CTSI also had the opportunity to support three Magic Leap awards to develop augmented/mixed reality biomedical innovations, with one such innovation focused on augmented reality 3D brain imaging to guide neurological surgery. The Miami CTSI also helped amplify minority perspectives in the media by supporting fellows in the Public Voices program, including faculty members in the departments of psychology and neurology. Additional achievements over the past year include holding 130 training events with 1,690 total attendees, enrolling more than 119,000 diverse patients into the Consent to Contact for Research program, completing the first year of the Research Mentoring Training program, and expanding and enhancing informatics support for research, such as URIDE, a de-identified clinical data tool, to house more than 15 million encounters representing 1.26 million unique patients.

  The Miami CTSI also responded to the COVID-19 Pandemic, supporting three COVID-19 research projects through Emerging Disease Awards. The CTSI worked closely with

institutional partners to enable methods to support virtual clinical research, including HIPAA-compliant Zoom, eConsent training, and eRegulatory Binder. Finally, the Miami CTSI created a website to act as a clearinghouse of all COVID-19 research occurring at the University of Miami, developed COVID-specific university message boards to facilitate collaborations, and launched Translational Tuesdays, a weekly moderated webinar highlighting COVID-19 research advances.

- **Dr. Xiaoyan Sun** has conducted the following research:
  - Characterization of the synaptic function in gene levels using post-mortem brains. Using a large-scale transcriptomic dataset, she examined the association of neurogranin (*NRGN*) gene expression with amyloid and tau pathology in post-mortem brains. She studied the association of *NRGN* expression with the Clinical Dementia Rating (CDR) and neuropathological diagnosis of AD. She analyzed the *NRGN*-centered integrative gene network in AD. *NRGN* expression is correlated with amyloid and tau pathology in the perirhinal cortex of post-mortem brains. *NRGN* expression is associated with the diagnosis of AD and correlated with CDR. The positively correlated genes with *NRGN* in AD are involved in synaptic transmission and caution channel pathways. Transcriptional regulation of the genes encoding for synaptic proteins is involved in selective synaptic damage in AD.

  - "Systolic blood pressure and cognition in race/ethnic population" - **Dr. Sun** and colleagues examined the relationship between blood pressure and cognition cross-sectionally and longitudinally in the elderly. They found a cross-sectional and longitudinal association of systolic blood pressure (SBP) with cognitive domains. This association was independent of demographics, vascular risk factors, white matter hyperintensity volume and carotid intima-media thickness. The cross-sectional and longitudinal association of SBP with cognition was attenuated or diminished after adjusting anti-hypertension medications in the models. Diastolic blood pressure was not associated with cognition in this cohort.

## Basic Science Programs

### 1. New Programs

- **Dr. Perez-Pinzon** received a supplemental grant award from the National Institute of Neurological Disorders and Stroke (NINDS) to conduct studies using a rodent model of vascular cognitive impairment (VCI). In 2021, he and **Dr. Dave** will establish a rodent model of VCI in the lab.

### 2. Update on Existing Research

- **Drs. Dave and Perez-Pinzon** worked on two major projects this year:

- In earlier studies, they observed that exposure to asphyxial cardiac arrest (ACA) induces cognitive impairment in rats and post-ACA physical exercise (PE) preserves cognitive function. Considering the importance of the limbic system in formation and retrieval of long-term memory, in the present study they evaluated the effect of ACA and PE on neuronal survivals in septal and anterior thalamic nuclei regions. Twelve days after ACA, a total of 8 rats (4 exercise and 4 sham) were euthanized for histological analyses. Following cardiac arrest, histopathology revealed significant differences in neuronal survival in both septal and thalamic nuclei in rats that underwent physical exercise post-ACA compared to those that did not exercise. This specifically accounted for a 31% increase in neuronal survival. Moreover, exercised rats also had a higher number of living neurons in the thalamic nuclei than non-exercised control representing a 45% increase of neuronal density. These results demonstrate that physical exercise preserves neuronal survival following asphyxial cardiac arrest in septal and thalamic nuclei.
- The second project involves how intensive anti-diabetic therapy aimed at controlling hyperglycemia delays the progression of secondary complications of diabetes. However, long-term therapy of diabetes increases the risk of patients' exposure to repetitive transient hypoglycemia. Exposure to recurrent hypoglycemia (RH) is common in diabetic patients receiving glucose-lowering therapies and is implicated in causing cognitive impairments. Increased susceptibility of patients to experience hypoglycemia is due to decreased responses in the hypothalamus: a brain area involved in restoring euglycemia. Therefore, they tested the hypothesis that prior exposure to RH produces metabolic alterations in the hypothalamus. Statistically significant differences were observed in the levels of metabolites of major metabolic pathways. In addition, network analysis showed that prior exposure of ITD rats to RH decreases the levels of metabolites belonging to either amino acid or amine metabolism and pyrimidine/purine metabolism and increases the levels of glycolate. This study demonstrates that the exposure to RH has a profound effect on metabolism in the hypothalamus. Understanding how RH affects metabolism in the hypothalamus and alters hypothalamic control of blood glucose levels may help in mitigating adverse effects of RH on brain function.

**Dr. Perez-Pinzon,**
**Dr. Dave and Team**

- **Dr. Della-Morte's** research was related to:
  - The role of Pereoxiredoxin6 on metabolism in aging phenotypes and may further elucidate the understanding of the role these antioxidant molecules have against chronic neurodegenerative diseases.

  - COVID-19 showed that COVID patients with lower levels of Plasminogen at hospital are significantly more prone to worse outcomes, including mortality, compared to patients with the normal levels of Plasminogen.

- **Dr. Pinto** has continued work on several projects that will be finalized in 2021: 1) Characterization of different phenotypes triggered by complex I or Complex III defects in dopaminergic neurons; 2) Analysis of the role of Mitochondrial Oxidative Phosphorylation Complex III defects in an Alzheimer's Disease mouse model; and 3) Mesenchymal Stem Cell treatment of mouse models of frontotemporal dementia.

- **Dr. Raval's** research on "Nicotine alters brain oxidative metabolism and exacerbates ischemic brain damage" demonstrated that nicotine in combination with oral contraceptives alters brain energy metabolism, which may be an underlying mechanism(s) of exacerbated ischemic brain injury observed in female rats.

**First year medical student Melissa Huberman looking at a histological slide and Jonathan Siegel, Masters in Biomedical Science student pipetting a sample in Dr. Raval's lab.**

- **Dr. Vontell** worked on the collaborative project with King's College London, assessing the morphology and pattern of radial glial expression in Trisomy 21 and euploid aged-matched brains. A new finding this year is from mid-gestation, the pattern of expression of radial glia markers had subtle deviations from age-matched euploid fetal brains.

## Technology transfer

N/A

## Patents/applications

**Dr. Della-Morte** Submitted a patent application to the University of Rome Tor Vergata entitled “Peroxiredoxin 6 as pharmacological hypoglycemic agent for the treatment of Type 2 Diabetes Mellitus.”

## Budget update, status of matching funds, projected budget for coming year

The status of matching funds is not available. The others are in **Appendix VI.**

# EDUCATIONAL PROGRAMS

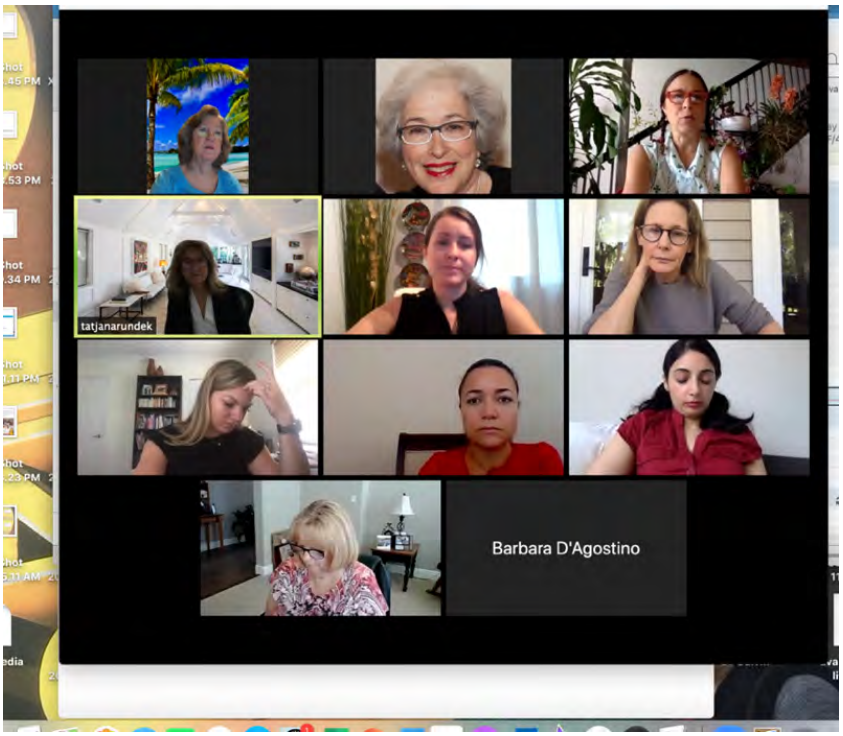
# Educational Programs Focusing on Age-Related Memory Loss

## 1. Scientific Education

**(MBI) Scientific Education Program Led by Dr. Xiaoyan Sun**

This year, MBI in-person meetings and research seminars/discussions were halted in April and began again virtually in May. Meetings were held bi-weekly and were well-attended. **Dr. Sun's** scientific educational program consisted of interesting, relevant and novel topics that garnered productive discussion. The scientific presentations are listed below.

**McKnight Team Zoom Meeting**



# MCKNIGHT BRAIN INSTITUTE RESEARCH SEMINARS 2020

| | |
|---|---|
| JANUARY 22ND | **Sonya Kaur, PhD** "Sleep, hippocampal volume, and cognition in adults over 90 years old" |
| JANUARY 29TH | **Michelle Marrero, MD** "Multimodality Imaging of Dementia" |
| FEBRUARY 5TH | **Regina Vontell, PhD** "Pathological evidence of neuroinflammation in neuropsychiatric disorders" |
| FEBRUARY 12TH | **Ashish Rehni, PhD** "PERK pathway of ER stress and recurrent hypoglycemia- induced increased ischemic brain injury intreated diabetic rats" |
| FEBRUARY 26TH | **Danielle Carns, PhD** "Accounting for sex may improve diagnosis of aMCI – how generalizable are these findings?" |
| APRIL 1ST | **Anita Seixas Saporta, MD** "The cerebellum in Alzheimer's disease: evaluating its role in cognitive decline" |
| APRIL 15TH | **Christian Camargo, MD** "Evidence for a synaptic approach to enhancing cognition in normal aging: the role of rate-limiting substrates" |
| APRIL 22ND | **Christian Camargo, MD** "Evidence for a synaptic approach to enhancing cognition in normal aging: the role of rate-limiting substrates" Continued. |
| APRIL 29TH | **Regina Vontell, PhD** "Guidelines for the Neuropathologic Assessment of Alzheimer's Disease" |
| MAY 13TH | **James Galvin, MD, MPH** "Can Dementia Be Prevented?" |
| MAY 27TH | **Sarah Getz, PhD** "Neurocognitive correlates of scam susceptibility in age-related hearing loss" |
| JUNE 10TH | **Michelle Caunca, PhD** "Racial Residential Segregation Throughout Young Adulthood and Cognitive Performance in Middle Age: the CARDIA Study" |

| | |
|---|---|
| JUNE 24TH | **Sonya Kaur, PhD**<br>"Sleep and Insomnia" |
| JULY 8TH | **Joyce Gomes-Osman, PT, PhD**<br>"An Exercise Study during and (hopefully!) after the COVID-19 Pandemic" |
| JULY 22ND | **Noam Alperin, PhD** "Different Relationship Between Systolic Blood Pressure and Cerebral Perfusion in Subjects with and Without Hypertension" |
| AUGUST 5TH | **Katalina McInerney, PhD & Josh Rooks, PhD**<br>"An Exercise in Mindfulness" |
| AUGUST 19TH | **Magdalena Tolea, PhD**<br>"Sarcopenia and Cognitive Performance" |
| AUGUST 26TH | **Christian Agudelo, MD**<br>"Using DTI to Assess Grey Matter Microstructure in Neurocognitive Aging" |
| SEPTEMBER 2ND | **Jinhua Wang, MD, PhD**<br>"Age-Related Alterations in Retinal Tissue Perfusion and Volumetric Density" |
| SEPTEMBER 16TH | **Nicole Sur, MD** "Discovery: Determinants of Incident Stroke Cognitive Outcomes and Vascular Effects on Recovery" |
| SEPTEMBER 30TH | **Gustavo Rey, PhD**<br>"Aging and Epilepsy" |
| OCTOBER 14TH | **Dr. Schork, PhD** *SPECIAL INVITED SPEAKER*<br>"Polygenic Longevity Scores" |
| OCTOBER 28TH | **Roger McIntosh, PhD** "Endothelial progenitor cell function in chronic HIV and cerebrovascular disease" |
| NOVEMBER 18TH | **Rosie Curiel, PsYD** "Cognitive Errors and Functional Dysconnectivity in Middle-aged Offspring of Persons with Late-onset Alzheimer's Dementia" |
| DECEMBER 2ND | **Michelle Marrero, MD** "Mediterranean Diet and Cognitive Health: Initial Results from the Helenic Longitudinal Investigation of Ageing and Diet" |
| DECEMBER 16TH | **Mohammed Goryawala, PhD**<br>"The MRI Visual Rating Scale and Diagnosis and AD" |
| DECEMBER 16TH | **Alexandra Cocores, MD** *Resident Cognitive Journal Club*<br>"Detection of Phosphorylated Alpha-Synuclein in the Muscularis Propria of the Gastrointestinal Tract Is a Sensitive Predictor for Parkinson's Disease" |

## Scientific Education by Faculty

**Dr. Sun** oversees the Neurology Resident Rotation in Cognitive and Behavioral Neurology shown in Figure 1 as well as the Neurocognitive Fellow Curriculum shown in Figure 2.

**Figure 1.**

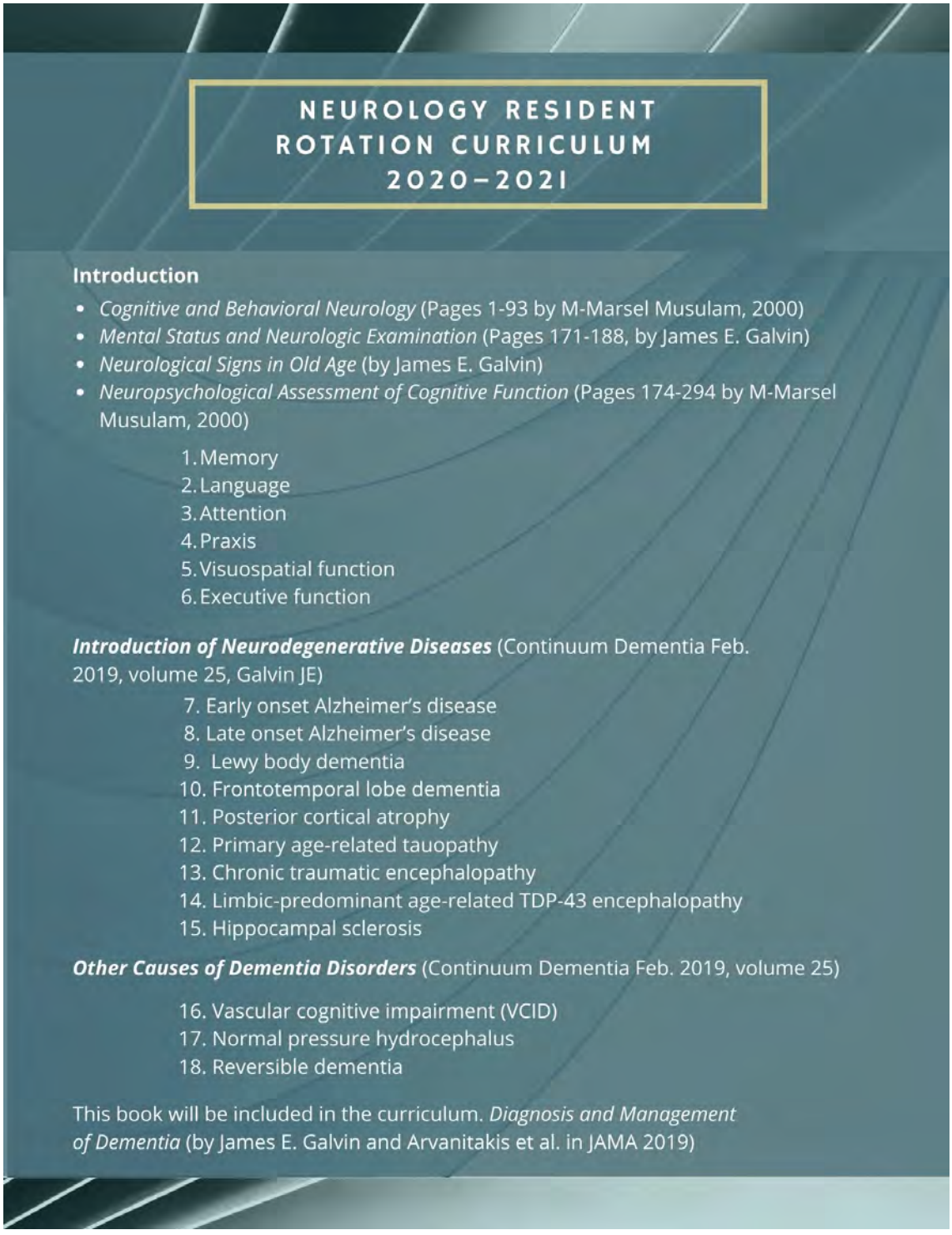
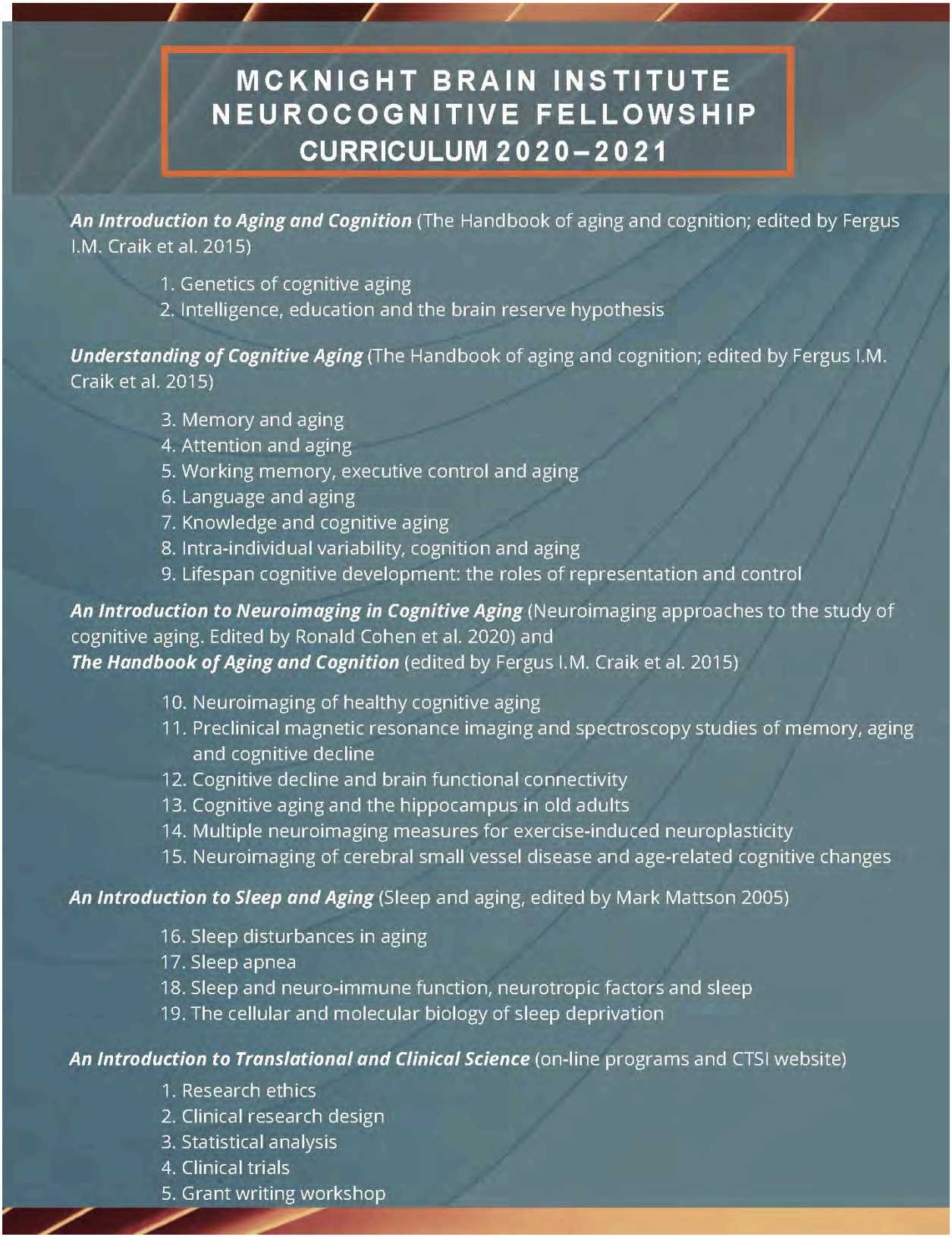


**Figure 2.**


MCKNIGHT BRAIN INSTITUTE
NEUROCOGNITIVE FELLOWSHIP
CURRICULUM 2020–2021
An Introduction to Aging and Cognition (The Handbook of aging and cognition; edited by Fergus I.M. Craik et al. 2015)
1. Genetics of cognitive aging
2. Intelligence, education and the brain reserve hypothesis
Understanding of Cognitive Aging (The Handbook of aging and cognition; edited by Fergus I.M. Craik et al. 2015)
3. Memory and aging
4. Attention and aging
5. Working memory, executive control and aging
6. Language and aging
7. Knowledge and cognitive aging
8. Intra-individual variability, cognition and aging
9. Lifespan cognitive development: the roles of representation and control
An Introduction to Neuroimaging in Cognitive Aging (Neuroimaging approaches to the study of cognitive aging. Edited by Ronald Cohen et al. 2020) and
The Handbook of Aging and Cognition (edited by Fergus I.M. Craik et al. 2015)
10. Neuroimaging of healthy cognitive aging
11. Preclinical magnetic resonance imaging and spectroscopy studies of memory, aging and cognitive decline
12. Cognitive decline and brain functional connectivity
13. Cognitive aging and the hippocampus in old adults
14. Multiple neuroimaging measures for exercise-induced neuroplasticity
15. Neuroimaging of cerebral small vessel disease and age-related cognitive changes
An Introduction to Sleep and Aging (Sleep and aging, edited by Mark Mattson 2005)
16. Sleep disturbances in aging
17. Sleep apnea
18. Sleep and neuro-immune function, neurotropic factors and sleep
19. The cellular and molecular biology of sleep deprivation
An Introduction to Translational and Clinical Science (on-line programs and CTSI website)
1. Research ethics
2. Clinical research design
3. Statistical analysis
4. Clinical trials
5. Grant writing workshop

## Scientific Education by Faculty – Continued

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

- **Dr. Ramos** was chair of the Department of Neurology Grand Rounds and was instrumental in planning for several speakers to present to faculty and staff on topics of aging, dementias and neurocognitive aging.

- **Dr. Crocco conducted the following scientific education:**
  - *Geriatric Psychiatry Lecture Series Jackson Memorial (JMH) General Psychiatry Residency Training* Program to develop and implement comprehensive geriatric specialty lectures in all 4 years of general psychiatric residency training.
  - *Weekly Case Conference JMH Geriatric Psychiatry Training Program*: Coordinate and supervise all geriatric psychiatry Fellow's weekly presentations of patient's case history including biological, psychological and sociological data and formulate an integrated treatment plan.
  - *Weekly Journal Club JMH Geriatric Psychiatry Residency Training Program*: Weekly coordination and supervision of all geriatric psychiatry Fellows with the objective of critical evaluation of peer-reviewed, original research articles and application of the knowledge to the care of their geriatric patients.
  - *Geriatric Psychiatry Seminar JMH Geriatric Psychiatry Residency Training Program*: Develop and implement a weekly core curriculum-focused conference that covers knowledge and skill areas necessary for the successful completion of the geriatric psychiatry training program and commonly seen diagnoses.
  - *Doctoring II: Dementia Small Groups Miller/UM School of Medicine Students*: Lead small groups of 20-25 medical students in diagnosis and evaluation of cognitive disorders.

- **Dr. Levin** taught the course Foundation of "Neuropsychology and Cognitive Neuroscience" to upper level graduate students. She also gave weekly clinical teaching rounds attended by practicum and graduate students, post-doctoral Fellows and faculty in the Division of Neuropsychology and Cognitive Neuroscience. She coordinated the case presentation and led the discussion each week.

- **Dr. Rundek** continues teaching MS classes in Clinical Translational Investigations and a UM CTSI grant writing course annually (she is director of the MS CTI program at UM).

## Scientific Education by Trainees

- **Judith Lobo** taught/mentored graduate students on successful agers among older adults living with HIV.

- **Katalina McInerney, PhD** taught "Coping and self-care strategies during quarantine" during a Clinical Staff meeting for the UM Neurology Department, Selected Divisions in March. This presentation intended to provide information on self-care and healthy coping strategies relevant to administrative staff working during a Pandemic.

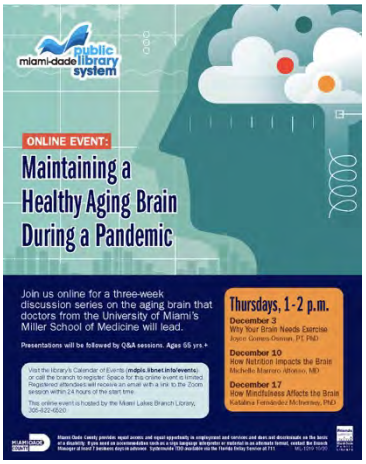
- **Katalina McInerney, PhD** and **Joshua Rooks, PhD** started an 8-week mindfulness, stress management and relaxation program for patients diagnosed with neurological disorders and their caregivers. The goal of the program is to promote wellness through improved coping mechanisms and self-care. The first program took place in February. The March program was postponed due to the Pandemic.

- **Katalina McInerney, PhD, Sonya Kaur, PhD** and **Gustavo Rey, PhD** taught a class on "Wellness and Mindfulness" for the Epilepsy division meeting series on self-care for clinicians in May. This presentation aimed to educate providers in the benefits of mindfulness for self-care, improved patient care and avoiding burnout.

- **Sonya Kaur, PhD** gave these lectures to the UM PSY 615 class:
  - "Temporal Lobes-Anatomy and Systems"
  - "Homeostasis, Memory, olfaction, hallucinations"
  - "Biomarkers of Neurodegenerative Diseases"

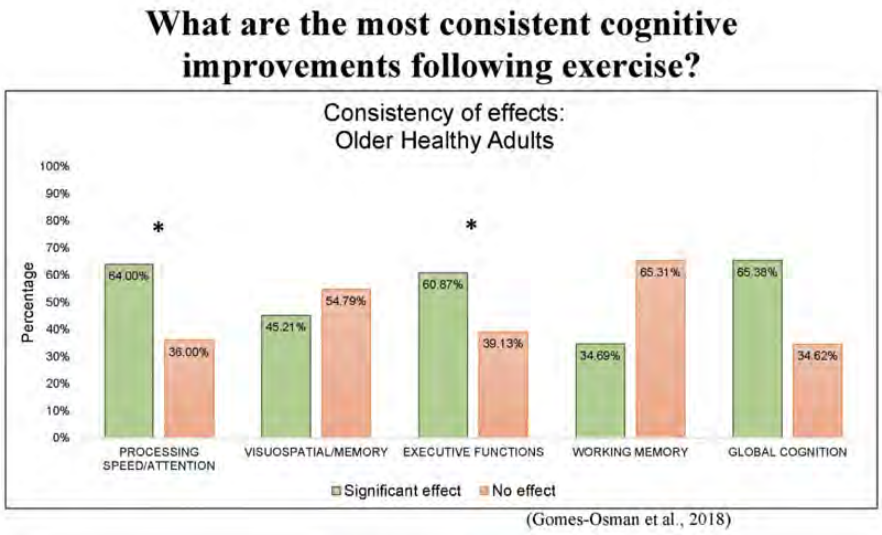
## 2. Public Education

**MBI Public Education Program Led by Dr. Sun**

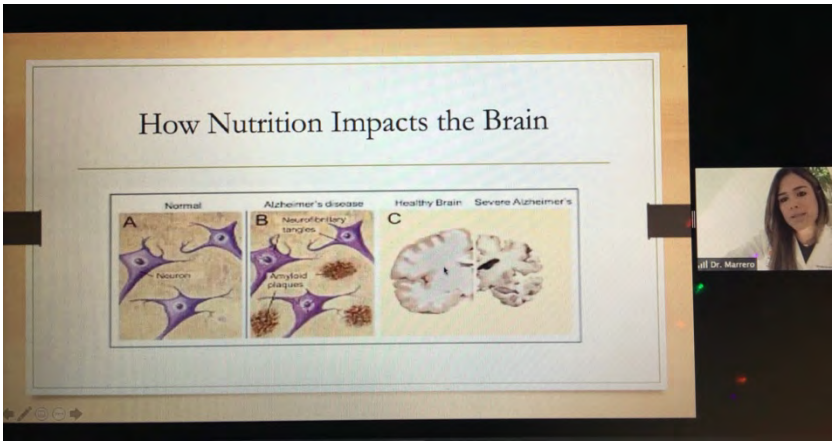



Two series were scheduled this year as part of our alliance with the Miami-Dade County Mayor's Initiative on Aging. One in English and one in Spanish. All 8 presentations were cancelled due to the COVID-19 Pandemic. We approached our community partners about continuing our education and outreach mission virtually. We scheduled several Zoom presentations. It took some time to get enrollees as our senior population was getting acclimated to the new virtual presentation format. During our MBI regular weekly meetings, we discussed how older adults were faring, being isolated and removed from their usual routines. Hence, we designed the *Pandemic and the Aging Brain* 3-part virtual Seminar Series in partnership with the Miami-Dade Public Library System. (It started late in the year as they were acquiring a Zoom license.) The series included:

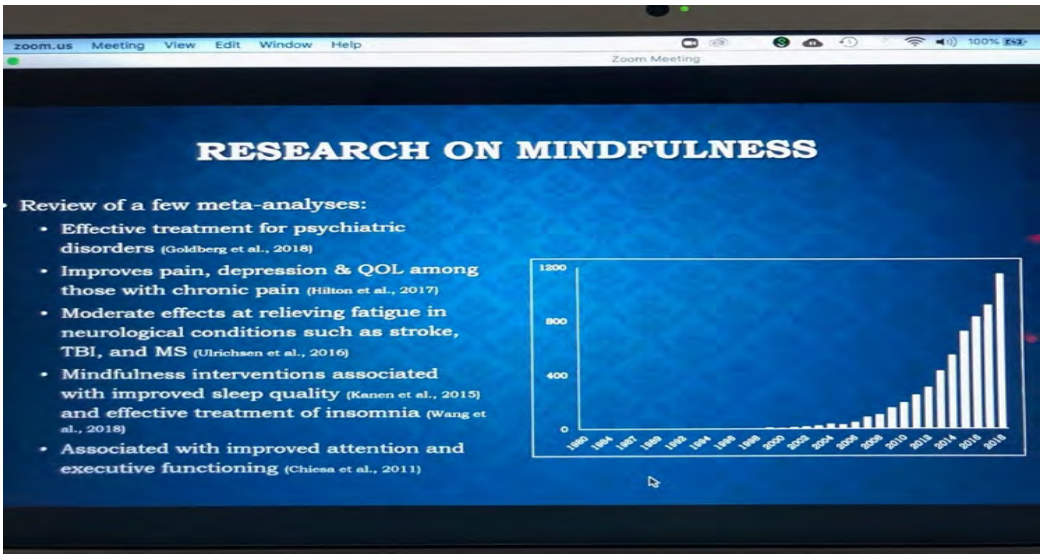
- "Why Your Brain Need Exercise" by **Joyce Gomes-Osman, PT, PhD** on December 3.




- "How Nutrition Impacts the Brain" by **Michelle Marrero, MD** on December 10.




- "How Mindfulness Affects the Brain" by **Katalina McInerney, PhD** on December 17.



We continued our outreach with some important aims. We wanted to make sure that minority seniors and caregivers were aware of community resources available to them and to teach about sleep, nutrition and exercise. This outreach is listed below.

**Dr. Crocco** developed and conducted the following public education:

Training/Lectures for Community and Caregivers

- Alzheimer's disease Initiative (ADI) Caregiver Training Seminars in Dementia, Miami-Dade County, FL.
- Develop and coordinate 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.
- 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.
- COVID-19 and the Risk to Aging Adults, 2020 ADI Special Series: COVID-19 and Dementia Care: Meeting the Challenge, Webinar, June, 2020.

# COLLABORATIONS

# Collaborations

## 1. Collaborative Programs with Other McKnight Brain Institutes, Institutions and Research Programs

- Under the leadership of **Drs. Rundek** and **Levin**, we are collaborating with the University of Arizona McKnight Brain Institute on the "Precision Aging Network Pilot Project." Work on the project this year included recruiting for the pilot to obtain data in support of the U19 resubmission. If funded (pending NIA review), this will be a tremendous inter-institutional collaboration. A separate report on this work is provided in **Appendix VII**.

- **Drs. Levin and Getz** are collaborating with the University of Florida and Arizona McKnight Brain Institutes on the "Aging Online" study that seeks to understand scamming and to design detection techniques to disseminate in the community.

- All four McKnight Brain Institutes are collaborating on the "McKnight Brain Aging Registry (MBAR)." **Drs. Rundek, Levin** and **Alperin** are the leaders of the UM site. The collaborations will continue by working on analyses and publication as they use these data to apply for grants and to present at scientific meetings.

- The MBRF Cognitive Aging and Memory Intervention Core - **Dr. Levin** co-chaired the MBRF Cognitive Aging and Memory Intervention Core with Dr. Ronald Lazar at UAB. She initiated the announcements, rewrote the review guidelines, initiated new award criteria to ensure that at least one award would be granted to a young investigator, sent out reminders of pending deadlines, identified reviewers and organized the review process in collaboration with Dr. Lazar. The overall goal is to facilitate grant submissions for extramural funding sources for multi MBI site cognitive aging and memory intervention trials.

- The 1FL ADRC (Alzheimer's Disease Research Center) is a collaborative project between the University of Florida, Mt. Sinai Medical Center in Miami Beach, Florida International University and Florida Atlantic University. **Drs. Rundek, Loewenstein** and **Sun** are the UM Clinical Investigators and Core Co-Leaders.

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

We have been collaborating with **Dr. Loewenstein** and **Dr. Galvin** on two important non-McKnight partnerships this year. Their Centers are described below.

- **The Center for Cognitive Neuroscience and Aging (CNSA)** is in the Department of Psychiatry and Behavioral Sciences at the University of Miami. The CNSA director **David**

**Loewenstein, PhD, ABPP**, serves on our MBI Scientific Advisory Board. Dr. Loewenstein along with the CNSA faculty are close collaborators on MBI research studies. Dr. Loewenstein is the Principal Investigator on several large NIH and Florida Department of Health funded studies, is Associate Director of the 1Florida Alzheimer's Disease Research Center (1FLorida ADRC) and Leads the 1Florida ADRC Clinical Core at University of Miami. The CNSA's mission is to be a national and international leader in understanding the aging brain and a hub to develop and implement the most state-of-the-art techniques for the study of brain disorders. The CNSA has a three tier focus on research, clinical care and education. The Center's specialists are experts in the provision of clinical care for aging adults and their families. The CNSA is home to the State of Florida Memory Disorders Center. As part of a major academic medical center, the CNSA is committed to training the next generation of leaders in the fields of gerontology, geriatric psychiatry, neuropsychology and cognitive neuroscience. Their established training program aims to equip future health professionals with the most advanced knowledge to successfully intervene using evidence-based methods to diagnose and treat cognitive disorders. Our continued partnership with Dr. Loewenstein's Center has increased our research base, enabled research collaborative grants (e.g., the VIP study and 1FL ADRC) and enhanced our mission to understand changes in memory and overall cognitive functions through the aging process.

- **The Comprehensive Center for Brain Health (CCBH)** is a new Center established at the University of Miami within the Department of Neurology. The Center is led by **Dr. James Galvin, MD, MPH** who brings a multitude of funded grants (both NIH and Foundation grants) and projects as well as an outstanding team of faculty and staff. The Center's core mission is on brain health and prevention of cognitive disorders. The Center provides comprehensive clinical care, conducts cutting edge research and offers outstanding educational training and outreach programs on healthy brain aging and prevention of neurodegenerative diseases. Dr. Galvin's multi-disciplinary approach is to better understand functions of the aging brain and to design treatments and prevention interventions to increase quality of life through the aging process. The CCBH will expand UM's scope of clinical care to Broward County and to Palm Beach County, where it will be located. The CCBH will foster substantial fundraising and philanthropy efforts drawing upon private and family foundations. The Center will develop educational opportunities to increase knowledge, health literacy and research readiness in the community. Training and mentoring opportunities are planned for students, residents, fellows, staff and faculty to gain knowledge and expertise in brain health and neurodegenerative diseases. Our partnership with Dr. Galvin and the CCBH team will greatly expand our community outreach and ability to further our research on age-related memory loss and cognition changes in the aging brain.

- **Drs. Sacco** and **Rundek** have active research programs with the NOMAS team at Columbia University in New York.

- **Dr. Rundek** is a collaborative clinical researcher with established extensive collaborations on these large NIH-funded studies at Columbia University (INVEST and U01 eMERGE), at Albert Einstein in the Bronx (Einstein Aging Study), and with national and international consortia (NINDS SiGN, ISGC, MRI-GENE).

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

- **Drs. Sacco** and **Rundek** participate and collaborate with the Hispanic Community Health Study- Study of Latinos (HCHS/SOL), which is a multi-site NIH contract.

- **Dr. Rundek** collaborates with Mt. Sinai at Miami Beach, Florida International University (FIU) and Florida Atlantic University (FAU) on the Brain Vascular Imaging Phenotypes (VIP) study.

- **Dr. Rundek** collaborates with UM CFAR (Center for AIDS Research). As a result of this collaboration, the HIV Aging Scientific Working Group (HIV SWG) was recently established under co-leadership of Dr. Rundek.

- **Dr. Della-Morte** and **Dr. Rundek** are collaborating on a project aimed to evaluate the association between a well-established biomarker of systemic inflammation, the Arachidonic Acid/Eicosapentaenoic Acid (AA/EPA) ratio with biomarkers of carotid atherosclerosis and biomarkers of cognitive degeneration. A NIH R21 grant proposal is projected to be resubmitted after addressing the reviewers' comments.

- **Dr. Della-Morte** and Eng. Eugenio Martinelli launched as Co-Directors the IC-LOC (Interdisciplinary center for advanced studies on Lab-on-Chip and organ on-chip applications) Institute of Research at University of Tor Vergata, Rome.

# RESEARCH AND CLINICAL INITIATIVES IN 2021

# Briefly Describe Plans for 2021

## 1. The MBI Strategic Plan

Our plan is to move forward with the implementation of the MBI Strategic Plan in 2021. In the First phase of the implementation, we will present our MBI Strategic plan to all of our MBI constituency and familiarize them with our MBI mission/vision and strategic plans. We will work with our members and collaborators to adopt our Core values and clearly present our Guiding principles, Goals and Strategies, Competitive Advantages, Plans, Actions, Metrics and Deliverables. Multiple meetings with various constituency will be organized to present and adopt our MBI Strategic Plan.

It is imperative that in this first phase we clearly communicate:

- What we do the best,
- Who we are and why we exist,
- What we stand for,
- Where we are going and why,
- What the strategic topics and issues are we need to address; and
- What plans we need to align with.

It is likely that this first phase will take a significant amount of time in order to present our goals and objectives clearly and understandably, and most importantly, to articulate a crystal clear strategic direction of our MBI for the next 5 years.

The Second Phase will be planned in the later part of 2021 in order to clearly define who will be involved in specific goals, what their actions and deliverables will be, to provide tools and support, and estimate timelines for the completion of actions and goals.

Our MBI leadership will steer the MBI Strategic Plan implementation and manage its performance. The Scientific Advisory Board will oversee the MBI Strategic Plan implementation process and provide additional input if our Strategic Plan needs revisions during the process of implementation and execution.

The brief plans for 2021 presented below are listed by categories and selected individual MBI members and collaborators in alphabetical order:

## 2. Clinical-Translational and Population Based Research

- **Dr. Crocco** will develop a registry of well-characterized African American older adults at risk for Alzheimer's disease and related dementias for the project "Building an Advanced Cognitive and Biomarker Registry for African American Older Adults At-Risk for Alzheimer's Disease." The project aims to assist in closing the gap of health disparities for these vulnerable older adults through clinical evaluation, novel cognitive tests sensitive to early cognitive impairment, as well as blood biomarkers and neuroimaging.

- In addition to the work **Dr. Galvin** will perform on his currently funded studies he will work on these projects in 2021:

  - "Natives Engaged in Alzheimer's Research (NEAR)" aims to engage, enroll and study American Indians, Alaskan Natives, and Native Hawaiians and Pacific Islanders in novel Alzheimer detection and treatment interventions and encourage biomarker and autopsy program participation. This project is submitted to NIA with Buchwald, Galvin, Kauwe (MPI) with *Priority Score: 17 (No Percentile on P01 grants).*

  - *"*A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Phase 2 Study to Evaluate the Safety and Efficacy of CT1812 in Subjects with Dementia with Lewy Bodies" *was submitted to the /NIA.* The major goal of this project is to conduct a Phase 2 clinical trial of CT1812, a novel disease-modifying compound, in patients with mild to moderate dementia with Lewy bodies (DLB). Caggiano, Galvin (MPI) Role: MPI. *Priority Score: 31 (16$^{th}$ Percentile).*

  - *"*Multicultural Community Dementia*"* *Screening* will conduct a population-based dementia screening, validate findings in a longitudinal study of ADRD biomarkers, and establish the potential benefits and harms of dementia screening in a multicultural sample. This proposal is submitted to the NIA, Role: PI*. Priority Score: 34 (14$^{th}$ Percentile).*

  - "Wabanaki Native American Research Centers for Health (NARCH)" was submitted to the NIGMS. The major goals of this project are to create research infrastructure to enable the Wabanaki Confederation to develop sustainable clinical and translational research programs in brain aging and dementia. Role: Project 1 Co-Lead. *Priority Score: 26 (No Percentile on S06 grants).*

- **Dr. Gomes-Osman** will work on two proposals:

  - 'K01 Career Development Award,' which was submitted to NIH in February 2020, scored but not funded. She resubmitted this grant in November 2020 and the reviews are pending.

  - She submitted a grant proposal to the McKnight Research Foundation (MBRF) Cognitive Aging and Memory Intervention Core to research: Harnessing Optimal Mechanisms of Exercise for Cognitive Gains (HOME-Cog). It is a collaborative project between the Evelyn F. McKnight Brain Institutes (MBI) at University of Miami and University of Florida that aims to inform the knowledge gap on the mechanistic action of exercise on the brain by characterizing important mechanisms of neuroplasticity and cardiovascular capacity, proposed to underlie cognitive response to exercise. The awardees haven't been announced yet.

- **Drs. Jiang and Wang** will study the effect of circuit resistance training on retinal vascular and neuronal functions in older people. They plan to submit an R01 application to the NIH in 2021.

- **Dr. Levin** will work on these projects:

  - "Vestibular Outcomes in Adults with Cognitive Impairment," which was submitted to NIH in collaboration with Dr. Liu from ENT. This study examines the interactions and overlap between vestibular, auditory and cognitive networks and their shared relationship throughout the aging process. If funded, it will begin in 2021.

  - **Dr. Levin** will be working on the study recently funded by the Ed and Ethel Moore Alzheimer Disease Research Program (DOH). The plan is to develop an educational intervention for Hispanic and non-Hispanic elderly individuals and their caregivers/partners who are residing independently in the community but susceptible to being scammed.

  - **Dr. Levin** and her team will delve into data analysis for the psychosocial and neuropsychological components of the McKnight Brain Aging Study (MBAR). **Dr. Rundek** will lead the development of manuscript proposals from MBAR results.

- **Dr. Ramos** started a new project with Avadel Pharmaceutical in 2020 titled "Open label study evaluating the effect of single dose sodium oxybate in Narcolepsy." Work has started with planning the logistics, budget and IRB, but study recruitment will take place in 2021.

- **Dr. Rundek** will be working on a number of projects in the next year, including:

  - "Carotid Ultrasound Imaging Markers of AGINg and Endothelial function in Risk of Alzheimer's Disease: The Florida IMAGINE Study of AD Risk," which is new FL DOH Ed and Ethel Moore Alzheimer Disease Research funded research project.

  - Dr. Rundek will continue her work on the "Family study and genetic and epigenetic risk of cognitive impairment," funded by the NIH.

  - She will continue her work as on the "Brain Vascular Imaging Phenotypes and Vascular Comorbidities in Risk of Alzheimer Disease" that is funded by the NIH.

  - Training and education in Clinical translational research as a part of "OneFLorida ADRC REC AlzSTARS" program funded by NIA and working in the Clinical Core of 1FL ADRC on dementia adjudication.

  - "COVID-19, Social Distancing, and Cognitive Impairment in 1Florida ADRC participants," which is a new supplement awarded to 1FL ADRC. Dr. Rundek is MPI together with Dr. Curiel (UM) and Dr. Smith (UF).

- "Einstein Aging Study" competitive renewal will be submitted in 2021 and Dr. Rundek will be a MPI on a project on vascular contribution to the sleep and cognition in aging together with Dr. Carol Derby from Albert Einstein in NY.

- "HIV and Aging Scientific Working Group (SWG)" collaboration is a new group established by the UM CFAR (Center for AIDS Research) under co-leadership of Dr. Rundek. A UM CFAR competitive renewal will be submitted in 2021 and HIV SWG will be a separate proposal that Dr. Rundek will work on closely with the CFAR leadership.

- **Dr. Sacco** will continue his multiple and large research projects and leadership programs. A planning phase for a renewal of the UM CTSI that he leads will start in 2021. He will also work on a resubmission of the NINDS NOMAS project in 2021 with the important goal to determine the role of specific immune and innate immunity pathways as well as gut microbiota-derived metabolites in longitudinal cognitive impairment. This program will provide data needed for a discovery of novel targets in the immune and specific metabolite pathways to prevent cognitive decline.

- **Dr. Seixas-Saporta** is currently working on the analysis of the McKnight Frailty Project data and plans to publish the results in 2021.

## 3. Basic Science

- **Dr. Della-Morte** will work on two projects:

  - "The Batman Project" that aims to investigate the mechanisms of defense against virus typical of bats that can be translated to fight against COVID-19 Pandemic. This project is funded by the University of Tor Vergata.

  - "The role of PUFAs in Subclinical Cerebro-vascular Imaging Phenotypes and Clinical Vascular Disease" This project was submitted as R21 to NIH with plans for resubmission this year.

  - "PERSEO - Biological utilization of Organ on a Chip Technology" this project was submitted to the Italian Minister of Health and work will start in 2021 if funded.

- **Dr. Raval** will be working on the research project "Therapeutic interventions for post-stroke rehabilitation." She will aim to get a better understanding of how nicotine in combination with oral contraceptive leads to altered energy metabolism. This will help her to design novel therapeutic targets to lower cerebral ischemic damage in co-morbid ischemic patient populations which is the goal of this upcoming research.

- **Dr. Vontell** will be working next year on one of the proteins thought to be involved is Neurogranin (Ng), which is a protein kinase C substrate that binds calmodulin in the nonphosphorylated state in the presence of low $Ca^{2+}$ concentrations. Ng is thought to play

a role in the cascade of events for the postsynaptic transmission and it is triggered by the binding of glutamate to NMDA receptors, particularly in the hippocampal region. Therefore, it plays an important role in learning and memory and CSF Ng is considered a biomarker for synaptic dysfunction. She will explore the mechanism underlying selective synaptic damage and memory loss seen in aging and AD.

### 4. Education

We see the need now more than ever to develop a robust scientific educational program. With faculty and staff working in separate locations, education is a great way to keep all informed and connected, albeit virtually. Our MBI 2020 Research Seminars Series via Zoom was better attended than ever, with attendance by faculty, clinicians, trainees and researchers from various Centers, Institutes and affiliations. We were able to learn more about other UM aging programs and disciplines, to have great scientific discussions, to hear fresh ideas and truly utilize every moment of meeting time to collaborate and plan future MBI collaborations. We are planning more interactive brainstorming/collaborating research meetings and new research seminars in our series in 2021.

Providing outreach and education to the senior community on aging and healthy brain initiatives is part of our strategic plan and it is especially essential to reach this population now. We will continue to partner with the Miami-Dade Public Library System and other community resources. The Miami-Dade Mayor's office changed leadership this fall but we hope to connect with the new mayor in 2021 about continuing the Mayor's Initiative on Aging program. We will be partnering with the city of Doral's Silver Club which encompasses 900 members, of which 200 are currently very active to provide education and outreach. The Connection with the Doral Silver Club has already been made through the Councilwoman Digna Cabral in the City of Doral. We are planning an array of virtual educational offerings and activities both in English and Spanish.

### 5. 12th Annual McKnight Brain Research Foundation Inter-Institutional Meeting

The agenda has been finalized and logistical details and further plans will be finalized in 2021. The draft agenda is attached in **Appendix VIII.**

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

N/A

## Endowment Investment Results and Budget

See **Appendix VI**.

