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

UNIVERSITY OF MIAMI EVELYN F. McKNIGHT BRAIN INSTITUTE

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

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

January 16th, 2020

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Trustees, The Evelyn F. McKnight Brain Research Foundation, Inc.
SunTrust Banks, Inc.
Foundations & Endowments Specialty Practice
333 Garland Avenue
15th Floor
Orlando, FL 32801

Dear Trustees,

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

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

Thank you for your attention.

Yours Sincerely,

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

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

RLS/TR/SSM/bd

cc: Amy Porter
Melanie Cianciotto
Susan Fox Rosellini
Stacy Merritt

LAST YEAR'S GOALS

SUMMARY OF SCIENTIFIC AND EDUCATIONAL ACHIEVEMENTS

SECTION 1

Introduction

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

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

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

- Our main goal for 2019 was to create our five-year MBI Strategic Plan. The second phase of our **Strategic Plan** was ongoing throughout the year. This included bi-monthly meetings to prioritize and finalize our goals and to assess and brainstorm the availability and attainability of needed resources. With these goals in mind, we set forth to determine what our strategies and tactics for each goal would entail. The University of Miami Miller School of Medicine (UMMSOM) has been working on its strategic plan and is moving to its final phase this year. It is encouraged that entities within the medical school align their individual strategic plans with the overall plan of our Medical School. **Drs. Sacco and Rundek** participate in the (UMMSOM) strategic plan and will communicate our plan to Dean Henry Ford and the Dean for Research, Carl Schulman, once their strategic plan is completed and our strategic plan aligned. (See **Appendix II**)

- **Dr. Ralph Sacco**, director of the University of Miami Clinical Translational Science Institute (UM CTSI) completed the first year of the newly funded grant cycle. In 2019, the Miami CTSI successfully reached 1,900 individuals throughout the Hub and across the region, and it collaborated with 11 other CTSAs institutions across the country. See **Section 9** for more information on the success of the UM CTSI.

- **Dr. Ralph Sacco** and collaborators furthered their analysis this year on the longitudinal NOMAS program (See **Section 9**). They expanded their focus on the role of the immune mechanisms in vascular cognitive impairment and dementia. They enhanced their methods to explore inflammation networks in cerebrovascular disease as determinants of cognitive trajectories and functional decline. As a result, key research data and findings were published.

- **Drs. Tatjana Rundek** and **David Loewenstein** in collaboration with Dr. Todd Golde at the University of Florida successfully competed for renewal of the 1FL ADRC (newly named ADC). Dr. Rundek will co-lead the Research Educational Core with Dr. Glenn Smith from UF. Dr. Loewenstein will lead the UM Clinical Site. Both Drs. Rundek and Loewenstein will participate in the 1FL ADC Steering Committee and Recruitment Core. Details are provided in **Section 9.**

- **Drs. Bonnie Levin** and **Katalina McInerney** continued building the registry for The McKnight Frailty Project. Our McKnight Frailty Registry is **unique** to the University of Miami and presents a critical research source for our young investigators to develop their clinical research skills, present and publish results and plan future research grants. The Registry