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

No

## Did all activities during the report period further the Purpose?

Yes- Completion of our Strategic plan will considerably further our MBI purpose.

## 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.

The Pandemic and resulting lockdown affected some MBI plans for 2020 including many research studies being on hold and canceling the McKnight Brain Research Foundation 12th Annual Inter-Institutional Meeting. The 12th Annual Inter-Institutional Meeting will be held virtually on April 28-29, 2021.

## 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

## What social media platforms are you active on and how many followers do you have?

Our MBI is active on the social media channels using the University Miller School of Medicine @Umiamimedicine and the Department of Neurology @Umiamineuro channels with hashtags #UMMBI. The channels have developed substantial followers over the past 5+ years, thus offering a much broader platform than just the one the UM-MBI could develop and create. We have a presence on Facebook, Twitter and Instagram. Facebook has 6,300 followers with an average of 150 reached by UM-MBI related posts. Twitter has 800 followers with an average of 100 reached by UM-MBI related posts. Finally, while our Instagram channel has 1,599 followers, we have not used it for MBI posts. We utilized social media to recruit for the Precision Aging Pilot Project. These are explained in **Appendix VII.**

## Number of media impressions and placements secured mentioning the MBI and/or your leadership/researchers

**Drs. McInerney** and Bure have participated in on-air radio discussions in partnership with the Latino Center on Aging for the La Ponderosa Spanish Radio show "Para Mayores." Sponsored by the AARP, it has a wide-reaching audience throughout the greater South Florida area. Their discussions include memory decline signs and symptoms as well as cognitive testing available via telehealth at UM. This is a great opportunity for them to talk about the McKnight Brain Institute, its research and clinicians.

## Number of monthly visitors to your website and any peak areas of interest or engagement

In the fourth quarter of 2020 we embarked on the revamping and recreation of our MBI website with the goal of launching it in the first part of 2021. This is still on schedule and was driven by the fact that the analytics were not available and had not been installed. Thus, the number of visitors and most successful post data is not available. We have included this in our website design moving forward and will be able to report on a regular basis once launched.

## Outline topics and attendance for any new podcasts, blogs, webinars, You Tube videos, etc.

Our MBI, its clinicians and researchers have contributed to a number of blogs. **Dr. Gomes-Osman** wrote on "Neuroplasticity of the brain and physical exercise: keeping a sharp mind." **Dr. Marrero** wrote on "Why everyone is obsessed with the MIND diet." **Dr. Kaur** wrote on "Sleep and the brain." All of these were written and posted in partnership with MindCrowd on their website and our MBI website.

The Miller School of Medicine Health Talk Series was relaunched virtually during the second quarter of 2020. A "Brain Health" Virtual Talk was held June 25th and an October Talk "Science of the Aging Brain," featured **Drs. Sacco**, **Rundek**, **Levin** and **Galvin** with at least 500 attendees combined.

Through a partnership forged with The Miami Dade Public Library System, the virtual webinar series "Maintaining a Healthy Brain During a Pandemic" was created. It took place on the first three Thursdays in December. The Series featured **Drs. Gomes-Osman**, **Marrero** and **McInerney**. Total attendance was approximately 140 participants.

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

January 14th, 2021

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

Date

# APPENDIX I

## THE UNIVERSITY OF MIAMI
## EVELYN F. MCKNIGHT BRAIN INSTITUTE
## STRATEGIC PLAN

**Appendix I: Strategic Plan**

# University of Miami
# Miller School of Medicine
# Evelyn F. McKnight Brain Institute
# 2020-2025

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

# INTRODUCTION

This is the first strategic plan for the University of Miami Miller School of Medicine Evelyn F. McKnight Brain Institute (UM-MBI). The UM-MBI was created through an endowment from the McKnight Brain Research Foundation. It is one of only four in the country. UM-MBI brings together a cross-disciplinary team of translational scientists and clinicians to accelerate discoveries of age-related memory loss and cognitive impairment produced by various brain related disorders. It seeks to train the next generation of clinical translational investigators capable of translating scientific discoveries into clinical practice and advance brain health in communities.

# DEVELOPMENT OF THE STRATEGIC PLAN

Commencing in 2018 we created an outline for a strategic plan. The following year, we convened the expanded Advisory Board and a multi-disciplinary group of physicians, scientists and research professionals from the Departments of Neurology, Neurosurgery, Psychiatry, Radiology, Internal Medicine, Psychology, Kinesiology and Sport Sciences, Brain Endowment Bank, Center for Cognitive Neuroscience and Aging (CNSA), Center for AIDS Research (CFAR), Clinical Translational Science Institute (CTSI), Hussman Institute for Human Genomics (HIHG) and others to evaluate current UM-MBI research and educational programs and plan the direction and develop goals and strategies of our Institute over the next 5 years.

The rationale for this strategic plan was to evaluate and emphasize the strengths of UM-MBI, to acknowledge the weaknesses, recognize challenges and opportunities, and to create and execute the strategic plan to achieve our goals in support of advancing our mission and vision in alignment with the University of Miami Miller School of Medicine (UM-MSOM) strategic plan.

# MISSION

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

# VISION

To become a *leading center for clinical and translational research* into the causes, treatments and prevention of age-related cognitive disorders and promotion of brain health.

# VALUES

| | |
|---|---|
| **D**iversity | Include people from all cultures and backgrounds. |
| **I**ntegrity | Demonstrate honesty and fairness in our actions. |
| **R**esponsibility | Exhibit pride and accountability in the performance of duties ensuring long-term success. |
| **E**xcellence | Strive to accomplish our goals with quality, rigor, passion and distinction. |
| **C**reativity | Embrace innovation, flexibility and originality. |
| **T**eamwork | Work across disciplines, departments, institutes and specialties to achieve optimal results. |

## GOALS, STRATEGIES AND METRICS

# GOAL 1: DEVELOP A SCIENTIFIC PROGRAM DIRECTLY RELATED TO UM-MBI AND THE MCKNIGHT BRAIN RESEARCH FOUNDATION MISSION

**The UM-MBI focuses its efforts on age-related memory loss, brain health and translating research discoveries into clinical practice.**

### CLINICAL TRANSLATIONAL RESEARCH STRATEGIES

- **Continue** research programs examining vascular, genetic, inflammatory, behavioral, psychosocial, sensory, environmental and imaging biomarkers of cognitive vascular impairment
- **Develop** new clinical translational research projects in age-related memory loss, cognitive decline and brain health; and leverage existing networks, NIH projects, databases and biorepositories (i.e., ADNI, MBAR, 1FL ADRC, OneFlorida, CFAR and others)
- **Develop** a strong clinical interventional program in age-related memory loss, cognitive decline and brain health based on restorative-stem cell, synaptic plasticity, sleep, cognitive-behavioral and lifestyle interventions
- **Identify funding opportunities** (NIH and others) and submit collaborative grants
- **Develop** seed/pilot research grant program for junior faculty and leverage institutional research funding (SAC, CFAR, CTSI pilots)
- **Prioritize** translation of evidence-based research findings into clinical practice
- **Develop** screening programs for cognitive impairment throughout UHealth for memory loss and promotion of brain health

### CLINICAL TRANSLATIONAL RESEARCH METRICS

- **Aim** for annual research and/or training grant submissions by UM-MBI members
- **Track** grant submissions and success among UM-MBI members, collaborators and trainees
- **Track** publications of UM-MBI members, collaborators and trainees
- **Increase** utilization of the research MRI at the UM Coral Gables Campus
- **Complete** a charter, research and business plans for the clinical interventional program and for the screening program in age-related memory loss, cognitive decline and promotion of brain health

## GOALS, STRATEGIES AND METRICS

# GOAL 2: EDUCATION AND MENTORSHIP

**The UM-MBI provides education and mentorship in age-related memory loss, cognitive decline and brain health.**

### EDUCATION STRATEGIES

- **Establish** a Neuro-Cognitive Post-Doctoral Fellowship
- **Integrate** cognitive aging education program with neurology resident training program
- **Expand** Schoninger Neuropsychology fellowship to include formal training in cognitive interventions focused on age-related memory loss
- **Develop** training program in age-related memory loss and cognitive decline (e.g., NIH T32, R25, F, K)
- **Provide** training in age-related memory loss to students, post doctoral fellows, physicians and scientists using multi-disciplinary seminar series, journal clubs, brain cutting sessions, research roundtables
- **Establish** a MD/PhD and MD/MS research thesis/capstone programs to fund a mentored project in age-related memory loss, cognitive decline and brain health
- **Partner** with the CTSI, CFAR, 1FL ADRC, VA, UM Geriatrics, FIU, Miami Jewish and other institutions in educational activities
- **Develop and strengthen** mentorship programs and leverage mentorship programs through CTSI Mentor-Mentee program and 1FL ADRC AlzSTARS (Alzheimer's Science Training to Advance Research Success) program

### EDUCATION METRICS

- **Conduct** at least 10 McKnight Research Seminars annually focused on age-related memory loss and brain health
- **Conduct** quarterly neurology resident journal club lectures focused on age-related memory loss and brain health
- **Conduct** quarterly education lectures focused on neuropsychology, brain image and neuropathology and cognitive neurology
- **Create and annually update** a curriculum for the Evelyn F. McKnight Fellowship
- **Create and annually update** the age-related memory education and training curricula in age-related memory loss, cognitive decline and brain health for students, post doctoral trainees, residents and fellows
- **Host** annual McKnight Brain Institute Grand Rounds
- **Participate** in CTSI Mentor-Mentee program (UM-MBI trainees and faculty)
- **Track transition** of UM-MBI trainees to faculty postions, promotions and successful applications for F, K and R grants

## GOALS, STRATEGIES AND METRICS

# GOAL 3: PROMOTE COMMUNICATION AND COLLABORATION

**The UM-MBI promotes and provides a structure to share information and collaborate across clinical translational research, education and clinical landscapes at UM as well as between MBIs focusing on our clinical and translational research strengths and UM-MSOM strategic plan.**

### RESEARCH SPECIFIC STRATEGIES

- **Enhance** research environment & collaborative interactions across disciplines and across UM departments and institutes, and with other MBIs and non-MBI institutions
- **Identify** leaders across disciplines and departments to develop scientific working groups (SWG)
- **Secure space** for collaborative projects, interactions and seminars/conferences in partnership with the UM-CTSI (leverage CTSI Connection and other collaborative activities)
- **Build upon** the existing Miami CTSI research infrastructure to promote team science in age-related memory loss and brain health
- **Increase c**ommunication across UHealth to develop integrated treatment plans that include referrals and research opportunities

### RESEARCH METRICS

- **Track** inter-disciplinary activities (webinars, conferences, seminars, participation in team science classes and activities) among members, collaborators and trainees
- **Create** at least one active SWG by UM-MBI members and apply for a research or education grant
- **Create** the UHealth clinical and research interventional protocols in age-related memory loss, cognitive decline and brain health
- **Reorganize** the UM-MBI website and update regularly on new activities, partnerships and collaborations

## GOALS, STRATEGIES AND METRICS

# GOAL 4: DEVELOP COMMUNITY OUTREACH

**The UM-MBI leads community research in age-related memory loss and cognitive decline and provides information on cognitive decline in communities.**

### COMMUNITY OUTREACH STRATEGIES

- **Establish** a community-based education network and develop community programs to inform community of issues on age-related memory, cognitive decline and to promote brain health
- **Provide** knowledge-based education series to community
- **Develop** social media community outreach to promote brain health
- **Disseminate** research achievements to the community using media, web, social media, etc.
- **Prioritize** translation of evidence-based research findings into community
- **Partner with community leaders** to develop integrated treatment plans that include referrals and research opportunities

### COMMUNITY OUTREACH METRICS

- **Identify and track** community activities, i.e new partners, ALFs, community centers and town governments (e.g., Silver Club in Doral) through number of events and community participation in research activities
- **Develop** education programs for community through libraries, senior centers, Mayor's Initiative on Aging (new mayor in Miami-Dade and don't know if initiative will continue)
- **Expand** ongoing radio outreach programs to educate Latinx community on healthy lifestyle interventions to promote brain health
- **Track** our webpage and social media traffic
- **Develop** and conduct at least one outreach program annually for the community of South Florida

# APPENDIX II

The Schoninger Neuropsychology Program has expanded its services to provide a full range of interventions designed to mitigate age-related memory loss and other cognitive changes associated with the aging process. Used in conjunction with neuropsychological testing to identify areas of cognitive weakness, patients are offered a uniquely tailored program administered over 8-12 weeks addressing their specific needs in areas that offer potential for intervention. This precision based delivery of services focuses on developing realistic goals and utilizing a practical, accessible plan of action. *A major strength of this new program is that nearly all of the interventions can be administered on either a virtual platform or face-to- face meeting.* A schematic of the program is on the next page.

Although each member in the Division of Neuropsychology and Cognitive Neuroscience is trained to administer all services offered as interventions, some faculty have pursued additional expertise in order to offer more advanced interventions as well as supervision and training of post-doctoral fellows in these areas. Below is a breakdown of the services and their respective providers:

Psychotherapy: Drs. McInerney, Slugh, Kaur, Bure-Reyes
Mindfulness
Supportive Psychotherapy
CBT/Emotion Regulation
CBT for Insomnia

Educational Interventions: Drs. McInerney, Slugh, Kaur, Getz, Levin, Rey, Sarno
Psychoeducation
Multidisciplinary Lifestyle Modifications
IADL Enhancement
Caregiver Support and Guidance
Deception Recognition Training
Building Social Connectivity

Compensatory Cognitive Rehabilitation: Drs. Slugh, Levin, Rey
Metacognitive Strategy Training
Executive/Goal Management
Prospective Memory Training
Building Resilience
Social Communication Enhancement

Remediative Cognitive Interventions: Dr. Slugh
Attention/Tracking Training
Improving Mental Flexibility
Individualized Tailored Cognitive Enrichment Programs

# Division of Neuropsychology
# Cognitive Rehabilitation Services

Cognitive Rehabilitation

Used in conjunction with neuropsychological evaluation to define specific needs and identify areas with greatest potential for intervention focusing on identified strengths. Designed for 8 to 12 week intervention. Can be administered on virtual platform or face-to-face meeting.

Comprehensive Neuropsychological Evaluation for Precision Based Delivery of Service
Develop Realistic Goals and Planned Course of Rehabilitation

**Therapy**

Mindfulness
Supportive Psychotherapy
CBT/Emotion Regulation
CBT for Insomnia

**Educational Interventions**

Psychoeducation
Multidisciplinary Lifestyle Modifications
IADL Enhancement
Caregiver Support and Guidance
Deception Recognition Training
Building Social Connectivity

**Compensatory Cognitive Rehabilitation**

Metacognitive Strategy Training
Executive/Goal Management
Prospective Memory Training
Building Resilience
Social Communication Enhancement

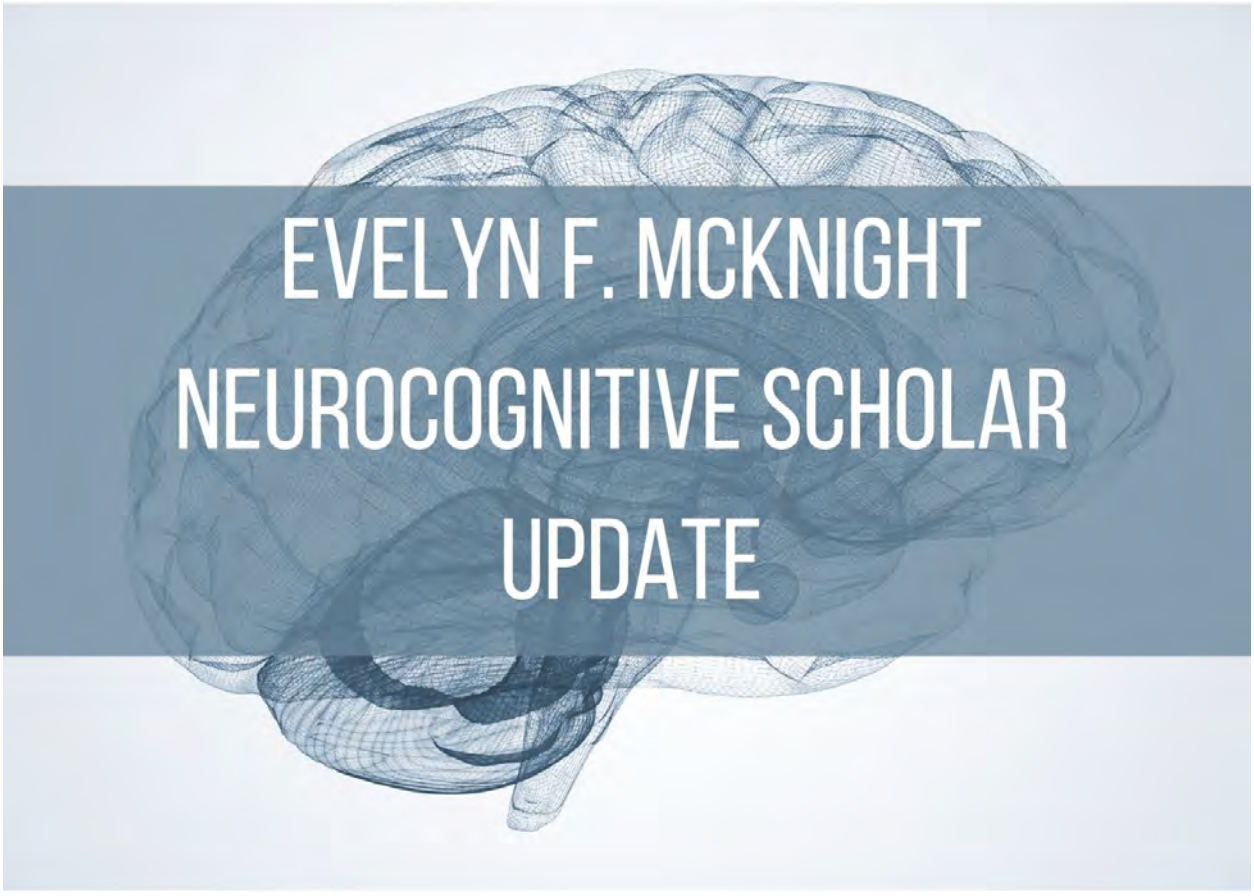
**Remediative Cognitive Interventions**

Attention/Tracking Training
Improving Mental Flexibility
Individualized Tailored Cognitive Enrichment Programs

**Late Adolescent Cognitive Interventions**

Study Skills for Return to Learn
Lifestyle Interventions to Promote Optimal Recovery

# APPENDIX III



# EVELYN F. MCKNIGHT NEUROCOGNITIVE SCHOLAR UPDATE

# Evelyn F. McKnight Neurocognitive Scholar Update

**Christian Agudelo, MD** is our first **Evelyn F. McKnight Neurocognitive Scholar.** He joined us in July, 2020. He received his medical degree from the University of Pittsburgh School of Medicine where he also completed a post-doctoral research fellowship. His research included using multimodal neuroimaging (functional MRI, structural MRI, and PET) to study late-life cognitive and mood disorders. He completed his residency training in neurology at the University of Miami Miller School of Medicine / Jackson Memorial Hospital. Then he completed a fellowship in sleep medicine at the University of Miami. Dr. Agudelo's research interests are in the ways sleep influences memory and cognitive decline in aging. His research aims to identify sleep-specific mechanisms responsible for cognitive decline and to develop sleep-related biomarkers of cognitive aging. Such biomarkers could be used to diagnose pre-symptomatic cognitive disease, track disease progression, be used as targets for intervention and assess the efficacy of future therapies. As sleep can be modified pharmacologically, surgically and behaviorally, Dr. Agudelo believes that sleep could one day be engineered to mitigate cognitive aging and optimize cognitive and brain health. His bio is included at the end of this report.

His mentors are Tatjana Rundek, MD, PhD, Xiaoyan Sun, MD, PhD and Alberto Ramos, MD. He meets weekly with his mentors. Together with his mentoring team, he has developed an Individualized Development Plan and mapped his research curriculum. He is driven and focused and has promising research ideas. His first six months as the McKnight Scholar have been productive yielding noteworthy success.

**Dr. Agudelo** submitted a manuscript and a supplement to peer reviewed journals that were accepted for publication**.** Also, 2 refereed abstracts and a poster were accepted at an important sleep conference. References for these are below.

1. Agudelo C, Tarraf W, Wu B, Wallace DM, Patel SR, Redline S, Kaur S, Daviglus M, Zee PC, Simonelli G, Mossavar-Rahmani Y, Sotres-Alvarez D, Zeng D, González HM, Ramos AR. Actigraphic Sleep Patterns and Cognitive Decline in the Hispanic Community Health Study/Study of Latinos. *Alzheimer's and Dementia* (In press).

2. Agudelo C, Tarraf W, Wu B, et al. 1144 Actigraphy-defined Sleep And Neurocognitive Decline In Middle-age Hispanic/Latino Adults. *Sleep.* 2020;43(Supplement_1):A435-A436.

3. Gei E, Agudelo C, Ascher K, Sun X, Velez-Ruiz N, Ramos AR. An unusual presentation of narcolepsy in an elderly man. Annual Meeting of the Associated Professional Sleep Societies Virtual Meeting; August 2020.

4. Agudelo C, Tarraf W, Wu B, Wallace DM, Pate SR, Redline S, Daviglus M, Zee PC, Simonelli G, Mossavar-Rahmani Y, Sotres-Alvarez D, Zeng D, González HM, Ramos AR. Actigraphy-defined Sleep and Neurocognitive Decline in Middle-age Hispanic/Latino Adults. Poster presented and abstract accepted at the Annual Meeting of the Associated Professional Sleep Societies Virtual Meeting; August 2020.

**Dr. Agudelo's** achievements, awards and recognitions include:

1. He was selected for the *Sleep and Circadian Workshop on Indispensable Methods* hosted by the University of Pittsburgh Center for Sleep and Circadian Science.
2. He joined other early career investigators that participated in the Sleep and Circadian Workshop on Indispensable Methods to Establish a Group. It was led by the University of Pittsburgh's Martica Hall, PhD, and Sanjay Patel, MD, and explored how to study racial disparities more effectively as they relate to sleep and health.
3. He attended the annual Trainee Symposia Series hosted by the Sleep Research Society; August 2020.
4. He attended the annual Florida Consortium on the Neurobiology of Cognition Meeting; August 2020.
5. He submitted an application for the NIH Loan Repayment Program award. This award provides up to $50,000 per year to pay for eligible federal educational debt.
6. He submitted an application for the *American Academy of Sleep Medicine's Young Investigator Research Forum Award*.
7. He reviewed manuscripts for the *British Medical Open Access Journal* and *Frontiers in Aging Neuroscience*.

**Dr. Agudelo** regularly attends these meetings:

1. Bi-monthly mentorship meetings with Drs. Rundek, Ramos and Sun
2. Monthly Sleep Medicine Division Journal Club
3. Bi-monthly Vascular Imaging Phenotype of the 1FL ADRC study group
4. Bi-monthly McKnight Brain Institute Research Seminars
   - He presented "A biomarker of grey matter microstructure integrity in neurocognitive aging" for the August McKnight Research Seminar. This presentation discussed specific aims of his research proposals about using grey matter diffusion MRI as a biomarker of neurocognitive aging.

Update on **Dr. Agudelo's** Projects:

He has established a plan for his empirical mentored research for the next two years, which consists of three projects. The overarching theme of the three projects is to identify sleep-related pathological biomarkers of cognitive aging.

- **Project 1**: Using diffusion MRI to investigate the relationship of gray matter microstructure integrity in cognitive aging.

The One Florida Alzheimer's Research Center has an ongoing observational study of older adults in Florida to characterize progression from normal cognition to dementia. Mentored by Dr. Rundek, he will use diffusion MRI to measure the diffusivity of cerebral gray matter regions. These measures are proxies for gray matter microstructure integrity. Higher diffusivity implies lower microstructure integrity. He hypothesizes that gray matter microstructure integrity will be lower in participants with lower neurocognitive function. Similarly, gray matter microstructure integrity will be lower in participants with greater diagnostic severity of their cognitive disease. Additionally, he will explore whether enlarged perivascular spaces (EPVS) are associated with MRI-based measures of gray matter microstructure integrity and neurocognitive function. EPVS's have been considered proxy measures for glymphatic function (an extra-arterial cerebral clearance network). The existence of EPVS's may imply glymphatic stasis and a diminished ability to clear cognitively damaging substances, such as beta-amyloid. He hypothesizes that higher concentration of EPVS's will be associated with higher gray matter diffusivity and lower neurocognitive function.

- **Project 2**: Using diffusion MRI to investigate the relationship between subjective measures of sleep and the integrity of white matter tracts associated with the mesial temporal lobe (MTL).

The Alzheimer's Disease Neuroimaging Initiative (ADNI) is an ongoing study that explores the progression from intact cognition to dementia. Among the many data collected from participants, they have performed MRI, PET, neurocognitive evaluations, questionnaires, and kept track of their cognitive diagnosis severity. Mentored by Dr. Ramos and Dr. Sun, he will study the relationship between subjective assessment of sleep quality and the integrity of white matter tracts associated with the MTL (cingulum, fornix, uncinate fasciculus). He hypothesizes that lower subjective assessments of sleep quality will be associated with lower integrity of white matter tracts associated with the MTL.

- **Project 3 (beginning in the second half of 2021)**: The relationship between sleep and cerebral gray matter microstructure integrity.

The Hispanic Community Health Study/Study of Latinos (HCHS/SOL) is an ongoing multi-site observational study of U.S. Hispanic/Latino Adults, with measures of sleep actigraphy, home sleep apnea studies, repeat neurocognitive evaluations, and ongoing MRI. Mentored by Dr. Ramos, he will study the relationship between subjective and actigraphic measures of sleep and MRI-based measures of cerebral gray matter microstructure integrity (diffusivity). As gray matter diffusivity may be a pathological biomarker of cognitive aging, it is important to explore how sleep is related to gray matter diffusivity. Sleep is a ubiquitous and highly modifiable biobehavioral process, thus sleep can serve as a potential target for intervention that can ameliorate age-related cognitive decline.

We are grateful for the funding to support Dr. Agudelo and look forward to his scientific and academic progress and achievements.

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Dr. Christian Agudelo grew up in Miami, Florida. He received his Bachelor Degree in Science in Engineering from Duke University, where he studied biomedical engineering. He received his medical degree from the University of Pittsburgh School of Medicine. His research in medical school included the study of psychophysiology and dysautonomia in Parkinson's Disease. During a post-doctoral research fellowship at the University of Pittsburgh, his research included using multimodal neuroimaging (functional MRI, structural MRI, and PET) to study late-life cognitive and mood disorders. He completed his residency training in neurology at the University of Miami Miller School of Medicine / Jackson Memorial Hospital. Then he completed a fellowship in sleep medicine at the University of Miami. He is continuing his training in neurocognitive neurology and studying the effects of sleep on age-related memory loss and cognitive decline as the Evelyn F. McKnight Neurocognitive Scholar. Dr. Agudelo is a member of these professional and scientific organizations, the American Academy of Neurology and the American Academy of Sleep Medicine, and is dedicated to clinical practice, research, and service to the scientific and professional neurology community.

Dr. Agudelo is interested in the ways sleep influences memory and cognitive decline. His research aims to identify sleep-specific mechanisms responsible for cognitive decline and to develop sleep-related biomarkers of cognitive aging. Such biomarkers could be used to diagnose pre-symptomatic cognitive disease, track disease progression, be used as targets for intervention, and possibly assess the efficacy of future therapies. As sleep can be modified pharmacologically, surgically, and behaviorally, Dr. Agudelo believes that sleep could one day be engineered to mitigate cognitive aging and optimize cognitive and brain health.

# APPENDIX IV

# PUBLICATIONS

## Publications Relevant to Our MBI Mission

**Agudelo C**, Tarraf W, Wu B, Wallace DM, Patel SR, Redline S, **Kaur S**, Daviglus M, Zee PC, Simonelli G, Mossavar-Rahmani Y, Sotres-Alvarez D, Zeng D, González HM, **Ramos AR**. Actigraphic Sleep Patterns and Cognitive Decline in the Hispanic Community Health Study/Study of Latinos. *Alzheimer's and Dementia* (In press).

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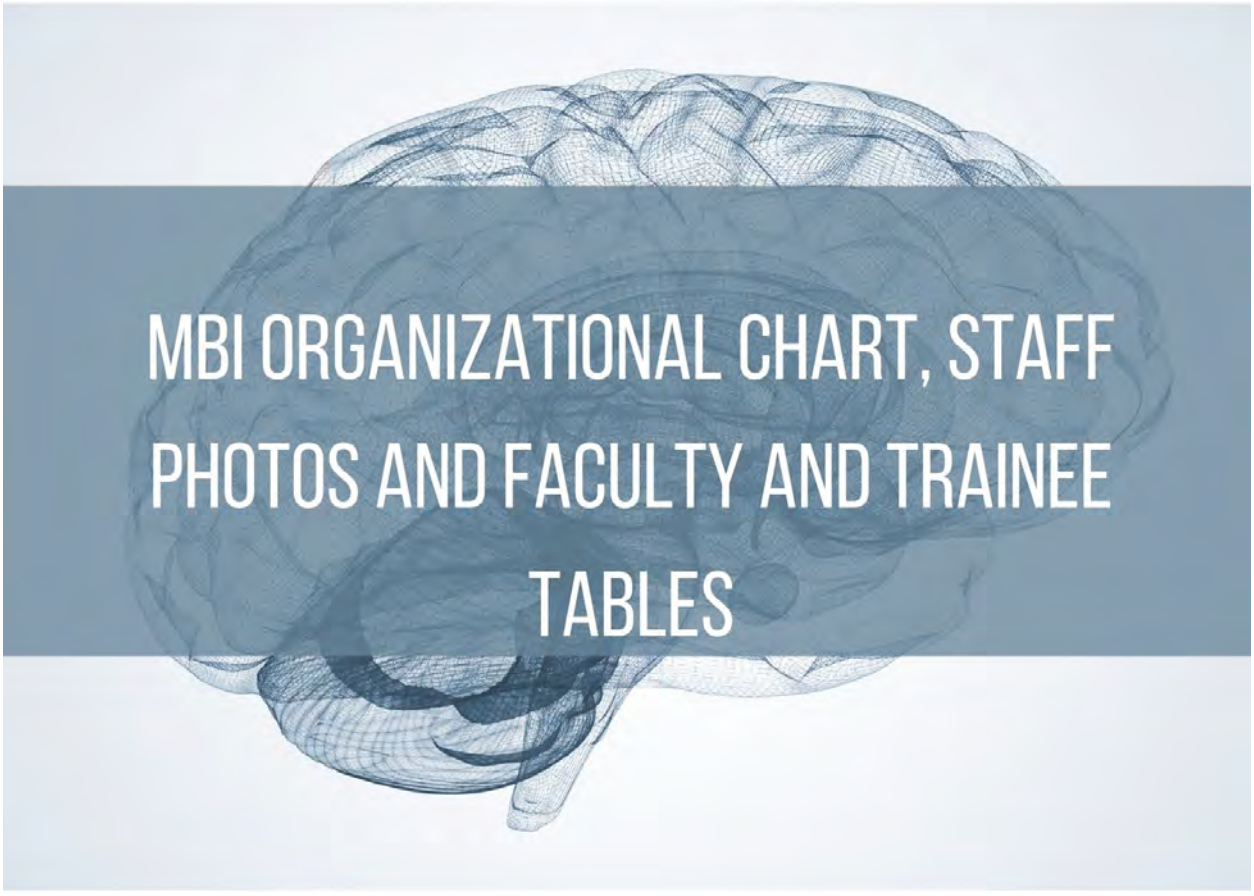
# APPENDIX V



## MBI ORGANIZATIONAL CHART, STAFF PHOTOS AND FACULTY AND TRAINEE TABLES

# Miami McKnight Brain Institute Organizational Chart

## LEADERSHIP

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Director, Clinical and Translational Science Institute
Senior Associate Dean for Clinical and Translational Science
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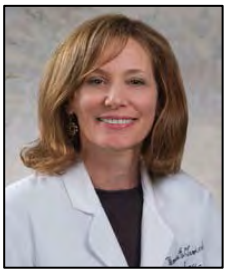

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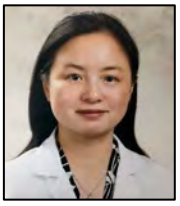

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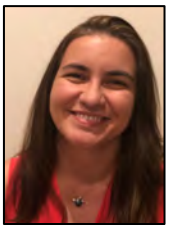

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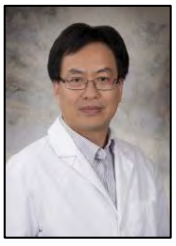

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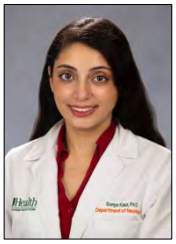
**Sonya Kaur, Ph.D.**
**Evelyn F. McKnight Brain Institute Collaborator**
Instructor
Department of Neurology, Division of Neuropsychology
University of Miami, Miller School of Medicine



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**Katalina Fernández McInerney, Ph.D.**
**Evelyn F. McKnight Brain Institute Collaborator**
Assistant Professor
Department of Neurology, Division of Neuropsychology
University of Miami, Miller School of Medicine

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**Milena Pinto, Ph.D.**
**Evelyn F. McKnight Brain Institute Collaborator**
Research Assistant Professor
Department of Neurology
University of Miami, Miller School of Medicine

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**Alberto Ramos, M.D., MSPH, FAASM**
**Evelyn F. McKnight Brain Institute Collaborator**
Associate Professor of Clinical Neurology
Co-Director of the Sleep Disorders Program
University of Miami, Miller School of Medicine

---

**Ami Pravinkant Raval, Ph.D.**
**Evelyn F. McKnight Brain Institute Collaborator**
Research Associate Professor
Basic Science Division
Department of Neurology
University of Miami, Miller School of Medicine

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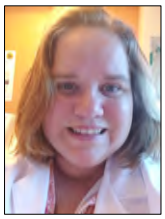
**Regina Vontell, Ph.D.**
**Evelyn F. McKnight Brain Institute Collaborator**
Research Assistant Professor of Neurology
Associate Director of Clinical and Histopathology
University of Miami, Miller School of Medicine



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

## **Faculty** (Leadership & Members)

Biosketches are provided at the end of the report.

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

## **Faculty** (Collaborators)

Biosketches are provided at the end of the report.

| Name | Institute Role | Area of Expertise |
|---|---|---|
| Susan Blanton, PhD | Collaborator | Genetics |
| Scott Brown, PhD | Collaborator | Public Health |
| Elizabeth Crocco, MD | Collaborator | Psychiatry |
| Chuanhui Dong, PhD | Collaborator | Epidemiology, Biostatistics |
| James Galvin, MD, MPH | Collaborator & Scientific Advisory Board | Neurology |
| Sarah Getz, PhD | Collaborator | Neuropsychology |
| David Loewenstein, PhD | Collaborator & Scientific Advisory Board | Neuropsychology |
| Katalina McInerney, PhD | Collaborator | Neuropsychology |
| Roger McIntosh, PhD | Collaborator | Psychology |
| Milena Pinto, PhD | Collaborator | Neuroscience |
| Alberto Ramos, MD | Collaborator | Neurology, Sleep Medicine |
| Ami P. Raval, PhD | Collaborator | Neuroscience, Epidemiology |
| Regina Vontell, PhD | Collaborator | Neurology |
| Jianhua Wang, MD, PhD | Collaborator | Neuro-ophthalmology, Neurology |

# Trainees

| Name | Institute Role | Academic Focus | Mentor |
|---|---|---|---|
| Christian Agudelo, MD | McKnight Cognitive Fellow | Neurology | Alberto Ramos, MD<br>Tatjana Rundek, MD, PhD<br>Xiaoyan Sun, MD, PhD |
| Shriya Airen | MD Student | Neurology | Hong Jiang, MD<br>Jinhua Wang, MD, PhD |
| Taylor Ariko, BS | PhD Student | Biomedical Engineering | Tatjana Rundek, MD, PhD<br>Andrew Dykstra, PhD |
| Nikhil Sebastian Banerjee, PhD | Postdoctoral Fellow | Neuropsychology | Bonnie Levin, PhD |
| Justin Burgess | Practicum Student | Neuropsychology | Bonnie Levin, PhD |
| Marlene Cabrera, PsyD | Postdoctoral Fellow | Neuropsychology | Bonnie Levin, PhD |
| Danylo Cabral, BS, PT | PhD Student | Physical Therapy/Cognition | Joyce Gomes-Osman, PT, PhD |
| Marlene Cabrera, PsyD | Postdoctoral Fellow | Neuropsychology | Bonnie Levin, PhD |
| Ileana Pacheco-Colon | Practicum Student | Neuropsychology | Bonnie Levin, PhD |
| Iris Escobar | PhD Student | Neurology | Miguel Perez-Pinzon, PhD |
| Min Fang | Postdoctoral Fellow | Neuro-ophthalmology | Hong Jiang, MD<br>Jinhua Wang, MD, PhD |
| Eric Fargali | PhD Student | Neuroscience | Miguel Perez-Pinzon, PhD |
| Meghan Gilmore | Practicum Student | Neuropsychology | Bonnie Levin, PhD |
| Zachary Goodman | Practicum Student | Neuropsychology | Bonnie Levin, PhD |
| Ryan Gober, BS | PhD Candidate | Neuroscience | Regina Vontell, PhD |
| Melissa Huberman | Medical Student | Neuroscience | Ami P. Raval, PhD |
| Sonya Kaur, PhD | Instructor | Neuropsychology | Bonnie Levin, PhD<br>Tatjana Rundek, MD, PhD<br>Alberto Ramos, MD |

| | | | |
|---|---|---|---|
| Che Liu | Graduate Student | Neuroradiology | Noam Alperin, PhD |
| Zhiping Liu | MD/PhD Candidate | Neurology | Hong Jiang, MD<br>Jinhua Wang, MD, PhD |
| Judith Lobo | Graduate Student | Cognitive Behavioral Neuroscience | Roger McIntosh, PhD |
| Michelle Marrero, MD | Cognitive Fellow | Neurology | Xiaoyan Sun, MD, PhD |
| Emily Cecilia Morales | Graduate Student | Biochemistry | Ami P. Raval, PhD |
| Amanda Neves | Post-Doctoral Trainee | Basic Science Neurology | Milena Pinto, PhD |
| Qismat Niazi | Student | Neuroscience | Ami P. Raval, PhD |
| Christina Nunez | Graduate Student | Physical Therapy | Joyce Gomes-Osman, PT, PhD |
| Damin Hadorn-Papke | Practicum Student | Neuropsychology | Bonnie Levin, PhD |
| Sonya Patel | Undergrad Student | Neuroscience | Ami P. Raval, PhD |
| Varun Reddy | Student | Neuroscience | Ami P. Raval, PhD |
| Ashish Rehni, PhD | Post-Doctoral Fellow | Neuroscience | Kunjan Dave, PhD |
| Jordyn Rice, PT, DPT | Graduate Student | Physical Therapy/Cognition | Joyce Gomes-Osman, PT, PhD |
| Joshua D. Rooks, PhD | Postdoctoral Fellow | Neuropsychology | Bonnie Levin, PhD |
| Anita Seixas Dias Saporta, MD | McKnight Fellow | Neurology, Imaging | Tatjana Rundek, MD, PhD |
| Sharnikha Saravanan | Undergrad Student | Neuroscience | Ami P. Raval, PhD |
| Christina Stutts | Graduate Student | Music Therapy | Xiaoyan Sun, MD, PhD |
| Jonathan Siegel | Graduate Student | Biochemistry | Ami P. Raval, PhD |
| Chiara Villa | Post-Doctoral Trainee | Neurology | Milena Pinto, PhD |
| Juan Zhang, PhD | Post-Doctoral Trainee | Neurology | Hong Jiang, MD<br>Jinhua Wang, MD, PhD |

# APPENDIX VI

## BUDGETS AND GRANTS UPDATE
## PROJECTED BUDGET FOR COMING YEAR
## ENDOWMENT AND INVESTMENT RESULTS

**McKnight - FY21 - Budget Actuals**
**June 1, 2020 - May 31, 2021**

| | | | Budget Summary |
|---|---|---|---|
| **Revenue Based on FY20 Endowment*** | | | **782,261.32** |
| **Personnel** | | | |
| **Faculty** | **Role In Project** | **Effort** | |
| Tatjana Rundek, MD (Suppliment) | Scientific Director | 95% | |
| Ralph Sacco, MD (only cost share) | Executive Director | 5% | |
| Xiaojan Sun, MD | Education Director | 15% | |
| Bonnie Levin, PhD | Neuropsychology | 20% | |
| Bonnie Levin, PhD(supplement-25%) | Neuropsychology | 25% | |
| Noam Alperin, MD - (MRI) | Radiology | 12% | |
| Jiang Hong | Neurology | 5% | |
| Christian Agueldo - McKnight Fellow (7/1/2020) | Neurology | 100% | |
| Sarah Getz (carry forward 40K given in FY20) | Neuropsychology | 8% | |
| Sonya Kaur | Neuropsychology | 8% | |
| Christian Camargo | Neurology | 5% | |
| Katalina McInereny | Neuropsychology | 10% | |
| **Subtotal Faculty Salary and CFB** | | | **391,873.52** |
| **Staff** | **Role in Project** | **Effort** | |
| Stacy Merritt | Project Mgr | 35% | |
| Sang Lee | Radiology | 10% | |
| Digna Cabral | Neurology | 25% | |
| MD-PhD Student | Neurology | 20% | |
| Anita Saporta | Neuropsychology | 25% | |
| Sang Lee | Radiology | 10% | |
| Marti Flothmann | Research/Communications Coordinator | 35% | |
| Susan Fox Rosellini | Administration/Marketing Director | 70% | |
| NeuroPsych 1 | Neuropsychology | 50% | |
| NeuroPsych 2 | Neuropsychology | 25% | |
| NeuroPsych 3 | Neuropsychology | 25% | |
| NeuroPsych 4 | Neuropsychology | 25% | |
| NeuroPsych 5 | Neuropsychology | 25% | |
| **Subtotal Staff and CFB** | | | **328,234.57** |
| **Total Personnel** | | | **720,108.09** |
| **Non Personnel Expenses** | | | |
| SC08818 - Publication Costs (Excluding Copying) | | | |
| SC08801 - Registration Conferences & Seminars | | | |
| SC08803 - Dues & Memberships - Other | | | |
| SC08611 - Employee Domestic Travel | | | |
| SC08619 - Meetings - Subsistence | | | |
| SC08624 - Entertainment - Food, Beverage, Recept | | | |
| SC08852 - Monthly - Lines & Sets & SC08858 - Monthly - Voice Mail | | | |
| SC08103 - Advertising - Email/Web | | | |
| SC08024 - Interdepartmental / Intercompany - Service | | | |
| SC08235 - Computer Hardware & Software Non-Capital | | | |
| SC08218 - Clerical Supplies | | | |
| SC08219 - Instructional supplies | | | |
| SC08229 - Photocopy, Publishing, & Printing Supplies | | | |
| SC08200 - Chemicals/blood samples storage/ship | | | |
| SC08011 - Interdepartmental / Intercompany - Animal Care Services - Internal | | | |
| SC08225 - Technical Supplies - Other | | | |
| **Total Non Personnel Expenses** | | | **15,154.23** |
| **Grand Total Expenses**** | | | **735,262.32** |

**Notes:**

* Revenue includes the Revenue for Fellow and Endowment Income

** Expenses are less than revenue this year since Covid limited travel and meetings and CFB was decreased. This revenue will be rolled over to FY22.

# McKnight - FY22 - Budget Proposal
# June 1, 2021 - May 31, 2022

| | | | Budget Summary |
|---|---|---|---|
| ***Revenue (based on FY21 endowment)*** | | | |
| **Endowment - McKnight Project** | | | |
| **Revenue Based on FY21 Endowment*** | | | **832,261.41** |
| **Personnel** | | | |
| ***Faculty*** | ***Role In Project*** | ***Effort*** | |
| Tatjana Rundek, MD (supplement) | Scientific Director | 100% | |
| Ralph Sacco, MD (only cost share) | Executive Director | 5% | |
| Xiaojan Sun, MD | Educational Director | 10% | |
| Bonnie Levin, PhD | Neuropsychology | 25% | |
| Kunjan Dave | Neurology - Basic Science | 5% | |
| Chuanhui Dong | Neurology -Statistician | 5% | |
| Noam Alperin, MD | Radiology | 15% | |
| Jiang Hong, MD | Neurologist | 5% | |
| McKnight Fellow (7/1/2020) | Neurology | 100% | |
| Sarah Getz | Neuropsychology | 5% | |
| Sonya Kaur | Neuropsychology | 10% | |
| Christian Camargo | Neurology | 5% | |
| Katalina McInereny | Neuropsychology | 10% | |
| Christian Agueldo - McKnight Fellow | Neurology | 100% | |
| ***Subtotal Faculty Salary and CFB*** | | | ***411,467.19*** |
| ***Staff*** | ***Role in Project*** | ***Effort*** | |
| Stacy Merritt | Project Mgr | 80% | |
| Sang Lee | Radiology | 10% | |
| Marti Flothmann | Clinical Research Coordinator | 75% | |
| MD-PhD Student | MD/PhD Student - Neuro | 100% | |
| Isabel Saul | Research Support Specialist-Basic S | 15% | |
| Anita Saporta | Neuropsychology | 25% | |
| Susan Fox Rosellini | Admin | 80% | |
| NeuroPsych 1 | Neuropsychology | 50% | |
| NeuroPsych 2 | Neuropsychology | 25% | |
| NeuroPsych 3 | Neuropsychology | 25% | |
| NeuroPsych 4 | Neuropsychology | 25% | |
| NeuroPsych 5 | Neuropsychology | 25% | |
| ***Subtotal Staff and CFB*** | | | **391,210.99** |
| ***Total Personnel*** | | | ***802,678.18*** |
| ***Non Personnel Expenses*** | | | |
| SC08818 - Publication Costs (Excluding Copy | | | |
| SC08801 - Registration Conferences & Semi | | | |
| SC08803 - Dues & Memberships - Other | | | |
| SC08611 - Employee Domestic Travel | | | |
| SC08619 - Meetings - Subsistence | | | |
| SC08624 - Entertainment - Food, Beverage, | | | |
| SC08852 - Monthly - Lines & Sets & SC08858 - Monthly - Voice Mail | | | |
| SC08103 - Advertising - Other | | | |
| SC08024 - Interdepart/ Intercomp - Service | | | |
| SC08235 - Computer Hardware & Software Non-Capital | | | |
| SC08218 - Clerical Supplies | | | |
| SC08219 - Instructional supplies | | | |
| SC08229 - Photocopy, Publishing, & Print Su | | | |
| SC08200 - Chemicals/blood samples store/s | | | |
| SC08011 - Interdepartmental / Intercompany - Animal Care Services - Internal | | | |
| SC08225 - Technical Supplies - Other | | | |
| ***Total Non Personnel Expenses*** | | | ***29,583.23*** |
| ***Grand Total Expenses*** | | | **832,261.41** |

**Notes:**

* Revenue includes Revenue for Fellow and Endowment Income
It also includes rollover from 2021 and increase to normal CFB

**McKnight - FY21 - Budget Actuals**
**June 1, 2020 - May 31, 2021**

| | | | | Budget Summary |
|---|---|---|---|---|
| **McKnight Project - Precision Aging Network Pilot Study** | | | | |
| **Revenue** | | | | **$ 173,500.00** |
| | | | | |
| **Personnel** | | | | |
| ***Faculty and Staff*** | ***Role In Project*** | ***Effort*** | | |
| Tatjana Rundek, MD | Scientific Director | 5% | | |
| Katalina McInereny | Neuropsychology | 5% | | |
| Stacy Merritt | Project Mgr | 65% | | |
| Marti Flothmann | Communications Coordinator | 20% | | |
| Susan Fox Rosellini | Administration/Marketing Director | 10% | | |
| | | | | |
| ***Total Personnel*** | | | | **$ 142,400.00** |
| | | | | |
| | | | | |
| ***Non Personnel Expenses*** | | | | |
| SC08103 - Advertising - Email/Social Media | | | | **$31,100.00** |
| | | | | |
| ***Total Non Personnel Expenses*** | | | | ***$31,100.00*** |
| | | | | |
| ***Grand Total Expenses*** | | | | ***$173,500.00*** |

# McKnight Members Grants

*Stroke Incidence and Risk Factors in a Tri-ethnic Region*
Source: NIH, NINDS (R01 NS029993)
Principal Investigator: **Ralph Sacco**
2020 Budget: $1,731,055 (NCE)

Miami Clinical and Translational Science
Institute Source: NIH//NCRR/NIMHD
Principal Investigator: **Ralph Sacco**
2020 Budget: $3,591,518

*Family Study of Stroke Risk and Carotid Atherosclerosis*
Source: NIH/NINDS R01 NS040807
Principal Investigator: **Tatjana Rundek**
2020 Budget: $615,412

*Family Study of Atherosclerosis and Vascular Cognitive Dysfunction – Administrative Supplement*
Source: NIH/NINDS R01 NS040807-S1
Principal Investigator: **Tatjana Rundek**
2020 Budget: $391,140

*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 2020 Budget: $697,910

*Disparities in Care Delivery in Patients with Atrial Fibrillation: FLiPER-AF Study*
Source: ARISTA-USA CV185-564, Pfizer/BMS
Principal Investigator: **Tatjana Rundek**
2020 Budget: $199,428

*Brain Vascular Imaging Phenotypes, Vascular Comorbidities and the Risk for Alzheimer Disease: The Florida VIP Study of AD Risk*
Source: State of Florida, Ed and Ethel Moore Alzheimer's Disease Research Program
(FDOH) Principal Investigator: **Tatjana Rundek**
2020 Budget: $237,500

University of Miami Memory Disorder
Clinic Source: State of Florida, Division
of Elder Affairs Co-Investigator:
**Xiaoyan Sun**
2020 Budget: $222,801

*Nicotine Exposure and Intracerebral Hemorrhage*
Source: State of Florida, James and Esther King Biomedical Research Program, FDOH
(9JK08)
Principal Investigator: **Kunjan Dave**
2020 Budget: $245,611

*Ischemic Preconditioning: Mechanisms of Neuroprotection*
Source: NIH, NINDS (R01NS034773)

Principal Investigator: **Miguel Perez-Pinzon**
2020 Budget: $173,224 NCE

*Mechanism of Neuroprotection Against Cardiac Arrest*
Source: NIH/NINDS
Site Principal Investigator: **Miguel Perez-Pinzon**
2020 Budget: $383,750

*Strategies to Ameliorate Cognitive Decline Following Cerebral Ischemia in Nicotine-Exposed Rats*
Source: State of Florida, James and Esther King Biomedical Research Program, FDOH (20K11)
Site Principal Investigator: **Miguel Perez-Pinzon**
2020 Budget: $142,826

*Metabolic Master Regulators for Ischemic Neuroprotection*
Source: NIH/NINDS
Site Principal Investigator: **Miguel Perez-Pinzon**
2020 Budget: $335,781

*Metabolic Master Regulators for Ischemic Neuroprotection – Administrative Supplement*
Source: NIH/NINDS
Site Principal Investigator: **Miguel Perez-Pinzon**
2020 Budget: $373,174

*Exploring Sleep in Neurocognitive Aging and Alzheimer's Research (eSANAR)*
Source: NIH/NIA (1R21AG056952)
Principal Investigator: **Alberto Ramos**
2020 Budget: $63,965

*Sleep Apnea Phenotypes in Latinos (SLEPT)*
Source: NIH/NINDS
Principal Investigator: **Alberto Ramos**
2020 Budget: $150,000

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

September 29, 2020

Michael L. Dockery, MD
Richard Isaacson, MD
Susan L. Pekarske, MD
Gene G. Ryerson, MD
Madhav Thambisetty, MD, PhD
Robert M. Wah, MD
J. Lee Dockery, MD, Emeritus

The Evelyn F. McKnight Brain Research Foundation
SunTrust Bank
Mail Code FL-ORL-1503
333 S. Garland Avenue, 15th Floor
Orlando, FL 32801

Dear Trustees:

On behalf of the University of Miami Leonard M. Miller School of Medicine, please find enclosed the growth pool annual investment report for the fiscal year ending May 31, 2020. Per the terms of our gift agreement (section 7.3) the University of Miami forwards this report to you annually. I have also included the market value analysis for the endowment for the same fiscal period.

Should you have any questions, please feel free to contact Susan Fox-Rosellini at (305) 243-5198.

Thank you for your continued support and collaboration in our efforts.

Warmest regards,

Ralph L. Sacco MD, MS, FAHA, FAAN
Chairman Department of Neurology
Olemberg Family Chair in Neurological Disorders
Executive Director, EvelynNF. McKnight Brain Institute
Director, Clinical and Translational Science Institute
Senior Associate Dean for Clinical and Translational Science
Miller Professor of Neurology, Public Health Sciences, Human Genetics and Neurosurgery
Leonard M. Miller School of Medicine
Immediate Past President, American Academy of Neurology 2019-21

Enclosures

cc: Tatjana Rundek, MD, PhD
Susan Fox-Rosellini, MBA.
Amy Porter
Melanie A. Cianciotto

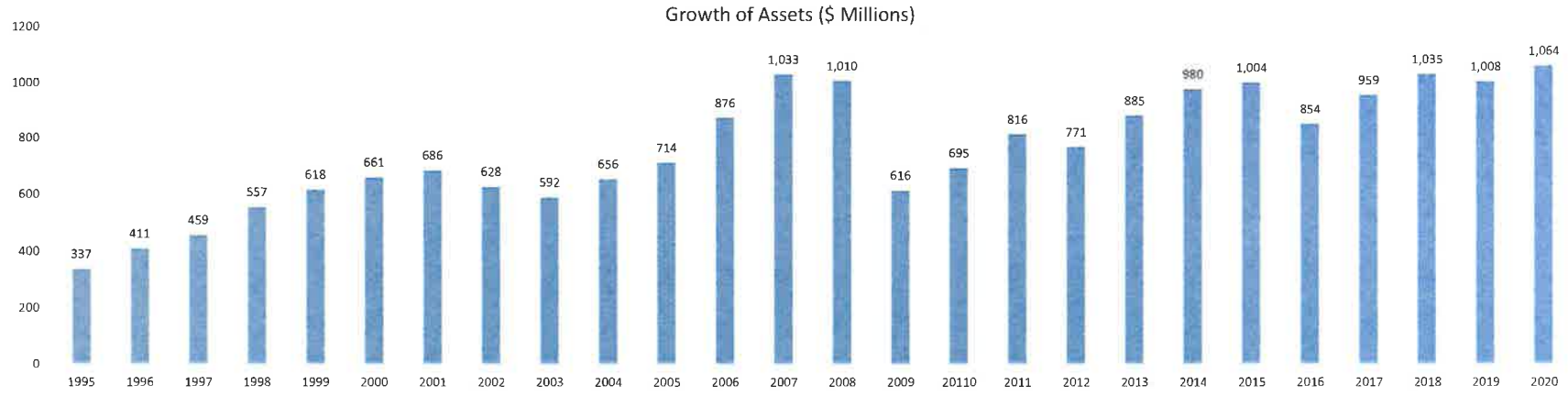
# UNIVERSITY OF MIAMI - ALL MANAGED ASSETS
## Performance Periods Ending: May 31, 2020

| Total Returns (Periods Greater Than 1 Year are Annualized) | | | | | | |
|---|---|---|---|---|---|---|
| **Growth Pool** | **Inception** | **1 Year (%)** | **3 Year (%)** | **5 Year (%)** | **7 Year (%)** | **10 Year (%)** |
| **Growth Pool Total Composite*** | **12/31/1990** | **2.2** | **3.8** | **4.0** | **5.1** | **6.6** |
| **Growth Pool Market Benchmark**** | **12/31/1990** | **4.4** | **4.4** | **4.8** | **6.0** | **7.7** |
| **Value (+/-)** | | **-2.2** | **-0.6** | **-0.8** | **-0.9** | **-1.1** |

| Inception-to-Date Growth Pool Risk/Return as of May 31, 2020 | | |
|---|---|---|
| **Growth Pool** | **15 Year Return** | **15 Year Standard Deviation** |
| **Growth Pool Total Composite** | **5.4** | **10.3** |
| **Growth Pool Market Benchmark** | **5.6** | **11.3** |

*Net of fee returns

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



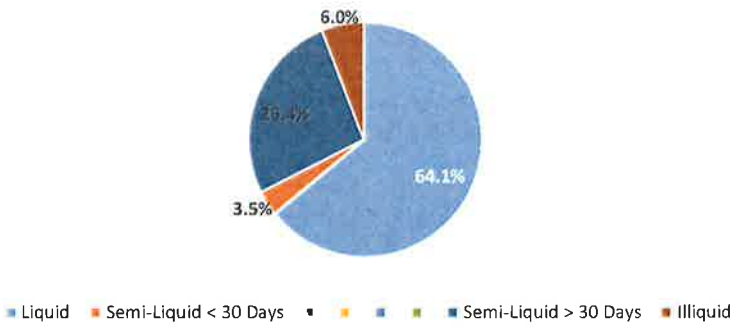
# UNIVERSITY OF MIAMI - GROWTH POOL

## Manager Structure - Market Values and Allocations Period Ending May 31, 2020

| Growth Pool | | | |
|---|---|---|---|
| Manager | Asset Class | Market Value ($) | % of Total Fund |
| **Large/Mid/All Cap Equity** | | **382,994,957** | **36.0%** |
| Vanguard Institutional Index (10/31/14) | US Large Cap Core Equity | 187,223,860 | 17.6% |
| Adage Capital Mgmt (6/30/04) | US Large Cap Core Equity | 101,767,550 | 9.6% |
| Columbia Dividend Income (2/2/17) | US Large Cap Core Equity | 24,982,091 | 2.3% |
| MFS Large Cap Value (2/2/17) | US Large Cap Value Equity | 17,466,153 | 1.6% |
| Earnest Partners Mid Cap (8/31/2018) | US Midcap Value Equity | 16,049,391 | 1.5% |
| Janus Enterprise Mid Cap Growth (2/2/17) | US Midcap Growth Equity | 16,403,731 | 1.5% |
| Vanguard Mid Cap (2/2/17) | US Midcap Core Equity | 19,102,181 | 1.8% |
| | | | |
| **Small Cap Equity** | | **55,062,559** | **5.2%** |
| Ariel Small Cap (8/31/2018) | US Small Cap Value Equity | 28,335,039 | 2.7% |
| Vanguard Small Cap (2/2/17) | US Small Cap Equity | 26,727,520 | 2.5% |
| | | | |
| **International Equity** | | **265,707,850** | **25.0%** |
| **Developed International Equity** | | **188,619,457** | **17.7%** |
| Silchester International (6/30/05) | Non-US DM/EM Value Equit | 55,085,201 | 5.2% |
| Vanguard Developed Markets (2/2/17) | Non-US DM Core Equity | 111,033,515 | 10.4% |
| GQG International (4/1/2020) | Non-US DM Core Equity | 22,500,741 | 2.1% |
| **Emerging Markets** | | **77,088,393** | **7.2%** |
| Neuberger Berman (9/30/2018) | Non-US EM Equity | 28,215,120 | 2.7% |
| Vanguard FTSE Emerging Markets (2/2/17) | Non-US EM Equity | 29,525,420 | 2.8% |
| WGI Emerging Markets (10/31/08) | Non-US EM Equity | 19,347,853 | 1.8% |
| | | | |
| **Total Alternative Investments** | | **149,297,598** | **14.0%** |
| **Credit Strategies** | | **32,918,577** | **3.1%** |
| Davidson Kempner (10/01/93) | Credit Strategy | 14,578,418 | 1.4% |
| Watershed Capital (1/01/08) | Credit Strategy | - | 0.0% |
| Regiment Capital (6/30/07) | Credit Strategy | 38,442 | 0.0% |
| Octagon CLO III (1/31/2019) | Credit Strategy | 2,333,994 | 0.2% |
| Shenkman Opp Crd (8/31/2018) | Credit Strategy | 15,967,723 | 1.5% |
| **Equity Long/Short** | | **59,142,620** | **5.6%** |
| Viking Global Equities III (11/30/10) | Equity Long/Short | 27,200,700 | 2.6% |
| Renaissance Institutional (8/31/17) | Equity Long/Short | 31,664,097 | 3.0% |
| Glenview Capital Management (2/01/06) | Equity Long/Short | 277,823 | 0.0% |
| **Multi-Strategy** | | **57,236,401** | **5.4%** |
| AQR Risk Parity (2/21/17) | Multi-Strategy | 29,641,483 | 2.8% |
| AQR Style Premia (12/14/16) | Multi-Strategy | 12,100,160 | 1.1% |
| Janus Multi-Strat (4/1/20) | Multi-Strategy | 15,494,758 | 1.5% |
| | | | |
| **Private Equity** | | **39,273,605** | **3.7%** |
| TIFF Partners IV (01/31/01) | Private Equity | 249,835 | 0.0% |
| TIFF Partners V (04/30/04) | Private Equity | 158,266 | 0.0% |

| Manager | Asset Class | Market Value ($) | % of Total Fund |
|---|---|---|---|
| **Private Equity (continued)** | | | |
| TIFF Partners 2006 (04/30/06) | Private Equity | 251,903 | 0.0% |
| TIFF Partners 2007 (01/31/07) | Private Equity | 1,361,081 | 0.1% |
| TIFF Partners 2008 (01/31/08) | Private Equity | 3,690,928 | 0.3% |
| ESG Fieldcrest Cannon | Private Equity | 2,500 | 0.0% |
| OCM Principal Opportunities IV (12/31/06) | Private Equity | 63,081 | 0.0% |
| Denham Commodity Fund V (6/30/08) | Private Equity | 487,355 | 0.0% |
| Clayton, Dubilier & Rice Fund IX (5/31/2014) | Private Equity | 6,701,313 | 0.6% |
| Carlyle Strategic IV (11/30/16) | Private Equity | 2,641,916 | 0.2% |
| KKR Americas XII (9/30/16) | Private Equity | 5,390,487 | 0.5% |
| HIG Advantage Buyout (4/30/18) | Private Equity | 732,465 | 0.1% |
| Carlyle Partners VII (12/31/2018) | Private Equity | 3,356,178 | 0.3% |
| Apollo Investment Fund IX (3/15/2019) | Private Equity | 1,297,554 | 0.1% |
| Silver Lake Partners (6/30/2018) | Private Equity | 7,121,483 | 0.7% |
| General Atlantic (12/31/19) | Private Equity | 716,431 | 0.1% |
| CINVEN Fund VII (1/31/19) | Private Equity | 1,157,553 | 0.1% |
| Broadway Strategic (6/30/19) | Private Equity | 1,029,628 | 0.1% |
| Spark Capital (5/31/19) | Private Equity | 216,666 | 0.0% |
| Spark Growth III (2/29/20) | Private Equity | 300,000 | 0.0% |
| Vista Equity Partners (6/30/2018) | Private Equity | 2,346,982 | 0.2% |
| | | | |
| **Private Real Assets** | | **35,282,270** | **3.3%** |
| WCP Real Estate Fund I (7/31/06) | Private Real Assets | 97,404 | 0.0% |
| WCP Real Estate Fund II (11/30/08) | Private Real Assets | 1,280,504 | 0.1% |
| Metropolitan Real Estate Fund (9/30/06) | Private Real Assets | 183 | 0.0% |
| SRI Nine REIT (3/31/08) | Private Real Assets | 623,730 | 0.1% |
| LBA Realty IV (10/31/09) | Private Real Assets | 1,099,681 | 0.1% |
| Warburg Energy (5/31/14) | Private Real Assets | 5,799,813 | 0.5% |
| Ishares Inf. Global ETF (6/30/2018) | Public Real Assets | 13,755,167 | 1.3% |
| ITE Rail (1/31/20) | Private Real Assets | 5,865,946 | 0.6% |
| JPMorgan GTIF (2/29/20) | Private Real Assets | 5,005,760 | 0.5% |
| GS Renew PWR LLC (8/31/2018) | Private Real Assets | 1,754,082 | 0.2% |
| | | | |
| **Total Fixed** | | **132,188,160** | **12.4%** |
| CIFC Sr. Secured Corp Fund (8/31/2018) | Corporate Bonds | 25,105,461 | 2.4% |
| PIMCO Income Fund (7/24/17) | Aggregate Bonds | 21,938,215 | 2.1% |
| Prudential US High Yield (2/2/17) | High Yield Bonds | 20,008,199 | 1.9% |
| SSGA 1-3 YR UST (7/31/19) | Short Duration Bonds | 45,785,714 | 4.3% |
| SSGA US Agg (7/31/19) | Aggregate Bonds | 19,350,571 | 1.8% |
| | | | |
| **Cash** | | **4,621,486** | **0.4%** |
| | | | |
| **Total Managed Assets** | | **1,064,428,485** | **100.0%** |
| **Allocation to Index or Enhanced Index Strategies** | | | |
| | | **Growth Pool** | |
| **% of Total:** | | **41.2%** | |

## UNIVERSITY OF MIAMI - GROWTH POOL
### Portfolio Liquidity Restrictions: Based on Market Value



# UNIVERSITY OF MIAMI - GROWTH POOL

## Inception to Date Performance vs. Relevant Benchmark(s)

## Periods ending - May 31, 2020

Net of Fees

| Total Returns (%) - Annualized if Greater than 1 | ROR | Value Added (+/-) | Years |
|---|---|---|---|
| **Large/Mid/All Cap Equity** | | | |
| Vanguard Institutional Index (9/30/14) | 9.67 | -0.53 | 5.7 |
| S&P 500 | 10.2 | | 5.7 |
| Adage Capital Mgmt (6/30/04) | 11.28 | 2.57 | 15.9 |
| S&P 500 | 8.71 | | 15.9 |
| Earnest Partners Mid Cap (8/31/2018) | 3.91 | 5.02 | 1.8 |
| Russell Midcap | -1.11 | | 1.8 |
| Columbia Dividend Income (2/2/17) | 9.75 | -1.32 | 3.3 |
| Russell 1000 Value | 11.07 | | 3.3 |
| MFS Large Cap Value (2/2/17) | 5.74 | 2.7 | 3.3 |
| Russell 1000 Value | 3.04 | | 3.3 |
| Janus Enterprise Mid Cap Growth (2/2/17) | 13.89 | -1.09 | 3.3 |
| Russell Midcap Growth | 14.98 | | 3.3 |
| Vanguard Mid Cap (2/2/17) | 7.02 | -0.03 | 3.3 |
| CRSP MidCap Index | 7.05 | | 3.3 |
| **Small Cap Equity** | | | |
| Ariel Small Cap (8/31/2018) | -11.62 | 5.38 | 1.8 |
| Russell 2000 Value | -17 | | 1.8 |
| Vanguard Small Cap (2/2/17) | 4.13 | 0.07 | 3.3 |
| CRSP US Small Cap TR Index | 4.06 | | 3.3 |
| **Developed International Equity** | | | |
| Silchester International (6/30/05) | 6.35 | 2.42 | 14.9 |
| MSCI EAFE Value ND | 3.93 | | 14.9 |
| GQG International (4/1/20) | 12.5 | 1.4 | 0.2 |
| MSCI ACWI ex US | 11.1 | | 0.2 |
| Vanguard Developed Markets (10/31/2014) | 2.1 | -0.23 | 5.6 |
| FTSE Dev All Cap ex US | 2.33 | | 5.6 |
| **Emerging Markets** | | | |
| Neuberger Berman (9/30/2018) | -3.59 | 1.06 | 1.7 |
| MSCI Emerging Markets ND | -4.65 | | 1.7 |
| Vanguard FTSE Emerging Markets (2/2/17) | 2.26 | -0.63 | 3.3 |
| MSCI Emerging Markets ND | 2.89 | | 3.3 |
| WGI Emerging Markets (10/31/08) | 7.5 | 5.34 | 1.6 |
| MSCI Emerging Markets ND | 2.16 | | 1.6 |
| **Credit Strategies** | | | |
| Davidson Kempner (10/01/93) | 8.33 | 0.05 | 26.7 |
| HFR Event-Driven | 8.28 | | 26.7 |
| Shenkman Opp Crd (8/31/2018) | 4.8 | 9.83 | 1.8 |
| HFRI ED: DIST RS (USD) | -5.03 | | 1.8 |
| **Equity Long/Short** | | | |
| Viking Global Equities III (11/30/10) | 10.45 | 1.89 | 9.5 |
| MSCI World Index | 8.56 | | 9.5 |
| Renaissance Institutional (8/31/17) | -0.98 | -5.28 | 2.8 |
| MSCI ACWI ND | 4.3 | | 2.8 |
| **Multi-Strategy** | | | |
| Janus Multi-Strat (4/1/20) | 3.3 | 3.29 | 0.2 |

| Total Returns (%) - Annualized if Greater than 1 | ROR | Value Added (+/-) | Years |
|---|---|---|---|
| FTSE 1-Month T-Bill | 0.01 | | 0.2 |
| AQR Risk Parity (2/21/17) | 4.56 | | 3.3 |
| 60 MSCI AC WORLD/40 BB Barclays U.S. Aggrega | 6.17 | | 3.3 |
| AQR Style Premia (12/14/16) | -10.11 | -11.73 | 3.5 |
| ICE ML 3M US Treasury Bill | 1.62 | | 3.5 |
| Fixed Income | | | |
| SSGA US Agg (7/31/19) | 6.33 | -1.49 | 0.8 |
| BB Barclays U.S. Aggregate | 7.82 | | 0.8 |
| Pimco Income Fund (7/24/17) | 2.63 | -2.54 | 2.9 |
| BB Barclays U.S. Aggregate | 5.17 | | 2.9 |
| Prudential US High Yield (2/2/17) | 4.15 | 0.47 | 3.3 |
| BB Barclays U.S. Corporate High Yield | 3.68 | | 3.3 |
| CIFC Sr. Secured Corp Fund (8/31/2018) | 0.24 | 0.46 | 1.8 |
| S&P/LTSA Lev Loan Index | -0.22 | | 1.8 |
| SSGA 1-3 YR UST (7/31/19) | 3.66 | -0.56 | 0.8 |
| BB Barc US Agg Treasury 1-3 Yrs | 4.22 | | 0.8 |

McKnight053120

Summary

# Evelyn F. McKnight Brain Institute's Endowments
# at the Miller School of Medicine
# Market Value Analysis
# 05/31/2020

## ***2002 Gift & Match***

| | |
|---|---|
| McKnight Contribution | $5,000,000 |
| UM Match | 5,050,913 |
| Transfers from Other University Funds | 1,362,153 |
| Investment Return | 6,562,640 |
| Distributions for Spending | (6,603,157) |
| 05/31/20 Endowment Balance | $11,372,549 |
| Unmatched Balance | $0 |

## ***2014 Gift & Match***

| | |
|---|---|
| McKnight Contribution | $2,000,000 |
| UM Match | 2,000,000 |
| Transfers from Other University Funds | 0 |
| Investment Return | 946,061 |
| Distributions for Spending | (768,525) |
| 05/31/20 Endowment Balance | $4,177,536 |
| McKnight Foundation Pledge Balance | $0 |

McKnight053120
Annual

**University of Miami**
**Evelyn F. McKnight Brain Institute's Endowments**
**Summary Analysis at Market Value**
**June 1, 2019 - May 31, 2020**

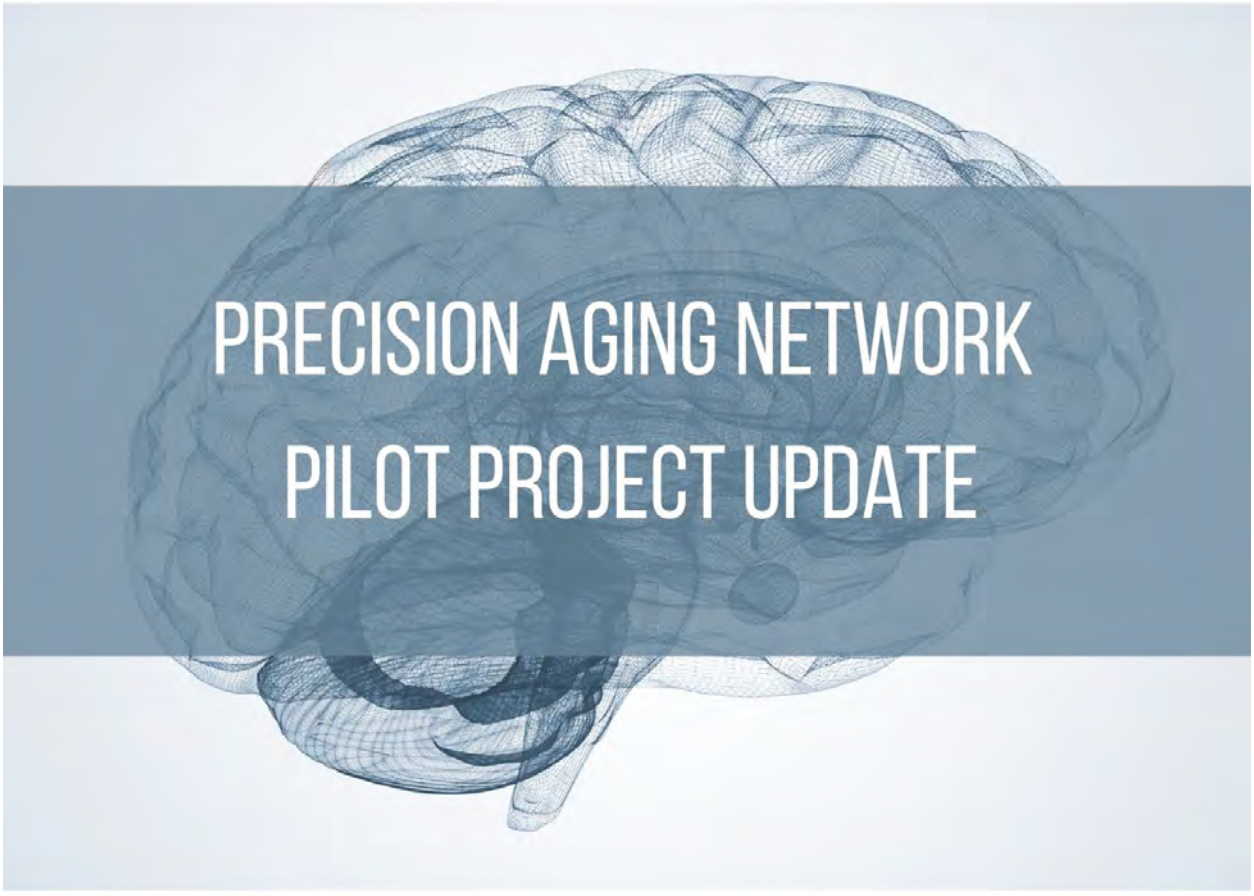
## *2002 Gift & Match*

| | Evelyn F. McKnight 262080 | F.Peterson/ McKnight 262293 | Schoninger Professorship in Neurology 262453 | Schoninger Neuropsychology Clinic 262454 | Other sources | Total |
|---|---|---|---|---|---|---|
| Beginning Balance at Market, 6/1/19 | $7,072,945 | $1,094,251 | $993,576 | $2,483,938 | $0 | $11,644,710 |
| Investment Return | 148,689 | 23,004 | 20,887 | 52,218 | | 244,797 |
| Distributions for Spending | (313,998) | (48,579) | (44,109) | (110,273) | | (516,960) |
| Transfers from other University funds | | | | | | 0 |
| Matching gifts | | | | | | 0 |
| Ending Balance at Market, 05/31/20 | $6,907,635 | $1,068,676 | $970,354 | $2,425,883 | $0 | $11,372,549 |

## *2014 Gift & Match*

| | Schoninger Professor in Memory Disorders 262471 | Evelyn F. McKnight Endowed Chair 262490 | | | | Total |
|---|---|---|---|---|---|---|
| Beginning Balance at Market, 6/1/19 | $2,034,659 | $2,242,851 | $0 | $0 | $0 | $4,277,510 |
| Investment Return | 42,773 | 47,150 | | | | 89,923 |
| Distributions for Spending | (90,327) | (99,570) | | | | (189,897) |
| Transfers from other University funds | | | | | | 0 |
| Matching gifts | | | | | | 0 |
| McKnight Foundation gifts | | | | | | 0 |
| Ending Balance at Market, 05/31/20 | $1,987,103 | $2,190,430 | $0 | $0 | $0 | $4,177,536 |

# APPENDIX VII



## PRECISION AGING NETWORK PILOT PROJECT UPDATE

# Precision Aging Network Pilot Project Update

We received funding to conduct a pilot study with the McKnight Brain Institute at the University of Arizona (UA) on a multi-site collaborative project, the ***Precision Aging Network: Closing the Gap Between Cognitive Healthspan and Human Lifespan***. (The budget for the study is included in **Appendix VI**.) The Precision Aging Network led by Dr. Carol Barnes is a U19 application to the NIA with an objective to develop in-depth profiles of risk for brain and cognitive function using a combination of demographic and lifestyle factors; psychosocial measures; biometric measures; physical and sensory measures; and markers of brain function derived from sweat, blood, cerebrospinal fluid, neuroimaging and genetics. The plan is to use these functional markers to predict cognitive maintenance or decline in prospective follow-up across four domains of cognition – memory, executive function, visuospatial functioning and processing speed. The findings of these proposed studies would contribute to our understanding of optimal brain performance and healthy and unhealthy cognitive and brain functioning using big-data approaches and precision medicine concepts. This research program addresses several goals within the NIA's strategic plan for aging research, and will contribute to the development of interventions to maintain health, well-being and function to prevent or reduce the burden of AD. The Network is comprised of seven Cores and four research Projects. UM will participate in the Network Clinical Core (Dr. Rundek is Core Co-Director with Dr. Ryan at UA and Dr. Levin is Co-Investigator), in the Imaging Core (Dr. Rundek) and Recruitment Core (Dr. Sacco). The structure of the Network includes an executive committee, a steering committee and an external advisory committee. The grant was reviewed, and resubmission was recommended after more pilot data became available.

Therefore, this pilot data will be critical in the success of this collaborative U19. We began the pilot by organizing a multi-faceted team at our MBI to brainstorm the best way to conduct a pilot during the COVID-19 Pandemic. We have conducted a series of internal zoom meetings as well as zoom meetings with our UA collaborators. We decided to focus on MindCrowd recruitment to obtain pilot data needed for the resubmission of the U19 grant. We have highlighted the specifics below. We thank the McKnight Brain Research Foundation for allowing us this opportunity to be part of the efforts to gather these important pilot data.

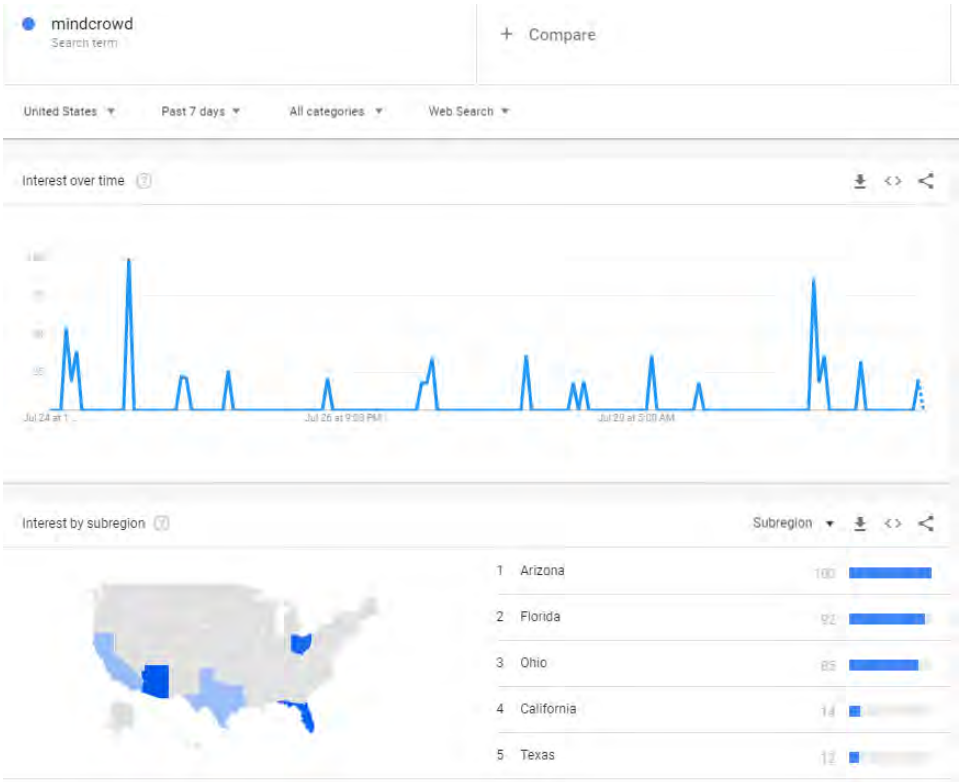
As part of our collaboration on the "Precision Aging Network Pilot Study," we set out to recruit participants to the MindCrowd website. MindCrowd is an easy-to-use web-based cognitive testing tool (www.mindcrowd.org) that has already reached over 135,000 individuals. MindCrowd was developed in 2013 with an objective to explore electronic cohort recruitment as a way to increase the size of studies that utilize cognitive testing. The rationale for this approach was that many cognitive tasks had already been "computerized" – typically to be performed by a participant while in an MRI machine – and that the barrier to conducting large scale testing via the Internet was therefore very low. The MindCrowd site consists of a main landing page that describes the study and investigators, an electronic consent form, a few demographic questions about the participant, a simple visual reaction time task (svRT) consisting of five trials whereby the participant must react as quickly as possible following the appearance of a pink sphere on the computer screen, a paired associates learning task (PAL) consisting of three rounds of 12

modernized model for broad and deep characterization of the drivers of brain aging and cognitive decline in individuals, extending knowledge in existing AD Center networks to empower data rich comparisons between normative aging and AD.

The University of Miami McKnight Brain Institute (UM-MBI) team employed various recruiting outlets in both English and Spanish to raise awareness of MindCrowd and to increase recruitment and traffic to the *mindcrowd.org* website. These included: 1) We mailed 100,00 IRB approved postcards to registered voters in the greater Miami-Dade area to invite them to participate in MindCrowd; 2) We launched 50,000 postcard adapted emails to a general consumer list in the 30 mile radius of our MBI with an "echo"; 3) We reached out to current and former research study participants by phone; 4) We promoted the information to neighborhood community centers and high occupancy resident buildings and communities; 5) We reached out to UM faculty, clinicians, students, residents and patients along with posting on UM Neurology and UM-MBI web channels; 6) We advertised on La Poderosa 670 AM, a local Latino radio station and on *Univision*, a local television station in Spanish; and 7) We used traditional channels of social media outreach as well as less conventional ones such as memes, *WhatsApp* and *Nextdoor* which are explained below.

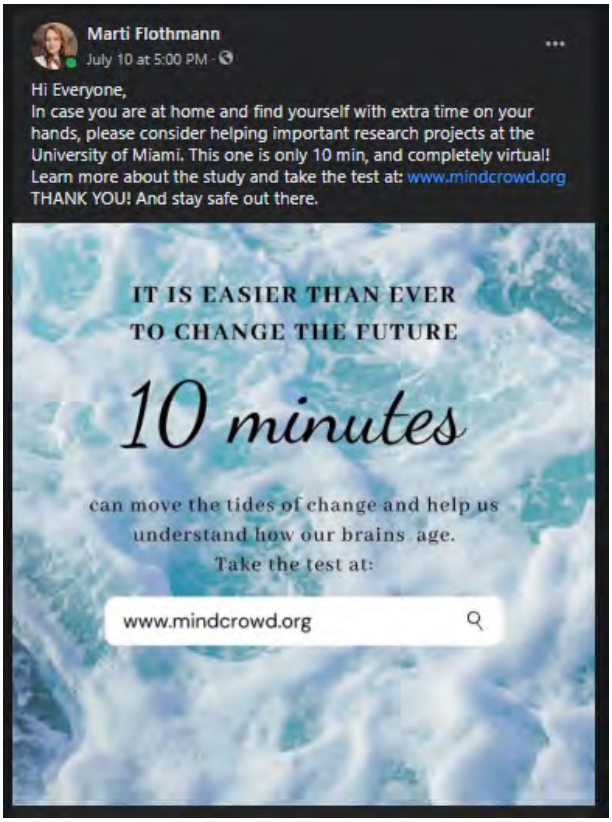
Our strategic use of social media outreach yielded the most measurable and lucrative results. Using *Google Trends* we searched for current trending topics to make our outreach more engaging. We also checked the popularity of any search term by location. After two months of outreach, Florida's interest in MindCrowd showed a significant upward trend as notated in the figure below. We have shown that interest in participating in MindCrowd is sustainable and can gain a wide-spread momentum as our outreach efforts expand further.

Google Trending Charts

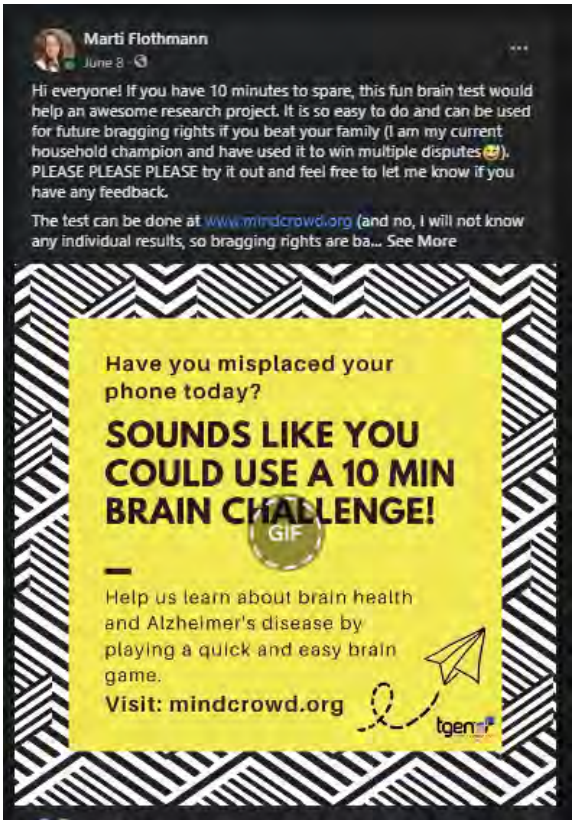


We also used meme marketing through 9gag and other strategies that can reach larger populations, while posting regularly on mainstream social media sites like *Facebook*, *Twitter*, *Instagram* and *WhatsApp*. See Meme examples below.

Meme 1.




Meme 2.




We posted information about MindCrowd using the *Nextdoor* App, a forum for individual locales to post events and share information specific to each community.

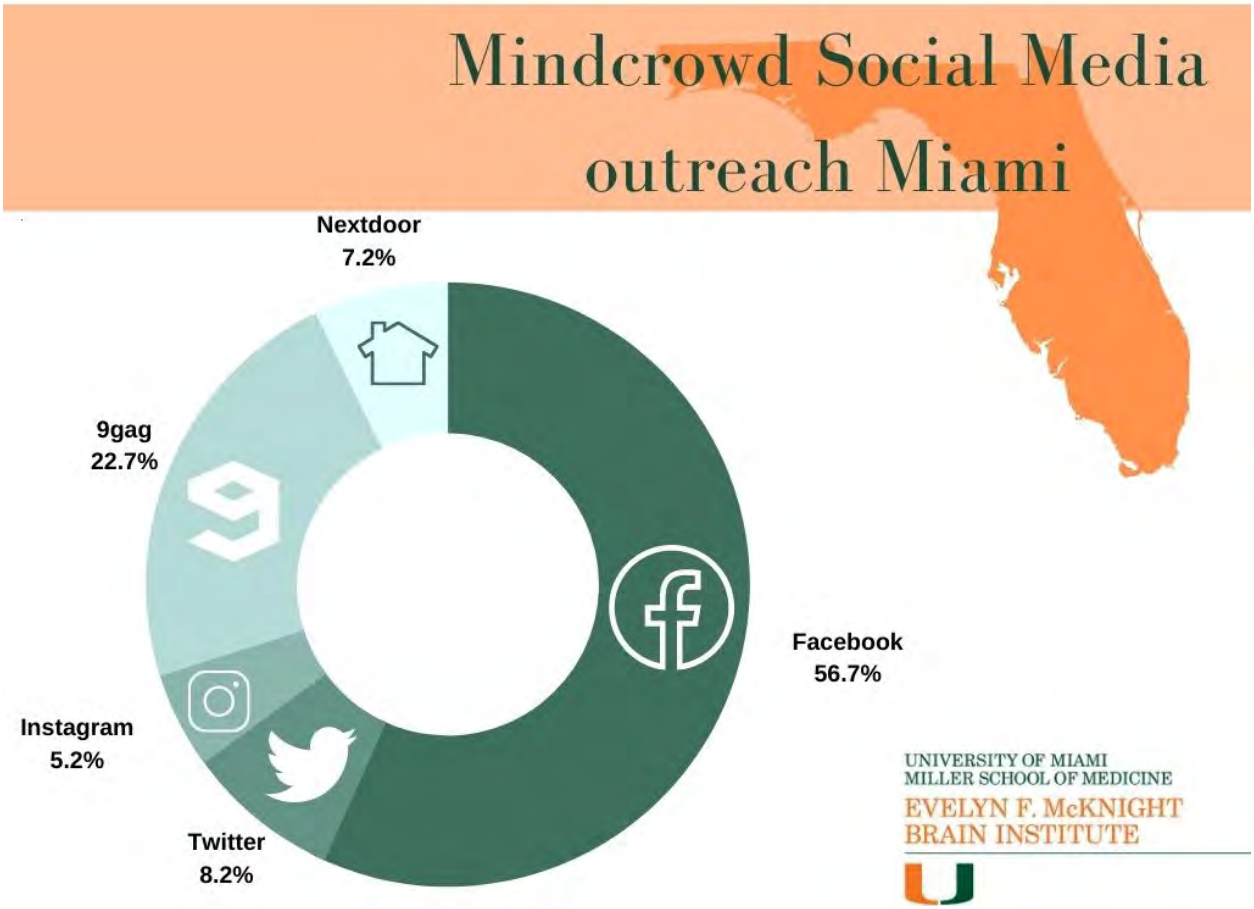
We created a *YouTube* channel to showcase UM McKnight Brain Institute presentations via short video clips on brain and relevant health related topics that are easily digestible. Once up and running, this station will serve as an archive to store video content. Our aim is to refer viewers to MindCrowd during each segment.

We tracked MindCrowd related social media posts and conversations to gauge the effectiveness of the outreach efforts and types. When we got spikes in MindCrowd enrollment, we sought to identify the sources and timelines that led to the increases.

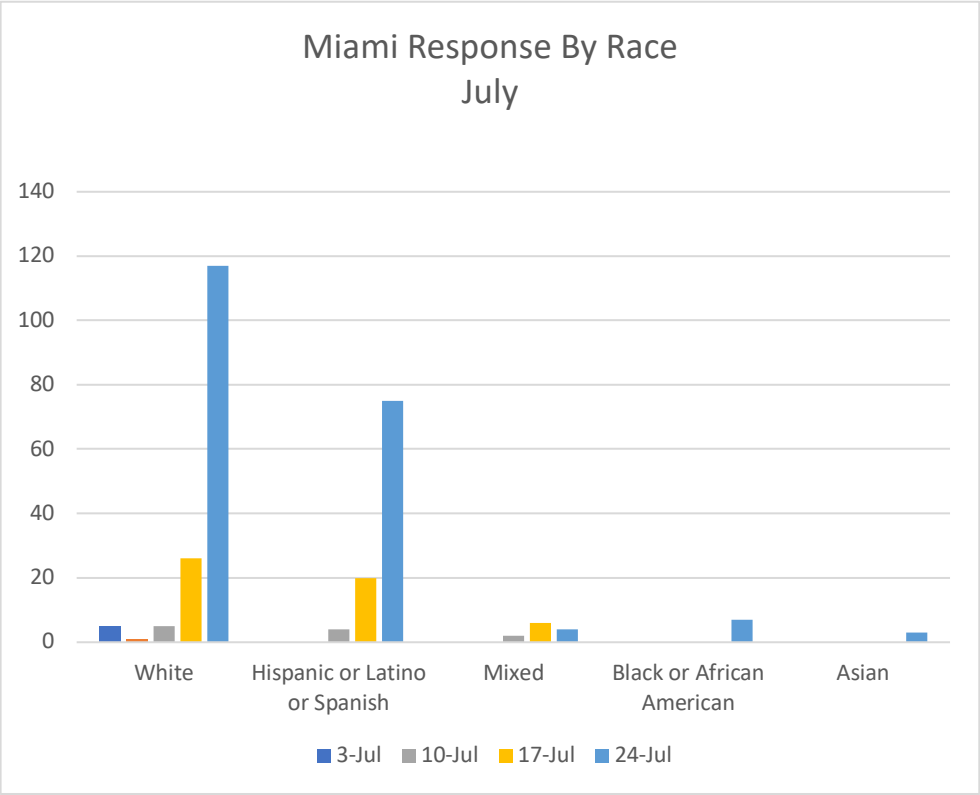
We successfully generated multiple MindCrowd related posts weekly, and sparked awareness of and conversations about MindCrowd among chatrooms, families, workplaces, community centers, aging residences and the University of Miami medical campus.

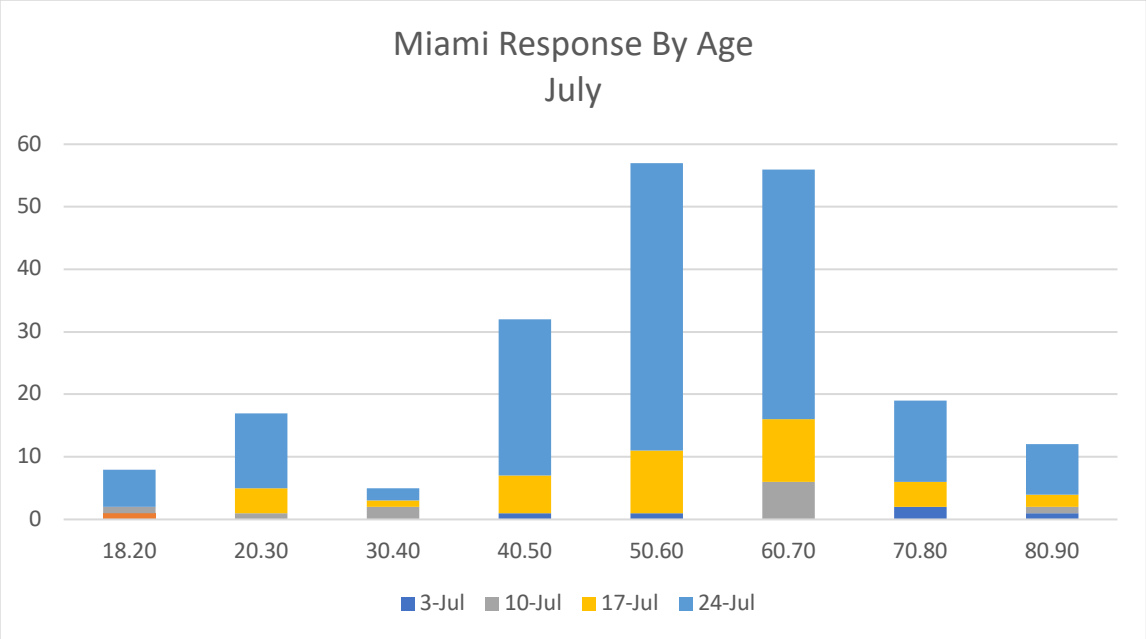
We have presented these results to the Precision Aging Network leadership at UA and included them in the U19 resubmission.

Overview of Social Media Outreach by Type



# July MindCrowd Website Traffic



# Communication Efforts to Boost Outreach
# University of Miami McKnight Brain Institute

1. Social
   - Facebook – Neuro Dept./Personal pages
   - Twitter
   - Tumblr
   - Pinterest
2. Neighborhood Channels
   - Nextdoor
3. Miami-Dade County
   - Registered Voter List – Mail Postcards
   - Emails
   - Mayor's Initiative on Aging
4. Community
   - Condo Towers – Coconut Grove -700 Units
   - Latino Center on Aging
   - Senior L.I.F.T. Center - Email List Serve
   - Pinecrest Community Center Bulletin & Newsletter
   - Retirement Communities (4)
5. Media
   - Radio
   - Univision
6. University of Miami
   - McKnight Website
   - Neurology Clinics - Faculty, Patients & Caregivers
   - Center for Cognitive Neuroscience and Aging
   - HIHG Researchers & Website
7. McKnight Study Participants
   - MindCrowd information
   - Alzheimer's Event Flyers

1

# Communication Efforts to Boost Outreach
# University of Miami McKnight Brain Institute
## Neurology Facebook

June 2020
A week post

Outcome:
- Reach 200+
- 6000+ followers



2

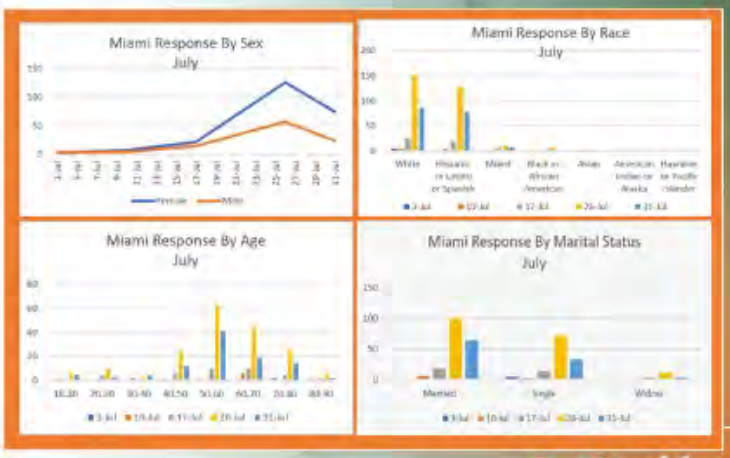
## MindCrowd Bilingual Postcard

July 2020
Dropped on July 14-15
Estimated receipt between July 20-28

- 100,000 pieces sent via direct bulk mail
- Sent to Miami-Dade County registered voters list
- To ages 40+
- Within a 30-mile radius
- Minimum income of $30,000

Outcome

- Increase in visitors/registrations July 26-31




## Email Campaign

July/August 2020

- Email sent to 90,000 consumers (45,000 male and 45,000 female)
- Within 30-mile radius
- Incomes of $30,000 - $100,000

Outcome

- Total rate of opening: 13% (10% industry average)
- July mailing: 1.8% (1,619) clicks
- August mailing: 1.4% (1,298) clicks

  (1% clicks is industry average)

## Communication Efforts to Boost Outreach
## University of Miami McKnight Brain Institute

***The Latino Center on Aging (LCA)**, funded in 1992 seeks to advocate for improved services for Latino seniors and educate seniors about resources available to them.*

Activity:

- Disseminated our information to their South Florida members (over 200K seniors)
- Appearances on their radio program
- Presentations at Virtual National Conference

5

## Communication Efforts to Boost Outreach
## University of Miami McKnight Brain Institute

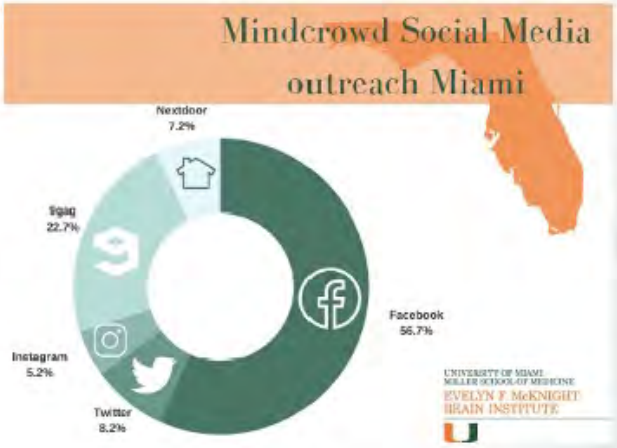
Social Media Activity:

- Local Facebook groups
- Continue to look for more groups who are willing to share posts about MindCrowd.
- WhatsApp groups, Instagram, Nextdoor, and other personal social media platforms.