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

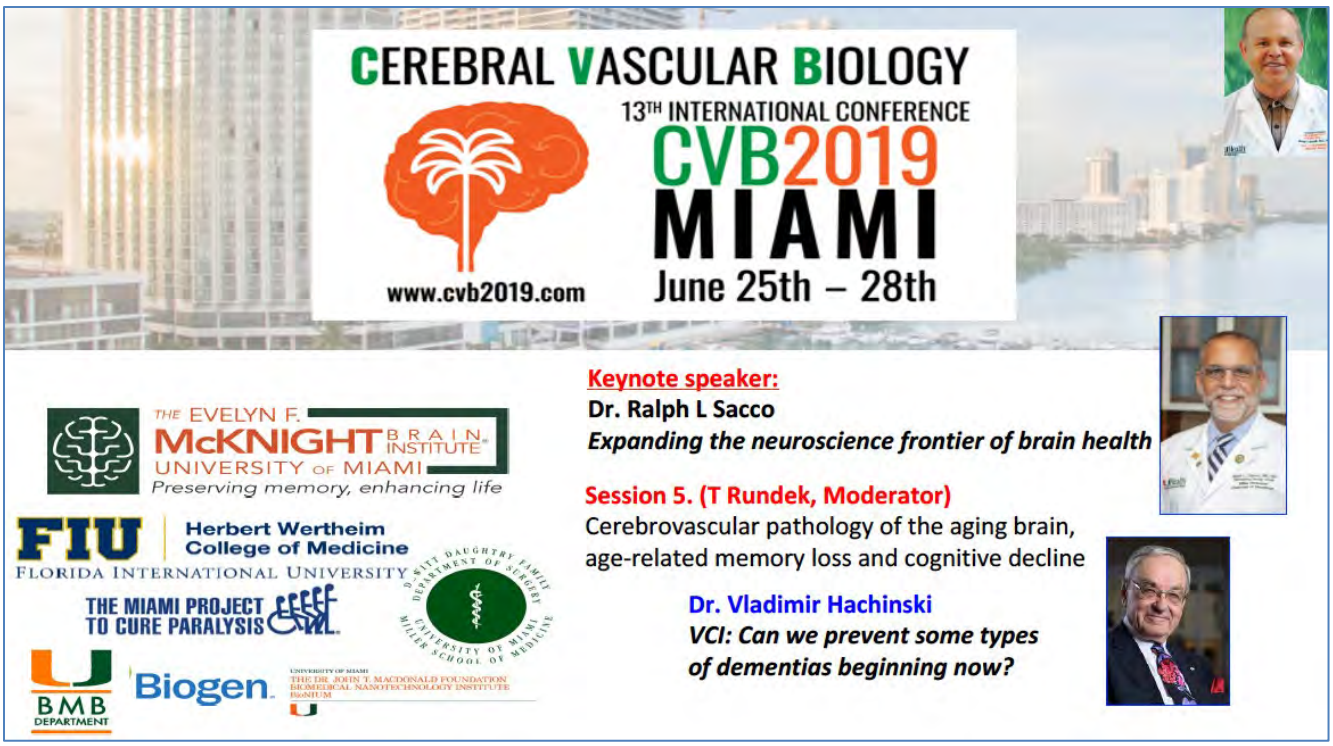
- **Dr. Xiaoyan Sun**, Director of our McKnight Education program expanded the scope of the program at the University of Miami and in the community of South Florida. Partnerships with the city of Miami were strengthened and new collaborations formed. Educational training geared towards residents, fellows and students was enhanced. Through our education and outreach program, we reached over 400 community members. We organized new brain cutting sessions with the Department of Pathology with multi-disciplinary team education. More details are presented in **Section 12**.

- We started planning **The Evelyn F. McKnight Brain Research Foundation 12th Annual Inter-Institutional Meeting** in Miami, April 1st - 3rd, 2020. The hotel rooms, meeting space and logistics are confirmed. Discussions on topics and presenters took place and the draft agenda is prepared and will soon be finalized. We are looking forward to hosting the McKnight Brain Research Foundation Trustees, other McKnight Brain Institutes, and the *McKnight Clinical Translational Research Scholars in Cognitive Aging and Age-related Memory Loss* fellows and their mentors.

Notable Scientific and Educational Achievements

13th International Conference of Cerebral Vascular Biology

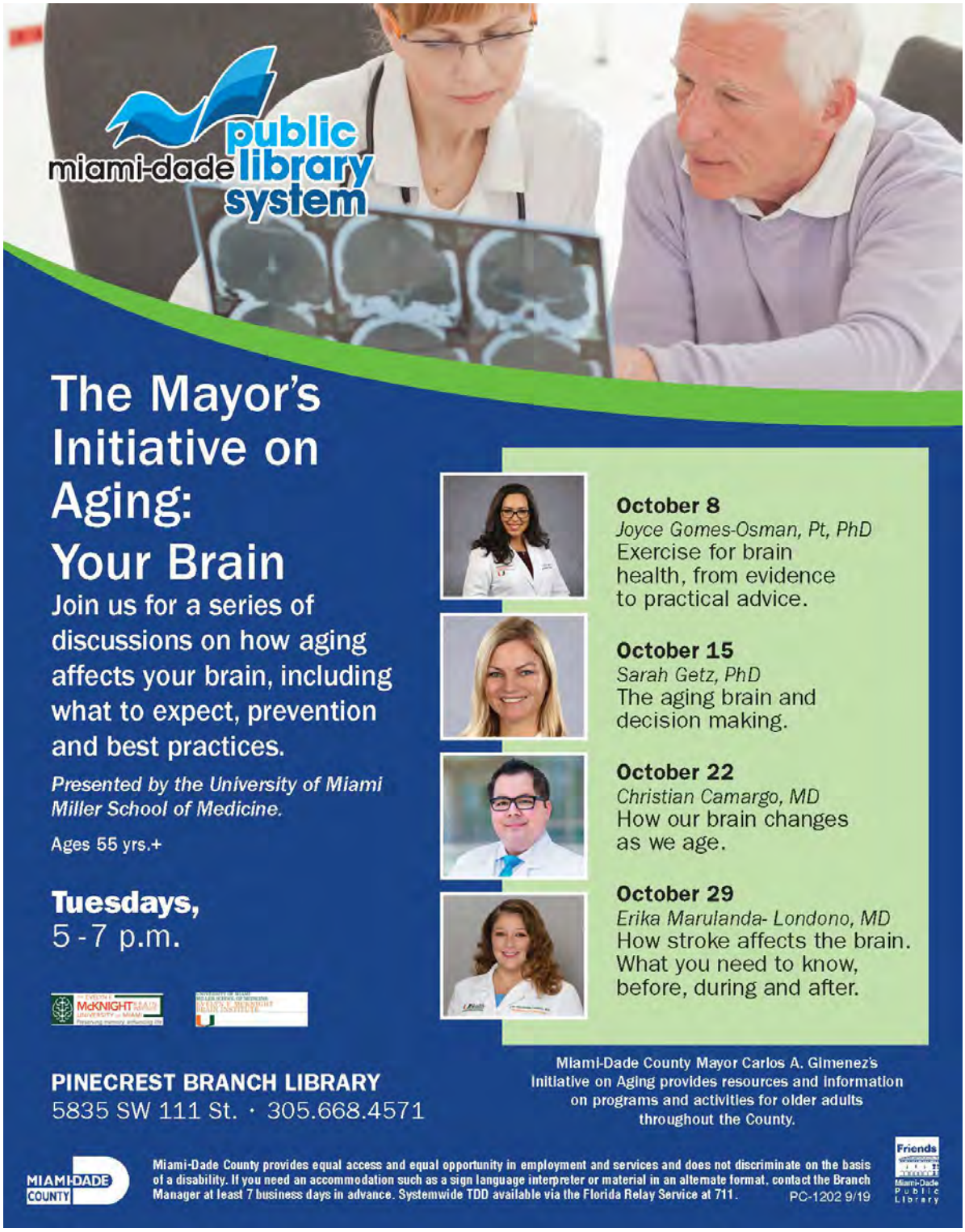
The UM McKnight Brain Institute (MBI) was one of the organizers and sponsors of the ***13th International Conference of Cerebral Vascular Biology***, held in Miami, June 25-28, 2019. **Dr. Ralph Sacco** was one of the keynote speakers and **Dr. Tatjana Rundek** was a moderator of a session on the *aging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



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

The Mayor's Initiative on Aging: Your Brain

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



CFAR HIV & Aging SWG Symposium

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

Additional Notable Scientific and Educational Achievements

- **Dr. Ralph Sacco** was elected to serve on the Steering Committee of the national network of Clinical and Translational Science Awards (CTSA) program at the National Center for Advancing Translational Sciences (NCATS). He also received the prestigious honor as the 2019 C. Miller Fisher Visiting Professor from Massachusetts General Hospital.

- **Dr. Tatjana Rundek** formally became a Contact Principal Investigator of the Miami CTSI KL2 mentored research training award program at NCATS to support newly trained clinicians in successful clinical and translational research.

- We were able to fund a new **Cognitive and Behavioral Neurology Fellow**, **Dr. Michelle Marrero** in the Neurology Department at the McKnight Brain Institute. Trainees in this field are lacking but greatly needed. Our program trains physician-scientists in skills needed to translate research findings to clinical practice and treat the ever-growing aging population. **Section 12.**

- **The Florida Stroke Registry** (**Drs. Sacco** and **Rundek**) program was awarded its third round of state appropriated funds to manage and maintain the Stroke Registry across hospitals treating stroke patients in Florida. Since last year, the Registry has added 34 new hospital members increasing the total number of participating Florida stroke centers to 114 (out of a total of approximately 160). The ongoing collection of Florida stroke cases (from 2010 to current) has collected clinical and outcome data on approximately 290,000 stroke patients to date. **Section 9.**

- **Drs. Jinhua Wang** and **Hong Jiang** received a NIH NINDS R01 grant on retinal changes in aging and small vessel brain disease. They were also awarded a grant for the project "Retinal biomarkers for monitoring vascular contributions to Alzheimer's Disease" from the Ed and Ethel Moore Alzheimer's Disease Research Program through the Florida Department of Health (DOH).