Facebook in (Spanish & English)

- Lifestyle Miami
- USF medical sciences master's group 2018
- Miami, FL group
- Cubans and Hispanics who grew up in Miami during the 60's and 70's
- Cubanos en Miami
- South Florida Events, Activities and Places
- USF Masters in Medical Sciences
- Venezolanos para el Doral en Miami
- Friends & Family
- Instagram post to friends & family - using Alzheimer's hashtags

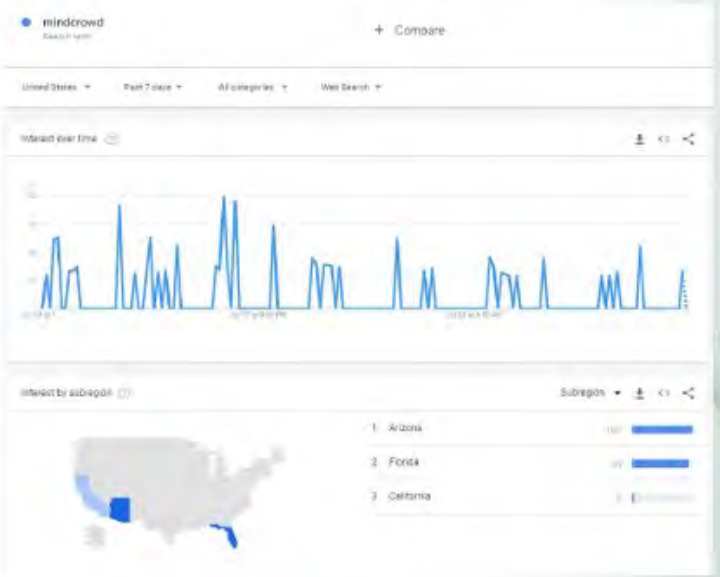
## Social Media Outreach Overview




- January - June, 2020 Miami registration was 191, about 31 responses per month
- July had 388 responses, increasing total to 579
- In July a 1,200% monthly increase as a result of social media outreach

UHealth
UNIVERSITY OF MIAMI HEALTH SYSTEM

## Tracking Outcomes: Google Trends

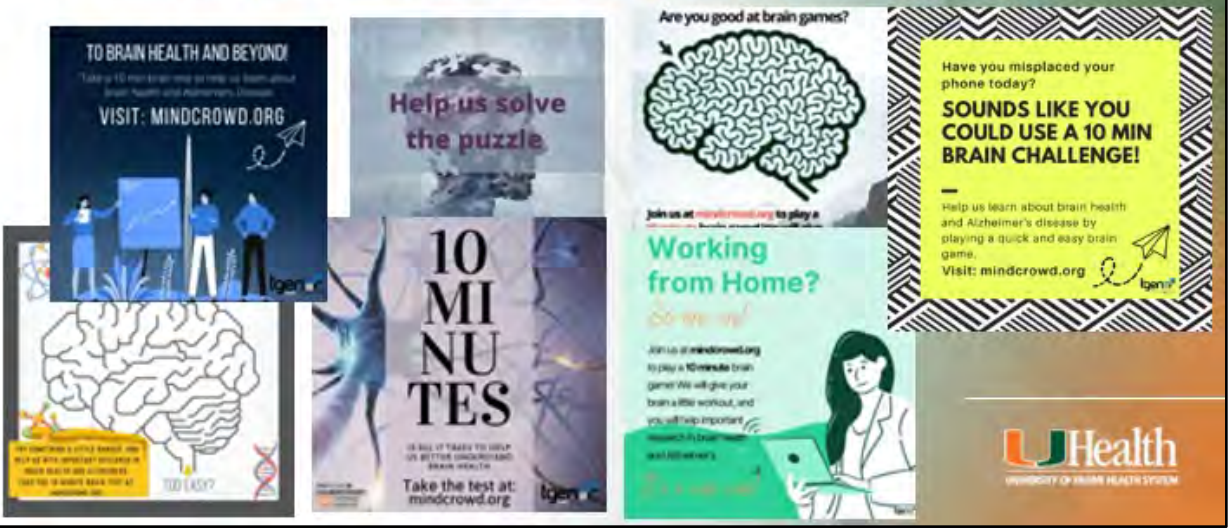



- Searched for current trending topics
- Checked the popularity of search term by location
- In 2 months Florida showed significant upward trend

UHealth
UNIVERSITY OF MIAMI HEALTH SYSTEM

## Communication Efforts to Boost Outreach
## University of Miami McKnight Brain Institute

**Some Examples of Social Media Posts Being Used to promote MindCrowd**




UHealth

## Communication Efforts to Boost Outreach
## University of Miami McKnight Brain Institute






### And lastly, why not have some fun with it?

In an attempt to branch out a bit, we have decided to create some memes! Who hasn't gotten a funny picture with some text that gave them a chuckle? It turns out, that we are not the only ones. Meme marketing is something that companies have been trying to break into for many years. Some with great success and others with utter failure. Brands like Netflix, Apple, and many others have tried to create the perfect meme, because if you go viral, you have a good chance of having your post seen by millions. And even if you don't become the next viral meme, it is free advertising that takes very little effort and puts a smile on people's faces.

Using **Google Trends**, we can see the search popularity of just about anything in the world. This allows us to search the popularity of specific memes and see what's trending. For instance, we can see when the notorious #birdbox meme came about, or when good old grumpy cat reached his peak (Dec. 2012 for those who are curious, and he got one last spike in May of 2019 when he passed away). Using such information can help us see what people like and try to use memes that are already popular in sharing MindCrowd (as well as throwing in some classics).



UHealth

## The University of Miami McKnight Brain Institute:

Multiple outreach strategies in English and Spanish

- Direct mailing
- Email
- Phone calls/emails to research study participants
- Social media
- Radio, Univision
- Mayor's Initiative on Aging
- Latino Center on Aging
- UM and McKnight Website

Tracking

- Google Trends to find trending topics
- MindCrowd
- Website registrations

# APPENDIX VIII

## DRAFT AGENDA - 12TH ANNUAL MCKNIGHT BRAIN RESEARCH FOUNDATION INTER-INSTITUTIONAL MEETING

McKNIGHT BRAIN INSTITUTES

University of Alabama at Birmingham
University of Arizona
University of Florida
University of Miami

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

## 12th Annual Inter-Institutional Meeting

**Evelyn F. McKnight Brain Institutes**

**McKnight Brain Research Foundation and University of Miami MBI**

**April 28-29, 2021**

## POWER OF COLLABORATION AND TEAM SCIENCE

# DRAFT

## Wednesday, April 28, 2021

1:00pm - 1:30pm **Welcome**

**Ralph L. Sacco, M.D.,** Executive Director of U Miami MBI & Chair of Neurology
**Tatjana Rundek, M.D.,** Scientific Director of U Miami MBI

**Michael L. Dockery, M.D.,**
**Chair, Board of Trustees, McKnight Brain Research Foundation**
***Building on MBRF History to Forge the Future***

**Introduction to Program and Meeting Overview**
**Tatjana Rundek, M.D., Ph.D.**
Scientific Director of Evelyn F. McKnight Brain Institute

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**SESSION I** **INTER-INSTITUTIONAL PROJECTS AND COLLABORATIONS**
**1:30pm - 3:30pm** **Moderators: Ronald Lazar, Ph.D. (UAB) and Tatjana Rundek, M.D., Ph.D. (UM)**

**1:30pm - 2:30pm** **McKnight Brain Aging Registry (MBAR), Moderator: Ronald Lazar, Ph.D.**
3 presentations (15 min each) + 15 min discussion at the end

1:30pm - 1:45pm **Bonnie Levin, Ph.D. (UM): *Cognitive and Social Determinants of Health***

1:45pm - 2:00pm **Gene E. Alexander, Ph.D. (UA): *Physical Activity and Brain Health***

2:00pm - 2:15pm **Kristina M. Visscher, Ph.D. (UAB) - *Resting State***

2:15pm - 2:30pm Discussion

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| **2:30pm - 3:30pm** | **MBRF Cognitive Aging and Memory Interventional Core Pilot Projects**<br>**Moderator: Bonnie Levin, Ph.D.**<br>3 pilot presentations (10 min each), 5 min discussion after each presentation |
| 2:30pm - 2:45pm | **John B. Williamson, PhD (UF, UA):** *Transcutaneous Vagal Nerve Stimulation and Cognitive Training to Enhance Cognitive Performance in Healthy Older Adults* |
| 2:45pm - 3:00pm | **Natalie Ebner, PhD (UF, UM, UA):** *Detecting Deceptive Information in Scamming Paradigms: A Training Intervention* |
| 3:00pm - 3:15pm | **Dawn Bowers, PhD (UF, UA):** *Transcranial Near Infrared Stimulation (NIR-NIH)* |
| 3:15pm - 3:30pm | **Announcement of new MBRF Pilot awards**<br>**Bonnie Levin, Ph.D. and Ronald Lazar, Ph.D.** |
| 3:30pm - 3:45pm | Break |

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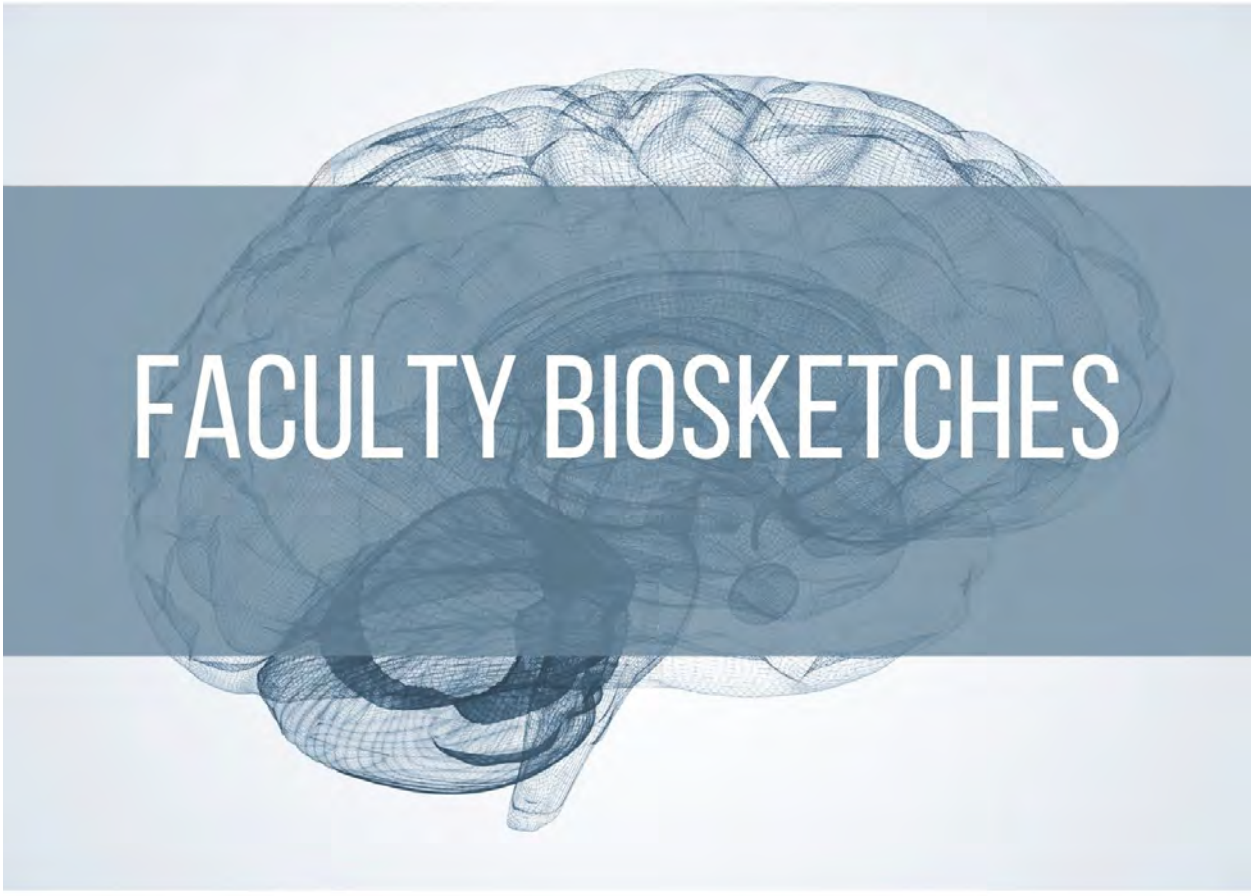
| **SESSION II**<br>**3:45pm - 5:05pm** | **COGNITIVE AGING - CLINICAL AND TRANSLATIONAL INTERVENTIONS AND COLLABORATIONS**<br>**Moderator: Thomas C. Foster, Ph.D. (UF)**<br>4 talks (15 min each) with 5 min discussion |
| 3:45pm - 4:05pm | The *Precision Aging Network*<br>**Lee Ryan, Ph.D. (UA)** |
| 4:05pm - 4:25pm | *Exercise for Brain Health*<br>**Joyce Gomes-Osman, P.T., Ph.D. (UM)** |
| 4:25pm - 4:45pm | *The Multi-Site ACT Study*<br>**Adam Woods, PhD (UF)** |
| 4:45pm - 5:05pm | *Nonpharmacological Approaches for Improving Cognitive Decline in Aging*<br>**Sara Burke, Ph.D. (UF)** |

# APPENDIX IX



# FACULTY BIOSKETCHES

## 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

I am a medical physicist with training and substantial expertise in MRI data acquisition and analyses. I graduated from the medical physics program from the University of Chicago with focus on diagnostic imaging. Initially my work involved x-ray angiography but soon after I transition to MRI. I was fascinated by the wealth of information that can be obtaining using different MRI modalities. My first work was to integrate XR Angiography and MRI angiography (1). I then expanded from static to dynamic imaging focusing on measuring flow and motion. We were one of the first group to apply velocity imaging both to blood flow and cerebrospinal fluid (CSF) flow. We established that the net transcranial blood flow is the driving force for the cranio-spinal CSF pulsation which lead to the development of a novel methodology to noninvasively measure intracranial pressure by MRI (MRICP) (2). I was a Principal Investigators on a number of NIH projects to demonstrate the feasibility of the MRICP method and its application to Chiari Malformations. We quickly realized that brain morphology and hemodynamics are both needed to understand the pathology were studied, Chiari Malefaction (3). (WE published 8 papers on CMI as a results of the data we collected during this project). We then expanded our research focus on brain parcelation and were the first group to tailor advanced brain parcelation method to automatically quantify the posterior cranial fossa volumetry for the diagnosis of Chiari Malformation. After relocating to Miami I became a member of the McKnight institute for brain research focusing our work toward aging and trying to answer the question about the causal relationship between age related reduction in brain perfusion and tissue in volume loss. We focus more on the brain hemodynamics using MRI technologies such as Arterial Spin Labeling in conjunction with phase contrast. Our current goal is to develop a tool that will provide a quantitative map of the perfusion regulation by the small vessels in the brain in different brain regions. Such a tool is badly needed to better understand the process of aging and wide range of neurological problems associated with brain volume loss.


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, 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.
3. 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.

    a. 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.
    b. 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.
    c. 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.
    d. 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. 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.

3. 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 1$^{st}$ 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)

4. 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. Additional Information: Research Support and/or Scholastic Performance**

1 R01HL145165-01 (PI:Goldberger) 02/15/19-01/31/22
Novel medical adjunctive therapy to catheter ablation for atrial fibrillation

20A19 LF DOH Alperin(PI) 03/2020-02/2023
Lifestyle Stressors of Hippocampus and AD Related Brain Regions: Potential for Intervention

8AZ22 FL DOH Alperin(PI) 03/2018-02/2020
Cardiovascular and Lifestyle Stressors of Hippocampus and Alzheimer's Disease related brain regions.

NNX16AG96G NASA Alperin(PI) 03/01/16-09/28/19
Comparing Globe Distortions Following Head-Down Bed Rest to those Measured in Astronauts in Short and Long-Duration Spaceflights
The goal of this solicited project is to assess the efficacy of head-down tilt bed rest a ground analogue model for spaceflight induced visual impairment intra-cranial pressure syndrome in astronauts

# 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: Agudelo, Christian

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

POSITION TITLE: Clinical Instructor and Evelyn F. McKnight Neurocognitive Scholar

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) | END DATE MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| Duke University, Durham, NC | BENG | 05/2006 | Biomedical Engineering |
| University of Pittsburgh School of Medicine, Pittsburgh, PA | MD | 05/2015 | Medicine |
| Western Reserve Health Education, Youngstown, OH | Resident | 06/2016 | Internal Medicine Internship |
| University of Miami School of Medicine, Miami, FL | Resident | 06/2019 | Neurology Residency |
| University of Miami School of Medicine, Miami, FL | Fellow | 06/2020 | Sleep Medicine Fellowship |

## A. Personal Statement

I am committed to my development as an interdisciplinary physician-scientist investigating the sleep-dependent mechanistic underpinnings of cognitive aging. I seek to develop sleep-dependent biomarkers of cognitive pathology to ultimately engineer sleep to ameliorate cognitive decline. Building upon my mentored research throughout my education and my background in biomedical engineering, medicine, neurology, and sleep medicine, I am well positioned to integrate diverse perspectives to build successful multidisciplinary collaborations. Leveraging the strength of my mentorship team, my ability to dedicate 100% of my effort to research as the Evelyn F. McKnight Neurocognitive Scholar, and the strength of the University of Miami's scientific infrastructure, I believe I have the tools necessary to develop into an independent clinical scientist.


1. **Agudelo C**, Tarraf W, Wu B, Wallace DM, Patel SR, Redline S, Kaur S, Daviglus ML, Zee PC, Simonelli G, Mossavar-Rahmani Y, Sotres-Alvarez D, Zeng D, Gallo LC, González HM, Ramos A. Actigraphic Sleep Patterns Predict Cognitive Decline in the Hispanic Community Health Study/Study of Latinos. Alzheimer's and Dementia. Forthcoming;
2. **Agudelo C**, Ramos AR, Williams NJ, Wallace DM. Do symptoms of sleepiness and insomnia in US veterans with obstructive sleep apnea vary by age?. Sleep Breath. 2020 Mar;24(1):159-166. PubMed PMID: 31044372; PubMed Central PMCID: PMC6824916.
3. Edelman K, Tudorascu D, **Agudelo C**, Snitz B, Karim H, Cohen A, Mathis C, Price J, Weissfeld L, Klunk W, Aizenstein H. Amyloid-Beta Deposition is Associated with Increased Medial Temporal Lobe Activation during Memory Encoding in the Cognitively Normal Elderly. Am J Geriatr Psychiatry. 2017 May;25(5):551-560. PubMed PMID: 28161156; PubMed Central PMCID: PMC5400712.
4. **Agudelo C**, Aizenstein HJ, Karp JF, Reynolds CF 3rd. Applications of magnetic resonance imaging for treatment-resistant late-life depression. Dialogues Clin Neurosci. 2015 Jun;17(2):151-69. PubMed PMID: 26246790; PubMed Central PMCID: PMC4518699.


## B. Positions and Honors

### Positions and Employment

2008 - 2008 Research Associate, Florida International University, Department of Biological Sciences, Study: Neurobiology of behavior and communication in electric fish (PI: Philip Stoddard, Ph.D.), Miami, FL

2008 - 2009 Research Associate, University of Miami Miller School of Medicine, Department of Physiology

| | |
|---|---|
| | and Biophysics, Study: Cellular and molecular physiology of sensory organs (PI: Nirupa Chaudhari, Ph.D.), Miami, FL |
| 2011 - 2011 | Medical Student Summer Research Trainee, University of Pittsburgh School of Medicine, Rehabilitation Research Experience for Medical Students (PI: Brad Dicianno, M.D.), Study: Age-dependent axonal regeneration post spinal cord injury in zebrafish (Mentor: Martin Oudega, Ph.D.), Pittsburgh, PA |
| 2012 - 2013 | Medical Student Research Trainee, University of Pittsburgh School of Medicine, Recruitment of Medical Students to Careers in Mental Health Research (R25, PI: Haas, Gretchen), Study: Psychophysiological dysfunction in Parkinson's Disease (Mentor: Samay Jain, M.D.), Pittsburgh, PA |
| 2014 - 2015 | Postdoctoral Research Fellow, University of Pittsburgh School of Medicine, Clinical and Translational Research Training in Late-Life Mood Disorders (T32, PI: Charles F. Reyndolds III, M.D.), Study: Neuroimaging in late-life mood and cognitive disorders (Mentor: Howard J. Aizenstein, M.D., Ph.D.), Pittsburgh, PA |
| 2015 - 2016 | Intern (Internal Medicine), Western Reserve Health Education, Northside Medical Center, Youngstown, OH |
| 2016 - 2019 | Resident (Neurology), University of Miami Miller School of Medicine, Jackson Memorial Hospital, Miami, FL |
| 2019 - 2020 | Fellow (Sleep Medicine), University of Miami Miller School of Medicine, Miami Veterans Affairs Healthcare System, Miami, FL |
| 2020 - | Clinical Instructor and Evelyn F. McKnight Neurocognitive Scholar, University of Miami Miller School of Medicine, Department of Neurology, Miami, FL |

## Other Experience and Professional Memberships

| | |
|---|---|
| 2016 - | Member, American Medical Association |
| 2019 - | Member, American Academy of Sleep Medicine |
| 2019 - | Member, Sleep Research Society |

## Honors

| | |
|---|---|
| 2018 - 2019 | Neurology Resident Teaching Award, University of Miami School of Medicine |
| 2020 - 2022 | Evelyn F. McKnight Neurocognitive Scholar, Evelyn F. McKnight Brain Institute |
| 2020 - 2020 | Selected to participate in the Sleep and Circadian Workshop on Indispensable Methods, University of Pittsburgh Center for Sleep and Circadian Science |

## C. Contribution to Science

1. In medical school, studying psychophysiology in Parkinson's Disease (PD), I made my first small contribution to science. Compared to healthy controls, those with PD had diminished blood pressure reactivity to visual emotional stimuli. This supported the idea that autonomic dysfunction in PD extends to psychophysiological reactivity. In post-doctoral research, I used MRI to study late-life mood and cognitive disorders. I was first author on a manuscript discussing the applications of MRI neuroimaging in the study of late-life depression. I also began to explore DTI as a measure gray matter microstructure integrity in relation to late-life cognitive disorders. During clinical training in neurology and sleep medicine, I focused my research to sleep-related biomarkers and mechanisms of cognitive aging. My collaborative analysis and first-author publication (in press) of data from the Hispanic Community Health Study/Study of Latinos demonstrated that actigraphy-derived sleep-onset latency predicted declines in cognitive function in middle-age. This implicates sleep in middle-age cognitive decline and suggests that sleep efficiency and homeostatic sleep drive may be dimensions of sleep involved in cognitive aging. My current work integrates my prior use of DTI to measure gray matter microstructure integrity and my study of sleep-related mechanisms of cognitive aging. I am investigating DTI-based gray matter microstructure integrity as a sleep-related pathologic biomarker of early cognitive pathology.

    a. **Agudelo C**, Tarraf W, Wu B, Wallace DM, Patel SR, Redline S, Kaur S, Daviglus ML, Zee PC, Simonelli G, Mossavar-Rahmani Y, Sotres-Alvarez D, Zeng D, Gallo LC, González HM, Ramos A.

Actigraphic Sleep Patterns Predict Cognitive Decline in the Hispanic Community Health Study/Study of Latinos. Alzheimer's and Dementia. Forthcoming;

b. **Agudelo C**, Ramos AR, Williams NJ, Wallace DM. Do symptoms of sleepiness and insomnia in US veterans with obstructive sleep apnea vary by age?. Sleep Breath. 2020 Mar;24(1):159-166. PubMed PMID: 31044372; PubMed Central PMCID: PMC6824916.

c. Edelman K, Tudorascu D, **Agudelo C**, Snitz B, Karim H, Cohen A, Mathis C, Price J, Weissfeld L, Klunk W, Aizenstein H. Amyloid-Beta Deposition is Associated with Increased Medial Temporal Lobe Activation during Memory Encoding in the Cognitively Normal Elderly. Am J Geriatr Psychiatry. 2017 May;25(5):551-560. PubMed PMID: 28161156; PubMed Central PMCID: PMC5400712.

d. **Agudelo C**, Aizenstein HJ, Karp JF, Reynolds CF 3rd. Applications of magnetic resonance imaging for treatment-resistant late-life depression. Dialogues Clin Neurosci. 2015 Jun;17(2):151-69. PubMed PMID: 26246790; PubMed Central PMCID: PMC4518699.

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

### Completed Research Support

T32 MH019986-18, National Institute of Mental Health (NIMH)
Reynolds III, Charles F (PI)
06/01/14-05/31/15
Clinical and Translational Research Training in Late-Life Mood Disorders
TITLE: Neuroimaging of Late-Life Mood and Cognitive Disorders DESCRIPTION: Applied various neuroimaging techniques to investigate potential pathogenic mechanisms of late-life depression and cognitive impairment. This was a year-long dedicated research opportunity after the completion of medical school and before clinical residency. Project mentor: Howard Aizenstein, MD PhD.
Role: PDC

R25 MH054318-16, National Institute of Mental Health (NIMH)
Haas, Gretchen L (PI)
06/01/12-05/31/13
Recruitment of Medical Students to Careers in Mental Health Research
Title: Psychophysiological Dysfunction in Parkinson's Disease. Description: Investigated psychophysiological responses to emotional stimuli in Parkinson's Disease. This was a year-long dedicated research opportunity between 2nd and 3rd year of medical school. Project Mentor: Samay Jain, MD.
Role: TA

Rehabilitation Research Experience for Medical Students (RREMS), Association of Academic Physiatrists (AAP)
Dicianno, Brad (PI)
05/01/10-08/30/10
Rehabilitation Research Experience for Medical Students
TITLE: Age-dependent impaired axonal regeneration after spinal cord injury in zebrafish DESCRIPTION: Investigated age-dependent mechanisms of spinal cord regeneration in zebrafish. Project mentor: Martin Oudega, PhD.
Role: TA

## 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: Christian Johann Camargo

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

POSITION TITLE: Assistant Professor of Clinical 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 | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| Massachusetts Institute of Technology, Cambridge, MA | SB, SB | 06/2007 | Brain and Cognitive Sciences; Music |
| Cleveland Clinic Lerner College of Medicine of Medicine of Case Western Reserve University, Cleveland, OH | MD | 06/2012 | Medicine |
| Washington Hospital Center, Washington, DC | Internship | 06/2013 | Preliminary Surgery |
| Jackson Memorial Hospital / University of Miami Miller School of Medicine, Miami, FL | Residency | 06/2017 | Neurology |
| University of Miami Miller School of Medicine, Miami, FL | Fellowship | 06/2018 | Cognitive Neurology |

### A. Personal Statement

I am presently a neurologist in the Division of Cognitive Neurology at the University of Miami Department of Neurology, and Assistant Professor of Clinical Neurology at the University of Miami Miller School of Medicine. My research interests include identification of biomarkers for prediction of cognitive decline, the therapeutic use of stem cells in primary neurodegenerative diseases, and therapeutic interventions focused on restoring synaptic plasticity to ameliorate cognitive effects of aging. My research background has been focused in the study of the molecular and electrophysiological mechanisms of synaptic plasticity, and functional brain stimulation towards effecting neuromodulation. As faculty in the Department of Neurology I have also had a direct educational role, in direct Neurology resident clinical training, and by promoting and educating the local Miami community on brain health via radio and in-person engagement in retirement communities. My goals include attaining a better understanding of mechanisms of cognitive dysfunction in Alzheimer's Disease (AD), and improving the ability to better predict which patients are more likely to progress to AD-related dementia.

### B. Positions and Honors

**Positions and Employment**

2019 – Present Assistant Professor, University of Miami Miller School of Medicine
2017 – 2019 Instructor, University of Miami Miller School of Medicine
2017 – Present McKnight Brain Institute Cognitive Fellow

**Honors**

MIT Honorable Mention for Outstanding Research (2005), MIT Walle J.H. Nauta Award for Outstanding Research (2007), Silvero Cabellon Award for Best Performance by a Jr. Resident, Washington Hospital Center Dept. of Vascular Surgery (2013)

**C. Contributions to Science**

1. **Predicting progression to Alzheimer's Disease in patients with Mild Cognitive Impairment.** Based on the observation that about half of patients with Mild Cognitive Impairment will go on to develop further cognitive dysfunction and dementia while half remain with stable cognition, we sought to identify potential biomarkers that could predict this transformation. Our research led us to investigate Neurogranin as such a potential biomarker. I also collaborated on a review article, similarly discussing a relatively novel biomarker for early AD detection, retinal microvascular alterations.
    a. **Supporting Publications**
        i. Headley, A., De Leon-Benedetti, A., Dong, C., Levin, B., Loewenstein, D., **Camargo, C.,** Sun, X. (2018). Neurogranin as a predictor of memory and executive function decline in MCI patients. Neurology, 90(10), e887-e895. doi:10.1212
        ii. Jiang, H., Wang, J., Levin, B. E., Baumel, B. S., **Camargo, C. J.,** Signorile, J. F., & Rundek, T. (2020). Retinal Microvascular Alterations as the Biomarkers for Alzheimer Disease: Are We There Yet?. Journal of neuro-ophthalmology : the official journal of the North American Neuro-Ophthalmology Society, 10.1097/WNO.0000000000001140. Advance online publication. https://doi.org/10.1097/WNO.0000000000001140

2. **Utilizing Deep Brain Stimulation to Investigate Reward Function in Ventral Striatal Cells, and as a novel therapy.** Towards this end, we analyzed single-unit electrophysiological recordings of the ventral striatum in patients receiving Deep Brain Stimulation for Depression and OCD. Utilized single unit-acquisition and analysis techniques utilizing customized MATLAB scripts, Offline Spike Sorter, and Spike2. Further conducted and analyzed recordings in a patient with Pelizaeus-Merzbacher Disease as a potential therapy via compassionate-use. Separately, I designed and executed a retrospective consecutive case review/repeated-measures study for analysis of dystonia outcomes following Deep Brain Stimulation (DBS.)
    a. **Supporting Oral Presentations / Conference Posters**
        i. **Camargo, C**., Sheth, S., Gale J., Mian, M., Patel, S., Gerard, J., Dougherty, D., Eskandar, E. "Single-Unit Reward Encoding in the Human Nucleus Accumbens" Massachusetts General Hospital Department of Neurosurgery, Cleveland Clinic Neurological Institute Research Day, 05/2010, Cleveland, OH (Oral Presentation)
        ii. **Camargo, C**., Sheth S., Patel, S., Mian, M., Flaherty, A., Eskandar, E., Gale J "Thalamic Deep Brain Stimulation as a Treatment Option for Tremor in Pelizaeus-Merzbacher Disease " Massachusetts General Hospital Department of Neurosurgery, American Association of Neurological Surgeons Annual Meeting, 05/2010, Philadelphia, PA (Abstract/e-Poster)
        iii. Sheth S, Mian M, Gale J, Patel S, **Camargo C**, Gerrard J, Eskandar E. "Human Ventral Striatum Neurons Encode Reward Expectation" Massachusetts General Hospital Department of Neurosurgery, American Association of Neurological Surgeons Annual Meeting, 05/2010, Philadelphia, PA (Oral Presentation)
        iv. **Camargo, C.,** Monsalve G., Kubu C., Deogaonkar M. "A Proposed Retrospective Consecutive Case- Review for the Study of Dystonia Outcomes post-DBS" Cleveland Clinic Center for Neurological Restoration, Cleveland Clinic Neurological Institute Research Day Poster Session, 05/2009, Cleveland, OH. (Poster)
3. **Identifying the molecular mechanisms of hippocampal synaptic plasticity in rodent hipoocampal neurons.** I assisted postdoctoral fellow Kensuke Futai in investigating PSD-95 modulation of presynaptic glutamate release probability by designing and creating a viral vector for overexpression of PSD-95 in rat hippocampal slices. Established developmental profiles for various synaptic plasticity-related hippocampal synaptic proteins in the rat by utilizing the Odyssey LI-COR IR Scanner to perform a novel quantifiable expression analysis of immunoblots. Initiated process for purifying GluR1 from hippocampal membrane

fractions in order to apply quantitative tandem mass spectrometry techniques to characterize GluR1 phosphorylation in naïve synapses at various developmental points.

**a. <u>Supporting Oral Presentations / Conference Posters</u>**

i. **Camargo**, **C**., Futai, K., Hayashi, Y.,"Investigation of the Developmental Changes of Rat Hippocampal Synaptic Proteins," MIT Picower Institute for Learning and Memory, RIKEN Neuroscience Research Institute, RIKEN Retreat Poster Session, 11/2006, Shinrin-Koen, Saitama, Japan (Poster)

ii. **Camargo, C.,** Futai, K., Hayashi, Y.,“Comparison of the Expression of PSD95 in Rat Hippocampal Slice Culture and Tissue from Various Postnatal Ages," MIT Picower Institute for Learning and Memory, RIKEN Neuroscience Research Institute, MIT Department of Brain and Cognitive Sciences CPW Poster Session, 04/2004, Cambridge, MA. (Poster)

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

2019-2021 American Academy of Neurology- McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss

2007-2012 Physician Investigator Training Scholarship, Cleveland Clinic Lerner College of Medicine

## 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 Principal Investigator of the State of Florida funded University of Miami Memory Disorder Clinic and an active co-investigator in three large NIH funded grants that are focused on diversity, aging, cognition and the early detection of neurodegenerative diseases. As a clinician scientist serving the multi-ethnic population in South Florida, it has been central to both my clinical practice and research to address health disparities by way of developing initiatives to improve access to geriatric services for underserved populations. I have had an active role for over 10 years in community-based clinics, such as the San Juan Bosco Clinic and have engaged with numerous community partners and stakeholders to advance efforts for care of South Florida's uninsured and indigent older adult population. The recruitment of underserved communities, particularly the African-American community in Alzheimer's Disease research represents a state-wide and national priority that I am poised to contribute to, based on my active engagements and current success in recruiting African-Americans into ongoing studies into the CNSA. These experiences have prepared me to lead the proposed project to develop and advanced registry of cognitive, biomarkers, and environmental influences that impact disease in the African-American community.

### B. Positions and Honor

**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

2006-2018 Medical Director, Geriatric Medical/Psychiatry Inpatient Unit, Jackson Memorial Hospital, Miami, FL

2010- Medical Director/PI, Memory Disorder Clinic, 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

2018- Medical Director, Center for Cognitive Neuroscience and Aging, 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, UM/JHS, 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, UM/JHS, Miami, FL

2017 Psychiatry Residency Senior Faculty Teaching Award, UM/JHS, Miami, FL

**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 3, 5-year studies predicting rates of cognitive decline in the elderly using these measures over 5 years in conjunction with other select diagnostic biomarkers such as atrophy on structural Brain MRI, amyloid and tau imaging as well as CSF markers and ApoE4 genotype. I have worked closely with both Dr. David Loewenstein and Dr. Rosie Curiel in this important field and have had several significant publications documenting this important work.

   a. **Crocco, E.**, Curiel-Cid, R.E., Kitaigorodsky, M., González-Jiménez, C.J., Zheng, D., Duara, R. & Loewenstein, D.A. (2020). A brief version of the LASSI-L detects prodromal Alzheimer's disease states. *Journal of Alzheimer's Disease,* 78(2): 789-799.

   b. **Crocco, E.A.**, Loewenstein, D.A., Curiel, R.E., Alperin, N., Czaja, S.J., Harvey, P.D., Sun, X., Lenchus, J., Raffo, A., Penate, A., Melo, J., Sang, L., Valdivia, R. & Cardenas, K. (2018). 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*: 96: 33-38

**c.** **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.

**d.** Curiel, R.E., **Crocco, E.A.**, Duara, R., Garcia, J.M., Rosselli, M., DeKosky, S.T., Smith, G.,, Bauer, R., Chirinos, C.L., Adjouadi, M., Barker, W. & Loewenstein, D.A. (2020). A novel method of evaluating semantic intrusion errors to distinguish between amyloid positive and negative groups on the Alzheimer's disease continuum. *Journal of Psychiatric Research,* 124: 131-136.

**e.** Capp, K.E., Curiel Cd ,R.E., **Crocco, E.A.,** Sripling, A., Kitaigorodsky, M., Sierra, L., Melo, J.G. & Lowenstein, D.A. (2020).Semantic intrusion error ratio distinguishes between cognitively impaired and cognitively intact African American older adults. *Journal of Alzheimer's Disease*, 73(2): 785-790.

**f.** Loewenstein, D.A., Curiel, R.E., Wright, C., Sun, X., Alperin, N., **Crocco, E.**, Czaja, S.J., Raffo, A., Penate, A., Melo, J., Capp, K., Gamez, M. & Duara, R. (2017). Recovery from proactive semantic I interference in MCI and normal aging: relationship to atrophy in brain regions vulnerable to Alzheimer's d 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 also not well understood. I have published several journal articles related to cognition and ddepression 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, D.A., 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:**
**https://www.ncbi.nlm.nih.gov/myncbi/1Pg52WCUHj95C/bibliography/public/**

**D. Research Support**

**Ongoing Research Support**

XZ703 (Crocco, Elizabeth-PI) 7/1/2020-6/30/2022
Florida Department of Elder Affairs
***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

20A11 (Crocco, Elizabeth-PI) 04/01/2020 – 03/31/2022
Florida Department of Health

***Building an Advanced Cognitive and Biomarker Registry for African American Older Adults At-Risk for Alzheimer's disease***
The role of the PI is to develop a registry of well-characterized African American older adults at risk for Alzheimer's disease and related dementias. Through clinical evaluation, novel cognitive tests sensitive to early cognitive impairment developed at the CNSA, as well as blood biomarkers, and neuroimaging, this grant aims to assist in closing the gap of health disparities for these vulnerable older adults.
Role: Principal Investigator.

P30 AG066506 (Golde, Todd-PI) 06/01/2020-05/31/2025
NIA

***1Florida Alzheimer's Disease Research Center***

The role of the UM Medical Director of the Clinical Core of the 1FloridaADRC is to be responsible for blood marker acquisition, conduct clinical and CDR interviews with participants and study partners, as well as physical and neurological examinations and work closely with the PI's at UM and other sites to reach consensus diagnoses of all participants on an annual basis.

Role: UM Medical Director, Clinical Core

R01AG061106 (Loewenstein, David-PI) 02/01/2019 – 11/30/2023
NIA
***A Novel Computerized Cognitive Stress Test Designed for Clinical Trials in Early Alzheimer's: Relationship with Multimodal Imaging Biomarkers in Diverse Cultural Groups***
The role of the Co-investigator is to assist in the validation the Cognitive Stress Test for use in preclinical AD trials by examining the performance of Hispanic and non-Hispanic individuals with early stage MCI (eMCI), in relation to traditional measures employed in AD clinical trials such as the ADAS-Cog. The new CST will be examined in relation to sensitive AD biomarkers such as amyloid PET, tau and MRI.
Role: Co-investigator

1R01AG055638-01A1 (Curiel, Rosie-PI) 04/01/2018-01/31/2023
NIA
***Precision-based Assessment for the Detection of Mild Cognitive Impairment in Older Adults***
The role of the Co-investigator is to be responsible for ApoE acquisition, conduct clinical and CDR interviews with participants and study partners, and work closely with the PI and the diagnostic team to reach consensus diagnoses of all of our participants on an annual basis. The study is an innovative longitudinal examination of the utility of three novel computerized cognitive stress tests to detect amnestic Mild Cognitive Impairment (MCI) versus normal cognition among community-dwelling elderly.
Role: Co-investigator

9AZ24 (Loewenstein, David-PI) 02/25/2019 – 02/28/2021
Florida Department of Health
***Middle-Aged Offspring of Late Alzheimer's Probands: Novel Cognitive and Biomarker Assessment.***
The proposed investigation provides an unprecedented opportunity to examine the underpinnings of the earliest manifestations of AD in at-risk middle-aged O-LOAD participants. The role of the co-investigator is to study the middle-aged offspring (O-LOAD) of individuals with LOAD (clinically diagnosed Alzheimer's Disease using structural and functional MRI), using a combination of: a) a novel cognitive stress test, the Loewenstein-Acevedo Scales for Semantic Interference and Learning (LASSI-L) uniquely sensitive to frPSI; b) fMRI measures of brain connectivity; c) structural MRI including diffusion tensor imaging (DTI); and d) genetic profile analyses.
Role: Co-investigator

R01AG051346 (Goldberg, Terry/Harvey, Phillip-PI's) 09/01/2018 - 05/31/2023
NIA
***Novel Cognitive and Functional Measures for Alzheimer's Disease Prevention Trials***
This proposal focuses on novel measures of cognition and everyday function that have robust psychometrics and reduced practiced effects. The role of the co-investigator in this study consists of the facilitation of recruitment of research participants and their coordination in the study. I will also be involved with clinical evaluations, assist with scientific analyses and dissemination of study results.
Role: Co-investigator

CNP520A2202J (Crocco, Elizabeth-PI) 05//01/2017-08/31/2025
Novartis Pharmaceuticals
***A randomized, double-blind, placebo-controlled, two cohort parallel group study to evaluate the efficacy and safety of CNP520 in participants at risk for the onset of clinical symptoms of Alzheimer's disease.***

## 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 the CVDRC, I have participated in several projects studying the different aspects of cerebral ischemia and intracerebral hemorrhage. One of the projects in my lab evaluates a strategy to lower hematoma growth following intracerebral hemorrhage. Another project is focused on improving the neurological health of patients with diabetes by decreasing the severity and incidence of cerebral ischemia as cerebral ischemia and heart disease are the most serious complications of diabetes, accounting for more than 84% of the mortality among diabetic patients. Since patients with diabetes are frequently exposed to episodes of mild / moderate hypoglycemia, we are interested in evaluating the impact of exposure to recurrent hypoglycemia on the risk of cerebral ischemia as well as cerebral ischemic damage. This R01 application is based on our studies evaluating the impact of recurrent hypoglycemia on cerebral ischemic damage in diabetics. We are a pioneer in this field. We have published several articles on this topic in recent years. This proposal proposes to evaluate new mechanisms by which exposure to recurrent hypoglycemia increases both the risk of cerebral ischemia and cerebral ischemic damage.

### 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.
- Neuroscience Graduate Program Faculty (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 (1999 – 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:**

- Reviewer, AHA Bugher phase 1 peer review committee, Fall 2020
- Reviewer, NIH ETTN-14 SEP peer review committee, 07/2020
- Reviewer, NIH SEP to review Renewal of Centers of Biomedical Research Excellence [COBRE] (P20): 3/2020
- Committee member, NINDS, ZNS1 SRB-O (04): 11/2019
- NIH- Acute Neural Injury and Epilepsy Study Section (ANIE): 6/2015, 10/2015, 2/2016, 6/2016, 10/2016, 2/2017, 10/2017, 6/2018, 10/2018, 2/2019, 6/2019, 10/2019
- Reviewer, VA NURC Study section: 10/2019, 05/2020, 11/2020
- Chair and Reviewer, AHA Brain 2 Study section: Fall 2019
- Reviewer, FWF Austrian Science Fund: Fall 2018, Fall 2019
- Reviewer, AHA Allen Brain Health Phase 1 and Phase 2 review committees: Fall 2018
- Chair and Reviewer, AHA Brain 2 Study section: Fall 2018
- Co-Chair AHA Brain 3 Study section: Spring 2017
- AHA Brain 3 Study section: Spring 2016, Fall 2016, Spring 2017
- AHA scientific sessions abstracts: June 2016
- AHA Cardiac Arrest Resus CL/Pop Merge with Basic Science Study section: Fall 2015
- AHA Cardiac Arrest Resuscitation Basic Study section: Spring 2015, Spring 2016
- Croatian Science Foundation: 2014
- AHA Innovative Research Grant Study section: Fall 2014, Fall 2015, Fall 2016
- Bando Giovani Ricercatori "Alessandro Liberati": 2013 (Italian funding agency)
- AHA Brain 1 study section: Fall 2013
- AHA Brain 5 Study section: Spring 2013, Spring 2014, Spring 2015

C. Contributions to Science

1. Cerebral ischemia and heart disease are the most serious complications of diabetes, accounting for more than 84% of the mortality among patients with diabetes. 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 streptozotocin-diabetic rats, 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 the risk of cerebral ischemia as well as 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. Smith L, Chakraborty D, Bhattacharya P, Sarmah D, Koch S, Dave KR. Exposure to hypoglycemia and risk of stroke. Ann N Y Acad Sci. 2018 Nov;1431(1):25-34.

d. Rehni AK, Dave KR. Impact of Hypoglycemia on Brain Metabolism During Diabetes. Mol Neurobiol. 2018 Dec;55(12):9075-9088. doi: 10.1007/s12035-018-1044-6.
e. Shukla V, Fuchs P, Liu A, Cohan CH, Dong C, Wright CB, Perez-Pinzon MA, Dave KR. Recurrent Hypoglycemia Exacerbates Cerebral Ischemic Damage in Diabetic Rats via Enhanced Post-Ischemic Mitochondrial Dysfunction. Transl Stroke Res. 2019 Feb;10(1):78-90.
f. Rehni AK, Shukla V, Perez-Pinzon MA, Dave KR. Acidosis mediates recurrent hypoglycemia-induced increase in ischemic brain injury in treated diabetic rats. Neuropharmacology. 2018 Jun;135:192-201.
g. Klingbeil KD, Koch S, Dave KR. Potential link between post-acute ischemic stroke exposure to hypoglycemia and hemorrhagic transformation. Int J Stroke. 2020 Jul;15(5):477-483.
h. Shukla V, Shakya AK, Perez-Pinzon MA, Dave KR. Cerebral ischemic damage in diabetes: an inflammatory perspective. J Neuroinflammation. 2017 Jan 23;14(1):21.
i. Rehni AK, Nautiyal N, Perez-Pinzon MA, Dave KR. Hyperglycemia / hypoglycemia-induced mitochondrial dysfunction and cerebral ischemic damage in diabetics. Metab Brain Dis. 2015 Apr;30(2):437-47.

2. Mitochondria play an important role in neurodegeneration in acute (e.g. cerebral ischemia) and chronic (e.g. Amyotrophic lateral sclerosis) neurodegenerative conditions. Besides, mitochondria also play an important role in neuroprotection. I participated in studies aimed to determine the contribution of mitochondrial dysfunction in brain damage following cerebral ischemia in a mouse model of amyotrophic lateral sclerosis. We characterized and identified potential mechanisms of mitochondrial dysfunction in the above-mentioned conditions. I also participated in studies aimed to determine the mechanisms by which mitochondria contribute to ischemia tolerance in the brain.
   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. 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.
   d. Dave K.R., Saul I., Busto R., Ginsberg M. D., Sick T. J., Perez-Pinzon M. A. Mitochondrial function following global cerebral ischemia in rat hippocampus. Journal of Cerebral Blood Flow and Metabolism, 21:1401-1410, 2001.

3. Ischemic tolerance in the 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 the 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.

4. 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 a 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.

5. Amyotrophic lateral sclerosis (ALS) is a devastating disease, which results in the 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 the 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.

I have collaborated with investigators outside the US: Dr. Rolando A Gittens, INDICASAT AIP, Centro de Biodiversidad y Descubrimiento de Drogas, Centro de Neurociencias, Panama; Dr. Pallab Bhattacharya, National Institute of Pharmaceutical Education and Research (NIPER) – Ahmedabad, India; Dr. David Della-Morte, University of Rome Tor Vergata, Rome, Italy.