- **Dr. Joyce Gomes-Osman** was selected from a competitive pool of early career investigators at the University of Miami to be among the 4 participants to attend the prestigious *11th Annual International Certificate Course, Eureka Institute for Translational Medicine* in Syracusa, Italy. Eureka is a weeklong immersive program that focuses on the fundamentals of translational medicine and trains scientists to be leaders in the translational medicine field through coaching, networking and mentorship opportunities. More information can be found in **Section 9.**

- **Michelle Caunca**, our MD/PhD student received the P.E.O. Sisterhood award for the 2019-2020 academic year. Michelle is one of 150 women in the US and Canada to receive this merit-based award for women pursuing a doctoral-level degree at an accredited college or university. Recipients are a select group of women chosen for their high level of academic achievement and their potential for having a positive impact on society. Michelle began her third year of the program after defending her dissertation last summer. Her thesis research work, "A Population Neuroscience

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

- Several grants and awards were given to these McKnight researchers in the basic and translational sciences, **Drs. David Della-Morte**, **Miguel Perez-Pinzon** and **Kunjan Dave**. See **Section 6.2**.

- **Drs. Sarah Getz** and **Bonnie Levin** submitted an application for an AAN McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss for the project "Neurocognitive correlates of scam susceptibility in age-related hearing loss." (Principal Investigator: Sarah Getz, Mentors: Drs. Levin and Rundek).

- **Dr. Bonnie Levin** participated in a widely publicized press conference, which described the findings and explored the energy source producing hearing loss and cognitive impairments among diplomats in Cuba.

Participation in McKnight Brain Research Foundation Events

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

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

Attendees:

2018 Scholars and Mentors
Brice McConnell, MD, PhD (Scholar – University of Colorado, Denver)
Benzi Kluger, MD, MS (Mentor – University of Colorado, Denver)

2019 Scholars and Mentors
Christian Camargo, MD (Scholar – University of Miami)
Richard Wurtman, MD (Mentor)

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

UM Evelyn F. McKnight Brain Institute Representation
Tatjana Rundek, MD, PhD
Ralph Sacco, MD, MS
Susan Fox-Rossellini, MBA
Stacy Merritt, MA
Raphaelle Depuhl (Christian Camargo's Guest)

McKnight Brain Research Foundation Representation
Richard Isaacson, MD
Gene Ryerson, MD
Amy Porter

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

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

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

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

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

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

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

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

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

"Relationship of Brain Functional Connections to Behavior in the Oldest Old"

"Frontal GABA Concentrations in the Oldest Old in the MBR: An Update"

McKnight Brain Research Foundation 10th Poster Reception

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

Posters Presented by the University of Miami McKnight Brain Institute:

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

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

McKnight Brain Institute Collaborative Inter-Institutional Posters:

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

PUBLICATIONS AND PRESENTATIONS

SECTIONS 2-5

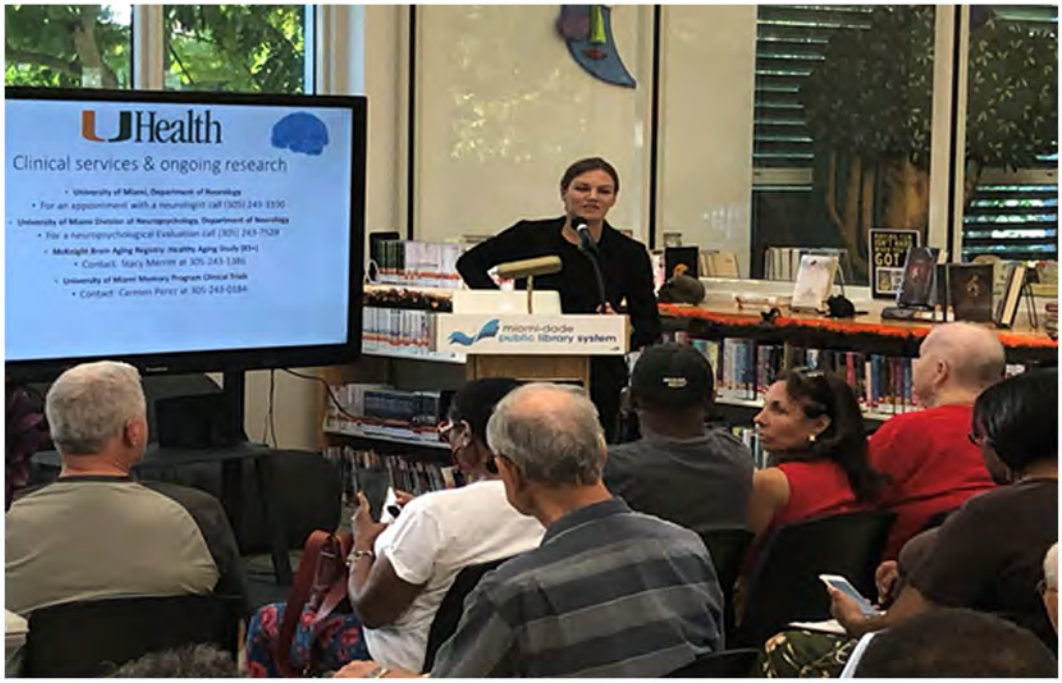
McKnight Brain Research Foundation 10th Poster Reception at the Society for Neuroscience (SFN) Meeting in Chicago, Illinois, October 20th, 2019.