**Complete List of Published Work in PubMed:** https://www.ncbi.nlm.nih.gov/sites/myncbi/kunjan.dave.1/bibliography/44169146/public/?sort=date&direction=descending

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

R21NS094896 (IGNITE mechanism) Dr. Dave, P.I. R21 phase: 2/1/2016 – 1/31/2017
NIH/NINDS R33 phase: 2/1/2017 – 7/31/2020
**(no cost extension)**

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

9JK08 Dr. Dave, P.I. 07/2019 – 06/2022
James and Esther King Biomedical Research Program, Florida Department of Health
Nicotine exposure and intracerebral hemorrhage
Role: Principal Investigator

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

R01 NS097658 Dr. Perez-Pinzon, P.I. 08/2017 – 04/2022
NIH/NINDS
Metabolic master regulators for ischemic neuroprotection
Role: co-investigator

20K11 Dr. Perez-Pinzon, P.I. 5/1/20-4/30/23
Florida Dept of Health/James & Esther King Discovery Research Grant
*Strategies to ameliorate cognitive decline following cerebral ischemia in nicotine-exposed rats*
Addresses prevention and treatment of post-stroke motor and cognitive recovery by studying the impact of smoking cessation and the intervention of PE on stroke outcomes.
Role: Co-Investigator

20K09 Dr. Raval, P.I. 5/1/20-4/30/23
Florida Dept of Health/ James & Esther King Discovery Research Grant
*Nicotine alters brain metabolism and exacerbates ischemic brain damage*
The study will contribute to better understanding of the consequences of nicotine on the brain specific to OC-exposed females for future translational research.
Role: Co-Investigator

2R01NS045676-10 Dr. Perez-Pinzon, PI 8/20-7/25
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.
Role: Co-Investigator

**Recently completed**
NIH 1R01NS073779 (PI: Dave) 03/2012 – 4/2018
Increased cerebral ischemic injury by repeated hypoglycemic episodes in diabetes.
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: Assistant Professor of Neurology, (Associate Professor Pending Position) 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- 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 (Associate Professor Position Pending) — Dept. of Systems Medicine, University of Rome, Italy
2014- Qualification as Associate Professor — Italian National Scientific Council

**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 *International Journal of Diabetology & Vascular Disease Research, Cell R4, Clinical & Experimental Cardiology, JSM 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.
2015-17 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 9 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. 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
   b. 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
   c. **Della-Morte D**, Gardener H, Dong C, Markert M, Cabral D, Elkind MSV, Sacco RL, Rundek T. Association Between Carotid Artery Function and Structure in the Northern Manhattan Study. Front Neurol. 2018 Apr 16;9:246. PMID: 29713306. PMCID: PMC5911635
   d. **Della-Morte D**, Dong C, Markert MS, Elkind MSV, Sacco RL, Wright CB, Rundek T. Carotid Intima-Media Thickness Is Associated With White Matter Hyperintensities: The Northern Manhattan Study. Stroke. 2018 Feb;49(2):304-311. PMID: 29284725. PMCID: PMC5780238

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. Experimental studies on the effect of antioxidant proteins against vascular risk factors and atherosclerosis. 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**

**Ongoing Research Support**

Award: M1800195 Rundek (PI) 09/01/2018-8/31/2023
NIH
Title: Family Study of Carotid Atherosclerosis and Stroke Risk.
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**: David Della-Morte

ARISTA---USA Protocol ID# CV185-564 Rundek (PI) 01/01/2017-12/31/2019
Pfizer
Title: "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 by using a large Florida-Puerto Rico (FL---PR) Stroke Registry.
**Role: Co-PI**: David Della-Morte

No Award No. B88F12000730005
Italian Minister of Health Guadagni (PI) 01/01/2014-12/30/2020
POR FESR CAMPANIA 2014-2020 – B-TECHNOLOGY PLATFORM AGAINST RARE CANCERS
Title: RARE.PLAT.NET. Innovazioni diagnostiche e terapeutiche per tumori neuroendocrini, endocrini e per il glioblastoma attraverso una piattaforma tecnologica integrata di competenze cliniche, genomiche, ICT, farmacologiche e farmaceutiche.
This award is specifically designed to develop through a cluster of National Biological Banks and Big Data a technological platform that will be able to improve prevention, prediction and treatment for brain cancers, neuroendocrin cancers, and cerebrovascular diseases. To find novel algorithms of prediction developed by using genetic, IT, and biological data is the main scope of this project.
**Role: Co-I:** David Della-Morte

No Award No. F/050383/01-03/X32 Guadagni (PI) 01/01/2014-12/31/2020
Italian Minister of Economic Development - Divisione VII – Interventi per ricerca e sviluppo.
NET4HEALTH - NETwork for HEALTH management. Title: “HORIZON 2020” PON I&C 2014-2020 MISE – Direzione Generale per gli Incentivi alle Imprese.
This project is manly aimed to develop a National central Biobank by clustering the most important Italian Biobanks. These Biobanks are especially dedicated in collecting biospecimens from patients with chronic diseases (e.g. cancer, diabetes, cardiovascular diseases). A central Biobank would further help researchers in better analyzing data and to reach in a better prediction and prevention for these pandemic diseases.
**Role: CoI:** David Della-Morte

Lauro (PI) 09/23/2018-09/22/2021
Rome Foundation- Title: “Diabetes Mellitus, Regenerative and Reparative Processes, and Improvement of Pancreatic Beta Cell Function: Role of Bone Marrow-Mesenchymal Stem Cells, Micrornas, M2 Macrophages And Myeloid Derived Suppressor Cells”. This project is mainly aimed to develop novel therapeutic strategies to regenerate and preserve pancreatic beta cell mass, which is dramatically affected in diabetes mellitus.
**Role: CoPI:** David Della-Morte

No Award No. PNR 2015-2020 ARS01_01163 PerMedNet Guadagni (PI) 10/01/2018-09/31/2021
European Social Fund, under the Italian Ministries of Education, University and Research. Title: “Personalized medicine for innovative strategies in neuropsychiatric and vascular diseases”.
This project is manly aimed to develop novel and more personalized drugs for neurodegenerative disorders particularly focused on stroke.
**Role: CoPI:** David Della-Morte

**<u>Completed Research Support</u>**
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 a 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**

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**

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**

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**

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**

## 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: James E. Galvin, MD, MPH

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

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 |
|---|---|---|---|
| New York University, New York, NY | BA | 06/1986 | Chemistry |
| Rutgers University, New Brunswick, NJ | MS | 06/1991 | Nutrition |
| UMDNJ-NJ Medical School, Newark, NJ | MD | 06/1992 | Medicine |
| Saint Louis University, St Louis, MO | MPH | 05/2004 | Epidemiology |

### A. Personal Statement

The major focus of my clinical and research career has been to improve the clinical care and quality of life for all older adults from diverse backgrounds and their family caregivers who are dealing with neurodegenerative disorders in order to initiate early intervention, alleviate psychosocial burden on the patient and family, reduce the impact of race, language, culture, and class on the delivery of health services, and improve health outcomes. My wife and her family are from the West Indies (Antigua) and I have spent the better part of three decades fighting to ensure that my mother-in-law (Alzheimer's disease) and father-in-law (Vascular Dementia) received the respect and medical care they deserved, even if they were unwilling or unable to stand up for themselves. Towards the ends of their lives, medical complication after medical complication whittled down their resistance and they eventually died from inanition and vascular events. I also witnessed firsthand the struggles my grandmother faced caring for my grandfather's Lewy Body Dementia, not only the lack of effective medications, but psychological effects of delayed diagnosis and the absence of available caregiver support mechanisms. Traditional approaches to medicine care failed them, in part because of the seriousness of their illnesses, but also because each individual's unique presentation, needs, and progression required more than the "one-size-fits-all" approach embedded in conventional medicine. To me, the need to understand root causes of disease, provide strategies for early detection of disease that will work in all older adults regardless of background, improve health outcomes while containing healthcare costs, and do this in culturally-sensitive and personalized fashion is not just a professional activity, it has been a personal battle.

Over the course of my research career, I pioneered dementia screening measures that offer quick, valid, reliable, and culturally sensitive assessments of older adults regardless of race, language, or educational attainment in collaborative projects across North and South America, Europe and Asia. I also developed regression models characterizing the transition from healthy aging to dementia with inflection points in cognitive performance that occur 1-3 years before the clinical detection of cognitive impairment. These activities guided the selection of brief cognitive measurements sensitive to early decline for use in screening programs in two R01 grants. I characterized the older adults' intention to consent to dementia screening using population-based survey methods and helped develop MRI biomarkers of dementia. To assist family caregivers, I led efforts to characterize the diagnostic experience of family caregivers getting a diagnosis for their loved ones, analyzed the societal and economic costs of disease, and studied caregiver burden, grief, and well-being to develop novel interventions. I have been productive, authoring 271 scientific manuscripts (h-index 58) and directing 45 ADRD clinical trials. In my clinical practice, I created an innovative transdisciplinary collaborative care model to provide personalized care using precision-medicine principles to patients and support mechanisms for family caregivers.

In prior positions at Washington University and NYU, I served as Leader of the Outreach, Recruitment, and Education Core for NIA-funded Alzheimer Disease Centers (ADC) developing protocols to improve the research recruitment and retention of older adults from multicultural backgrounds; interprofessional education programs; and dissemination of research findings back to the community. I also obtained an Administrative Supplement from the National Library of Medicine to create an open-access database for other investigators to benefit from a rich multicultural cohort. Throughout my career, I have been able to maintain continuous funding to support my research efforts. My current research program focuses on four themes: (1) Developing and validating new clinical assessment scales to improve detection of cognitive impairment in multicultural community samples to improve health outcomes; (2) Studying the interaction between race, ethnicity, socioeconomic status, and multiple chronic conditions on the risk of cognitive impairment; (3) Characterizing the clinical, cognitive, behavioral, and biomarker features of neurodegenerative disorders; and (4) Creating novel precision-medicine based interventions based on individual phenotypic, biomarker, and genomic profiles aimed at ADRD risk reduction and dementia prevention. I have had the opportunity to demonstrate personal and professional growth and leadership in multi-component program projects and center grants as an investigator, Associate Core Leader, Satellite Leader, Core Leader, and Associate Director of NIH-funded P01, P30 and P50 Centers. My expertise, scientific productivity, and leadership in brain aging, cognitive health, neurodegenerative disease and health disparities qualify me to direct the Comprehensive Center for Brain Health.

**B. Positions and Honors**

1992 – 1993 Intern, Dept of Internal Medicine, Hackensack University Hospital, Hackensack, NJ
1993 – 1995 Resident, Dept of Neurology, Thomas Jefferson University, Philadelphia, PA
1995 – 1996 Chief Resident, Dept of Neurology, MCP Hahnemann University, Philadelphia, PA
1996 – 2000 Post-Doctoral Fellow (Laboratory of John Q. Trojanowski, MD, PhD and Virginia M-Y Lee, PhD), Center for Neurodegenerative Disease Research, University of Pennsylvania, Philadelphia, PA
1996 – 1997 Instructor, Dept of Neurology, MCP Hahnemann University, Philadelphia, PA
1997 – 2000 Assistant Professor, Dept of Neurology, MCP Hahnemann University, Philadelphia, PA
2000 – 2007 Assistant Professor, Dept of Neurology, Washington University, St Louis, MO
2003 – 2007 Assistant Professor, Dept of Anatomy and Neurobiology, Washington University
2006 - 2010 Director, Memory Diagnostic Center, Washington University
2007 – 2010 Director, Education Core and Community Outreach, Washington University
2007 - 2010 Associate Professor, Dept of Neurology, Psychiatry and Neurobiology, Washington University
2010 - 2015 Professor, Dept of Neurology and Psychiatry, New York University, New York, NY
2010 - 2015 Director, Pearl Barlow Center for Memory Evaluation and Treatment, New York University
2010 - 2015 Director of Clinical Operations, Center of Excellence on Brain Aging, New York University
2010 - 2015 Associate Director, Alzheimer Disease Center, New York University
2015 - 2019 Professor and Associate Dean for Clinical-Translational Research, Charles E. Schmidt College of Medicine, Florida Atlantic University
2019 - Professor of Neurology and Director, Comprehensive Center for Brain Health, University of Miami Miller School of Medicine.

**Honors, Awards, Editorial and Advisory Boards**

Advisory Committee to the Claude Pepper Older Americans Center Program Coordinating Center, 2016-present; Strategic Planning Panel for Alzheimer Disease Centers Program, NIH, 2016-present; Chair: Lewy Body Dementia Module Workgroup, National Institute on Aging Alzheimer Disease Center Program: 2015-present; Member, CNN Study Section, NIH, 2015-present; Alzheimer's Disease-Related Dementia Summit, NIH, Health Disparities Committee, 2013, US Department of Justice/International Association of Chiefs of Police, Missing Alzheimer Patient Initiative Advisory Board (2010-present), Geriatric Neurology Section, American Academy of Neurology, Research Award Committee (2011-present, Councilor, 2007-2010), Chair: Lewy Body Dementia Module Workgroup, National Institute on Aging Alzheimer Disease Center Program: 2015-present; Advisory Committee to the Claude Pepper Older Americans Center Program Coordinating Center, 2016-2018; Strategic Planning Panel for Alzheimer Disease Centers Program, NIH, 2016-2018; Member, CNN Study Section, NIH, 2015-2019; Alzheimer's Disease-Related Dementia Summit, NIH, Health Disparities Committee, 2013, US Department of Justice/International Association of Chiefs of Police, Missing Alzheimer Patient Initiative Advisory Board (2010-present), Geriatric Neurology Section, American Academy of Neurology, Research Award Committee (2011-present, Councilor, 2007-2010), American Neurological Association (2009-present), External Advisor Committee, University of Wisconsin Alzheimer Disease Center (2009-present), Chair Steering Committee Education Cores, NIA Alzheimer Disease Program (2008-2010), Board of Directors Lewy Body

Dementia Association (2007-present), Dorothy Dillon Eweson Lectureship on Advances in Aging Research, American Federation for Aging Research (2007), Research Award in Geriatric Neurology, American Academy of Neurology (2006), Board of Directors, Lewy Body Dementia Association (2006-present), Scientific Advisory Board, American Federation for Aging Research (2005-present), Editorial Board, Clinical Practice (2011-present), Editorial Board, Acta Neuropathologica, (2006-present), Editorial Board, Alzheimer's Disease and Associated Disorders (2004-present), Associate Editor Neuroscience Letters (2004-2008), Alene and Meyer Kopolow Award for Excellence in Geriatric Psychiatry and Neurology, Washington University (2002)

**C. Contributions to Science** (selected from 271 publications, h-index=58, i10 index=137)
**URL for published work:** http://www.ncbi.nlm.nih.gov/pubmed/?term=galvin+je

**1. Use of Deep Phenotyping to Developing Novel Screening Tests, Biomarkers of Neurodegenerative Disease, and Predictors of Response to Therapy:** Deep phenotyping (the use of multimodal markers from a single individual) is a novel approach to characterizing individuals with and without disease. Application of deep phenotyping offers the possible to model disease, develop new diagnostics and therapeutics, and predict and monitor response over time. We have used these methods to combine detailed clinical, cognitive, imaging, and fluid biomarker data to characterize cross-sectional and longitudinal cohorts.

1. Jelescu IO, Sherpherd TM, Novikov DS, Ding YS, Smith J, Koesters T, Babb, JS, Friedman KP, **Galvin JE,** Fieremans E. Comprehensive integrated PET-MRI characterization of region-specific correlations between amyloid deposition, cortical atrophy, and white matter degeneration due to underlying AD pathology. Neurobiol Aging 89:118-128, 2020
2. Shim YS, Roe CM, Benzinger TL, Cairns NJ, Xiong C, **Galvin JE,** Coats MA, Yang D-W, Morris JC. Pathological Correlates of White Matter Hyperintensities on MRI. Dementia Geriatr Cogn Disord, 39:92-104;2014 (PMCID: 4312498)
3. **Galvin JE,** Price JL, Yan L, Morris JC, Sheline YI. Patterns of resting BOLD functional MRI activation differentiate Dementia with Lewy Bodies from Alzheimer Disease. Neurology 76:1797-1803,2011. (PMCID: 3100121)
4. **Galvin JE**, Fagan AM, Holtzman DM, Mintun MA, Morris JC. Relationship of dementia screening tests with biomarkers of Alzheimer's Disease. Brain, 133:3290-3300,2010. (PMCID: 2965421).

**2. Development, Evaluation, and Dissemination of Dementia Screening Instruments and Their Translation to Practice and Policy:** MCI and Dementia are poorly detected in community samples, in part due to the lack of brief validated instruments. I have led the creation of 11 screening and assessment instruments including the AD8, Quick Dementia Rating System (QDRS), and Healthy Aging Brain Care Monitor (HABC-M) with translation and use in 17 countries, application of these instruments in State Medicaid eligibility evaluations in Iowa, Missouri, and Pennsylvania, inclusion in longitudinal studies, and recommended in tool kits by NIA, the Alzheimer Association and Professional Societies.

1. **Galvin JE,** Tolea MI, Chrisphonte S. Using a Patient-Reported Outcome to Improve Detection of Cognitive Impairment and Dementia: The Patient Version of the Quick Dementia Rating System (QDRS). PLoS One, In Press 2020.
2. **Galvin JE.** The Quick Dementia Rating System (QDRS): A rapid dementia staging tool. Alzheimer Dem (DADM)1:249-259; 2015 (PMCID: 4484882)
3. **Galvin JE.** Improving the detection of Lewy body dementia with the Lewy Body Composite Risk Score. Alzheimer Dem Diag Assess Dis Manage 1:316-324, 2015. (PMCID: 4576496)
4. Monahan PO, Boustani M, Alder C, **Galvin JE**, Perkins A, Healy P, Chehreza A, Shepard P, Bubp C, Callahan C. A Practical Clinical Tool to Monitor Dementia Symptoms: The HABC-Monitor Clinical Interven Aging 7:143-157;2012. (PMCID: 3393358)

**3. Use of Surveys and Internet Questionnaires to Collect Data Characterizing Patient-, Caregiver-, and Societal Outcomes:** In many instances, sampling of large disease cohorts and populations is not possible at a single site. The use of survey data to sample large numbers of older adults with validated questionnaires enables the collection and analyses of data to explore topics ranging from intention to undergo cognitive screening, physician practice patterns, diagnostic experiences of patients and caregivers, concepts of burden, grief and well-being, and medical economic outcomes.

1. Rigby T, Ashwill RT, Johnson DK, **Galvin JE**. Differences in the Experience of Caregiving between spouse and adult child caregivers in Dementia with Lewy Bodies. Innov Aging, 3:igz027 2019. (PMCID: 6736163).
2. Besser L, Denny S, Tatton N, **Galvin JE.** The Diagnostic Experience and Challenges Facing Patients with Frontotemporal Degeneration. Neurol: Clin Prac, In Press 2020

3. **Galvin JE,** Howard DH, Denny SS, Dickinson S, Tatton N. The Social and Economic Burden of Frontotemporal Degeneration. Neurology 2017 89:2049-2056. (PMCID:5711509)
4. **Galvin JE,** Fu Q, Nguyen JT, Glasheen C, Scharff DP. Psychosocial Determinants of Intention to Screen for Alzheimer Disease. Alzheimer Dement 4:353-360;2008. (PMCID: 2608720)

**4. Novel Studies Linking Physical Decline to Cognitive Impairment:** While a cure for ADRD is desirable, it may be possible that by identifying important co-morbid diseases that are potentially modifiable, we may be able to prevent or mitigate development. My lab has focused on the intersection between physical performance, frailty, sarcopenia and vascular risk factors as root causes of dementia and affective disorders to develop predictive models of disease and novel intervention strategies.

1. Tolea MI, Chrisphonte S, **Galvin JE.** Sarcopenic obesity and cognitive performance. Clin Interv Aging 13:1111-1119; 2018 (PMCID: 5995418).
2. Tolea MI, **Galvin JE.** Physical dysfunction staging and global cognition. Alz Dis Assoc Disord, 2016; 30:230-236 (PMCID: 4970960)
3. Tolea MI, Morris JC, **Galvin JE**. Trajectory of physical functional decline by type of dementia Alz Dis Assoc Disord 30:60-66, 2016 (PMCID: 4592781)
4. Tolea MI, Morris JC, **Galvin JE.** Longitudinal Associations between Physical and Cognitive Function among Community-dwelling Older Adults. PLoS One 2015 Apri 13;10(4):e0122878 (PMCID: 4395358)

**5. Health System Re-Design and Re-Orientation to Improve Health Outcomes:** An important aspect of reducing health disparities and improving health outcomes is to change the way we deliver care and services to different populations. We have implemented a number of novel programs to shift care from expensive hospital-based programs to ambulatory and home settings to reduce costs and increase access of services.

1. **Galvin JE,** Howard DH, Denny SS, Dickinson S, Tatton N. The Social and Economic Burden of Frontotemporal Degeneration. Neurology, 89(20):2049-2056;2017. (PMCID: 5711509)
2. Brody AA, Guan C, Cortes T, **Galvin JE.** Development and testing of the Dementia Symptom Management at Home (DSM-H) Program: An interprofessional home healthcare intervention to improve quality of life for persons with dementia and their caregivers. Geriatr Nurs, 37:200-206, 2016. (PMC-In process)
3. Boltz M, Chippendale T, Resnick B, **Galvin JE**. Testing family-centered, function-focused care in hospitalized persons with dementia. Neurodegen Dis Manage 5:203-215; 2015 (PMCID: 4529403)
4. **Galvin JE,** Kuntemeier B, Al-Hammadi N, Germino J, Murphy-White M, McGillick J. "Dementia-Friendly Hospitals: Care not crisis" Improving the care of the hospitalized patient with dementia. Alz Dis Assoc Disord, 24:372-379,2010. (PMCID: 2955811)

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

**ACTIVE**

R01 AG069765-01 Boustani, Ben-Miled, Galvin (MPI) 9/15/20 - 8/31/25
*Digital Detection of Dementia ($D^3$)*
The major goals of $D^3$ includes two complementary studies at diverse urban, suburban, and rural primary care practices within Central Indiana and South Florida that will evaluate the predictive performance, the utility and effectiveness of the Passive Digital Marker, the Quick Dementia Rating Scale (QDRS), and the combined approach (Passive + QDRS) in the early detection of Alzheimer's disease and related dementia (ADRD).
Role: MPI

R01 AG057681-01A1 Butler, Galvin, Atwood (MPI) 9/1/19-8/31/24
*The LUCINDA Trial: Lupron + Cholinesterase Inhibition to Reduce Neurologic Decline in Alzheimer's Disease*
The major goal is to conduct a randomized double-blind, placebo controlled trial of Lupron and donepezil in women with mild to moderate Alzheimer's disease to improve cognition and activities of daily living. Role: Multi-PI

R01 NS101483-01A1 Galvin (PI) 9/1/19-8/31/24
*Reducing Disparities in Dementia and VCID Outcomes in a Multicultural Rural Population*
The major goals of this project are to study disparities in health outcomes related to vascular contributions to cognitive impairment and dementia (VCID) in a multicultural rural community, determine rates of impairment, and provide community-based interventions to improve care and reduce costs. Role: PI

P30 AG059295 Buchwald, Manson, Galvin (MPI) 9/1/18-6/30/23

*Native Alzheimer's Disease Resource Center for Minority Aging Research (NAD-RCMAR)*
The major goals of this Center is to describe, understand, intervene on, and mitigate the Alzheimer's disease health disparities experienced by American Indians, Alaska Natives, Native Hawaiians, and Pacific Islanders by funding social and behavioral Pilot Studies that advance the field, emphasizing the recruitment and mentorship of Native junior and mid-level researchers. Role: Multi-PI

U54AG063546 Mor & Mitchell (MPI) 09/01/19 – 10/31/24
*NIA AD/ADRD Health Care Systems Research Collaboratory*
The NIA AD/ADRD Collaboratory will provide the national infrastructure necessary to catalyze and support embedded pragmatic clinical trials of non-pharmacological interventions for persons with dementia. By convening national experts to provide consultation and guidance to Collaboratory-funded pilot projects and NIA-funded trials, the Collaboratory has the potential to transform care delivery, quality, and outcomes for millions of Americans suffering with AD/ADRD. Role: Pilot Core Steering Committee

R01 AG056531-01A1 Osorio (PI) 4/1/18-3/31/23
*Slow Wave Sleep and the Effect of African Ancestry on Amyloid Burden: A Longitudinal Study*
The major goal of this project is to study the effect of disruption of sleep wave sleep duration and efficacy on the accumulation of amyloid protein in the brains of African American older adults. Role: Co-Investigator

5U01NS100610-02 Leverenz (PI) 9/30/16-9/29/21
*Dementia with Lewy Bodies Consortium*
The major goals of this project is to develop a national network to study Dementia with Lewy bodies including longitudinal clinical and cognitive characterization, imaging and CSF biomarkers, and autopsy. Role: Site PI

1R01AG056610-01 Brody (PI) 8/1/17-3/31/22
*A Multi-Site Cluster RCT of the Dementia Symptom Management at Home Program*
The major goal of this project is to conduct a randomized trial of the Dementia Symptom Management at Home Program for efficacy in improving quality of care for persons living with dementia and their informal caregivers receiving home healthcare. Role: Site PI

1R01AG054425-01A1 Boltz (PI) 5/1/17-4/30/22
*Reducing Disability via a Family-centered Intervention for Acutely-Ill Persons with Alzheimer's disease and Related Dementias*
The major goals of this project are to test and validate a family-centered function focused care (Fam-FFC) plan to improve physical function, cognitive function, and medicoeconomic outcomes in hospitalized patients with dementia. Role: Co-Investigator

9AZ05 Ghoraani (PI) 2/1/19-1/31/21
*Technology-based Systems to Measure Dual-Task (Motor-Cognitive) Performance as a Biomarker for Early Detection of Alzheimer's Disease*
The major goal of this project is to develop an accurate data analysis approaches to translated body movement and speech data using sensor-based assessment systems into biomarkers that can identify individual at risk for MCI. Role: Co-Investigator

**Completed Research Support (within past 3 years)**
7R01AG040211-06 Galvin (PI) 9/30/11-5/31/20
*Multicultural Community Dementia Screening*
The major goals of this project are to provide cross-cultural validation of dementia screening methods and biological validation against imaging and CSF biomarkers of Alzheimer disease and related disorders. Role: PI

5R01NS088040-04 Fieremans/Novikov (PIs) 9/1/14-7/31/19
*Mesoscopic Biomarkers of Neurodegeneration with Diffusion MRI*
The major goals of this project are to distinguish and quantify the different underlying white matter pathological processes *in vivo* by means of magnetic resonance imaging (MRI). Role: Co-Investigator

The Michael J. Fox Foundation Galvin (PI) 3/9/18-3/8/19
*LRRK2-002*
Goals: The major goals of this study is to characterize the role of LRRK2 mutation in the onset and progression of Parkinson's disease. 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: Getz, Sarah J

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

POSITION TITLE: Instructor of Neuropsychology

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 |
|---|---|---|---|
| Reed College, Portland, OR | BA | 05/2004 | Psychology |
| Princeton University, Princeton, NJ & Suffolk University, Boston, MA | PHD & Respecialization Certificate in Clinical Psychology | 07/2016 | Psychology and Cognitive Neuroscience/ Clinical Respecialization in Neuropsychology |
| Miami VA Healthcare System, Miami, FL | Clinical Internship | 07/2016 | Clinical Psychology and Neuropsychology |
| University of Miami, Miller School of Medicine, Miami, FL | Residency | 08/2018 | Neuropsychology |

**Personal Statement**

I am an early stage investigator in my second year as an Instructor at the University of Miami Miller School of Medicine. My research interests as a graduate student at Princeton University focused on impulsive and maladaptive decision-making and the imbalance between motivational brain circuitry and regulatory control circuitry. My dissertation employed a neuroeconomics framework to examine impulsivity and cognitive control in decision-making and led to a dissertation grant funded by the Center for Health and Wellbeing's Demography of Aging Center, which is supported by the National Institute of Aging at the Woodrow Wilson School of Public and International Affairs. In other lines of my doctoral research, I examined working memory training and intelligence. After earning my PhD, I began postdoctoral re-specialization training in Boston where I completed research interventions and advanced neuropsychology practica, including training experiences at Brigham and Women's Hospital Harvard Medical School and Beth Israel Deaconess Harvard Medical School. As the Chief Intern and Neuropsychology Intern at the Miami VA, I evaluated patients with a wide range of neurodegenerative disorders. During my fellowship, under the mentorship of Dr. Bonnie Levin in the Department of Neurology Division of Neuropsychology, at the University of Miami Miller School of Medicine, I evaluated patients from diverse backgrounds and cultures and participated in a number of research projects examining prodromal features of cognitive decline in patients with movement disorders, memory loss, mild traumatic brain injury, and physical frailty. In my new role as an instructor, my research efforts have focused on the cognitive, behavioral, and psychological features of susceptibility to deception

among the vulnerable elderly and have led to a multisite McKnight pilot grant with Dr. Levin and collaborators at the Universities of Arizona and Florida as well as the development the "Assessment of Situational Judgement" questionnaire. I am currently the recipient of the McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss Award funded by the McKnight Brain Research Foundation through the American Brain Foundation and the American Academy of Neurology for my research on deception and age related hearing loss. My specialized research background in cognitive neuroscience and decision making combined with my clinical training in neuropsychology provide the necessary background and credentials to serve as a primary investigator on this project.

Representative Publications and Presentations:

a. Casey, B. J., **Getz, S.** Galvan, A. (2008). The adolescent brain. *Developmental Review, 28*, 62-77.
b. Kool, W., **Getz, S. J**.*, & Botvinick, M. M. (2013). Neural Representation of Reward Probability: Evidence from the Illusion of Control. *Journal of Cognitive Neuroscience*, *25*(6), 852-861. ***Indicates co-first authorship**
c. Hakim, Z. M., Ebner, N. C., Oliveira, D. S., **Getz, S. J.,** Levin, B. E., Lin, T., ... & Wilson, R. C. (2020). The Phishing Email Suspicion Test (PEST) a lab-based task for evaluating the cognitive mechanisms of phishing detection. Behavior Research Methods, 1-11.
d. Grilli, M.D., McVeigh, K.S., Hakim, Z.M, Wank, A.A., Ebner, N.C., **Getz, S.J**., Levin, B.E., & Wilson, R.C. (under review). Is this phishing? Older age is associated with greater difficulty discriminating between safe and fraudulent emails.

## A. Positions and Honors

**Clinical Positions**

| | |
|---|---|
| 2013-2014 | Practicum Clinician, Center for Anxiety and Related Disorders (CARD), Psychological Services Clinic, Boston University, Boston, MA |
| 2014-2015 | Research Interventionist, Department of Psychiatry/Behavioral Medicine, Brigham and Women's Hospital/ Harvard Medical School, Boston, MA |
| 2014-2015 | Advanced Neuropsychology Practicum Student and Technician, Child and Family Psychological Services, Norwood, MA |
| 2014-2015 | Advanced Neuropsychology Practicum Student, Cognitive Neurology Unit, Beth Israel Deaconess Medical Center/ Harvard Medical School, Boston, MA |
| 2015-2016 | Neuropsychology Intern and Chief Intern, Miami VA Medical Center, Miami, FL |
| 2016-2018 | Neuropsychology Fellowship, University of Miami/Miller School of Medicine, Department of Neurology/Division of Neuropsychology, Miami, FL |
| 2018-present | Instructor of Neuropsychology, Department of Neurology, University of Miami/Miller School of Medicine, Department of Neurology/Division of Neuropsychology, Miami, FL |

**Research Positions and Employment**

| | |
|---|---|
| 2005-2006 | Research Assistant, Kosslyn Laboratory, Harvard University, Cambridge, MA |
| 2006-2008 | Senior Research Aide, Sackler Institute for Developmental Psychobiology, Weill Cornell Medical College, New York, NY |
| 2013 | Research Consultant at Educational Testing Services, Princeton, NJ |

**Other Experience**

| | |
|---|---|
| 2009-2010 | Psychology Graduate Representative, Princeton University |
| 2010-2012 | Co-director of Neuroscience of Social Decision-Making Speaker Series, Princeton University |
| 2012-2013 | Resident Graduate Fellow, Forbes College, Princeton University |
| 2015-2016 | Chief Intern, Miami VA Medical Center |
| 2017 | Ad hoc Reviewer for the Journal of the International Neuropsychological Society and Neuropsychology |

**Honors and Awards**

| | |
|---|---|
| 2004 | Recommendation for Academic Excellence, Reed College |
| 2005 | Mind and Life Summer Research Institute Fellow |

2005 Mind and Life Initiative Grant (PI: Daniel Reisberg)
2008 Princeton University Admission Merit Award
2008 Princeton University Graduate Student Fellowship
2012 Princeton University Residential Graduate Fellow, Forbes College
2013 Dissertation Grant, Princeton Center for Health and Wellbeing, Demography of Aging Center, Woodrow Wilson School of Public and International Affairs, Princeton University
2015 Women in Leadership Sponsorship, National Academy of Neuropsychology
2018 University of Miami Medical Faculty Association Travel Award
2018 McKnight Brain Research Foundation – Pilot Study Award (Co-I with Bonnie Levin, PhD (UM), Robert Wilson, PhD (UA), Matthew Grilli, PhD (UA), Natalie Ebner PhD (UF), and Daniela Oliveira, PhD (UF))

## B. Contributions to Science

### 1. Decision making across the lifespan (Early Career and Graduate Research)

This research examined the hypothesis that suboptimal decision-making may result from an imbalance between brain regions involved in reward and executive control processes. When this imbalance occurs, the reward-oriented system may override the control system and give rise to impulsive decision-making. I examined this imbalance in both the developing brain as well as via experimental manipulations in young adults. Experimentally, I investigated intertemporal choice—decisions over time that involve trade-offs between costs and benefits. I hypothesized that choosing larger long-term rewards over smaller short-term rewards requires control mechanisms and preferentially recruits brain regions involved in cognitive control. Frequently, decisions are made while tasks that also require control are simultaneously performed, which can cause interference of limited capacity control mechanisms necessary for patient decision-making. My research examined how interference of control mechanisms leads to decisions that are impulsive, maladaptive, or suboptimal.

Representative Publications and Presentations:

a. Casey, B. J., **Getz, S.** Galvan, A. (2008). The adolescent brain. *Developmental Review, 28*, 62-77.
b. Mulder, M. J., Gold, J. I., Durston, S., Heasly, B., Millner, A., Simen, P., **Getz, S**., Voss, H., Ballon, D., & Casey, B. J. (2009). BOLD Correlates of Reward-Related Decision Bias on a Visual Discrimination Task. *Neuroimage*, *47* (Supplement 1).
c. **Getz, S. J.,** Tomlin D., Nystrom, L. E., Conway, A. R. A., & Cohen, J. D. (2010, October). *Executive control of intertemporal choice: Effects of cognitive load on impulsive decision-making*. Poster presented at Neuroeconomics. Evanston, IL.
d. Kool, W., **Getz, S. J**.*, & Botvinick, M. M. (2013). Neural Representation of Reward Probability: Evidence from the Illusion of Control. *Journal of Cognitive Neuroscience*, *25*(6), 852-861. ***Indicates co-first authorship**

### 2. Cognitive training and rehabilitation (Graduate Research)

The scope of my research has expanded to focus on training of working memory. I am an author on an opinion paper and chapter that argue for a better understanding of the durability and transfer of working memory training to other cognitive domains. Specifically, in this work we argue that the efficacy of our current training paradigms—particularly those that focus on rehabilitation and enhancement of cognitive resources—warrant concerns about the construct measurement, underlying cognitive and neural mechanisms, and durability of cognitive gains. Accordingly, this line of research may produce a means of improving cognitive rehabilitation outcomes for the elderly as well as a range of neuropsychological conditions.

Representative Publications:

a. Conway, A.R.A. & **Getz, S.** (2010). Cognitive ability: Does working memory training enhance intelligence? *Current Biology*, *20*, 362-4.
b. Conway, A. R. A., **Getz, S**., Macnamara, B., & Engel, P. (2011). Working memory and fluid intelligence: A multi-mechanism view. In R. Sternberg and S. B. Kaufman (Eds.). Cambridge Handbook of Intelligence.

### 3. Prodromal features and neuropsychological sequelae of several neurologic conditions (Residency Research)

As a resident, my research has examined prodromal features and neuropsychological sequelae of several neurologic conditions. In one line of research, we have synthesized multidisciplinary evidence to examine the early prodromal phase of Parkinson's disease pathology. Better understanding of the earliest biomarkers of Parkinson's disease is crucial for the development of neuroprotective, disease modifying, cognitive, and psychiatric interventions. In a separate line of research, my co-authors and I examined the constellation of acute and post-acute cognitive and emotional changes associated with mTBI, as well as effects on vestibular functioning. A greater understanding of the intersection between cognition and neurosensory function will provide a valuable framework to study the complex array of cognitive, emotional, and behavioral changes following a mild traumatic head injury. In a third line of research, I have applied the Fried Frailty Syndrome to assess whether adverse childhood events are selectively linked to one or more of the five frailty subcomponents. Findings from this work add to the growing literature showing that early life stress is associated with negative health outcomes in older age. Specifically, self-reported fatigue in the context of the frailty syndrome in middle and later life may be best viewed for select individuals from a developmental perspective that takes into account the long-range impact of childhood trauma.
Representative Publications and Presentations:

a. **Getz, S. J.**, & Levin, B. (2017). Cognitive and neuropsychiatric features of early Parkinson's disease. Archives of Clinical Neuropsychology, 32(7), 769-785.
b. **Getz S.J.,** McInerney K.F., Sun-Suslow S., Banerjee N.S., Bure-Reyes A., Sarno M., Levin B.E. Low Emotional Reserve as a Risk Factor for the Frailty Syndrome. Journal of the International Neuropsychological Society, 2018:24(1).
c. **Getz, S.** (2018). Cognitive, Cultural and Affective Dimensions of Frailty. Presentation at the Tenth McKnight Inter-Institutional Meeting, Birmingham, Alabama.
d. Banerjee, N., **Getz, S. J.**, & Levin, B. E. (2019). Cognitive-Emotional-Vestibular Triad in Mild Traumatic Brain Injury. In Neurosensory Disorders in Mild Traumatic Brain Injury (pp. 183-198). Academic Press.
e. **Getz, S.J.,** Rooks, J., McInerney, K.F., Banerjee, N.S. & Levin, B.E. (Submitted). Fatigue as a powerful influence in the relationship between childhood exposure to adversity and frailty in later life.

**4. Decision Making and the Aging Brain (Early Stage Investigator Research)**

In my role as Instructor at the University of Miami Miller School of Medicine, I continue to hone my specialized skills in the neuropsychological correlates of neurodegenerative disorders. In addition, I am involved in ongoing studies within the McKnight Brain Research Foundation to alleviate memory loss and promote brain health in the aging. I am the co-principle investigator on a multidisciplinary pilot grant with the Universities of Arizona and Florida that examines the emotional and cognitive correlates of susceptibility to scamming among the elderly. My current efforts are focused on screening measures and primary interventions to reduce deception among the vulnerable elderly with memory loss.
Representative Publications and Presentations:

a. **Getz, S** (2018). Susceptibility to Deception: Decreasing Vulnerability in Age Related Memory Loss. Presentation at the University of Miami Evelyn F. McKnight Brain Institute Research Symposium, Miami, FL December.
b. **Getz, S.** (Spring, 2019). Detecting Deceptive Information in Scamming Paradigms: A Training Intervention. Presentation at the Eleventh McKnight Inter-Institutional Meeting, Gainesville, FL.
c. Hakim, Z. M., Ebner, N. C., Oliveira, D. S., **Getz, S. J.,** Levin, B. E., Lin, T., ... & Wilson, R. C. (2020). The Phishing Email Suspicion Test (PEST) a lab-based task for evaluating the cognitive mechanisms of phishing detection. Behavior Research Methods, 1-11.
d. Grilli, M.D., McVeigh, K.S., Hakim, Z.M, Wank, A.A., Ebner, N.C., **Getz, S.J**., Levin, B.E., & Wilson, R.C. (under review). Is this phishing? Older age is associated with greater difficulty discriminating between safe and fraudulent emails.

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

**<u>Ongoing Research Support</u>**

**Neurocognitive Correlates of Scam Susceptibility in Age-Related Hearing Loss funded by the McKnight Brain Research Foundation through the American Brain Foundation and the American Academy of Neurology.** PI: Sarah Getz. UM Mentors: Tatjana Rundek, M.D. and Bonnie Levin, PhD July 2020-July 2022 ($150k)

McKnight Inter-Institutional Cognitive Aging and Memory Intervention Core pilot grant
Getz, Levin, Ebner, Oliveria, Wilson, & Grilli (Co-PIs)
$40,000
2018 – 2020
The long-term goal of this multi-site collaboration is to develop and validate a decision-supportive device to reduce online scam susceptibility in late midlife and old age.

## 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): JOYCEGOMES-OSMAN

POSITION TITLE: Assistant Professor, Departments of Physical Therapy and Neurology
Faculty, Transcranial Magnetic Stimulation Intensive Course, Berenson-Allen Center for Non-invasive Brain Stimulation, Beth Israel Deaconess Medical Center, Harvard Medical School.

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, Salvador, Bahia, Brazil | B.S. | 06/07 | Physical Therapy |
| University of Miami Miller School of Medicine, FL, USA | Ph.D. | 09/13 | Motor Control Physiology |
| Harvard Medical School, Boston, MA, USA | Post Doctoral Fellowship | 09/15 | Non-Invasive Brain Stimulation Neurology |

### A. Personal Statement

I am a rehabilitation scientist with expertise in clinical and translational research that harnesses neuroplasticity through neuromodulation and exercise to promote functional and cognitive improvements in different clinical populations. I am an Assistant Professor of Clinical Physical Therapy and Neurology where I Direct Neuromotor Plasticity Laboratory at the University of Miami Miller School of Medicine (UM). I am a KL2 scholar from the Clinical and Translational Science Institute at UM. Additionally, I am Faculty at the Transcranial Magnetic Stimulation Intensive Course, Harvard Medical School. My early studies used neuromodulation techniques to augment rehabilitation targeting functional hand use after spinal cord injury. In recent years, my research interest has focused on better understanding how to use exercise to promote neuroplasticity for improving cognitive brain health for aging individuals. This stemmed both from scientific curiosity and also from experiencing cognitive deficits as a family member. The research study proposed in this K01 application will investigate the mechanisms underlying cognitive gains after a 16-week aerobic exercise intervention in adults aged 55-80 years by combining the use of an assessment of neuroplasticity using transcranial magnetic stimulation (TMS) and electroencephalography (TMS-EEG), cardiorespiratory fitness testing. This K01 Award will allow me to advance my academic career by protecting my time for research, additional training and mentorship from a multi-disciplinary group of established researchers at UM and Harvard. By expanding my skills in Cognitive Aging, Advanced Cardiorespiratory Testing, and Clinical Trials and Biostatistics, this K01 grant will enable me to develop and test exercise interventions that can be personalized to an individual, and likely to be more effective at improving cognition in aging adults. The successful completion of the research and training aims will allow me to approach my long-term goal of developing into a successful independent investigator and a research leader dedicated to improving cognitive health through exercise interventions targeting optimal cognitive health in aging adults. Finally, the results of this study will inform an R01 proposal to precisely and rigorously investigate mechanisms driving cognitive gains associated with different exercise doses and modalities in Year 3 of this proposed Award. Given the stage of my clinical and research training, my research field and interests, and strong support from my mentorship team and the Chairs of Physical Therapy and Neurology, I believe I am an excellent candidate for this K01 award.

**B. Positions and Honors**

**Positions and Employment**

| | |
|---|---|
| 2018- | Assistant Professor (secondary appointment), Department of Neurology, University of Miami Miller School of Medicine. |
| 2016- | Member, Center on Aging, University of Miami Miller School of Medicine. |
| 2014- | Member, Evelyn F. McKnight Brain Institute University of Miami Miller, School of Medicine. |
| 2014- | Assistant Professor, Department of Physical Therapy, University of Miami Miller School of Medicine. |
| 2013- | Faculty, Transcranial Magnetic Stimulation Intensive Course, Berenson-Allen Center for Non-invasive Brain Stimulation. Beth Israel Deaconess Medical Center, Harvard Medical School. |
| 2013-2015 | Postdoctoral Research Fellow, Berenson-Allen Center for Noninvasive Brain Stimulation, Beth Israel Deaconess Medical Center, Harvard Medical School. |
| 2010-2013 | Research Support Specialist, The Miami Project to Cure Paralysis, University of Miami Miller School of Medicine. |
| 2007-2010 | Research Associate, the Miami Project to Cure Paralysis, University of Miami Miller School of Medicine. |

**Honors**

| | |
|---|---|
| 2019 | Dr. Gomes-Osman and Dr. Loewenstein (Primary Mentor on this Application) were nominated as a model mentee-mentor pair, and selected to participate in a formal Mentoring training and Certification program. CTSI, Miami, FL, USA |
| 2019 | Dr. Gomes-Osman's PhD student Jordyn Rice won a prestigious Promotion of Doctoral Studies (PODS) II Scholarship award from the Foundation for Physical Therapy Research for her dissertation work, supervised by Dr. Gomes-Osman. |
| 2019 | Dr. Gomes-Osman was selected to participate in the prestigious 11th Annual International Certificate Course for Translational Medicine, Eureka Institute for Translational Medicine, Italy. |
| 2018 | Dr. Gomes-Osman was selected to participate in the prestigious Training for Grantsmaship in Rehabilitation Research (TIGRR), funded by NIH/NICHD. |
| 2007 | Outstanding Student of the Year, Humberto de Castro Lima Award by the Bahiana School of Medicine and Public Health. |
| 2005 | Scholarship for Young Rising Scientists Foundation for Research, State of Bahia, Brazil "Fundacao de Amparo a Pesquisa do Estado da Bahia (FAPESB)". |

**Other Experience and Professional Memberships**

| | |
|---|---|
| 2020 | Guest Editor for the *Journal of Neurologic Physical Therapy* for a Special Issue: "Harnessing and Evaluating Neuroplasticity in Physical Therapy" |
| 2020 | Reviewer, *Neurology* |
| 2018- | Reviewer, *Experimental Gerontology* |
| 2017- | Reviewer, *Frontiers in Aging Neuroscience* |
| 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. **Investigating dose of exercise needed to promote cognitive improvements in older adults, and determining consistency of cognitive improvements following exercise.** My recent major contribution to the field and relevant to this proposal was a systematic review and regression analysis of 98 randomized clinical trials proposing exercise to improve cognition in older adults with and without cognitive impairments. This study aimed at describing various exercise dose measures, assessing their relationship with improved cognitive performance, and identifying consistent patterns of reported effects on cognition. I found that among various aspects of dose (session duration, weekly minutes, frequency, total weeks, total hours), only total hours was statistically tied to improved cognitive outcomes, and the most stable and consistent cognitive improvements were seen in the cognitive domains of executive function and processing speed/attention. In a second study, I reviewed the neurobiological underpinnings of exercise-induced cognitive improvements. These studies advance the field by: 1) producing practical, evidence-based dose parameters of exercise to improve cognitive function, and 2) further investigating the mechanisms responsible for such cognitive benefits after exercise. I served as primary/corresponding author on these publications. The first publication seen below was selected for a media release and widely publicized in the media.

1. **Gomes-Osman J**, Cabral D, Morris TP, McInerney K, Oliveira A, Rundek T, and Pascual-Leone A. Exercise for cognitive brain cognitive health in aging: a systematic review for an evaluation of dose. ***Neurology: Clinical Practice***; 2018; 1-9.
2. Cabral DF, Rice J, Morris TP, Rundek T, Pascual-Leone A, **Gomes-Osman J.** Exercise for Brain Health: An Investigation into the Underlying Mechanisms Guided by Dose, ***Neurotherapeutics*****,** 2019; 580-599.

C2**. Characterizing TMS Neuroplasticity and genetic differences in response of aerobic exercise on cognitive performance in middle-aged sedentary adults.** In my post-doctoral work, I assessed the feasibility and safety of evaluating the effects of a month-long exercise intervention on cognitive performance, a TMS Measure of Neuroplasticity, and brain derived neurotrophic factor (BDNF) Met carrier status in young sedentary adults. I found cognitive improvements in executive function following 4 weeks of regular aerobic exercise. In addition, neuroplasticity appeared to differ according to BDNF allelic status. I additionally worked on a team and assessed neuroplasticity and cortical excitability with TMS in response to acute aerobic exercise. This work contributes to the literature by introducing an innovative neuroplasticity assessment and exploring genetic factors that may be useful in further elucidating exercise-mediated improvements in cognitive performance. This was the first study proposing TMS to assess neuroplasticity related to exercise-mediated cognitive improvements in humans and I served as first author.

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***; 2017; 547-556.
2. Morris TP, Fried PJ, Macone J, Stillman A, **Gomes-Osman J**, Costa-Miserachs D, Tormos Muñoz JM, Santarnecchi E, Pascual-Leone A. Light aerobic exercise modulates executive function and cortical excitability. ***European Journal of Neuroscience***, 2019; 1723-1734.

C3. **Determining stability of TMS measures and developing guidelines to improve internal consistency in TMS studies.** In my earlier work I observed inter-individual variability in TMS outcomes, leading to my interest in improving the reproducibility of this technique during my post-doctoral work. I worked in a team on a study to calculate the internal consistency in different TMS measures (including TMS Plasticity). I have continued to contribute to this work, which led to the formation of the 'Big TMS Data Collaboration', pooling data from over 60 TMS researchers across the world to conduct a large-scale analysis of consistency in TMS outcomes. 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. I served as a co-author in these studies.

1. 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; ***Clinical Neurophysiology***; 2016; 2892-2897.
2. Corp DT, Bereznicki HGK, Clark GM, Youssef GJ, Fried PJ, Jannati A, Davies CB, **Gomes-Osman J**, Stamm J, Chung SW, Bowe SJ, Rogasch NC, Fitzgerald PB, Koch G, Di Lazzaro V, Pascual-Leone A, Enticott PG; 'Big TMS Data Collaboration'. ***Brain Stimulation***, 1476-1488, 2020

C4. **Transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS) and exercise promote neuroplasticity that supports unimanual and bimanual fine motor performance.** My doctoral work focused on comparing non-invasive brain stimulation protocols for harnessing plasticity to augment motor function, both in neurologically healthy individuals and individuals with chronic incomplete tetraplegia. I found that TMS and tDCS applied to the primary motor cortex individually augmented the effects of neurorehabilitation exercise programs designed to improve fine motor hand function, both in neurologically healthy individuals and individuals with tetraplegia. This body of work provides evidence that TMS and tDCS can be used to improve the results of rehabilitation programs aimed at improving fine motor control of the hand. I served as primary author on these publications.

1. **Gomes-Osman J**, Field-Fote EC; Improvements in hand function in adults with chronic tetraplegia following a multi-day 10Hz rTMS intervention combined with repetitive task practice***; Journal of Neurologic Physical Therapy***; 2015; 23-30.
2. **Gomes-Osman J**, Field-Fote EC; Bihemispheric Anodal Corticomotor Stimulation Using Transcranial Direct Current Stimulation Improves Bimanual Typing Task Performance; ***J Motor Behavior***; 2013; 361-367.
3. **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***; 2016; 1-13.
4. **Gomes-Osman J**, Field-Fote EC; Cortical versus afferent stimulation as an adjunct to functional task practice training: a randomized, comparative pilot feasibility study in people with cervical spinal cord injury; ***Clinical Rehabilitation***; 2015; 771-782.

Complete List of Published Work in My Bibliography:

https://www.ncbi.nlm.nih.gov/myncbi/1xg4wvaMqVQQE/bibliography/public/

1. Morris TP, Fried PJ, Macone J, Stillman A, **Gomes-Osman J**, Costa-Miserachs D, Tormos Muñoz JM, Santarnecchi E, Pascual-Leone A. Light aerobic exercise modulates executive function and cortical excitability. ***European Journal of Neuroscience***, 2019; 1723-1734.
2. Shpiner DS, McInerney KF, Miller M, Allen J, Rice J, Luca CC, Adams D, **Gomes-Osman J.** High frequency repetitive transcranial magnetic stimulation for primary progressive apraxia of speech: A case series. ***Brain Stimulation***, 2019; 1581-158.
3. Cabral DF, Rice J, Morris TP, Rundek T, Pascual-Leone A, **Gomes-Osman J.** Exercise for Brain Health: An Investigation into the Underlying Mechanisms Guided by Dose, ***Neurotherapeutics*****,** 2019; 580-599.
4. Morris TP, Costa-Miserachs D, Rodriguez-Rajo P, Finestres J, Bernabeu M, **Gomes-Osman J**, Pascual-Leone A, Tormos-Muñoz JM. Feasibility of Aerobic Exercise in the Subacute Phase of Recovery from Traumatic Brain Injury: A Case Series. ***Journal of Neurologic Physical Therapy***; 2018; 268-275.
5. Corp DT, Youssef GJ, Clark RA, **Gomes-Osman J**, Yücel MA, Oldham SJ, Aldraiwiesh S, Rice J, Pascual-Leone A, Rogers MA, Reduced motor cortex inhibition and a 'cognitive-first' prioritisation strategy for older adults during dual-tasking, ***Experimental Gerontology*****,** 95-105, 2018
6. **Gomes-Osman J**, Indahlastari A, Fried PJ, Cabral DLF, Rice J, Nissim NR, Aksu S, McLaren ME and Woods AJ. Non-invasive Brain Stimulation: Probing Intracortical Circuits and Improving Cognition in the Aging Brain. ***Frontiers in Aging Neuroscience***; 2018; 1-25.
7. **Gomes-Osman J**, Cabral D, Morris TP, McInerney K, Oliveira A, Rundek T, and Pascual-Leone A. Exercise for cognitive brain cognitive health in aging: a systematic review for an evaluation of dose. ***Neurology: Clinical Practice***; 2018; 1-9.
8. Spagnuolo G, Farias CDCM, da Silva BA, Ovando, AC, **Gomes-Osman J**, Swarowsky A. Are functional mobility tests responsive to group conventional physical therapy intervention in individuals with Parkinson's disease? ***Neurorehabilitation***; 2018; 465-472.
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***; 2017; 547-556.

10. **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***; 2016; 1-13.
11. 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.
12. 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; ***Clinical Neurophysiology***; 2016; 2892-2897.
13. **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. ***Journal of Neurotrauma***; 2016; 425-438.
14. **Gomes-Osman J**, Field-Fote EC; Improvements in hand function in adults with chronic tetraplegia following a multi-day 10Hz rTMS intervention combined with repetitive task practice***; Journal of Neurologic Physical Therapy***; 2015; 23-30.
15. **Gomes-Osman J**, Field-Fote EC; Cortical versus afferent stimulation as an adjunct to functional task practice training: a randomized, comparative pilot feasibility study in people with cervical spinal cord injury; ***Clinical Rehabilitation***; 2015; 771-782.
16. **Gomes-Osman J**, Field-Fote EC; Bihemispheric Anodal Corticomotor Stimulation Using Transcranial Direct Current Stimulation Improves Bimanual Typing Task Performance; ***J Motor Behavior***; 2013; 361-367.
17. 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. ***Journal of the Peripheral Nervous System***; 2009; 285-293.
18. Baptista AF, **Gomes JR**, Oliveira JT, Santos SM, Vannier-Santos MA, Martinez AMB; High and low frequency transcutaneous electrical nerve stimulation delay sciatic nerve regeneration in the mouse. ***Journal of Neuroscience Methods***; 2008; 71-80.
19. Baptista AF, **Gomes JR**, Oliveira JT, Santos SM, Vannier-Santos MA, Martinez AMB; A new approach to assess function after sciatic nerve lesion in the mouse-Adaptation of the sciatic static index. ***Journal of Neuroscience Methods***; 2007; 259-264.
20. Corp DT, Bereznicki HGK, Clark GM, Youssef GJ, Fried PJ, Jannati A, Davies CB, **Gomes-Osman J**, Stamm J, Chung SW, Bowe SJ, Rogasch NC, Fitzgerald PB, Koch G, Di Lazzaro V, Pascual-Leone A, Enticott PG; 'Big TMS Data Collaboration'. ***Brain Stimulation***, 1476-1488, 2020
21. Koch S, Tiozzo E, Simonetto M, Loewenstein D, Wright CB, Dong C, Bustillo A, Perez-Pinzon M, Dave KR, Gutierrez CM, Lewis JE, Flothmann M, Mendoza-Puccini MC, Junco B, Rodriguez Z, **Gomes-Osman J**, Rundek T, Sacco RL.Randomized Trial of Combined Aerobic, Resistance, and Cognitive Training to Improve Recovery From Stroke: Feasibility and Safety. ***Journal of the American Heart Association***, e015377, 2020

**D. Research Support**

2018 **Miami Clinical and Translational Science Institute Mentored Translational Research Scholars Program Awards (KL2).** Assessing Cognitive Improvements, Brain Neuroplasticity and the Role of Genetic Factors After Aerobic Exercise in Sedentary Adults. This study is aimed at investigating mechanisms underlying cognitive benefits after an 8-week exercise intervention in sedentary adults over 55 years of age. This study utilizes Transcranial Magnetic Stimulation (TMS) to gain insights into neuroplasticity, neuropsychological measures, and examines potential effect modifications by brain-derived neurotrophic factor (BDNF) and and apolipoprotein E (APOE) factors. **Role: Principal Investigator.** Grant amount: 75% of current salary plus $32,500 per year for the award period.

Past

2017-2018 **Evelyn F. McKnight Brain Institute Internal Pilot Grant.** 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.

# 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 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 |
| 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

Accumulating evidence implicates the significance of the microvascular alternation in contributing to age related cognitive impairment and dementia such as late onset Alzheimer's disease (AD). However, cerebral microvasculature is difficult to access. The retina has been used as a model to study central nervous system disorder because brain and retina shares similar anatomic and physiologic and vascular features. We propose to study retinal microvascular changes at the capillary level using advance ophthalmic imaging techniques in patients with mild cognitive impairment (MCI), and correlate the retinal microvascular alterations with cognitive impairment. The goal is to develop retinal vascular biomarkers for monitoring disease progression and therapeutic efficacy. 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 8 years. My work relevant to this project has been reflected in my recent publications in the field of retina functional imaging. My expertise and experience make me well equipped and qualified for working in this proposed project.


1. Lin Y, **Jiang H**, Liu Y, Gameiro GR, Gregori G, Dong C, Rundek T, Wang J. Age-related alterations in retinal tissue perfusion and volumetric vessel density. Investigative Ophthalmology and Vision Research. 2019;60;685-693. PubMed PMID: 30786280; PubMed Central PMCID: PMC6383727.
2. **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. J Neuroophthalmol. 2018 Sep; 38(3):292-298. PubMed PMID: 29040211; PMCID: PMC5902666.
3. Shao Y, **Jiang H**, Wei Y, Shi Y, Shi C, Wright CB, Sun X, Vanner, EA, Rodriguez AD, Lam BL, Rundek T, Baumel BS, Gameiro GR, Dong C**,** Wang J. Visualization of Focl Thinning of the Ganglion Cell-Inner

Plexiform Layer in Patients with Mild Cognitive Impairment and Alzheimer's Disease J *Alzheimers Dis* 64(4):1261-127. PubMed PMID: 30040712.

4. Gameior GR, **Jiang H**, Liu Y, Deng Y, Sun X, Nascentes B, Baumel B, Rundek T, Wang J. Retinal tissue hypoperfusion in patients with clinical Alzheimer's disease. Eye Vis (Lond). 2018;17;5:21. PubMed PMID: 30140712; PubMed Central PMCID: PMC6097197

## 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 – 5/2018 | Clinical Assistant Professor, Neuro-ophthalmology & Neurology, Bascom Palmer Eye Institute & Dept. of Neurology, University of Miami, Miami, FL |
| 6/2018 - now | Clinical Associate 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 |
| 2019 | The J. Lawton Smith Award 2019 from NANOS for the paper published in JNO titled "Altered macular microvasculature in mild cognitive impairment and Alzheimer's disease. |

## C. Contribution to Science

1. I have initiated the development of automatic segmentation of 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. J Neuroophthalmol. 2018 Sep; 38(3):292-298. PubMed PMID: 29040211; PMCID: PMC5902666

    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 in studying cerebral small vessel diseases, a system called functional slit-lamp biomicroscope (FSLB) was developed and a patent of single shot for generating conjunctival microvascular network map was filled. 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 and Alzheimer's dementia, I have contribute to the development of slit-lamp based ultra-high resolution OCT for imaging the retina. Our segmentation software can segment 9 retinal sub-layers. Recent development of segmentation 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. Shao Y, Jiang H, Wei Y, Shi Y, Shi C, Wright CB, Sun X, Vanner, EA, Rodriguez AD, Lam BL, Rundek T, Baumel BS, Gameiro GR, Dong C**, Wang J**. Visualization of Focl Thinning of the Ganglion Cell-Inner Plexiform Layer in Patients with Mild Cognitive Impairment and Alzheimer's Disease J *Alzheimers Dis* 2018;64(4):1261-127. PubMed PMID: 30040712

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

UM Dean Bridge Award DBA 2019-3 Jiang, Hong (PI) 8/1/18-3/31/20
Novel retinal microvascular biomarker of vascular contribution to dementia
The goal is to run a preliminary study to bridge NIH grant application.
Role: PI

NMSS, National Multiple Sclerosis Society (no cost extension) Jiang, Hong (PI) 04/01/16-03/31/20
The Role of retinal microvascular impairment on Neurodegeneration in Multiple Sclerosis
Role: PI

R01 R01NS111115A1 Detre and Wang (MPI) 08/15/2019-03/31/2024
NIH/NINDS
Novel Biomarkers of Small Vessel Contributions to Vascular Cognitive Impairment and Dementia (VCID)
This project will investigate the biological and technical determinants of brain MRI cerebral blood flow (CBF) and OCTA-derived microvascular density, associate changes in retinal microvasculature with brain perfusion, and preliminarily show their predictive value in small vessel disease (SVD) by correlating baseline measures with longitudinal changes in healthy and clinical cohorts of SVD.
Role: Co-investigator

SUN1, Sun Yat-sen University Collaboration Award Wang, Jianhua (PI) 10/01/15-09/30/20
Clinical applications of advanced ophthalmic imaging
Role: Co-Investigator

Food UM 01, Global Healthcare Focus LLC Wang, Jianhua (PI) 01/01/17-12/31/19
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: Co-Investigator

CR-5879 Johnson & Johnson Vision Care Jiang, Hong (PI) 03/1/2018-12/31/19
Lid-wiper microvascular response as an indicator of contact lens discomfort
The goal of this study is to characterize lid-wiper microvasculature in contact lens wear.
Role: PI

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

US202, Toyama (pharmaceutical company) Wright, Baumel (PIs) 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'ss Disease (US202)
Role: Co-Investigator

NANOS Pilot 2015, North American Neuro-Ophthalmology Society Jiang, Hong (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, Hong (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 Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Kaur, Sonya

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

POSITION TITLE: Instructor

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) | END DATE MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| Monash University, Melbourne, Victoria | BA | 02/2009 | Psychology |
| University of Texas at Austin, Austin, Texas | PHD | 05/2017 | Clinical Psychology |
| Henry Ford Health System, Detroit, Michigan | Resident | 07/2017 | Internship in Clinical Neuropsychology |
| University of Miami , Miami, Florida | Postdoctoral Fellow | 10/2019 | Postdoctoral fellow in Neuropsychology |

## A. Personal Statement

I am a neuropsychologist with a broad research interest in the area of cognitive aging. As an instructor at the University of Miami Miller School of Medicine, I am heavily involved with the McKnight Brain Research Institute, where I have participated in multi-site collaborations characterizing cognition in the oldest old, frailty and cognition in middle aged to older adults with subjective memory complaints. Prior to my appointment, I conducted multi-modal neuroimaging research examining the neural consequences of metabolic syndrome in middle aged adults who do not exhibit cognitive decline. My long term goal is to identify the mechanisms of cognitive aging in order to develop useful targeted interventions.


1. Oleson S, Eagan D, Kaur S, Hertzing WJ, Alkatan M, Davis JN, Tanaka H, Haley AP. Apolipoprotein E genotype moderates the association between dietary polyunsaturated fat and brain function: an exploration of cerebral glutamate and cognitive performance. Nutr Neurosci. 2020 Sep;23(9):696-705. PubMed PMID: 30465491; PubMed Central PMCID: PMC6531361.
2. Banerjee N, Slugh M, Kaur S, Sun-Suslow N, McInerney KF, Sun X, Levin BE. Neuropsychological correlates of subjective fatigue in non-demented older adults and the moderating effect of physical activity. Neuropsychol Dev Cogn B Aging Neuropsychol Cogn. 2020 Mar;27(2):254-269. PubMed PMID: 31025596.
3. Kaur S, Banerjee N, Miranda M, Slugh M, Sun-Suslow N, McInerney KF, Sun X, Ramos AR, Rundek T, Sacco RL, Levin BE. Sleep quality mediates the relationship between frailty and cognitive dysfunction in non-demented middle aged to older adults. Int Psychogeriatr. 2019 Jun;31(6):779-788. PubMed PMID: 31006402.
4. Haley AP, Oleson S, Pasha E, Birdsill A, Kaur S, Thompson J, Tanaka H. Phenotypic heterogeneity of obesity-related brain vulnerability: one-size interventions will not fit all. Ann N Y Acad Sci. 2018 Sep;1428(1):89-102. PubMed PMID: 29741211.


## B. Positions and Honors

### Positions and Employment

2008 - 2009 Research Psychologist, National University Health System, Singapore
2010 - 2016 Teaching Assistant, University of Texas at Austin
2016 - 2017 Neuropsychology Intern, Henry Ford Health System

| | |
|---|---|
| 2017 - 2019 | Post Doctoral Fellow, University of Miami Miller School of Medicine |
| 2018 - 2019 | Ad-hoc reviewer, Journal of the International Neuropsychological Society |
| 2018 - 2019 | Ad-hoc reviewer, Neurobiology of Aging |
| 2019 - | Instructor, University of Miami |

## Other Experience and Professional Memberships

| | |
|---|---|
| 2010 - | Member, American Academy of Clinical Neuropsychology |
| 2018 - | Member, Sleep Research Society |
| 2019 - | Member, American Academy for Sleep Medicine |

## Honors

| | |
|---|---|
| 2010 | Ira and Lousie Ischoe Fellowship, University of Texas at Austin |
| 2016 | Lee Willerman Award for Research Excellence, University of Texas at Austin |
| 2016 | Graduate student travel award, University of Texas at Austin |
| 2019 | Young Investigators Research Forum, American Academy of Sleep Medicine Foundation |
| 2020 - 2021 | Sleep Research Program for Advancing Careers (SOAR) fellowship, American Academy for Sleep Medicine Foundation |

## C. Contribution to Science

1. Examining the association between cardio-metabolic risk and brain vulnerability and elucidating the mechanisms that drive these relationships has been an important focus of my research. In particular, I have demonstrated that obesity in midlife is strongly associated with multi-modal imaging markers of brain vulnerability even prior to onset of cognitive decline.

    a. Birdsill AC, Oleson S, Kaur S, Pasha E, Ireton A, Tanaka H, Haley A. Abdominal obesity and white matter microstructure in midlife. Hum Brain Mapp. 2017 Jul;38(7):3337-3344. PubMed PMID: 28390146; PubMed Central PMCID: PMC5632566.

    b. Kaur S, Birdsill AC, Steward K, Pasha E, Kruzliak P, Tanaka H, Haley AP. Higher visceral fat is associated with lower cerebral N-acetyl-aspartate ratios in middle-aged adults. Metab Brain Dis. 2017 Jun;32(3):727-733. PubMed PMID: 28144886; PubMed Central PMCID: PMC6802935.

    c. Kaur S, Gonzales MM, Strasser B, Pasha E, McNeely J, Tanaka H, Haley AP. Central Adiposity and Cortical Thickness in Midlife. Psychosom Med. 2015 Jul-Aug;77(6):671-8. PubMed PMID: 26098178.

    d. Gonzales MM, Kaur S, Eagan DE, Goudarzi K, Pasha E, Doan DC, Tanaka H, Haley AP. Central adiposity and the functional magnetic resonance imaging response to cognitive challenge. Int J Obes (Lond). 2014 Sep;38(9):1193-9. PubMed PMID: 24418893; PubMed Central PMCID: PMC4097967.

2. Given my clinical background, I have pursued research with regards to neurobiological markers of cognition in diverse samples of middle aged and older adults. In particular, I have explored the effects of neurotrophins, pro-inflammatory cytokines and vascular risk in cognitively healthy middle aged adults. In highlighting the mediating effect of these peripheral markers on cognition, I have added to the literature on the significant effect of vascular risk on cognitive outcomes.

    a. Gourley D, Pasha EP, Kaur SS, Haley AP, Tanaka H. Association of Dementia and Vascular Risk Scores With Cortical Thickness and Cognition in Low-risk Middle-aged Adults. Alzheimer Dis Assoc Disord. 2020 May 27;PubMed PMID: 32467426.

    b. Kaur S, Gonzales MM, Tarumi T, Villalpando A, Alkatan M, Pyron M, Tanaka H, Haley AP. Serum Brain-Derived Neurotrophic Factor Mediates the Relationship between Abdominal Adiposity and Executive Function in Middle Age. J Int Neuropsychol Soc. 2016 May;22(5):493-500. PubMed PMID: 27026196.

    c. Kaur SS, Gonzales MM, Eagan DE, Goudarzi K, Tanaka H, Haley AP. Inflammation as a mediator of the relationship between cortical thickness and metabolic syndrome. Brain Imaging Behav. 2015 Dec;9(4):737-43. PubMed PMID: 25376331; PubMed Central PMCID: PMC4424190.

3. An important aspect of my research program has involved examining the mediating and moderating effects of lifestyle (i.e. poor sleep quality, dietary polyunsaturated fat, exercise) on cognitive and neuroimaging biomarkers. Given the fact that neurodegeneration is irreversible, it is crucial to examine potential markers that could prevent or delay disease onset.

    a. Kaur S, Banerjee N, Miranda M, Slugh M, Sun-Suslow N, McInerney KF, Sun X, Ramos AR, Rundek T, Sacco RL, Levin BE. Sleep quality mediates the relationship between frailty and cognitive dysfunction in non-demented middle aged to older adults. Int Psychogeriatr. 2019 Jun;31(6):779-788. PubMed PMID: 31006402.
    b. Oleson S, Eagan D, Kaur S, Hertzing WJ, Alkatan M, Davis JN, Tanaka H, Haley AP. Apolipoprotein E genotype moderates the association between dietary polyunsaturated fat and brain function: an exploration of cerebral glutamate and cognitive performance. Nutr Neurosci. 2020 Sep;23(9):696-705. PubMed PMID: 30465491; PubMed Central PMCID: PMC6531361.
    c. Haley AP, Oleson S, Pasha E, Birdsill A, Kaur S, Thompson J, Tanaka H. Phenotypic heterogeneity of obesity-related brain vulnerability: one-size interventions will not fit all. Ann N Y Acad Sci. 2018 Sep;1428(1):89-102. PubMed PMID: 29741211.
    d. Gonzales MM, Tarumi T, Kaur S, Nualnim N, Fallow BA, Pyron M, Tanaka H, Haley AP. Aerobic fitness and the brain: increased N-acetyl-aspartate and choline concentrations in endurance-trained middle-aged adults. Brain Topogr. 2013 Jan;26(1):126-34. PubMed PMID: 22926147; PubMed Central PMCID: PMC3537918.

4. Given the underrepresentation of minorities in clinical research, I have made conducting research that includes diverse samples an important priority. To that end, I have contributed to publications that have highlighted important differences in arterial stiffness, cortical thinning and cognitive dysfunction among non-demented participants who identify as Hispanic/Latino.

    a. Gourley D, Pasha EP, Kaur SS, Haley AP, Tanaka H. Association of Dementia and Vascular Risk Scores With Cortical Thickness and Cognition in Low-risk Middle-aged Adults. Alzheimer Dis Assoc Disord. 2020 May 27;PubMed PMID: 32467426.
    b. Banerjee N, Slugh M, Kaur S, Sun-Suslow N, McInerney KF, Sun X, Levin BE. Neuropsychological correlates of subjective fatigue in non-demented older adults and the moderating effect of physical activity. Neuropsychol Dev Cogn B Aging Neuropsychol Cogn. 2020 Mar;27(2):254-269. PubMed PMID: 31025596.
    c. Kaur S, Banerjee N, Miranda M, Slugh M, Suslow NS, McInerney KF, Sun X, Ramos A, Rundek T, Sacco RL, Levin BE. Sleep quality mediates the relationship between frailty and cognitive dysfunction in non-demented middle aged to older adults. Int Psychogeriatr. 2020 Feb 17;PubMed PMID: 32063237.
    d. Pasha EP, Kaur SS, Gonzales MM, Machin DR, Kasischke K, Tanaka H, Haley AP. Vascular function, cerebral cortical thickness, and cognitive performance in middle-aged Hispanic and non-Hispanic Caucasian adults. J Clin Hypertens (Greenwich). 2015 Apr;17(4):306-12. PubMed PMID: 25720950; PubMed Central PMCID: PMC4390456.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/1ziZ7VecpL8IYd/bibliography/public/

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

N/A

## 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: Bonnie E. Levin, Ph. D.

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

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)* | 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 and Cognitive Neuroscience, Department of Neurology at the University of Miami Miller School of Medicine. Currently, I hold the Bernard and Alexandria Schoninger Professorship in Neurology. I founded the Division of Neuropsychology and Cognitive Neuroscience and direct the Schoninger Neuropsychology Teaching Program. I supervise the research activities of PhD graduate students, interns and fellows as well as mentor post-doctoral fellows in clinical assessment and intervention. I have taught the graduate level course, Foundations of Neuropsychology and Clinical Neuroscience, for over 30 years. I work collaboratively with research teams in Neurology, Neurosurgery, Bascom Palmer Eye Institute, Radiology and Otolaryngology on multiple projects examining cognitive, behavioral and imaging changes associated with normal aging and neurodegenerative disease. I am currently the site PI of the cognitive core on a study examining cognitive and behavioral changes in the oldest old funded by the McKnight Brain Research Institute as well as the PI of the UM McKnight Frailty Project and a recently funded McKnight Brain Research Institute pilot study, Susceptibility to Deception in the Aged. I am also a co-investigator on the NIH-funded population based Northern Manhattan Study (NOMAS), in which I am a member of the dementia adjudication consensus panel. Other projects where I serve as a co-investigator include: a project investigating the role of gut microbiota on brain metabolism, inflammation and cognition in Alzheimer's disease, a DoD funded study examining PTSD in mild traumatic brain injury, and a multi-site study assessing traumatic risk and fitness for continued duty. My broad research expertise in cognitive, behavioral and socioemotional aging neuroscience over the lifespan and early biomarkers of behavioral and cognitive decline in neurodegenerative disease as well as my experience as the director of a large clinical neuroscience lab, puts me in an excellent position to direct the clinical assessments in the proposed application. I believe I have the necessary qualifications, expertise, administrative and leadership skills.


1. Banerjee, N., Slugh, M., Kaur, S., Sun-Suslow, N., McInerney, K.F., Sun, X., **Levin, B.E**. Neuropsychological correlates of subjective fatigue in non-demented older adults and the moderating effect of physical activity. Aging, Neuropsychology, and Cognition, 2019,
2. Hoffer ME, **Levin BE**, Snapp H, Buskirk J, Balaban C. Acute Findings in an Acquired NeurosensoryDysfunction. Laryngoscope Investig Otolaryngol. 2018 Dec 12;4(1):124-131. doi: 10.1002/lio2.231. eCollection 2019 Feb.
3. **Levin, BE**, Llabre. MM., Dong, C., Elkind, M.,Stern,Y.,Rundek,T.,Sacco, R., Wright, CB. Modeling metabolic syndrome and its association with cognition: The Northern Manhatten Study. Journal of the International Neuropsychology Society. 2014 Nov;20(10):951-60. PubMed PMID: 253821
4. Balaban, CD., Szczupak, M., Kiderman, A., Hoffer, ME, **Levin, BE**. Distinctive Convergence Eye Movements in an Acquired Neurosensory Dysfunction. Frontiers Neurology: Neur0Ophthalmology, 2020 (in press)

**B. Positions and Honors**

| | |
|---|---|
| 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 Study Section, 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 sensory, behavioral and cognitive decline in normal aging and neurodegenerative disease. As the Schoninger Professor of Neurology, I oversee the Division of Neuropsychology and Cognitive Neuroscience, 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. Tomer, R**, Levin, BE**, Differential affects of aging in two verbal fluency tasks. Perceptual and Motor Skills, 1993; 76: 465-466
2. Geldmacher, DS, **Levin BE**, Wright CB. Characterizing healthy samples for studies of normal cognitive aging. Front. Ag. Neurosci., 2012, 4:6
3. Kaur, S, Banerjee, N, Miranda, M, Slugh, M, Sun-Suslow, N, McInerney, K.F, Sun, X, Ramos, A.R., Rundek, T., Sacco, R.L., **Levin, B.E**. Sleep quality mediates the relationship between frailty and cognitive dysfunction in non-demented middle aged to older adults, International Psychogeriatrics 2019 Jun;31(6):779-788.
4. Airen S, Shi C, Liu Z, **Levin BE**, Signorile JF, Wang J, Jiang H. Focal alteration of the intraretinal layers in neurodegenerative disorders. Ann Eye Sci 2020;5:8.

**C.2.** Our group was among the earliest investigators to document and describe non-motor changes in Parkinson's disease. I 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 other imaging changes associated with normative aging, TBI, ALS and Parkinson's disease. These studies utilize 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 white matter changes, cortical brain volume, and 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. J Neurotrauma, 2016; 33(14):1380-9.
4. Headley, A., De Leon-Benedetti, A., Dong, C., **Levin, B.,** Loewenstein, D., Camargo C., Rundek, T., Zetterberg, H., Blennow, K., Wright, C., Sun, X. and AD Neuroimaging Initiative. Neurogranin as a Predictor of Memory and Executive Function Decline in MCI patients, 2018, *Neurology*, *90*(10), e887–e895. doi:10.1212/WNL.0000000000005057

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**

**7 R01 NS 029993 (PI: Sacco) NIH/NINDS 02/01/03-07/31/21 1.20 cal mos *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.
Role: Co-Investigator

**R01NS040807-S01 04/01/19-3/31/21 0.36 calendar NIH: The Family Study of Stroke Risk and Carotid Atherosclerosis (The Family Study) Supplement** evaluates genes and non-genes (epi-genes) that contribute to stroke in high-risk families for stroke from Dominican background. In this supplement proposal we would investigate the actions these genes and non-genes have on cognition (e.g., memory, speed of processing).

**Tassili Life Sciences Corp 3.6 cal mos**
**Further Characterizing the use of Cannabinoids and Psilocybin as a Pharmaceutical Countermeasure for Traumatic Brain Injury and Post Traumatic Stress Disorder.**

This project is designed to examine a novel combination of products administered orally in a pre-clinical Model of PTSD alone and combined in mTBI and PTSD.
Role: Co-Investigator

**HU0001201002 (Balaban) 11/22/19-11/21/20**
**DOD Through University of Pittsburgh**
**A Portable Method for Objective assessment of Fitness for Return to Duty**
UM site on multi-site study assessing traumatic injury and fitness for continued duty.

Role Co-Investigator

**McKnight Brain Research Institute 6/1/2018 - 6/1/20**
Uncovering Risk Profiles of Deception and Mitigating Susceptibility to Scamming in Midlife and Older Age: A Novel Intervention Tool. McKnight Brain Research Institute. Pilot Intervention Grant

**FL Department of Health**

Role of Gut Microbiota on the Brain Metabolism, Cognition, Immune Function and Inflammation in Alzheimer's disease: Novel Biomarkers and Understanding Mechanisms
(Co-I) **02/25/2019-2/29/2020**

The goal of this study is to test the associations between dysbiosis of the gut microbiome and intestinal permeability and microbial translocation markers with brain GABA, brain inflammation markers, peripheral amyloids and lipopolysaccharides, peripheral inflammation markers and cognitive function in patients at the early stage of cognitive impairment and age-matched healthy controls.

**7 R01 NS 029993 (PI, Sacco) NIH/NINDS** 02/01/03-03/31/2
***Stroke Incidence and Risk Factors in a TriEthnic 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. B. Levin, Co-Investigator

**Prior Research Support**

**Scythian Bioscience**
08/01/2016-7/30/2020
*The Effects of Cannabinoids on TBI*
This study will examine the inflammatory properties of cannabinoids and determine whether they can be used as a therapeutic intervention in traumatic brain injury.
B. Levin, Co-Investigator, Director of Clinical Trials

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

**AHA/ASA 14BFSC1759000 (PI: Sacco)**
04/01/14 – 03/31/18
**American Heart Association**
*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.
B. Levin, Co-Investigator

**DoD/CDMRP/USAMRMC (PI: Widerstrom-Noga)**
11/2015-10/2018
*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.
B. Levin, Co-Investigator

**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.

**NINDS 1 UO1 NS052478-01A2 (Adelson)**
7/30/07 – 6/30/2011
*Pediatric Traumatic Brain Injury Consortium: Hypothermia*
A multicenter clinical trial to determine the efficacy of early induced moderate hypothermia after severe TBI in a pediatric sample. Role: StudySite PI 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)*

## 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 Loewenstein, PhD, ABPP/CN

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

POSITION TITLE: Professor of Psychiatry and Behavioral Sciences and Director of Neuropsychology

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 South Florida | B.A. | 04/1981 | Psychology |
| University of South Florida | M.S. | 04/1983 | Psychology |
| Florida State University | Ph.D. | 09/1986 | Clinical Psychology |
| University of Washington School of Medicine | Internship | 08/1986 | Clinical Psychology |

### A. Personal Statement

I am the Director for the Center for Cognitive Neuroscience and Aging (CNSA) and a board certified neuropsychologist. I served as Principal Investigator on a number of NIH studies investigating novel cognitive and functional measures for the early detection of Alzheimer's disease (AD) and other cognitive disorders of aging, cross-cultural assessment as well as intervention studies involving the effects of cognitive and exercise in older adults with mild cognitive impairment (MCI). I am widely published in the identification of early stage MCI and its relationships to biomarkers data such as amyloid load, MRI, fMRI and DTI. I am Associate Director of the Clinical Core for the 1Florida, Alzheimer's Disease Research Center (ADRC) as Director of the Clinical Core site at the University of Miami. I previously served as Director of Research for the Wien Center for Alzheimer's Disease. and Memory Disorders at Mount Sinai Medical Center and currently am Principal investigator of a large NIH longitudinal study on novel cognitive and biomarkers for MCI and early Alzheimer's Disease.

### B. Positions and Honors

1986-1992 Research Assistant Professor, Department of Psychiatry, University of Miami School of Medicine, Miami, FL.

1986-2010 Director of Cognitive/Neuropsychological Laboratory and Psychological Services, Wien Center for Alzheimer's Disease and Related Disorders, Mount Sinai Medical Center, Miami Beach FL.

1990-Present Chief of Neuropsychological Laboratories, Department of Psychiatry, Mount Sinai Medical Center, an affiliated Program of Mount Sinai and University of Miami, School of Medicine.

1992- 2002 Associate Professor, Department of Psychiatry, University of Miami School of Medicine, Miami, FL.

2001-2010 Director of Research, Wien Center for Alzheimer's Disease and Memory Disorders, Mount Sinai Medical Center.

2002- Present Professor of Psychiatry and Behavioral Sciences, University of Miami School of Medicine.

2010-Present Director of Neuropsychology, Department of Psychiatry and Behavioral Sciences, University of Miami School of Medicine.

2018-Present Director of Cognitive Neurosciences and Aging (CNSA), Department of Psychiatry and Behavioral Sciences, University of Miami School of Medicine.

Other Experience and Professional Memberships
Adult Psychopathology and Disorders of Aging (Regular Study Section Member 2010-2014);
Senior Editor, Journal of Alzheimer's Disease
Determining Functional Capacity and the Need for Representative Payees (2015);
American Psychological Association (Division 40: Neuropsychology; Division 20: Aging;
American Academy of Clinical Neuropsychology).

**C. Contributions to Science**

**1. Development of tests for early detection of neurodegenerative diseases.** I am the author of 203 peer-review referenced journal articles and have been a funded NIH Principal investigator on a number of longitudinal studies investigating detection of Preclinical Alzheimer's Disease, assessment of MCI and PreMCI states, development of novel cognitive stress tests for the early detection of neurodegenerative disease, development of objective functional assessment measures, relating neuroimaging findings (e.g., MRI, amyloid PET) to cognitive function both cross-sectionally and longitudinally. Our focus has been on four major areas as outlined below.

First, my team and I have pioneered tests that employ proactive and retroactive semantic interference Tests (SIT: Loewenstein et al 2004: 2007); Loewenstein, Acevedo Scales of Semantic Interference Test (LASSI-L: Crocco et al.,2014; Curiel et al., 2013) and the newly developed Miami Test of Semantic Interference and Learning (MITSI-L: Curiel et al., 2016), We have also explored the relationship between these novel measures and have their relationship with neuroimaging measures in older adults with MCI and PreMCI.

A. Crocco E, Curiel RE, Acevedo A, Czaja SJ, **Loewenstein DA**. (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, 22(9), 889-897.

B**. Loewenstein DA**, Curiel RE, Greig MT, Bauer RM, Rosado M, Bowers D, Wicklund M, Crocco E, Pontecorvo M, Joshi AD, Rodriguez R. (2016). A Novel Cognitive Test for the Detection of Preclinical Alzheimer's Disease: Discriminative Properties and Relation to Amyloid Load. The American Journal of Geriatric Psychiatry, 24(10), 804-813..

C. **Loewenstein DA**, Curiel R, Duara R, Buschke H. (2018). Novel cognitive paradigms for the detection of Memory Impairment in Preclinical Alzheimer's Disease. Assessment. 2018 Apr;25(3):348-359.

D. **Loewenstein, DA,** Curiel, RE, DeKosky, S.,Bauer, RM, Rosselli, M, Guinjoan, S, Adjouadi,M. Peñate, A, ; Barker,W, Goenaga, S; Golde, T, Greig-Custo, M, Hanson, KS, Li, C,Lizarrag1, Marsiske, M, Duara, R. (2018). Utilizing Semantic Intrusions to Identify Amyloid Positivity in Mild Cognitive Impairment. Neurology. 976-984.

**2. Cross-Cultural Assessment and translation of neuropsychological measures.** Another focus of research is cross-cultural fair neuropsychological assessment and vast experience with translation, back-translation and committee translation of neuropsychological measures. I have vast experience in training psychometrics in community based epidemiological studies so that neuropsychological testing can be done in home-based settings.

A. **Loewenstein DA**, Argüelles T, Argüelles S. (1994). Potential cultural bias in the neuropsychological assessment of the older adult. Journal of Clinical and Experimental Neuropsychology, 16: 623- 629.

B. Acevedo A, **Loewenstein DA,** Agron J, Duara R. (2007) Influence of Socio-Demographic Variables on Neuropsychological Test Performance in Spanish-Speaking Older Adults. Journal of Clinical and Experimental Neuropsychology, 29(5) 363-368.

C. Matías-Guiu JA, Curiel RE, Rognoni T, Valles-Salgado M, Fernández-Matarrubia M, Hariramani R, Fernández-Castro A, Moreno-Ramos T, **Loewenstein DA**, Matías-Guiu J. (2016). Validation of the Spanish Version of the LASSI-L for Diagnosing Mild Cognitive Impairment and Alzheimer's Disease. Journal of Alzheimer's Disease, 56(2), 733-742.

D. Matias-Guiu JA, Cabrera-Martín MN, Curiel RE, Valles-Salgado M, Rognoni T, Moreno-Ramos T, Carreras, JL, **Loewenstein DA**, Matias-Guiu J. (2017).Comparison between FCSRT and LASSI-L to detect early stage Alzheimer's disease. J Alzheimers Dis doi: 10.3233/JAD-170604

**3. Development of functional assessment for dementia.** Third, my team also developed the first behaviorally-based functional assessment instrument for early dementia (The Direct Assessment of Functional Status: DAFS, Loewenstein et al., 1989), which has been translated into eight different languages, and has been used worldwide and was the basis for the current performance –based functional tests in schizophrenia such as the UPSA. My colleague Dr. Sara Czaja and myself have also developed other functional measures as well as cognitive and functional training paradigms.

A. **Loewenstein DA,** Amigo EA, Duara RD, Guterman A, Hurwitz D, Berkowitz N, Weinberg G, Black B, Gittleman B, Eisdorfer C. (1989) A new scale for the assessment of functional status in Alzheimer's disease and related disorders. Journals of Gerontology, 44, 114-121.

B. **Loewenstein DA**, Acevedo A, Czaja CJ, Duara R. (2004). Cognitive rehabilitation of mildly Impaired Alzheimer's disease patients on cholinesterase inhibitors. American Journal of Geriatric Psychiatry, 12, 395-402.

C. Acevedo A, **Loewenstein DA.** (2008). Non-Pharmacological Cognitive Interventions in Aging and Dementia. Journal of Geriatric Psychiatry and Neurology, 20(4), 239-249.

D. Czaja SJ, **Loewenstein DA**, Lee CC, Fu SH, Harvey PD. (2016). Assessing functional performance using computer-based simulations of everyday activities. Schizophrenia Research, 183, 130-136. PubMed PMID: 27913159.

**4. Changes in MRI and PET scans for preclinical Alzheimer's**. Fourth, our group has conducted a number of studies investigating preclinical Alzheimer's Disease and relating cognitive measures to changes in structural MRI and amyloid deposition on PET scans.

A. **Loewenstein DA**, Acevedo A, Small BJ, Agron J, Crocco E, Duara R. (2009). Stability of Different Subtypes of Mild Cognitive Impairment Among the Elderly Over a Two to Three Year Follow-Up Period. Dementia and Geriatric Cognitive Disorders, 17(5), 437- 440.

B. **Loewenstein DA,** Amarilis Acevedo A, Potter H, Schinka J, Raj A, Greig M, Agron J, Barker WW, Wu Y, Small B, Schoefield E, Duara R. (2009). Severity of Medial Temporal Atrophy and Amnestic MCI: Selecting type and number of memory tests. American Journal of Geriatric Psychiatry, 17(12), 1050-1058.

C. **Loewenstein DA**, Greig MT, Schinka JA, Barker W, Shen Q, Potter E, Raj A, Brooks L, Varon D, Schoenberg M, Banko J, Potter H, Duara R. (2012). An investigation of PreMCI: subtypes and longitudinal outcomes. Alzheimer's & Dementia, 8(3), 172-9.

D. **Loewenstein, D.A**., Curiel, R.E., DeKosky, S., Roselli, M., Bauer, R., Grieg-Custo, M., Penate, A., Li, C., Lizagarra, G., Golde, T., Adjouadi, M., Duara, R. (2017) Recovery from proactive semantic interference and MRI volume: A replication and extension study, *J Alzheimers Dis. 2017; 59(1):131-139. doi: 10.3233/JAD-170276*

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

1P30AG066506-01. 06/15/2020 – 03/31/2025
Todd Golde, PI University of Florida
David Loewenstein Associate
Director and UM Clinical Core Leader
Alzheimer's Disease Research Centers
The 1Florida ADRC is a consortium between the University of Florida, University of Miami, Mount Sinai Medical Center, Miami Beach and other top Florida academic institutions to longitudinally evaluate and follow older adults at higher and lower.risk for AD/ADRD through extensive clinical, neuroimginging, neuropsychological and genetic and other blood-based biomarkers on 600 older adults. We will be focusing on underserved and unrepresented minority populations such as African-American and different Hispanic groups. 2.0 CM

R01AG061106-01 (NIH-NIA) Loewenstein, David (PI) 2/1/2019- 10/1/2023 Novel Computerized Cognitive Stress Test Designed for Clinical Trials in Early Alzheimer's: Relationship with Multimodal Imaging Biomarkers in Diverse Cultural Groups . This will investigate a newly computerized cognitive stress test as it relates to amyloid deposition and tau distribution in older adults at risk for Alzheimer's disease. 1.8 CCM

1RO1AG047649-01A1 (NIH) Loewenstein, David (PI) 02/01/2015 - 01/31/2021
Novel Detection of Early Cognitive and Functional Impairment in the Elderly
This is an innovative longitudinal study that will examine the utility of two novel cognitive measures (LASSI-L; MPMT) and a series of newly developed computer-based functional task stimulations (FTS) in the detection of amnestic mild cognitive impairment (aMCI) and PreMCI versus normal elderly subjects.1.2 CM

R01AG054009-01 (NIH-NIA) Czaja, S and Loewenstein, D Multiple -PIs 09/01/2016- 04/30/2021
A nonpharmacological intervention for patients with Alzheimer's Disease and their family caregivers.
This intervention provides a dual target intervention involving cognitive training and enhancing caregiver skills through an innovative technological platform 1.2 CM

1R01AG055638 - 01A1 (NIA/NIH) Rosie Curiel (PI) 04/01/2017-1/31/2023
Precision-Based Assessment for Detection of MCI in Older Adults
The major goals of this project are to examine the psychometric properties of novel sensitive cognitive assessment tools among participants 70+ years of age and determine which cognitive markers are most predictive of baseline and longitudinal atrophy in AD-related signature brain regions on MRI. The measures will be compared to widely used cognitive outcome measures in current Alzheimer's disease clinical trials.
Role: Co-Investigator 1.8 CM

Grant Number: 8AZ23 State of Florida Ed and Ethel Moore Grant
PI: David Loewenstein PhD Project Title: The Relationships between Multimodal Neuroimaging Biomarkers and A Novel Cognitive Stress Test (CST) Among Ethnically Diverse Older Adults 02/01-18- 1/31/2020.This is a two year cross-sectional study designed to examine tau and amyloid deposition as it relates to the CST in a modest number of Hispanic and non-Hispanic participants. .6 CM

Grant Number: 9AZ24 State of Florida Ed and Ethel Moore Grant

David Loewenstein, David, PI 02/01/2019 – 01/31/2021
Grant # 9AZ24
State of Florida
Middle-Aged Offspring of Late Alzheimer's Probands: Novel Cognitive and Biomarker Assessment.
.6 CM

## 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: Katalina Fernández McInerney

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

POSITION TITLE: Assistant 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 | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| The Catholic University of America, Washington, D.C. | BA | 05/2001 | Architecture |
| The Catholic University of America, Washington, D.C., | MA | 05/2007 | General Psychology |
| Ohio University, Athens, OH | PhD | 08/2015 | Clinical Psychology |
| University of Miami Miller School of Medicine/Jackson Memorial Hospital, Miami, FL | Clinical Internship | 07/2015 | Adult Behavioral Medicine and Rehabilitation Track – Neuropsychology Emphasis |
| University of Miami Miller School of Medicine, Miami, FL, | Postdoctoral Fellowship | 09/2017 | Neuropsychology |

### A. Personal Statement

My research focuses on intervention and rehabilitation strategies for neurologically compromised individuals. I am currently involved in several clinical trials examining neuropsychological and affective changes in patient with Alzheimer's disease following interventions with medications, infusion of stem cells or nutritional supplements. I am also involved in research looking at the cognitive, medical and emotional correlates of frailty in a population of Hispanic/Latino and Non-Hispanic/Latino adults with memory complaints. The latter research stems from a database that utilizes data collected in our neuropsychology clinic. I am also collaborating in a study that aims to characterize psychosocial, cognitive and brain structure patterns of the oldest old. Prior research focused on the neurocognitive correlates of hazard perception in active driving older adults.

Representative Publications and Presentations:

a. **McInerney**, K. F. & Suhr, J. (2016). *Neuropsychological correlates of hazard perception in older adults.* Journal of the International Neuropsychological Society, *22*, 332-240.
b. Joyce Gomes-Osman, PT, PhD, Danylo F. Cabral, Timothy P. Morris, Katalina **McInerney**, PhD, Augusto Oliveira, Tatjana Rundek, MD, PhD and Alvaro Pascual-Leone, MD, PhD. (2018) *Exercise for cognitive*

*brail health in aging: a systematic review for an evaluation of dose.* Neurology Clinical Practice, 8(3):257-265.

c. **McInerney**, K. F., Gomes-Osman, J., Banerjee, N. S., Getz, S. J., Sun-Suslow, N., Bure-Reyes, A., Sarno, M., Merritt, S., Gaztanaga, W., Dong, C., Sun, X., Rundek, T., Levin, B. A comparison of frailty criteria in Hispanic/Latino and Non-Hispanic/Latino older adults in South Florida. The Journal of Frailty and Aging 2018, 7(1):114.

## B. Positions and Honors

### Positions and Employment

2014- 2015 Clinical Internship, University of Miami Miller School of Medicine/Jackson Memorial Hospital, Miami, FL, Adult Behavioral Medicine and Rehabilitation Psychology Track (Neuropsychology Emphasis)

2015- 2017 Postdoctoral Fellowship, University of Miami Miller School of Medicine, Miami, FL, Department of Neurology, Division of Neuropsychology

2017-present Assistant Professor, University of Miami Miller School of Medicine, Miami, FL, Department of Neurology, Division of Neuropsychology

### Other Experience and Professional Memberships

2009-2010 Graduate Student Representative, Clinical Internship Committee

2008-2009 Co-Leader, Graduate Representative Committee (GRC)

2007-2008 Graduate Student Representative, Ohio Psychological Association for Graduate Students (OPAGS)

2007-2009 Member, International Student Outreach (ISO) Team

2006-present Member, Clinical Neuropsychology, Division 40 of the American Psychological Association

### Honors

2012-2013 Martin and Willson Geropsychological Scholarship

2007-2008 Saundra Taylor Lawson Fellow

## C. Contributions to Science

**1. Clinical trials on Alzheimer's disease and Cognitive Aging**

Over the last four years I have actively worked on clinical trials for the treatment of Alzheimer's disease (AD). My contributions to these studies have spanned from administering neuropsychological tests and tracking/monitoring the cognitive abilities and mood of participants on large sponsored clinical trials, to assisting in the design and implementation of site initiated clinical trials at the University of Miami. Site initiated trials include two studies that evaluate the safety and potential efficacy of human mesenchymal stem cell infusions in patients with AD and a therapeutic intervention with an oral nutrient for age related memory loss.

Representative Publications and Presentations:

a. Co-Investigator: A Randomized, Double-Blind, Placebo-Controlled and Delayed-Start Study of LY3314814 in Mild Alzheimer's Disease Dementia (The DAYBREAK Study). PI: Bernard Baumel, M.D. Sponsor: Eli Lilly and Company
2016-2018

b. Co-Investigator: A Phase 3 Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of Aducanumab (BIIB037) in Subjects with Early Alzheimer's Disease. PI: Bernard Baumel, M.D. Sponsor: Biogen MA Inc.
2015-2018

c. Co-Investigator: A Phase I, Prospective, Randomized, Double-Blinded, Placebo-controlled Trial to Evaluate the Safety and Potential Efficacy of Longeveron Allogeneic Human Mesenchymal Stem

Cell (LMSC) Infusion Versus Placebo in Patients with Alzheimer's Disease. PI: Bernard Baumel, M.D. Sponsor: Longeveron LLC
2015-present

d. Co-Investigator: Reducing the Effects of Aging on Cognition with Therapeutic Intervention of an Oral Nutrient - The REACTION Study. AAN McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss. PI: Christian Camargo, MD
2019-present

e. Co-Investigator: A Phase I, Prospective, Open-Labeled Trial to Evaluate the Safety, Tolerability and Exploratory Outcomes of Multiple Allogeneic Human Mesenchymal Stem Cell (MSC) Infusions in Patients with Mild to Moderate Alzheimer's Disease.PI: Bernard Baumel, M.D.
2019-present

2. Cognitive aging
    a. Shpiner, D. S., McInerney, K. F., Miller, M., Allen, J., Rice, J., Luca, C. C., Adams, D., Gomes-Osman, J., (2019) High frequency repetitive transcranial magnetic stimulation for primary progressive apraxia of speech: A case series. Brain Stimulation. In press.
    b. Banerjee N, Slugh M., Kaur S, Sun-Suslow N, **McInerney** KF, Sun X, Levin BE. Neuropsychological correlates of subjective fatigue in non-demented older adults and the moderating effect of physical activity. Aging, Neurology, and Cognition. DOI: 10.1080/13825585.2019.1606889
    c. Kaur S, Banerjee N, Miranda M, Slugh M, Sun-Suslow N, **McInerney** KF, Sun X, Ramos A, Rundek T, Levin BE. (2019) *Sleep quality mediates the relationship between frailty and cognitive dysfunction in non-demented middle aged to older adults*. International Psychogeriatrics, 31(6), 779-788.
    d. Joyce Gomes-Osman, PT, PhD, Danylo F. Cabral, Timothy P. Morris, Katalina **McInerney**, PhD, Augusto Oliveira, Tatjana Rundek, MD, PhD and Alvaro Pascual-Leone, MD, PhD. (2018) *Exercise for cognitive brail health in aging: a systematic review for an evaluation of dose.* Neurology Clinical Practice 8(3):257-265.
    e. **McInerney**, K. F. & Suhr, J. (2016). *Neuropsychological correlates of hazard perception in older adults.* Journal of the International Neuropsychological Society, *22*, 332-240.

## PUBLICATIONS

### Other Works, Publications and Abstracts:

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.. Low Emotional Reserve as a Risk Factor for the Frailty Syndrome Independent of Gender. *The Journal of Frailty and Aging* 2018;7(1):114.

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. *The Journal of Frailty and Aging* 2018;7(1).

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

### Ongoing Research Support

Co-Investigator: A Phase I, Prospective, Randomized, Double-Blinded, Placebo-controlled Trial to Evaluate the Safety and Potential Efficacy of Longeveron Allogeneic Human Mesenchymal Stem Cell (LMSC) Infusion Versus Placebo in Patients with Alzheimer's Disease. PI: Bernard Baumel, M.D. Sponsor: Longeveron LLC
2015-present

Co-Investigator: Reducing the Effects of Aging on Cognition with Therapeutic Intervention of an Oral Nutrient - The REACTION Study. AAN McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss. PI: Christian Camargo, MD
2019-present

Co-Investigator: A Phase I, Prospective, Open-Labeled Trial to Evaluate the Safety, Tolerability and Exploratory Outcomes of Multiple Allogeneic Human Mesenchymal Stem Cell (MSC) Infusions in Patients with Mild to Moderate Alzheimer's Disease.PI: Bernard Baumel, M.D.
2019-present

## 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: Roger Christopher McIntosh, Ph.D.

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

POSITION TITLE: Assistant Professor of Psychology

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 |
|---|---|---|---|
| Jacksonville University, Jacksonville, Florida | B.S. | 05/2002 | Biology |
| Nova Southeastern University, Fort Lauderdale, Florida | M.S. | 05/2005 | Neuroscience |
| Florida Atlantic University, Boca Raton, Florida | M.A. | 05/2010 | Psychology |
| Florida Atlantic University, Boca Raton, Florida | Ph.D. | 07/2012 | Neuropsychology |
| University of Miami, Miami, Florida | Postdoctoral | 07/2014 | Psychoneuroimmunology CV Behavioral Medicine |

### A. Personal Statement

My program of research broadly examines the effects of aging and chronic disease on neuro-psychological outcomes with a focus on populations living with Human Immunodeficiency Virus (HIV). As a health psychologist I utilize a biopsychosocial model to elucidate factors associated with HIV and cardiovascular disease management. As a cognitive-behavioral neuroscientist I am interested in the neural correlates of neurocognitive, cardio-autonomic and inflammatory-immune function in the context of aging and chronic disease. My approach to elucidating these factors involves electroencephalography, neurocognitive testing as well as structural and functional neuroimaging. Amongst the biobehavioral mechanisms under investigation through the use of functional neuroimaging include: (1) neural correlates of inflammation and sickness behavior in the resting-state (2) central control of cardio-autonomic function, and (3) neural correlates of interoceptive (cardiac) awareness and psychopathology. This data is collected in conjunction with neuroendocrine and inflammatory-immune biomarkers in order to evaluate significance within the context of chronic disease. I am also funded through a National Heart Lung and Blood Institute-sponsored mentored K01 to investigate inflammatory-immune, cardio-autonomic and neural reactivity to stress in HIV+ and HIV-negative adults at risk for developing hypertension. The aim for this project is to identify the neural signature for maladaptive stress reactivity in the prodromal hypertensive state and determine how these processes are impacted by chronic HIV infection. My research is primarily conducted in underserved populations including African Americans and Hispanics/Latinos living South Florida. This work is of imperative due to the disproportionate burden of psychiatric, cardiovascular, cerebrovascular and HIV disease reported in these populations.

## B. Positions and Honors

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**Positons and Employment**

2012-2014 Postdoctoral Fellow, Department of Psychology, University of Miami, Miami FL

2014-2015 Research Assistant Professor, Department of Psychology, University of Miami, Miami FL

2015- Assistant Professor, Department of Psychology, University of Miami, Miami FL

**Other Experience and Professional Memberships**

2012- Member, Society for Neuroscience

2013- Member, American Psychosomatic Society

2014- Member, Psychoneuroimmunological Research Society

**Honors**

2011 APA Minority Fellowship award recipient

2015 American Psychosomatic Society Young Investigator's Award

2017 University of Miami, Department of Psychology Undergraduate Research Advising Award

## C. Contribution to Science

We published a series of studies showing a deficit in electrocortical response to affective cues in HIV positive AA women (1,2). Based upon these serendipitous findings, we developed an affect regulation paradigm to demonstrate that these deficits extend to the cognitive regulation of affect and are linked to a negative attention bias that occurs milliseconds within being presented an affective stimulus (3). We have also combined psychophysiology-neuroimaging to show reduced theta activity within the anterior cingulate was associated with depression in persons living with HIV.

1- Tartar, J.L., de Almeida, K.E., McIntosh, R.C., Rosselli, M., Nash, A.J. (2012). Emotionally negative pictures increase attention to an immediately subsequent auditory stimulus. International Journal of Psychophysiology. 83, 36–44. PMID: 22015918

2- Tartar, J. L., McIntosh, R. C., Rosselli, M., Widmayer, S. M., & Nash, A. J. (2014). HIV-positive females show blunted neurophysiological responses in an emotion–attention dual task paradigm. Clinical Neurophysiology, 125(6), 1164-1173. PMID: 24405904

3- McIntosh, R. C., Tartar, J. L., Widmayer, S., & Rosselli, M. (2015). Negative Attention Bias and Processing Deficits During the Cognitive Reappraisal of Unpleasant Emotions in HIV+ Women. The Journal of neuropsychiatry and clinical neurosciences. PMID: 25541865

4- Kremer, H., Lutz, F. P., McIntosh, R. C., Dévieux, J. G., & Ironson, G. (2015). Interhemispheric Asymmetries and Theta Activity in the Rostral Anterior Cingulate Cortex as EEG Signature of HIV-Related Depression Gender Matters. Clinical EEG and neuroscience, PMID: 25568149

Chronic HIV disease results in increased trafficking of peripheral monocytes and cytokines to the central nervous system and this may contribute to the prevalence of neurocognitive deficits and neuropsychiatric complaints (5). We have shown a cognitive vulnerability for depression in persons with HIV-associated Dementia (HAD) (6). We have also shown that HAD is associated with increased risk for mortality (7). Cross-sectional vidence of greater executive dysfunction in long-term HIV survivors with elevated levels of alexithymia (8) and longitudinal research showing trait alexithymia predicts 2-year changes in viral load (9) also support a model for cognitive-emotional dysfunction in poor HIV disease management.

5- McIntosh, R. C., Rosselli, M., Uddin, L. Q., & Antoni, M. (2015). Neuropathological Sequelae of Human Immunodeficiency Virus and Apathy: A review of neuropsychological and neuroimaging studies. Neuroscience & Biobehavioral Reviews, 55, 147-164. PMID: 25944459

6- McIntosh, R.C., Seay, J., Antoni M., Duran, R., Schneiderman, N. (2013). Cognitive vulnerability for depression in HIV: A Moderated Mediation Model. Journal of affective disorders, 150(3), 908-915. PMID: 23726660

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

8- McIntosh, R.C., Ironson, G., Antoni, M., Kumar, M., Fletcher, M., Schneiderman, N. (2013). Alexithymia is Linked to Neurocognitive, Psychological, Neuroendocrine, and Immune Dysfunction in Persons Living with HIV. Brain Behavior and Immunity, 36, 165-175. PMID: 24184475

9- McIntosh, R.C., Ironson, G., Antoni, M. et al.. (2017). Psychological Distress Mediates the Effect of Alexithymia on 2-Year Change in HIV Viral Load. Int.J. Behav. Med. 24: 294. PMID: 27882489

Persons living with HIV are at an increased risk for CVD comorbidity. Some of this risk can be attribute to psychobiological factors. For example, we demonstrate that elevated urinary cortisol excretion mediates the effect of angry/hostile mood on 9-month change in diastolic blood pressure amongst persons living with HIV (11). In addition to altered adrenal function we examined the prevalence of autonomic dysfunction in persons living with HIV/AIDS and provide evidence for HIV-related dysautonomia despite advancements in the antiretroviral therapy (12,13). Based upon the evidence of sympathetic over-arousal in HIV we have become interested in both functional and structural markers of cardio-autonomic regulation in the brain by examining brain metabolites (14) and functional brain connectivity (15). Most recently, we have begun to examine how other visceral signals such as the inflammation are reflected in resting-state networks of persons with HIV (16).

11- McIntosh R.C., Antoni, M., Carrico, A, Duran, R., Hurwitz, B., Ironson, G., Fletcher, M.A., Klimas, N., Kumar, M., Schneiderman, N. (2017). Change in urinary cortisol excretion mediates the effect of angry/hostile mood on 9 month diastolic blood pressure in HIV+ adults. Journal of Behavioral Medicine, 1-11. doi:10.1007/s10865-017-9827-1

12-McIntosh, R.C. (2016). A meta-analysis of HIV and heart rate variability in the era of antiretroviral therapy. Clin Auton Res, 26: 287. PMID: 27395409

13- McIntosh, R. C., Lobo, J. D., & Hurwitz, B. E. (2017). Current assessment of heart rate variability and QTc interval length in HIV/AIDS. Current Opinion in HIV and AIDS, 12(6), 528-533.

14- McIntosh, R. C., Lobo, J. D., Fajolu, O., Reyes E., Pattany, P.M., & Kolber, M.A. (2018). Greater N-Acetylaspartate to creatine ratio within left anterior insula predicts sympathetic imbalance in postmenopausal women living with hypertension and/or HIV. Heart Mind Journal. DOI: 10.4103/hm.hm_18_17

15- McIntosh, R. C., Chow, D. C., Lum, C. J., Hidalgo, M., Shikuma, C. M., & Kallianpur, K. J. (2017). Reduced functional connectivity between ventromedial prefrontal cortex and insula relates to longer corrected QT interval in HIV+ and HIV− individuals. Clinical Neurophysiology, 128(10), 1839-1850. DOI:10.1016/j.clinph.2017.07.398

16 - McIntosh, R. C., Paul, R., Ndhlovu, L. C., Hidalgo, M., Lobo, J. D., Walker, M., Shikuma, C.M., & Kallianpur, K.J. (2018). Resting-state connectivity and spontaneous activity of ventromedial prefrontal cortex predict depressive symptomology and peripheral inflammation in HIV. Journal of Neurovirology. DOI: https://doi.org/10.1007/s13365-018-0658-9

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

**Ongoing Research Support**

1R25HL105446-01. McIntosh (PI) $13,219.20 11/1/2020 – 10/31/2021
A psychoneuroimmune model for evaluating discrimination as a determent of arterial stiffness in HIV

FL DOH 20A11. Crocco (PI) $248,590 1 2/15/2019 – 12/14/2021
Building an Advanced Cognitive and Biomarker Registry for African American Older Adults At-Risk for Alzheimer's Disease

NIMHD U54MD002266-13 Prado (PI) $50,000 Direct Costs 12/17/19-12/16/20
Psychoneuroimmunological Outcomes Associated with a Culturally Adapted Written Emotional Disclosure Intervention in Traumatized Hispanic/Latina Women Living with HIV

K01 HL139722-01 McIntosh (PI) $668,490 2/6/2018 - 2/5/2023
HIV-Related Changes to the Central-Autonomic Network and Associated Risk for Hypertension
This study proposes the use of functional neuroimaging to determine whether HIV and/or pre- hypertension (pre-HTN) has an additive or interactive effect on cardiovascular (CV) reactivity via an altered brain activity and connectivity within structures that control heart rate and blood pressure. The study aims to examine these mechanisms at rest, during mental stress, and following anger rumination.

**Completed Research Support**

None for three years

## 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: Miguel A. Perez-Pinzon, PhD, FAHA

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

POSITION TITLE: Peritz Scheinberg Endowed Professor in 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 | DEGREE *(if applicable)* | Completion Date MM/YYYY | 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 Pertiz Scheinberg 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, cognitive, 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. For more than 10 years, I have been collaborating with Dr. Dave on his diabetes project, which he has led. I will continue to participate in this exciting and very crucial translational project.

**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

2019 – present Peritz Scheinberg Endowed Professor in 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.

2018-20 Chair of the Program Committee for the International Stroke Conference.

**C. Contribution to Science**

1. My group has been studying mitochondrial dysfunction for approximately 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 PKC activation provides neuroprotection while activation of PKC 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/pubmed/?term=perez-pinzon**

**D. Research Support.**

***Active***
R01 NS34773-19 **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 NS 097658-04 **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.

2R01NS045676-10 **Perez-Pinzon (PI)** 8/20-7/25
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.

FDOH-20K11- James and Esther King Biomedical Research Program **Perez-Pinzon (PI)** 8/20-7/23
NIH/NINDS
**Strategies to ameliorate cognitive decline following cerebral ischemia in nicotine exposed rats**
The main goals are the elucidation of mechanisms leading to improvements in cognitive deficits following focal cerebral ischemia using physical exercise.

***Past***
**American Heart Association/ASA-Bugher Foundation (14BFSC17690007). Sacco R. (PI)** 4/1/14-12/31/18
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.

## BIOGRAPHICAL SKETCH

NAME: Milena Pinto

eRA COMMONS USER NAME (credential, e.g., agency login): Pintom1n

POSITION TITLE: Research Assistant Professor

EDUCATION/TRAINING

| INSTITUTION AND LOCATION | DEGREE | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| • Universita' degli studi di Trieste, Italy | M.Sc. | 04/2005 | Medical Biotechnology |
| • International School for Advanced Studies (SISSA) Trieste, Italy | Ph.D. | 11/2009 | Neurobiology |

### A. Personal Statement

I have more than ten years of research experience on neurodegenerative disorders. During my Masters and PhD studies, I extensively worked on drug-induced and genetically modified animal models of neurodegeneration as well as on neuronal cellular models and primary cultures. For my postdoctoral training, I have been involved in understanding the neuronal-specific role of mitochondrial dysfunctions and mitochondrial DNA deletions and depletion in mouse models of neurodegenerative disorders. Recently I received a K01 from NIA to study the neuroprotective role of NMNAT in animal models of Alzheimer's disease. NMNAT is a central enzyme in NAD biosynthesis, and the coenzyme NAD has many potential sites of interaction with OXPHOS defects, including stimulation of Krebs cycle and substrate availability. With this grant, I want to determine if NMNAT neuroprotective capacity can also be utilized against neurodegeneration caused by Oxidative phosphorylation defects.

### B. Positions and Honors.

**PROFESSIONAL APPOINTMENTS**

**Mar 2017-present** Research Assistant Professor at Neurology department, University of Miami
**Apr 2015-Mar 2017** Sr. Research Associate at Neurology department, University of Miami
**Apr 2010-Apr 2015** Postdoctoral Associate at Neurology department, University of Miami
**Nov 2009-Apr 2010** Temporary Research Fellow, SISSA, Trieste, Italy

**HONORS**

| | |
|---|---|
| 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. Contribution to Science

1. I became involved in the study of neurodegenerative diseases during my Ph.D. at the International School for Advanced Studies (SISSA) in Trieste, Italy, under the supervision of Dr. Stefano

Gustincich. In my first years I was involved in the study of the role of PARK7/DJ-1 gene, whose mutations are associated to autosomal recessive early onset forms of Parkinson's disease (PD). We studied two DJ-1 missense mutations that cause misfolding of the protein, degradation or accumulation into insoluble cytoplasmic aggregates. By yeast-two hybrid screening, we identified two novel DJ-1 interactors (TRAF6 and TTRAP) that bound more strongly the mutated forms than the wild type form of DJ1, and we analyzed in vitro their role in physiologic and pathologic conditions.
Moreover, we discovered that both the proteins were present in the Lewy Bodies (neuropathological hallmarks of PD) of post mortem brains of PD patients, identifying them as new players not only in rare genetic cases of PD but also in the more common sporadic cases.

A. 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]
B. 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]
C. 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]

2. During my PhD I also studied the expression profile of A9 neurons of *substantia nigra*, a subpopulation of dopaminergic neurons that degenerate in patients affected by Parkinson's disease. This research project led to the discovery that these particular neurons express alpha and beta chains of hemoglobin, a well-known protein with essential role in binding and delivering oxygen, carbon dioxide and nitric oxide. This particular finding opened a new line of research since hemoglobin has a non-oxygen-carrying function as an antioxidant and a regulator of iron metabolism, both essential mechanisms involved in the pathogenesis of Parkinson's disease. These findings helped other researchers to look into the role of this protein in brain metabolism, finding correlations with Alzheimer's disease, Parkinson's disease and dementia with Lewy bodies. Moreover, Hemoglobin-derived peptides have been studied as novel type of bioactive signaling molecules.
We also discovered that 46% of genes that encode for subunits of mitochondrial complex I-V were induced in stable cell lines overexpressing hemoglobin chains, suggesting a link between hemoglobin expression and mitochondrial biogenesis/function.

A. **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]

3. As a result of this work in Italy, I was recruited to join the Neurology Department of the University of Miami, Miller School of Medicine as a Postdoctoral Associate. I joined Dr. Carlos Moraes laboratory to expand my knowledge and research in the study of the role of mitochondria in neurodegenerative diseases.

Neuronal OXPHOS deficiency, in fact, has been associated with a variety of late-onset progressive neurodegenerative diseases, including Parkinson's disease and Alzheimer's disease.
Almost all the animal models of PD available at that time were 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, we decided to induce mitochondrial defects in different neuronal subpopulations, mimicking the mitochondrial function decline that occurs naturally with aging.
We 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 we 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*. We then 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.
Because mitochondrial dysfunctions have been closely associated with PD, the creation of this new mouse models provided important clues to the pathophysiology of the disease. The PD mouse models have been widely received and accepted in the field and can provide also a valuable tool to test new mitochondrial therapies in the treatment of this disease.

A. 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]
B. **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]
C. **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]
D. **Pinto M**, Nissanka N, Moraes CT.
*Lack of Parkin Anticipates the Phenotype and Affects Mitochondrial Morphology and mtDNA Levels in a Mouse Model of Parkinson's Disease.*
J Neurosci. 2018 Jan 24;38(4):1042-1053. [PMID: 29222404]

4. Since mtDNA damage and the generation of reactive oxygen species have been associated with and implicated in the development and progression of Alzheimer's disease, we studied how mtDNA damage affects reactive oxygen species and amyloid beta pathology in vivo. We generated an Alzheimer's disease mouse model expressing an inducible mitochondrial-targeted endonuclease (Mito-PstI) in the central nervous system that cleaves mtDNA causing mtDNA depletion, which leads to a partial oxidative phosphorylation defect when expressed during a short period in adulthood. We found that a mild mitochondrial dysfunction in adult neurons decreased plaque pathology by altering the cleavage pathway of amyloid precursor protein without increasing oxidative stress in the brain. These data suggest that mtDNA damage is not a primary cause of Ab accumulation.

A. **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]

5. Even though my main line of research is focused on neurodegenerative disorders, my contribution has also been essential in other fields where mitochondrial dysfunctions play an important role, like aging, age-related cachexia, and mitochondrial diseases (Leber's hereditary optic neuropathy plus dystonia), as shown in recent publications in Human Molecular Genetics, Nature Medicine, and Cell Death and Differentiation.

   A. 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]
   B. Wang X, Pickrell AM, Rossi SG, **Pinto M**, Dillon LM, Hida A, Rotundo RL, Moraes CT.
   *Transient systemic mtDNA damage leads to muscle wasting by reducing the satellite cell pool.*
   Hum Mol Genet. 2013 Oct 1;22(19):3976-86 [PMID: 23760083]
   C. **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 and Differentiation 2016, December 2; doi: 10.1038/cdd.2016.123
   D. Bacman SR, Kauppila JHK, Pereira CV, Nissanka N, Miranda M, **Pinto M**, Williams SL, Larsson NG, Stewart JB, Moraes CT.
   *MitoTALEN reduces mutant mtDNA load and restores tRNAAla levels in a mouse model of heteroplasmic mtDNA mutation.* Nat Med. 2018 Nov;24(11):1696-1700 [PMID: 30250143]

**Complete List of Published Work in MyBibliography:**
http://www.ncbi.nlm.nih.gov/sites/myncbi/milena.pinto.1/bibliography/50578890/public/?sort=date&direction=ascending.

**D. Research Support**

K01AG057815 (Milena Pinto) 02/01/2019 – 10/31/2023
NIH/NIA
"Use of NMNAT chaperone activity against Alzheimer's related proteinopathy"
The goals of this project is to identify new targets for therapeutic options of Alzheimer's disease.
Role: PI

PDF-FBS-1316 (Milena Pinto) 7/1/2013 – 7/1/2014
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: Postdoc

**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: Ramos, Alberto Rafael

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 | DEGREE (if applicable) | END DATE MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| University of Puerto Rico, Rio Piedras, PR | BS | 06/1999 | Natural Sciences |
| U Central del Caribe, School of Medicine, Bayamon, PR | MD | 05/2003 | Medicine |
| Jackson Memorial Hospital-U. of Miami, Miami, Florida | Residency | 06/2007 | Neurology |
| Jackson Memorial Hospital-U. of Miami, Miami, Florida | Fellowship | 06/2008 | Sleep Medicine |
| Miller School of Medicine, U of Miami, Miami, Florida | MSPH | 05/2012 | Epidemiology |
| Miller School of Medicine, U. of Miami, Miami, Florida | MS | 05/2018 | Translational Research |

**A. Personal Statement**

Dr. Ramos is a new stage investigator with research experience in multi-site and interdisciplinary projects evaluating the determinants of sleep health in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). Dr. Ramos has training and experience in clinical sleep medicine, sleep epidemiology, cerebrovascular injury and neurocognitive aging. Dr. Ramos have been an HCHS/SOL investigator since 2010, when sleep apnea was assessed with home-sleep apnea studies in visit-1 of the nascent cohort of 16,000 participants across the Bronx, Chicago, Miami and San Diego. Further, Dr. Ramos was the Miami site-PI for the sleep ancillary study, Sueño (R01HL098297)-Sleep as a Risk Factor for Disease in HCHS/SOL. The aim of Sueño was to determine the prevalence of abnormal sleep patterns in 2,200 Latinos using actigraphy. He was the PI for an HCHS/SOL ancillary study that evaluated sleep apnea, actigraphic sleep duration with impaired cerebral hemodynamics using transcranial Doppler ultrasound in 98 participants at the Miami field site. The study was supported by a mentored research award from the Clinical Translational Research Institute at the Miller School of Medicine. Dr. Ramos has multiple high-impact publications, as well as two funded R21s (PI-Ramos; AG056952, HL140437). Dr. Ramos was the Chair of the Young Investigator Research Forum in 2019, for the American Academy of Sleep Medicine Foundation (AASMF). He is also the Founding Chair of the yearlong Sleep Research Fellowship Committee (SOAR program) of the American Academy of Sleep Medicine Foundation. Dr. Ramos continues mentors multiple young investigators by providing guidance and expertise in sleep research, grant writing, research design and career development.

1.**Gonzalez, H. M., W. Tarraf,** K. A. Gonzalez, M. Fornage, D. Zeng, L. C. Gallo, G. A. Talavera, M. L. Daviglus, R. B. Lipton, R. Kaplan, **A. R. Ramos**, M. Lamar, J. Cai, **C. DeCarli** and N. Schneiderman. Diabetes, Cognitive Decline, and Mild Cognitive Impairment Among Diverse Hispanics/Latinos: Study of Latinos-Investigation of Neurocognitive Aging Results (HCHS/SOL).Diabetes Care. 2020; doi: 10.2337/dc19-1676 PMID: 32139382

2. **Gonzalez HM, Tarraf W**, Schneiderman N, Fornage M, Vásquez PM, Zeng D, Youngblood M, Gallo LC, Daviglus ML, Lipton RB, Kaplan R, **Ramos AR**, Lamar M, Thomas S, Chai A, **DeCarli C**. Prevalence and correlates of mild cognitive impairment among diverse Hispanics/Latinos: Study of Latinos-Investigation of Neurocognitive Aging results. Alzheimers Dement. 2019; 15(12):1507-1515. PMID: 31753701

3. **Ramos, A. R., W. Tarraf**, M. Daviglus, S. Davis, L. C. Gallo, Y. Mossavar-Rahmani, F. J. Penedo, **S. Redline**, T. Rundek, R. L. Sacco, D. Sotres-Alvarez, C. B. Wright, P. C. Zee and **H. M. Gonzalez**. Sleep Duration and Neurocognitive Function in the Hispanic Community Health Study/Study of Latinos.SLEEP.2016; **39**: 1843-51

4. **Ramos, A. R., W. Tarraf**, T. Rundek, **S. Redline**, W. K. Wohlgemuth, J. S. Loredo, R. L. Sacco, D. J. Lee, R. Arens, P. Lazalde, J. P. Choca, T. Mosley, Jr. and **H. M. Gonzalez**. Obstructive sleep apnea and neurocognitive function in a Hispanic/Latino population. NEUROLOGY. 2015; **84**(4): 391-398

**B. Positions and Employment**

| | |
|---|---|
| 2006 - 2007 | Administrative Chief Resident, Neurology Residency Program, U of Miami, Miami, FL |
| 2007 - 2009 | Neurology Staff Physician, Miami VA Hospital, Miami, FL |
| 2009 - 2010 | Instructor, Miller school of Medicine, University of Miami, Miami, FL |
| 2010 - 2016 | Assistant Professor of Neurology, Miller School of Medicine, U. of Miami, Miami, FL |
| 2010 - | Research Director Sleep Medicine Program, Miller School of Medicine, U. of Miami, Miami, FL |
| 2013 - 2018 | Associate Graduate Faculty, College of Engineering & Computer Science, Florida Atlantic University, Boca Raton, FL |
| 2016 - | Associate Professor of Neurology, Miller School of Medicine, U. of Miami, Miami, FL |

**Other Experience and Professional Memberships**

| | |
|---|---|
| 2008 - | Member, American Academy of Sleep Medicine |
| 2008 - | Member, American Academy of Neurology |
| 2015 - | Collaborator, Evelyn McKnight Brain Institute, Miller School of Medicine |
| 2016 -2019 | Clinical Research Subcommittee member , American Academy of Neurology |
| 2017 | Topic Editor, Frontiers of Neurology, Sleep and Chronobiology Section |
| 2017 -2018 | Vice Chair, Young Investigator Research Forum, American Academy of Sleep Medicine Fdn |
| 2018 –2019 | Chair, Young Investigator Research Forum, American Academy of Sleep Medicine Foundation |
| 2018-2019 | Faculty Representative, Dept. of Neurology. Faculty Council, Miller School of Medicine, FL |
| 2018- | Editorial Board, *CHEST* Journal |
| 2018- | Clinical Guidelines Advisory Committee, American Academy of Sleep Medicine (AASM) |
| 2018-19 | Diversity Task Force, American Academy of Sleep Medicine |
| 2019- | Founding Chair, Sleep Research Fellowship Committee, AASMF |
| 2019- | Chair, Grand Rounds Planning Committee, Dept. of Neurology, Miller School of Medicine, FL |

**Ad Hoc Reviewer**

| | |
|---|---|
| 2017 | Scientific Review Committees: ZRG1-BBBP-J-56 for CSR; ZHL1-CSR-I-F3 for NHLBI |
| 2018 | Scientific Review Committees: ZHL1-CCT-I-C1 for NHLBI; HLBP-I for NHLBI |
| 2019 | Scientific Review Committees: CHSB for CSR; ZHL1-CCT-X-C1 for NHLBI; ADPA for NIMH; ZRG1-BBBP-X-64 for CSR |
| Current- | Journals: *Alzheimer's and Dementia*, SLEEP, Neurology, JCSM, Sleep Medicine, Sleep Health |

**Honors**

| | |
|---|---|
| 2003 | Cum Laude, U. Central Del Caribe, School of Medicine |
| 2003 | Alpha Omega Alpha, U. Central Del Caribe, School of Medicine |
| 2007 | Clinical Neuroscience Prize, Neurology Residency Program, U. of Miami |
| 2008 | Faculty Development Award, American Neurological Association |
| 2013 - 2014 | Scholar, Program to Increase Diversity among Individuals Engaged in Health-Related Research (PRIDE), NHLBI |
| 2013 | Fellow, American Academy of Sleep Medicine |
| 2015 | Diversity Leadership Development Program, American Academy of Neurology |
| 2015-2016 | Peer Mentor Program, PRIDE, Supported by grants from NHLBI/New York University |
| 2015 | Travel Award, U13 Conference Series: Sleep, Circadian Rhythms, and Aging: Supported by the National Institutes of Aging and the American Geriatrics Society |
| 2019 | Keynote Speaker, Plenary Session, Update in Clinical Research-*Sleep in cerebrovascular disease and Neurocognitive aging (May 10)*; >5,000 people in |

attendance. American Academy of Neurology Annual Meeting. Philadelphia, Pennsylvania

2020 Fellow, C-Change Institute, Brandeis University, MA

**C. Contribution to Science.**

**1.** Dr. Ramos has played a leading role in various multi-ethnic population based studies design to address the influence of sleep disorders on brain health, including cognitive aging, cognitive decline and cerebrovascular risk. Study results have provided important estimates of the effect that sleep disorders and sleep patterns have on cognitive performance and declines in memory, executive function and processing speed. These studies also determined the detrimental effect of sleep apnea and sleep patterns on cerebrovascular risk factors, including hypertension, non-dipping of blood pressure, left ventricular mass, cerebral hemodynamics, white matter hyperintensities and decreased brain volumes, among other outcomes.

a. **Ramos, A. R., W. Tarraf, B. Wu, S. Redline**, J. Cai, M. L. Daviglus, L. Gallo, Y. Mossavar-Rahmani, K. M. Perreira, P. Zee, D. Zeng and **H. M. Gonzalez**. Sleep and neurocognitive decline in the Hispanic Community Health Study/Study of Latinos. Alzheimers Dement. 2020;**16**(2): 305-315.

b. **Ramos AR**, Weng J, Wallace DM, Petrov MR, Wohlgemuth WK, Sotres-Alvarez D, Loredo JS, Reid KJ, Zee PC, Mossavar-Rahmani Y, Patel SR. Sleep Patterns and Hypertension Using Actigraphy in the Hispanic Community Health Study/Study of Latinos. CHEST. 2018; 153:87-93. PMID: 28970105; PMCID: PMC5812757.

c. **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; 87:1511-1516. PMID: 27590286; PMCID: PMC5075974.

d. **Ramos, A. R**., C. Dong, T. Rundek, M. S. Elkind, B. Boden-Albala, R. L. Sacco and C. B. Wright Sleep duration is associated with white matter hyperintensity volume in older adults: the Northern Manhattan Study. Journal of Sleep Research.2014.**23**(5): 524-530.

**2.** Dr. Ramos's research program identified the important role for ethnicity, and the sociocultural factors that could explain differences in sleep symptoms, sleep disorders and sleep patterns in minorities; as well as their associated impact on health. Published studies identified differences in sleep disturbances (snoring, sleepiness, long sleep) among Hispanic/Latinos, non-Hispanic blacks and non-Hispanic whites, associated with depression and cardiometabolic diseases. In addition, these studies determined the prevalence and the sociocultural correlates of sleep disorders and sleep patterns in a diverse sample of Hispanic/Latinos. In addition, collaboration with genetic statisticians help define traits of sleep apnea and hypoxemia in Hispanic/Latinos. The research program emphasized the existence of sleep health disparities and created the rationale for studies that address the contributors of these disparities.

a. Lippman S, Gardener H, Rundek T, Seixas A, Elkind MSV, Sacco RL, Wright CB, **Ramos AR**. Short sleep is associated with more depressive symptoms in a multi-ethnic cohort of older adults. Sleep Med. 2017; 40:58-62. PMCID: PMC5726583.

b. Cade BE, Chen H, Stilp AM, Gleason KJ, Sofer T, Ancoli-Israel S, Arens R, Bell GI, Below JE, Bjonnes AC, Chun S, Conomos MP, Evans DS, Johnson WC, Frazier-Wood AC, Lane JM, Larkin EK, Loredo JS, Post WS, **Ramos AR**, Rice K, Rotter JI, Shah NA, Stone KL, Taylor KD, Thornton TA, Tranah GJ, Wang C, Zee PC, Hanis CL, Sunyaev SR, Patel SR, Laurie CC, Zhu X, Saxena R, Lin X, Redline S. Genetic Associations with Obstructive Sleep Apnea Traits in Hispanic/Latino Americans. Am J Respir Crit Care Med. 2016; 194:886-897.PMID: 26977737

c. Patel SR, Sotres-Alvarez D, Castañeda SF, Dudley KA, Gallo LC, Hernandez R, Medeiros EA, Penedo FJ, Mossavar-Rahmani Y, **Ramos AR**, Redline S, Reid KJ, Zee PC. Social and Health Correlates of Sleep Duration in a US Hispanic Population: Results from the Hispanic Community Health Study/Study of Latinos. SLEEP. 2015; 38:1515-22. PMCID: PMC4576324.

d. Redline S, Sotres-Alvarez D, Loredo J, Hall M, Patel SR, **Ramos A**, Shah N, Ries A, Arens R, Barnhart J, Youngblood M, Zee P, Daviglus ML. Sleep-disordered breathing in Hispanic/Latino individuals of diverse backgrounds. The Hispanic Community Health Study/Study of Latinos. Am J Respir Crit Care Med. 2014; 189:335-44 PMCID: PMC3977733.

Link to complete list of publications (6/8/2020):
https://www.ncbi.nlm.nih.gov/myncbi/alberto.ramos.1/bibliography/public/

**D. Additional Information:** Ongoing Research

U01NS099043 Brown/Chervin (MPI) 8/15/2018-7/21/2023
Title: Sleep for Stroke Management and Recovery Trial (Sleep SMART). Leveraging the infrastructure of StrokeNet, this study is phase III multicenter, prospective randomized open-, blinded- endpoint controlled trial of positive airway pressure for stroke recovery and prevention in stroke patients with sleep apnea.
**Role: Miami site Co-I** (Jose Romano,MD Miami site-PI)

**Ongoing Research Support**

Avadel Pharmaceutical Ramos (site-PI) 11/ 2020-12/2022
Open label study evaluating the effect of single dose sodium oxybate in Narcolepsy. 5% effort.
**Role: Site-Principal Investigator**

JAZZ Pharmaceutical Ramos (PI) 6/2019-5/2021
Title: MR brain Atrophy and Neurocognition in Treated Obstructive sleep apnea (MAGNETO). Investigator initiated study to examine the neuroimaging and neurocognitive substrates of residual daytime sleepiness in patients with treated obstructive sleep apnea. Effort 15% **Role: Principal Investigator**

R21 HL140437 (Ramos) NIH/NHLBI 2/01/19 – 01/31/21 2.76 Cal Months
*Title: Sleep Apnea Phenotypes in Latinos (SLEPT).* This study will help develop risk-stratification strategies for sleep apnea and inform future intervention studies in cardiovascular risk and sleep apnea; providing a step towards personalized medicine in sleep. This study would contribute to reducing health disparities among diverse Latinos, burdened by increased risk for cardiovascular disease and a high prevalence of sleep apnea. Effort 12%
**Role: Principal Investigator**

**OVERLAP:** None

**PENDING:** R01AG063868 NIH/NIA-Sleep in Neurocognitive Aging and Alzheimer's Research. Role: Principal Investigator (To be paid)

1R41AG073066-01 An AI-assisted screening platform within a multivariate framework for biomarkers of mild cognitive impairment due to Alzheimer's disease. Role: MPI

**Completed Research Support**

Scientific Advisory Committee Pilot Study Award Ramos (PI) 02/01/18-04/01/2020

Miller School of Medicine, University of Miami, FL
*Title: Elucidating the link between sleep apnea and dementia using multimodal MRI and cognitive testing.* This pilot study compares MRI brain regions, total volumetric blood flow to the brain, and regional cerebral perfusion; and neurocognitive function in across sleep apnea phenotypes. **Role: Principal Investigator**

R21 AG056952 Ramos, Alberto Rafael (PI) 08/01/17-05/31/2020, 3.12 Cal Months
*Title: Exploring Sleep in Neurocognitive Aging and Alzheimer's Research (eSANAR)*
This study provides the framework for future SOL studies on sleep and ADRD risk in Latinos. Evaluating the severity of baseline sleep apnea, levels of hypoxemia, apnea duration, sleep duration and sleep fragmentation, provides an opportunity to refine the sleep phenotypes associated to early neurocognitive decline and mild cognitive impairment and Alzheimer's disease and related dementias. **Role: Principal Investigator**

Boehringer Ingelheim. Chaturvety/Ramos (PI) 05/2016-12/2019
*Title: Arrhythmia Detection In Obstructive Sleep apnea (ADIOS Title: 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: Principal Investigator**

KL2 TR000461-02/03
Szapocznik, Jose (PI) 06/27/12-05/31/16
Miami Clinical and Translational Science Institute
The goal of this study is to evaluate the cerebral hemodynamic as an early marker of cerebrovascular risk in participants with sleep apnea compared to controls. 75% effort. *Mentor: Tatjana Rundek, MD, PhD.* ***Role*: Scholar**

L60 MD005231-01-04 Ramos, Alberto Rafael (PI) 07/01/12-06/30/16
*Sleep apnea, cerebral blood flow and cognition.* Loan repayment program from the National Institutes of Health/National Institute of Minority Health and Health Disparities to evaluate associations between sleep apnea, sleep disturbances, cerebral blood flow and cognitive function in Latinos. **Role: Principal Investigator**

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.

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

## 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: Ami P. Raval

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

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 |
|---|---|---|---|
| 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, 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. 1994 - 2000
- Assistant scientist: University of Miami, U.S.A. 2003 –2006
- Research Assistant Professor: University of Miami, U.S.A. 2006 - 2018
- American Heart Association (AHA)- Innovative grant reviewer Fall 2014 - 2017
- American Heart Association- Career Development Award Committee Fall 2017 – Spring 2020
- NIH-NNRS Study Section Spring 2017 Ad-hoc
- AHA- Transformational Project Award Organ Sciences reviewer Spring 2018
- VA- Rehabilitation Research and Development grant reviewer Fall 2019 Ad-hoc

- 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
- NextGenMD Phase 1B facilitator Fall 2020-Present
- American Heart Association- Brain 1/2 study section reviewer Spring 2015 – Present
- Associate editor of Translational Stroke Journal Fall 2020-Present
- Technical editor of Stroke Journal Fall 2020-Present

**Scholarship and Awards:**

- 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

**Membership in Professional Societies:**

- Society for Neuroscience (SFN)
- Society for Cerebral Blood Flow & Metabolism
- American Heart Association (AHA)
- Organization for the Study of Sex Differences (OSSD)
- Society for Reproductive Biology and Comparative Endocrinology (SRBCE)

**C. Contribution to Science**

**Note:** * represents equal contribution; **** Corresponding author,** Google h-index = 31

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. Diaz F and **Raval AP**** Simultaneous nicotine and oral contraceptive exposure alters brain energy metabolism and exacerbates ischemic stroke injury in female rats. J Cereb Blood Flow Metab. 2020 Jun 14:271678X20925164.
b. d'Adesky N, Diaz F, Zhao WZ, Bramlett HM, Perez-Pinzon MA, Dave KR, and **Raval AP**. Nicotine exposure along with oral contraceptive treatment in female rats exacerbates post-cerebral ischemic hypoperfusion potentially via altered histamine metabolism. Translational Stroke Journal 2020 October (in press)
c. d'Adesky ND, de Rivero Vaccari JP, Bhattacharya P, Schatz M, Perez-Pinzon MA, Bramlett HM, **Raval AP****. Nicotine Alters Estrogen Receptor-Beta-Regulated Inflammasome Activity and Exacerbates Ischemic Brain Damage in Female Rats. Int J Mol Sci. 2018; 19(5)
d. **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.

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. 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.
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.
c. 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.
d. **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.

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. McCarthy M and **Raval AP****. The Peri-menopause in a Woman's Life: A Systemic Inflammatory Phase that Enables Later Neurodegenerative Disease. 2020 Oct 23;17(1):317.
b. Schatz M, Saravanan S, d'Adesky ND, Bramlett H, Perez-Pinzon MA, **Raval AP****. Osteocalcin, ovarian senescence, and brain health. Front Neuroendocrinol. 2020 Aug 8;59:100861.
c. **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.
d. **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.

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. Kerr N, Dietrich WD, Bramlett HM, **Raval AP**** Sexually dimorphic microglia and ischemic stroke. CNS Neurosci Ther. 2019 Dec;25(12):1308-1317
b. **Raval AP****,** Martinez CC, Mejias NH, de Rivero Vaccari JP. Sexual dimorphism in inflammasome-containing extracellular vesicles and the regulation of innate immunity in the brain of reproductive senescent females. Neurochem Int. 2018 Nov: S0197-0186(18)30536-9.

c. 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:**

**https://pubmed.ncbi.nlm.nih.gov/?term=Raval%20Ami%20P&sort=date**

## D. Active Support

Florida Department of Heath# 20K09 01/07/2020- 05/31/ 2023
Nicotine alters brain oxidative metabolism and exacerbates ischemic brain damage
The proposed study will investigates effects of smoking-derived nicotine (N) and oral contraceptives (OC) on cerebral ischemia risk in female rats.
**Role: PI**

Florida Department of Heath# 20K11 01/07/2020- 05/31/ 2023
Strategies to ameliorate cognitive decline following cerebral ischemia in nicotine exposed rats
The proposed study will determine whether physical exercise along with other therapies can ameliorate cognitive deficits in older cohorts of rats that ensue from stroke.
Principal Investigator: Dr. Pérez-Pinzón
**Role: Co-investigator**

NIH-NINDS-2R01NS045676-10A1 15/08/2020- 07/31/ 2025
Mechanisms of neuroprotection against cardiac arrest
Principal Investigator: Dr. Pérez-Pinzón
**Role: Co-investigator**

NIH-NINDS -5R01NS034773-19 01/08/2017- 07/31/ 2022
Mitochondria and cerebral ischemia: Intracellular Signaling
Principal Investigator: Dr. Pérez-Pinzón
**Role: Co-investigator**

Florida Department of Heath # 9JK08 09/01/2019-07/30/2022
Nicotine exposure and intracerebral hemorrhage
Principal Investigator: Dr. Kunjan R. Dave
**Role: Co-investigator** (15% efforts)

University of Miami, Scientific Review Committee funding 12/01/2020-11/30/2021
Therapeutic interventions for post-stroke rehabilitation
The proposed study will investigates underlying mechanisms of whole body low frequency vibration mediated ischemic neuroprotection.
**Role: PI**

Florida Department of Heath#7JK01 (NEC) 03/01/2017- 2/28/2021
Whole body vibrations improves stroke outcome in nicotine-exposed rats
The major goal of Florida Department of Health funding is to test the hypothesis that post-stroke whole body vibration reduces inflammation and increases circulating endothelial progenitor cells

(EPCs), thus reducing frailty and improving physical activity and cognition after ischemia in nicotine exposed rats.
Principal Investigator: Dr. Helen Bramlett
**Role: Co-PI**

***Completed Research Support:***
American Heart Association- Grant-in-aid (NCE)
AHA # 16GRNT31300011 07/01/16- 06/30/2019
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**

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**

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**

# 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**

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

POSITION TITLE: **Professor of Neurology, Vice Chair of Clinical 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)* | Start Date MM/YYYY | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|---|
| University of Zagreb, Croatia | BS | 09/1979 | 06/1983 | Applied Mathematics |
| Medical School U of Zagreb, Croatia | MD | 09/1984 | 06/1989 | Medicine |
| Medical School U of Zagreb, Croatia | MS | 08/1989 | 06/1991 | Epi/Bioinformatics |
| Ludwig-Maximillian U, Munich, Germany | PhD | 08/1991 | 05/1995 | Neuroscience |
| Medical School U of Zagreb, Croatia | Residency | 06/1991 | 06/1994 | Neurology |
| Grossharden Spital Munich, Germany | Fellow | 07/1994 | 07/1995 | Stroke |
| Columbia University, New York, NY | Fellow | 01/1998 | 06/2000 | Stroke/Epidemiology |

**A. Personal Statement**

As Scientific Director of the McKnight Brain institute (MBI), I provide leadership, strategic collaborations, and mentorship in cognitive and brain aging to the MBI scientific community and to the broader community of the Medical School and the UM through partnership with other Departments, Centers and Institutes. Together with the UM MBI Executive Director and Leadership, I provide strategic collaboration with other MBIs and national and international institutions on the issues of age-related memory loss, cognitive decline and promotion of brain health. I also provide opportunities to our MBI investigators at every stage of their career to utilize infrastructure and resources of MBI, including the opportunities to obtain the MBI pilot awards in cognitive aging. I am a neurologist, neuroscientist and epidemiologist by training with an extensive experience in vascular and cognitive neurology and neuroimaging studies. I serve as Executive Vice Chair of Research and Faculty Affairs in the Department of Neurology and direct Clinical Translational Research Division. At the institutional level, I am Director of a MS degree in Clinical Translational Investigations, and Director of the KL2 program and translational workforce development of the Miami CTSI. I am a co-Director of AlzSTARS research education program of the One Florida Alzheimer Disease Research Center and Director of the Research Educational Programs for NIH NeuroNext and StrokeNet. I have a 25+ year long track record of NIH funding as PI, collaborative investigator, and as a mentor. I have been conducting cross-disciplinary research in aging brain health and disease for the past 25 years using epidemiology, genetics, and neuroimaging. I have been a productive investigator with over 430 publications in the area of vascular cognitive impairment in aging populations. I am a true collaborative clinical researcher with established extensive collaborations on the large NIH-funded aging studies.

These 4 peer reviewed publications highlight my experience:


1. **Rundek T**, Gardener H, Dias Saporta AS, Loewenstein DA, Duara R, Wright CB, Dong C, Levin B, Elkind MSV, Sacco RL. Global Vascular Risk Score and CAIDE Dementia Risk Score Predict Cognitive Function in the Northern Manhattan Study. J Alzheimers Dis. 2020;73(3):1221-1231. PMC3628415
2. Fleysher R, Lipton ML, Noskin O, **Rundek T**, Lipton R, Derby CA. White matter structural integrity and transcranial Doppler blood flow pulsatility in normal aging. Magn Reson Imaging. 2018 ;47:97-102. PMC5828865
3. **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. PMC5780238
4. Ezzati A, **Rundek T**, Verghese J, Derby CA. Transcranial Doppler and Lower Extremity Function in Older Adults: Einstein Aging Study. J Am Geriatr Soc. 2017 ;65(12):2659-64. PMC5729099

**B. Positions and Honors**

**Positions and Employment**

| | | |
|---|---|---|
| 1994-96 | Assistant Professor of Neurology | Dept. of Neurology, University of Zagreb, Croatia |
| 1994-00 | Stroke Attending | Department 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 |
| 2002-07 | Director & Attending, Vasc Laboratory | Columbia University Medical Center, New York, NY |
| 2007-11 | Associate Professor of Neurology | Miller School of Medicine, Univ. of Miami, Miami, FL |
| 2007- | Director, Clinical Translational Div | Miller School of Medicine, Univ. of Miami, Miami, FL |
| 2010- | Vice Chair, Clinical Translational | Miller School of Medicine, Univ. of Miami, Miami, FL |
| 2011- | Professor of Neurology (with tenure) | Miller School of Medicine, Univ. of Miami, Miami, FL |
| 2014- | Director, MS Clinical Translational | Miller School of Medicine, Univ. of Miami, Miami, FL |
| 2016-17 | Interim Scientific Director, McKnight Brain Institute (MBI) | Miller School of Medicine, Univ. of Miami, Miami, FL |
| 2018- | Scientific Director, MBI | Miller School of Medicine, Univ. of Miami, Miami, FL |

**Other Experience and Professional Membership**

| | |
|---|---|
| 2009-14 | President, the Neurosonology Community of Practice, Am Institute of Ultrasound in Medicine |
| 2012- | Member, the Board of the Directors, Intersocietal Accreditation Committee (IAC)-Vascular |
| 2012-19 | Consulting Editor of *Stroke* |
| 2013- | Editorial Board Member of *Neurology, Cerebrovascular Disease, J of Ultrasound in Medicine* |
| 2014- | Member, the Clinical Standards Committee, Am Institute of Ultrasound in Medicine (AIUM) |
| 2015- | Secretary, the Executive Committee, Intersocietal Accreditation Committee (IAC)-Vascular |
| 2015- | Reviewer, NIH sections ZHL1 CT-K (C1)1, NHLBI 21, NIH LRP |
| 2016- | Intersocietal Accreditation Committee (IAC), Vascular Testing Board member |
| 2019- | Intersocietal Accreditation Commission (IAC), President elect |
| 2020 | Section Editor of *Stroke* |

**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 |
| 2015 | The American Heart Association Core Vitae Award for Stroke |
| 2018- | The Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging |
| 2020 | UMMSOM: The Women in Academic Medicine Career Achievement Award |

**C. Contribution to Science**

1. Extracranial and intracranial neuroimaging markers. 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 sleep breathing disorders, vascular cognitive impairment, memory loss and dementia. I have been an active member of IAC (Intersocietal Accreditation Committee), the largest US accreditation body that sets the standards for performance of clinical ultrasound, CT/MRI and cardiac Echo. I have been an advocate for advancing quality of clinical ultrasound and improving access to high-quality clinical ultrasound in medicine.

a. **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. PMCID: PMC2831775.
b. **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. PMC3738011.

c. **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):364-70. PMC4509793
d. Lorenz MW, Polak JF, Kavousi M, Mathiesen EB, Völzke H, Tuomainen TP, Sander D, Plichart M, Catapano AL, Robertson CM, Kiechl S, **Rundek** T, Desvarieux M, Lind L, Schmid C, DasMahapatra P, Gao L, Ziegelbauer K, Bots ML, Thompson SG; PROG-IMT Study Group. Carotid intima-media thickness progression to predict cardiovascular events in the general population (the PROG-IMT collaborative project): a meta-analysis of individual participant data. Lancet. 2012; 379(9831):2053-62. PMCID: PMC3918517.

2. Epidemiology of stroke and atherosclerosis, stroke disparities. Over the past 20 years I have pursued multi-disciplinary research in stroke epidemiology and stroke disparities. The central findings from this research include the discovery of novel stroke risk factors (e.g., insulin resistance, sleep duration, homocysteine, adiponectin, oral infection) in minority populations. Some of these reports were among the first in the literature. We conducted the seminal epidemiological investigation on 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. I am a strong believer in team science and many of my research products are the results of multiple collaborations between various national and international research teams and institutions.

a. **Rundek T**, Gardener H, Xu Q, Goldberg R, Wright C, Boden-Albala B, Disla N, Paik M, Elkind MSV, Sacco RL. Insulin Resistance and Risk of Ischemic Stroke Among Nondiabetic Women from the Northern Manhattan Study. Arch Neurol**.** 2010; 67:1195-200. PMCID: PMC2954671.
b. **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. PMCID: PMC2737546.
c. **Rundek T**, Sacco RL. Outcome following stroke. In “Stroke- Pathophysiology, Diagnosis, and Management”. Editors: J.P. Mohr, D.W. Choi, J.C. Grotta, B. Weir, P.A. Wolf; Fourth edition, Churchill Livingstone, Elsevier Inc.; 2016; Chapter 2: 58-67.
d. **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; 61:889-892. PMCID: PMC15210526.

3. Genetic contribution to atherosclerosis and stroke. I have been investigating genetic contribution to carotid disease for over the past 10 years as PI of 2 NINDS R01 grants and a NINDS K24 award, and recently as PI of family study of atherosclerosis and a site PI of the NINDS SiGN (ischemic Stroke Genetic Network). In one of my investigations I have taken 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.

a. **Rundek T**, Elkind MS, Pittman J, Boden-Albala B, Martin S, Humphries SE, Hank Juo SH, Sacco RL (2002). 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 333:1420-3. PMCID: PMC2692936.
b. Dong C, Della-Morte D, Wang L, Cabral D, Beecham A, McClendon MS, Luca CC, Blanton SH, Sacco RL, **Rundek T** (2011). Association of the sirtuin and mitochondrial uncoupling protein genes with carotid plaque. PLoS One. 6(11):e27157. PMCID: PMC3210138.
c. Battey TW, Valant V, Kassis SB, Kourkoulis C, Lee C, Anderson CD, Falcone GJ, Jimenez-Conde J, Fernandez-Cadenas I, Pare G, **Rundek T**, James ML, Lemmens R, Lee TH, Tatlisumak T, Kittner SJ, Lindgren A, Mateen FJ, Berkowitz AL, Holliday EG, Majersik J, Maguire J, Sudlow C, Rosand J (2015); International Stroke Genetics Consortium. Recommendations from the international stroke genetics consortium, part 2: biological sample collection and storage. Stroke. 46(1):285-90. PMCID: PMC4276505.
d. Meschia JF, Arnett DK, Ay H, Brown RD Jr, Benavente OR, Cole JW, de Bakker PI, Dichgans M, Doheny KF, Fornage M, Grewal RP, Gwinn K, Jern C, Conde JJ, Johnson JA, Lindgren A, Markus HS, McArdle PF, McClure LA, Mitchell BD, , Rosand J, Rothwell PM, **Rundek T**, Sacco RL, Sharma P, Shuldiner AR, Slowik A, Wassertheil-Smoller S, Sudlow C, Thijs VN, Woo D, Worrall BB, Wu O, Kittner SJ (2013); NINDS SiGN Study. Stroke Genetics Network (SiGN) study: design and rationale for a genome-wide association study of ischemic stroke subtypes. Stroke. 44(10):2694-702. PMCID: PMC4056331.

**Complete List of Published Work in MyBibliography:**
https://www.ncbi.nlm.nih.gov/myncbi/tatjana.rundek.1/bibliography/public/

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

**Ongoing Research Support**

NIH/NINDS R01 NS 40807 Rundek (PI) 05/01/02-09/30/23
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.

NIA P30AG066506 Golde (PI) 06/15/20- 04/30/25
1Florida Alzheimer's Disease Research Center (1FL ADRC)
1FL AD Science Training to Advance Research Success (AlzSTARS) Rundek (Co-Director)
The major goal of program is to create and maintain a longitudinal clinical cohort of aging individuals with memory complains, detailed cognitive and brain MR imaging phenotypes, and infrastructure for further clinical research and research education in cognitive aging, MCI and AD.
Role: Co-Director of AlzSTARS Research Education Core (REC) and Co-Investigator of UM Clinical Core

FL DOH 9AZ25 Rundek (PI) 01/01/19-12/31/21
Brain Vascular Imaging Phenotypes, Vascular Comorbidities and the Risk for Alzheimer Disease: The Florida VIP Study of AD Risk (PI)
The major goal is to determine imaging and vascular phenotypes associated with increased risk of AD.

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

U54TR002736-01 Sacco (PI) 06/28/18-05/31/23
1KL2TR002737 Rundek (PI) 06/28/18-05/31/23
NIH/NCATS
*Miami Clinical and Translational Science Institute*
The goals of the Miami CTSI are to improve the quality and efficacy of clinical and translational research, advance team science and culturalized health sciences.
Role: Co-Director of Translational Workforce Development

NIH/NIMHD R01MD012467 Rundek, Sacco, Romano (MPI) 10/30/17-06/30/22
Disparities in Transition of Care after Acute Stroke Hospitalization
The objective of this study is to identify disparities in post-hospital stroke care among stroke patients hospitalized for acute stroke hospitalization and discharged to home in Florida and to develop effective initiative to reduce disparities in post-hospital stroke care.

NIH/NINDS U10 NS 077423 Benatar, Sacco (MPI) 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: Training Director

NIH/NIA P01 AG003949 Lipton, Derby, Rundek (MPI) 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 U10 NS086528 Romano (PI) 09/30/13-07/31/23
Miami Regional Coordinating Center for NINDS Stroke Trials Network
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/NHLBI N01-HC65234 Schneiderman (PI) 06/01/14-05/31/24
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: Stroke Adjudication Core Investigator

ARISTA-USA CV185-564 Rundek (PI) 01/04/17-12/31/20
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.

**Completed Research Support**

NIH/NIDA R01DA034589 Kumar (PI) 09/15/14-08/31/19
Predictive Biomarkers of CVD Risk in Diverse HIV-1+ Cocaine Abusers
Role: Co-Investigator

NIH/NGRI Columba GENIE (GENomic Integration with EHR) Weng (PI) 09/01/15-05/31/19
Role: Co-Investigator

NIH/NINDS R01 NS084288-01A1 Romano (PI) 04/01/14-03/31/19
Mechanisms of Early Recurrence in Intracranial Atherosclerotic Disease (MyRIAD)
Role: Co-Investigator

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

AHA14BFSC17690000 Sacco (PI) 04/01/14-03/31/18
AHA-ASA/Bugher Foundation Center of Excellence in Stroke Collaborative Research
Role: Training Director

NIH/NINDS U54 NINDS SPIRP U54NS081763 Sacco (PI) 01/01/13-12/31/18
Stroke Prevention/Intervention Research Program in Hispanics
Role: PI of Core C and PI of Supplement- Stroke Outcome in Women

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

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

NIH/NIDCR R01 DE 13094 Desvarieux (PI) 06/15/06-05/31/17
Oral Infections, Carotid Atherosclerosis and Stroke (INVEST)
Role: Co-Investigator

NIH/NINDS U01 NS 069208 Kittner (PI) 04/01/10-03/31/16
The NINDS International Stroke Genetics Consortium Study: Ischemic Stroke Genetics
PI: S. Kittner, U Maryland; T. Rundek, Site PI
Role: Site PI; Sign Publication Committee Lead

## 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. I have an extensive research track record in stroke, vascular cognitive impairment, clinical trials and disparities research. As Executive Director of the McKnight Brain Institute I am committed to expanding translational research in cognitive aging. I am PI for several large-scale collaborative 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. As the NOMAS study cohort ages, our focus has expanded to include the vascular contributions to cognitive aging and functional impairment. In the Multi-PI Transition of Care Stroke Disparities Study), we seek to identify disparities and gaps in stroke care, which may limit cognitive recovery and severely affect quality of life after stroke. I also function as Program Director for the Florida Stroke Registry which is dedicated to improving the quality of stroke care and to addressing disparities. I also have an extensive record of accomplishments in clinical trials currently functioning as Co-PI for the Miami Regional Coordinating Center for NINDS. 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 700 peer-reviewed articles and over 120 invited articles in the areas of stroke prevention, treatment, epidemiology, risk factors, vascular cognitive impairment, and human genetics. I am member of the National Academy of Medicine and previously 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. I have helped train numerous fellows in stroke and epidemiology and was co-director of a T32 entitled Neuro-epidemiology Training Program designed to train neurologists in epidemiology, as well as to mentor MD, PhD, and graduate students. As former president of the American Heart Association and former president of the American Academy of Neurology, I am fully committed to advancing scientific collaborations and building partnerships for clinical and translational brain research in the areas of environmental determinants of stroke, cardiovascular disease, cognitive performance, brain health, and successful aging.

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

1. 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.
2. Zeki Al Hazzouri A, Caunca MR, Nobrega JC, Elfassy T, Cheung YK, Alperin N, Dong C, Elkind MSV, **Sacco RL**, DeCarli C, Wright CB. Greater depressive symptoms, cognition, and markers of brain aging: Northern Manhattan Study. **Neurology**. 2018 Jun 5;90(23):e2077-e2085. PMID: 29743209; PMCID: PMC5993180
3. Gardener H, Caunca M, Dong C, Cheung YK, Alperin N, Rundek T, Elkind MSV, Wright CB, **Sacco RL**. Ideal Cardiovascular Health and Biomarkers of Subclinical Brain Aging: The Northern Manhattan Study. **J Am Heart Assoc.** 2018 Aug 21;7(16). PMID: 30369305; PMCID: PMC6201403
4. Caunca MR, Gardener H, Simonetto M, Cheung YK, Alperin N, Yoshita M, DeCarli C, Elkind MSV, **Sacco RL**, Wright CB, Rundek T. Measures of obesity are associated with MRI markers of brain aging: The Northern Manhattan Study. **Neurology**. 2019 Aug 20. PMID: 31341005; PMCID: PMC6711659

## B. Positions and Honors

### POSITIONS AND EMPLOYMENT

**Academic Appointments:**

| | |
|---|---|
| 1989-97 | Assistant Professor of Neurology & Public Health (Epidemiology) in the Sergievsky Center |
| 1997-02 | Associate Professor of Neurology & Public Health (Epidemiology) (with tenure) |
| 2003-07 | Professor of Neurology & Epidemiology, Columbia University, College of Physicians and Surgeons, Mailman School of Public Health, and the Sergievsky Center (with tenure) |
| 2007- | 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 |
| 2016- | Senior Associate Dean of Clinical Research, Miller School of Medicine, University of Miami |

**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 |
| 2018 | National Academy of Medicine | 2019 | Neurologist Pioneering Award, SVIN |

**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 |
| 2019- 21 | AAN, Immediate Past President |

## C. Contribution to Science

C.1. Vascular Determinants of Cognitive Aging. Through the 27-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.2. Genetic Contribution to Atherosclerosis, Stroke, and Brain aging. As founding PI of a family study, I have been investigating the genetic contributions to carotid disease and other stroke precursor phenotypes. Through this work, extensive data for quantitative traits in family linkage studies, genome wide association studies, fine-mapping studies, and extreme phenotypes for carotid atherosclerosis and other cardiovascular traits has been evaluated. The results of these investigations are now contributing novel observations for future targeted therapies and prevention of CVD.

1. **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;40:2307-12. PMCID: PMC2737512.
2. Wang L, Di Tullio MR, Beecham A, Slifer S, Rundek T, Homma S, Blanton SH, **Sacco RL**. A comprehensive genetic study on left atrium size in Caribbean Hispanics identifies potential candidate genes in 17p10. **Circ Cardiovasc Genet** 2010;3:386-92. PMCID: PMC2923674
3. 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 Sep 25;3(5):e185. PMID: 28975155; PMCID: 5619914
4. Dueker ND, Beecham A, Wang L, Blanton SH, Guo S, Rundek T, **Sacco RL**. Rare Variants in NOD1 Associated with Carotid Bifurcation Intima-Media Thickness in Dominican Republic Families. **PLoS One** 2016;11(12):e0167202. PMCID: PMC5147882

C.3. Epidemiology of Stroke. Over the past 33 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.4. Health Disparities As Principal Investigator for both a 27-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. PMCID: PMC3396556
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 Feb 14;6(2). pii: e004073. doi: 10.1161/JAHA.116.004073. PubMed PMID: 28196814

C.5. 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. **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
4. Diener HC, **Sacco RL,** Easton JD, Granger CB, Bernstein RA, Uchiyama S, Kreuzer J, Cronin L, Cotton D, Grauer C, Brueckmann M, Chernyatina M, Donnan G, Ferro JM, Grond M, Kallmünzer B, Krupinski J, Lee BC, Lemmens R, Masjuan J, Odinak M, Saver JL, Schellinger PD, Toni D, Toyoda K; RE-SPECT ESUS Steering Committee and Investigators. Dabigatran for Prevention of Stroke after Embolic Stroke of Undetermined Source. **N Engl J Med**. 2019;380(20):1906-1917. PubMed PMID: 31091372

C.6. 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 PMID: 16432246 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. Research Support**

List of selected ongoing and completed research projects for the past three years:

**Ongoing Research Support**

Florida Dept. of Health #COHAN A1 Sacco (Director) 07/01/19-06/31/21
Florida Stroke Registry
Aims: To improve the quality of acute stroke care across the state of Florida and reduce disparities by sex, race, ethnicity, and region.
Role: PI

R01NS29993 Sacco (PI) 01/01/93-07/31/21
Risk Factors for Stroke and Cognitive Decline 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

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
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

UL1TR002736 Sacco (PI) 06/28/18-05/31/23
KL2TR002737 06/28/18-05/32/23
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

2R01NS240807 Rundek/Blanton (Multi-PI) 05/01/02-03/31/23
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-I

U10NS086528 Romano (PI) 08/01/18-07/31/23
Florida 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

U10NS077423-01 Benatar (PI) 07/01/18-06/30/23
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: Co-I

1U01NS086872 Broderick (PI) 10/01/18-09/30/23
NSTN National Clinical Coordinating Center (StrokeNET)
Role: Prevention, Co-chair, Co-I

# 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: Anita Seixas Dias Saporta

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

POSITION TITLE: Postdoctoral Researcher

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*)* | START DATE MM/YYYY | END DATE MM/YYYY | FIELD OF STUDY |
|---|---|---|---|---|
| Universidade Federal Fluminense (Rio de Janeiro, Brazil) | MD | 03/1996 | 09/2002 | Medicine |
| Universidade do Estado do Rio de Janeiro (Rio de Janeiro, Brazil) | N/A | 03/2003 | 02/2005 | Pediatric Residency |
| Instituto Fernandes Figueira (Rio de Janeiro, Brazil) | N/A | 02/2005 | 02/2007 | Pediatric Neurology (Clinical Fellowship) |
| Wayne State University (MI, USA) | N/A | 08/2007 | 07/2009 | Neuroimaging Research - Child Neurology (Post-doc) |
| Wayne State University (MI, USA) | N/A | 08/2009 | 07/2010 | Neurogenetics Research - Inherited Neuropathies (Post-doc) |
| University of California in San Francisco (CA, USA) | N/A | 10/2010 | 05/2012 | Neuroimaging Research - Neonatal Neurology (Post-doc) |
| University of Miami | N/A | 06/2017 | Current | Neuroimaging Research - Clinical and Translational Research, Cognitive disorders and Epilepsy (Post-doc) |

## A. Personal Statement

I am currently a research fellow at the University of Miami Evelyn F. McKnight Brain Institute. I am highly motivated to pursue an academic carrier and under the mentoring of Dr. Rundek (PI), my role is that of data collector and analyst (Imaging data post processing) in the present

project “Brain Vascular Imaging Phenotypes, Vascular Comorbidities and the Risk for Alzheimer’s Disease: The Florida VIP Study of AD Risk”.
My previous research work includes brain neuroimaging from the neonatal period to adulthood and utilizing multiple imaging modalities to analyze brain function and structure (PET, MRI, DTI, MRS). I also have experience with large database management and development of clinical tools. Since my clinical training in child neurology in Rio de Janeiro, Brazil, I developed an interest in the normal and pathological development of the brain, behavior and cognition. This interest brought me to pursue training and research projects in neuroimaging in reference centers including the PET Center at Wayne State University (Detroit, MI) and the Neonatal Brain Disorders Lab at UCSF (San Francisco, CA), and more recently at University of Miami. Ultimately, I believe my previous experience and the opportunity to collaborate with the present project will help me follow my main career goal which is to identify clinical and neuroimaging phenotypical correlations in neurological disorders throughout the human’s brain lifespan.

## B. Positions and Honors

- 1996 - 2002 School of Medicine - Fluminense Federal University (UFF), Rio de Janeiro, Brazil
- 2002 MD Graduation
- 2003 - 2005 Pediatric Residency Program, State University of Rio de Janeiro (UERJ), Brazil
- 2005 - 2007 Child Neurology Fellowship, Fernandes Figueira Institute – FIOCRUZ (Reference center for autistic disorders, epilepsy, and neurogenetics)
- 2006 Board Certification in Pediatrics - Brazilian Pediatric Society
- 2007 – 2009 Post-doctoral Fellow in Neuroimaging – Translational Imaging Center / Children’s Hospital of Michigan / Pediatric department - Wayne State University (Supervisor: Harry T. Chugani)
- 2009 – 2010 Post-doctoral Fellow in Neurogenetics – Charcot-Marie-Tooth North American Network / Neurology department - Wayne State University (Supervisor: Michael E. Shy)
- 2010 – 2012 Post-doctoral Fellow in the Neonatal Brain Disorders Lab, Department of Neurology - University of California, San Francisco (Supervisor: Donna M. Ferriero)
- 2014 Board Certification in Child Neurology – Brazilian Pediatric Society
- 2017 - to date Post-doctoral Research Fellow in Neuroimaging – Epilepsy Division, Neurology Department - University of Miami (Supervisor: Andres Kanner)
- June 2018 to date: McKnight Brain Institute Research Fellow at University of Miami (Supervisor: Tatjana Rundek)

## C. Contributions to Science

1. Neuroimaging Research:

My publications were focused in identifying neuroimaging anatomical correlations in a diverse spectrum of neurological disorders and by using multiple imaging modalities. Using Diffusion Tensor imaging (DTI), we identified abnormal frontal lobe tracts in children with socio-emotional deprivation, thought to be related to defective fiber pruning and the reason for the behavior and cognitive abnormalities found in these children (a). We also demonstrated that the phenotypical variation in language development in children with congenital bilateral perisylvian syndrome is associated with the presence or absence of the Arcuate Fasciculus, a major language tract detectable by DTI (d). We also used Positron Emission Tomography (PET) and DTI to study Tourette Syndrome and identified the presence of asymmetric synthesis of serotonin in basal ganglia in addition to microstructural abnormalities of the cortico-striato-thalamo-cortical circuit, providing an anatomical basis for future therapy development efforts (c).
In epilepsy, we used PET, structural MRI and intracranial electroencephalogram (iEEG) data to identify that the seizure onset zone often extends from the hypometabolic to adjacent normometabolic cortex, while large portions of hypometabolic cortex are not involved in seizure onset or early propagation(b).
Using proton magnetic resonance spectroscopy (H-MRS), we demonstrated that whole body hypothermia reduces disturbances of brain metabolism and preserve its microstructure in the setting of neonatal hypoxic encephalopathy(e).


a. Behen ME, Muzik O, Saporta AS, Wilson BJ, Pai D, Hua J, et al. Abnormal fronto-striatal connectivity in children with histories of early deprivation: A diffusion tensor imaging study. Brain Imaging Behav. 2009;3(3):292-7.

b. Alkonyi B, Juhasz C, Muzik O, Asano E, Saporta A, Shah A, et al. Quantitative brain surface mapping of an electrophysiologic/metabolic mismatch in human neocortical epilepsy. Epilepsy Res. 2009;87(1):77-87.

c. Saporta AS, Chugani HT, Juhasz C, Makki MI, Muzik O, Wilson BJ, et al. Multimodality neuroimaging in Tourette syndrome: alpha-[11C] methyl-L-tryptophan positron emission tomography and diffusion tensor imaging studies. J Child Neurol. 2010;25(3):336-42.

d. Saporta AS, Kumar A, Govindan RM, Sundaram SK, Chugani HT. Arcuate fasciculus and speech in congenital bilateral perisylvian syndrome. Pediatr Neurol. 2011;44(4):270-4.

e. Bonifacio SL, Saporta A, Glass HC, Lee P, Glidden DV, Ferriero DM, et al. Therapeutic hypothermia for neonatal encephalopathy results in improved microstructure and metabolism in the deep gray nuclei. AJNR Am J Neuroradiol. 2012;33(11):2050-5.


2. Epidemiology research:

As part of my academic career development, I have also contributed to epidemiological research in neurological disorders. I was responsible for curating a large registry of patients with Charcot-Marie-Tooth disease (CMT) as part of a natural history and prevalence study. The goal of this project was to design effective strategies for the molecular diagnosis of CMT. The resulting paper in Annals of Neurology is a highly cited paper in the field (345 citations) and has had significant impact in the clinical management of patients with CMT (a).

Recently, I collaborated with my mentor (Dr. Rundek) in a study demonstrating that the “Global Vascular Risk Score” (GVRS) was a stronger predictor of cognitive decline when compared to the “Cardiovascular Risk Factors, Aging, and Incidence of Dementia” (CAIDE) risk score in the Northern Manhattan Study (NOMAS)(b) cohort.

a. Saporta AS, Sottile SL, Miller LJ, Feely SM, Siskind CE, Shy ME. Charcot-Marie-Tooth disease subtypes and genetic testing strategies. Ann Neurol. 2011;69(1):22-33.

b. Rundek T, Gardener H, Dias Saporta AS, Loewenstein DA, Duara R, Wright CB, Dong C, Levin B, Elkind MSV, Sacco RL. Global Vascular Risk Score and CAIDE Dementia Risk Score Predict Cognitive Function in the Northern Manhattan Study. J Alzheimers Dis. 2020;73(3):1221-1231.

My bibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/1L53O30urrJsd9/bibliography/56618993/public/?sort=date&direction=ascending

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

None

## 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: Xiaoyan Sun

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

POSITION TITLE: Assistant Professor at Dept. 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 |
|---|---|---|---|
| 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 am a fully trained physician-scientist. Currently, I am an assistant professor in the Department of Neurology, a clinical director of Brain Endowment Bank, and an education director of McKnight Brain Institute, University of Miami Miller School of Medicine.

I am seeing about 1000 patients with cognitive complaint annually. I also work at brain bank weekly to make final diagnosis of donor brains based on combination of clinical history and formal neuropathology report of post-mortem brain. Brain Endowment bank at University of Miami Miller School of Medicine has a big collection of neurodegenerative diseases. We have capacity to support this proposed research grant by Dr. Yue.

My research experience includes basic science and clinical research. I worked with world renown pathologists to study pathological changes of Alzheimer's disease (AD) and other neurodegenerative diseases 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. Recently, I have conducted clinical research focused on identifying biomarkers for neurodegenerative diseases. My clinical and research experience have placed me on an unique position to participate in this research project. I am an author on fifty peer-reviewed journal articles. I continue dedicating my effort to understand the mechanism underlying dementia disorders.

### 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
2014.10-2020.5 Assistant professor in Dept of Neurology, University of Miami Miller School of Medicine, Miami, FL
2014.10-present Education director for McKnight Brain Institute of University of Miami Miller School of Medicine, FL
2017.12-present Clinical Director, Brain Endowment Bank, University of Miami School of Medicine, FL
2020. 6- present Associate professor in Dept of Neurology, University of Miami Miller School of Medicine,

**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. Contributions to Science

**1. 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*, 2018 Mar 6;90 (10):e887-e895

**2. 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. 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)
d. **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

**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. Characteristic of protein aggregation and cleavage in the post-mortem brains with neurodegenerative disease**

My early work was involved in understanding protein aggregation in the patients with ALS and Alzheimer's disease. I worked with world renown neuropathologists, Dr. Okamoto and Dr. Yamaguchi to characterize inclusion body in the brain with ALS and amyloid pathology in the brain with Alzheimer's disease. I also worked with Dr. Cole to understand the mechanism of cell death in the brain of Alzheimer's disease. The neuropathological research at my early career has laid a good foundation for me to understand protein aggregation in many different 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; 158:379-389 379-389

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

### Ongoing Research Support

75N95019C00050 Scott (PI) 9/1/2019-8/31/2024 2.4 calendar
National Institute of Health $972,533
**The NIH NeuroBioBank and Tissue Repository**
Development of a centralized brain and tissue biorepository to supply neurodegenerative, developmental and psychiatric diseased tissue to academic and industry scientists in order to advance biospecimen science and the economic opportunities emerging in the biomedical and biotechnology sectors.
Role: Co-Investigator

7R01NS029993 Ralph Sacco (PI) 08/01/2019-07/31/2021 1.2 calendar
NIH $339,168
**NOMAS 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.
Role: Co-Investigator

XZ903 Crocco, Elizabeth (PI) 07/01/2018-6/30/2022 0.60 calendar
Florida Department of Elder Affairs $222,801
**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: Co-Investigator

5R01AG055638-02 Curiel, Rosie (PI) 04/1/2018-1/31/2023 0.36 calendar
NIH/NIA $349,674
**Precision-Based Assessment for Detection of MCI in Older Adults**
The major goals of this project are to examine the psychometric properties of novel sensitive cognitive assessment tools among participants 70+ years of age and determine which cognitive markers are most predictive of baseline and longitudinal atrophy in AD-related signature brain regions on MRI. The measures will be compared to widely used cognitive outcome measures in current Alzheimer's disease clinical trials.
Role: Co-Investigator

AG066506 Golde (PI) 06/15/2020- 04/30/2021 1.2 calendar
University of Florida/NIH/NIA $689,760
**1Florida Alzheimer's Disease Research Center**
ADRC is a statewide initiative to study the effects of Alzheimer's Disease.

McKnight Brain Institute, University of Miami Miller School of Medicine

Toyama (clinical trial) PI: Barry Baumel SEP PROTOCOL ADC- 047-TCAD: A PHASE 2 MULTI-CENTER, RANDOMIZED

## 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

HHSN271201300028C Scott (PI) 09/1/13-8/31/21 0.96 calendar
National Institute of Health $623,651
**Brain and Tissue Repository Contract**
Development of a centralized brain and tissue biorepository to supply neurodegenerative, developmental and psychiatric diseased tissue to academic and industry scientists in order to advance biospecimen science and the economic opportunities emerging in the biomedical and biotechnology sectors.

HHSN271201300028C SUB 01 Scott (PI) 02/1/14-8/31/21 0.60 calendar
National Institute of Health $110,169
**Genotype Tissue Expression (GTEx) Contract Options**
NIH grantee supplement to extend biospecimen collection efforts to include receipt, processing, storage, archiving, and distribution of specimens in support of the GTEx project, an NIH Roadmap Initiative, which provides a research resource to the scientific community with which to study the relationship between genetic variation and regulation of gene expression.

5R01AG047649-05 Loewenstein, David (PI) 02/1/2015-1/31/2020 0.96 calendar
NIH/NIA $345,893
**Novel Detection of Early Cognitive and Functional Impairment in the Elderly**
The proposed investigation is highly innovative and designed to examine the efficacy of the newly developed and novel cognitive tests of cued recall and semantic interference (LASSI-L), time and event related prospective memory (MPMT), and novel computer-based functional task simulations (FTS) in detecting subtle cognitive and functional impairments, and progression of these impairments over time. Our sample will
include Spanish-speaking and English-speaking older adults diagnosed with traditional neuropsychological measures and clinical evaluations as: amnestic MCI (aMCI), preclinical
MCI (PreMCI), or cognitively normal (NC).
Role: Co-Investigator

**BIOGRAPHICAL SKETCH**

NAME: Regina Theresa Vontell

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

POSITION TITLE: Research 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 Society of Clinical Pathologists, Washington, DC | HTL | 1991 | Histology |
| University of Connecticut, Storrs, CT | BA | 2004 | Neuroscience |
| University of Connecticut, Storrs, CT | MA | 2008 | Behavioral Neuroscience |
| Healthcare Professions Council, London, UK | HPC | 2009 | Biomedical Scientist |
| King's College London, London, UK | PhD | 2016 | Neurobiology |

**A. Personal Statement**

I started my career in Histology in 1991, specializing in Neuroscience in 2000. My research has included studies of preterm birth and encephalopathy of prematurity, neurological inflammatory mediators in neonates and in adults. My research has been reported in over 21 articles, monographs, and presentations at national and international meetings. I have served as a British Chartered Scientist for the Healthcare Professional Council and on the American Society of Clinical Pathology Testing Committee. My current investigations include brain injury, microglia activation and diseases of the aging brain. My goal is to continue to enhance the application of immunohistochemical and in situ hybridization techniques in studying neurological impairments. My contribution to the proposed study will be to provide histological characterization of brain tissue samples and to participate in the generation of the neuropathological annotation of the study samples.

**B. Positions and Honors**

**Positions and Employment**

1991 – 2008 Senior Histologist, Hartford Hospital, Hartford, CT
2002 – 2005 Instructor//Director Health Career Collaborative Program, Hartford, CT
2008 – 2012 Research Assistant, Imperial College London, London, UK
2012 – 2016 Senior Research Associate, King's College London, London, UK
2016 – 2018 Senior Research Associate, University of Miami, Miami, FL
2018-present Research Assistant Professor, University of Miami, Miami, FL

**Other Experience and professional Memberships**

1991 – Present Member, American Society of Clinical Pathologists
2006 – 2008 Research Specialist, University of Connecticut, Storrs, CT
2009 – Present Member, Healthcare Profession Council, London, UK
2014 – Present Member, British Society of Chartered Scientists
2016 – Present Fellow, Institute of Biomedical Scientists

**Honors and Awards**

2003 University of Connecticut- Department of Psychology Undergraduate Research Grant
2004 DakoCytomation- Excellence in Standardization of Immunohistochemistry Techniques
2007 Robert A. Clark Memorial Education Scholarship Award
2009 Lee Luna International Travel Award

2010 The Biological Stain Commission-Detecting Neurofibrils in Immature Axons
2012 Ventana Medical Systems *In Situ* Hybridization Award
2014 BioGenex Award for Excellence in *In Situ* Hybridization
2020 Newcomber Scholarship

## C. Contributions to Science

1. My early publications were aimed at identifying receptor subtypes in the basal ganglia. We reported that striatopallidal regions are activated and regulated via adenosine A2A agonists which modulate the activity of dopaminergic (DA) D2 receptors and the effort related response. By creating immunohistochemical protocols we were able to visualize the receptors in the basal ganglia, which complemented the behavioral evidence in the animal model of effort related behavior. The protocols were expanded to include markers of activation for the cells of striatum support relevant data that demonstrated that Adenosine A2A antagonist maybe a candidate for the treatment of Parkinsonian Tremors. Additionally, since DA rich areas have an important role in regulating both motor activity and motivation, we compared the effects of central and peripheral administration of EtOH and acetaldehyde incorporating a cellular marker of brain activity (C-Fos) in DA innervated brain regions. I served as the primary investigator or co-investigator in all of these studies.

   a. Mingote, L. Font, A.M. Farrar, **R. Vontell**, L.T. Worden, C.M. Stopper, R.C. Port, K.S. Sink, J.G. Bunce, J.J. Chrobak, J.D. Salamone,"Nucleus Accumbens Adenosine A2a Receptors Regulate Exertion of Effort by Acting on the Ventral Striatopallidal Pathway,". Journal of Neuroscience (2008), 28(36):9037-9046doi: 10.1523/JNEUROSCI.1525-08.2008. PMID: 18768698

   b. A.J. Betz , **R. Vontell,** J. Valenta, L. Worden, K. S. Sink, L. Font, M. Correa T. N. Sager, J. D. Salamone, "Effects of the Adenosine $A_{2a}$ Antagonist Kw-6002 (Istradefylline) on Pimozide-Induced Oral Tremor and Striatal C-Fos Expression: Comparisons with the Muscarinic Antagonist Tropicamide,". *Journal of Neuroscience (2009)*, 29;163(1):97-108. doi: 10.1016/j.neuroscience.2009.05.040. PMID: 19467297

   c. **R. Vontell** , K.N. Segovia, A.J. Betz, S. Mingote, K. Goldring, R. W. Cartun, J. D. Salamone., "Immunocytochemistry Studies of Basal Ganglia Adenosine $A_{2a}$ Receptors in Rat and Human Tissue, " *Journal of Histotechnology (2010). 33(1):41-48.*

   d. Segovia KN, **Vontell R**, López-Cruz L, Salamone JD, Correa M. c-Fos immunoreactivity in prefrontal, basal ganglia and limbic areas of the rat brain after central and peripheral administration of ethanol and its metabolite acetaldehyde. Front Behav Neurosci. 2013 May 24;7:48. doi: 10.3389/fnbeh.2013.00048. PMID: 23745109; PMCID: PMC3662884.

2. My studies on perinatal brain injury and white matter malformations that result in cerebral palsy and cognitive impairments are summarized below. My doctoral research was on the cellular response to focal injury seen after white matter injury and how it cascades to secondary atrophy in the thalamus and internal capsule. This work examined the relationship between toll-like receptors (TLR) activation and autophagocytosis as an inflammatory mediation to white matter injury. These studies utilized in situ hybridization and immunohistochemical approaches to demonstrate that an increase in mRNA and protein expression leads to intracellular signals that regulate cytokine production, excessive autophagy and prolong inflammatory mediators.

**a.** Thornton C, Rousset CI, Kichev A, Miyakuni Y, **Vontell R**, Baburamani AA, Fleiss B, Gressens P, Hagberg H. Molecular mechanisms of neonatal brain injury. Neurol Res Int. 2012;2012:506320. doi: 10.1155/2012/506320. Epub 2012 Jan 26. PMID: 22363841; PMCID: PMC3272851

**b.** V.Supramaniam, **R.Vontell**, L.Srinivasan, J. Wyatt-Ashmead, M. Rutherford***, "***Microglia Activation in the Extremely Preterm Human Brain,". *Pediatr Res*. (2013) 73(3):301-9. doi: 10.1038/pr.2012.186. Epub 2012 Dec 7. PMID: 23364172

**c.** **R.Vontell**, V.Supramaniam, C.Thornton, J.Ashmead-Wyatt, C.Mallard, P.Gressen, M. Rutherford, H. Hagberg, "Toll-Like Receptor 3 Expression Identified in Glia and Neurons in the Developing Brain Alters in Response to Insult," *Developmental Neuroscience* (2013);35(2-3). doi: 10.1159/000346158. Epub 2013 Mar 16. PMID: 23548575

**d.** **R.Vontell**, V Supramaniam, J Wyatt-Ashmead, P Gressens, M Rutherford, H Hagberg, C Thornton, "Cellular Mechanisms of Toll-Like Receptor-3 Activation in the Thalamus are Associated with White Matter Injury in the Developing Brain," *J Neuropathol Exp Neurol.* (2015) 74(3):273-8. doi: 10.1097/NEN.0000000000000172. PMID: 25668563

3. I have spent over 8 years studying the complex question of brain immunity. When these studies began, inflammatory mediation was considered to be the result of over stimulated glial populations. My work on complexities that are involved in the developing brain has led to collaborations with similar groups around the world to evaluate other novel components in the immature brain that may precondition glial cells.

**a.** Baburamani AA, Miyakuni Y, **Vontell R**, Supramaniam VG, Svedin P, Rutherford M, Gressens P, Mallard C, Takeda S, Thornton C, Hagberg H. Does Caspase-6 Have a Role in Perinatal Brain Injury? Dev Neurosci. 2015;37(4-5):321-37. doi: 10.1159/000375368. Epub 2015 Mar 24. PMID: 25823427; PMCID: PMC4876595.

**b.** V Chhor, R Moretti, T Le Charpentier, S Sigaut, S Lebon, L Schwendimann, MV Oré, C Zuiani, V Milan, J Josserand, **R Vontell**, J Pansiot, V Degos, C Ikonomidou, L Titomanlio, H Hagberg, P Gressens, B Fleiss, "Role Of Microglia in a Mouse Model of Paediatric Traumatic Brain Injury.Brain Behav Immun (2017) Jul;63:197-209. doi: 10.1016/j.bbi.2016.11.001. Epub 2016 Nov 4. PMID: 27818218

**c.** Baburamani AA, Sobotka KS, **Vontell R**, Mallard C, Supramaniam VG, Thornton C, Hagberg H. Effect of Trp53 gene deficiency on brain injury after neonatal hypoxia-ischemia. Oncotarget. 2017 Feb 14;8(7):12081-12092. doi: 10.18632/oncotarget.14518. PMID: 28076846; PMCID: PMC5355327.

**d.** G.Girardi, J Fraser, R Lennen, **R Vontell**, M Jansen, G Hutchison. Imaging of activated complement using ultrasmall superparamagnetic iron oxide particles (USPIO)--conjugated vectors: an in vivo in utero non-invasive method to predict placental insufficiency and abnormal fetal brain development. *Mol Psychiatry.* 1017-1026 (2015) 20(8):1017-26. doi: 10.1038/mp.2014.110. Epub 2014 Sep 23. PMID: 25245499

4. My collaborators and I have identified several novel candidates that may contribute to a prolonged inflammatory response. The investigations suggests that potential biological pathways that maybe targeted for prevention or therapy. I worked analyzing and confirming several of these key components of T-cell and TWEAK receptors.

**a.** A.M. Albertsson, X. Zhang, **R.Vontell**, D. Bi, R. Bronson, A. Baburamani, V. Supramaniam, S.H.Arshed, S. Cardell, C. Mallard, H. Hagberg, C. Zhu, H. Cantor, J. Leavenworth, X. Wang. γδ T Cells Contribute to Preterm Brain Injury. *American Journal of Pathology* (2017). doi: 10.1016/j.ajpath.2017.11.012

**b.** X. Zhang X, E. Rocha-Ferreira, **R. Vontell**, D. Jabin, S. Hua, K. Zhou, A. Nazmi, AM Albertsson, K.Sobotka, J. Ek, C.Thornton, H. Hagberg, C. Mallard, J. W. Leavenworth, C. Zhu, X. Wang. γδT Cells but Not αβT Cells Contribute to Sepsis-induced White Matter Injury and Motor Abnormalities in Mice. *J Neuroinflammation*. (2017). doi: 10.1186/s12974-017-1029-9.

**c.** Nazmi A, Albertsson AM, Rocha-Ferreira E, Zhang X, **Vontell R**, Zelco A, Rutherford M, Zhu C, Nilsson G, Mallard C, Hagberg H, Lai JCY, Leavenworth JW, Wang X. Lymphocytes Contribute to the Pathophysiology of Neonatal Brain Injury. Front Neurol. 2018 Mar 19;9:159. doi: 10.3389/fneur.2018.00159. PMID: 29615958; PMCID: PMC5868390.

**d.** A. Kichev, A. Baburamani, **R. Vontell**, P. Gressens. L. Burkly, C. Thornton, H. Hagberg. TWEAK Receptor Deficiency Has Opposite Effects on Female and Male Mice Subjected to Neonatal Hypoxia-Ischemia doi: 10.3389/fneur.2018.00230. eCollection 2018.

.

5. I have been studying neuropathological conditions for the past 8 years seen in infants and in adults. My recent work, provides insight on how disturbances of important migratory signals may dramatically affect ongoing brain development.

**a.** V. Golubinskaya**, R. Vontell**, V. Supramaniam, J. Wyatt-Ashmead, H. Gustafsson, C. Mallard, H. Nilsson. Bestrophin-3 Expression In A Subpopulation Of Astrocytes In The Neonatal Brain After Hypoxic-Ischemic Injury. *Frontiers in Physiology* (accepted 2019)

**b.** **Vontell R**, Supramaniam VG, Davidson A, Thornton C, Marnerides A, Holder-Espinasse M, Lillis S, Yau S, Jansson M, Hagberg HE, Rutherford MA. Post-mortem Characterisation of a Case With an *ACTG1* Variant, Agenesis of the Corpus Callosum and Neuronal Heterotopia. Front Physiol. 2019 May 24;10:623. doi: 10.3389/fphys.2019.00623. PMID: 31231230; PMCID: PMC6558385.

**c.** H.B. Stolp, B. Fleiss, Y. Arai, V. Supramaniam, **R. Vontell**, S. Birtles, A. Yates, A. Baburamani, C. Thornton, M.A. Rutherford, D. Edwards, P. Gressens.Interneuron development is disrupted in preterm brains with diffuse white matter injury. Front Physiol. 2019 Jul 30;10:955. doi: 10.3389/fphys.2019.00955. eCollection 2019.

**d.** A. Baburamani, **R.Vontell**, A. Uus, M. Pietsch, P. Patkee, J. Wyatt-Ashmead, J. Chin-Smith, V. Supramaniam, JD. Tournier, M. Deprez, M. Rutherford. Assessment of Radial Glia in the frontal lobe of fetuses with Down Syndrome. *Acta Neuropathologica Communications.* doi.org/10.1186/s40478-020-01015-3

Complete List of Published Work in MyBibliography:

https://www.ncbi.nlm.nih.gov/myncbi/1fwnSgrdskqMow/bibliography/public/

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

Rosetrees Trust-Grant code A1563
(Professor Mary Rutherford) 2016-2020

We seek to enhance our understanding regarding the deviations in brain development that occur in DS by closely investigating the complex interplay between radial glia and neuronal development. Whilst current therapies target childhood and adulthood, our research could lead to earlier intervention designed to improve cognition and delay later cognitive decline. Dr. Regina T. Vontell is a Co-Investigator.

NIH Contract Number: 75N95019C00050 2019-2024
(Professor William Scott)

# 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. Add/delete rows as necessary.)*

| 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 electronic engineering, especially on advanced ophthalmic imaging and human studies. As an assistant professor at the University of Rochester, I have learnt optics and prototyped time domain optical coherence tomography (OCT) devices through the join work with OCT experts. After I moved to Miami, I have been working with other researchers to develop many other prototypes of spectral domain OCT devices. They are ultra-high resolution OCT, ultra-long scan depth OCT, dual-channel OCT, magnetomotive OCT and CMOS camera based ultra-high speed OCT. In recent 8 years, I have worked on vascular imaging of the eye and developed the methods and hardware to image microvasculature and microcirculation in the retina. Working with a group of clinicians, I focus on microvasculature and microcirculation in the retina as a window of the cerebral vasculature in aging, dementia and multiple sclerosis. As the PI or co-Investigator on many previous industrial- and NIH-funded grants, I worked out the proposed research and published more than 150 papers in top journals. Currently, I am the co-director of scientific experimental imaging laboratory at the Bascom Palmer Eye Institute and managing my own lab. In summary, I have a good record of successful research projects in the area of ophthalmic imaging and clinical research. My expertise and experience make me well equipped and qualified for working in this proposed project.


1. Lin Y, Jiang H, Liu Y, Gameiro GR, Gregori G, Dong C**,** Rundek T, **Wang J.** Age-related alterations in retinal tissue perfusion and volumetric vessel density. Investigative Ophthalmology and Vision Research. 2019;60;685-693. PubMed PMID: 30786280; PubMed Central PMCID: PMC6383727.
2. Gameior GR, Jiang H, Liu Y, Deng Y, Sun X, Nascentes B, Baumel B, Rundek T, **Wang J**. Retinal tissue hypoperfusion in patients with clinical Alzheimer's disease. Eye Vis (Lond). 2018;17;5:21. PubMed PMID: 30140712; PubMed Central PMCID: PMC6097197.
3. Shao Y, Jiang H, Wei Y, Shi Y, Shi C, Wright CB, Sun X, Vanner, EA, Rodriguez AD, Lam BL, Rundek T, Baumel BS, Gameiro GR, Dong C**, Wang J**. Visualization of Focl Thinning of the Ganglion Cell-Inner Plexiform Layer in Patients with Mild Cognitive Impairment and Alzheimer's Disease J *Alzheimers Dis* 64(4):1261-127. PubMed PMID: 30040712.
4. 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.


## 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 Palmer 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 Palmer Eye Institute, University of Miami, Miami, FL |
| 2010 - 2012 | Associate Professor, Bascom Palmer Eye Institute, University of Miami, Miami, FL |
| 2012 - | Associate Professor (Tenured), Bascom Palmer 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 significantly contribute the development of optical coherence tomography prototypes for clinical research, especially in the field of anterior segment imaging. Worked 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. Collaborated with clinicians and engineers, ultra-high resolution OCT devices for imaging the anterior segments were developed for imaging the tear film, epithelium and ocular tumor by conducting clinic 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. Worked with optics experts, I contributed significantly to long scan depth OCT for imaging the full eyes in studying accommodation and full eye biometry. A unique system consists of two spectral domain OCT devices equipped with wavefront sensor was developed.

    a. Ke B, Mao X, Jiang H, He J, Liu C, Li M, Yuan Y, **Wang J**. The relationship between high-order aberration and anterior ocular biometry during accommodation in young healthy adults. Invest Ophthalmol Vis Sci. 2017;58:5628-5635. PubMed PMID: 29094166; PubMed Central PMCID: PMC5667401.

b. 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.

c. 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.

d. 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 contribute significantly to image microvasculature on the ocular surface and retina. A system called functional slit-lamp biomicroscope (FSLB) was developed and a patent of single shot for generating conjunctival microvascular network map was filled. This novel system enables easily imaging 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.Worked with vascular experts in neuro-ophthalmology, we developed automatic segmentation of retinal microvascular network obtained using Retinal Function Imager (RFI) for studying retinal microvascular changes in multiple sclerosis, AD, diabetics 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 development of segmentation software enables automatic segmentation of 6 maps of retinal sub-layers. Furthermore, I adapted the RFI for the first time for imaging the retinal tissue perfusion and adapted OCT angiography to image volumetric vessel density.

   a. Lin Y, Jiang H, Liu Y, Gameiro GR, Gregori G, Dong C**,** Rundek T, **Wang J.** Age-related alterations in retinal tissue perfusion and volumetric vessel density. Invest Ophthalmol Vis Sci. 2019;60;685-693. PubMed PMID: 30786280; PubMed Central PMCID: PMC6383727.
   b. Gameior GR, Jiang H, Liu Y, Deng Y, Sun X, Nascentes B, Baumel B, Rundek T, **Wang J**. Retinal tissue hypoperfusion in patients with clinical Alzheimer's disease. Eye Vis (Lond). 2018;17;5:21. PubMed PMID: 30140712; PubMed Central PMCID: PMC6097197.
   c. 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.
   d. Hu L, Shi C, Jiang H, Shi Y, Sethi Z, **Wang J**. Factor affecting microvascular responses in the bulbar conjunctiva in habitual contact lens wearers. Invest Ophthalmol Vis Sci. 2018;59:4108-4114. PubMed PMID: 30098199; PubMed Central PMCID: PMC6088803.

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 detecting cochlin (a protein) in glaucomatous mice. This approached significantly improve 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

R01 R01NS111115A1 Detre and Wang (MPI) 08/15/2019-03/31/2024
NIH/NINDS
Novel Biomarkers of Small Vessel Contributions to Vascular Cognitive Impairment and Dementia (VCID)
This project will investigate the biological and technical determinants of brain MRI cerebral blood flow (CBF) and OCTA-derived microvascular density, associate changes in retinal microvasculature with brain perfusion, and preliminarily show their predictive value in small vessel disease (SVD) by correlating baseline measures with longitudinal changes in healthy and clinical cohorts of SVD.
Role: MPI

UM Dean Bright Award DBA 2019-3 Jiang, Hong (PI) 8/1/18-3/31/20
Novel retinal microvascular biomarker of vascular contribution to dementia
The goal is to run a preliminary study to bridge NIH grant application.
Role: Co-investigator

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 Jiang, Hong (PI) 04/01/16-03/31/20
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

Food UM 01, Global Healthcare Focus LLC Wang, Jianhua (PI) 01/01/17-12/31/19
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

CR-5879 Johnson & Johnson Vision Care Jiang, Hong (PI) 03/1/2018-12/31/19
Lid-wiper microvascular response as an indicator of contact lens discomfort
The goal of this study is to characterize lid-wiper microvasculature in contact lens wear.
Role: Co-investigator

Imaging Research, Bausch & Lomb, CooperVision and Allergan Wang, Jianhua (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

## Completed Research Support

JJVC, Johnson & Johnson Vision Product Jiang, Hong (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 Wang, Jianhua (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 Jiang, Hong (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 Wang, Jianhua (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