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

Sarah Getz

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

Mayor's Initiative On Aging: Your Brain Seminar Series



Sarah Getz, PhD

Christian Camargo, MD
Stacy Merritt, MA

Joyce Gomes-Osman, PT, PhD

2. Publications in Peer Reviewed Journals

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

Trainee (as first authors) Publications

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

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

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

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

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

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

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

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

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

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

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

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

Cross-Disciplinary and Collaborative Publications

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

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

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

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

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

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

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

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

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

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

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4. Presentations at Scientific Meetings

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

GRANTS AND AWARDS

SECTION 6

6. Grants and Awards

6.1. Trainee Grants and Awards

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

- Fellows
  Nicole Sur, MD received funding as a Florida Stroke Registry Fellow.
  Victor Del Brutto, MD received funding as a NINDS StrokeNet Fellow.

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

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

- Fellows
  Dr. Anita Saporta - UM Evelyn F. McKnight Research Fellow grant recipient
  Dr. Michelle Marrero - UM Department of Neurology Cognitive Behavioral Fellow

- Junior Faculty
  Dr. Joyce Gomes-Osman - recipient of a KL2 award and EUREKA.
  Dr. Christian Camargo - recipient of the AAN McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-Related Memory Loss
  Tali Elfassy - recipient of a KL2 award, R01 and Prevision Medicine Award from AHA.

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

- Training
  Michelle Caunca - Neurology candidate on Dissertation Committee funded by F30 Fellowship Award and the P.E.O. Sisterhood award
  Maya Elias, PhD School of Nursing Mentoring F32 Grant Application

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

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

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

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

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

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

6.2. Faculty Grants and Awards

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

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

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

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

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

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

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

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

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

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

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

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

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

FACULTY AND TRAINEES

SECTIONS 7-8

LEADERSHIP

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Evelyn F. McKnight Brain Institute Executive Director
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Senior Associate Dean for Clinical and Translational Science
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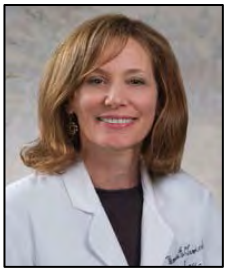
Bonnie E. Levin, Ph.D.



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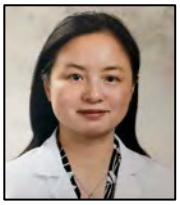

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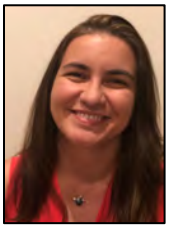

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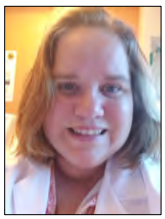

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University of Miami, Miller School of Medicine

Faculty (Members)

Biosketches are provided at the end of the report.

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

Faculty (Collaborators)

Biosketches are provided at the end of the report.

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

Trainees

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

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

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

CLINICAL AND TRANSLATIONAL PROGRAMS

SECTION 9

9. Clinical/Translational Programs

9.1. *Update on MBI Directly Related Clinical Translational Studies*

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

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

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

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

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

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

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

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

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

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

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

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

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

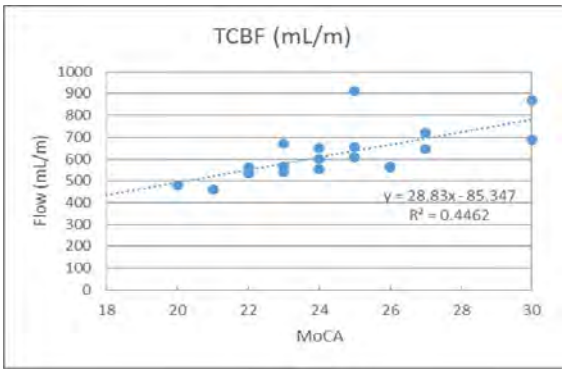
Stacy Merritt continued the recruitment efforts by sending out more flyers to the community as well as to almost every church in the Miami vicinity. MBAR flyers are displayed across the Miami-Dade library system. Additionally, the community outreach and education events, which she plans and attends,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

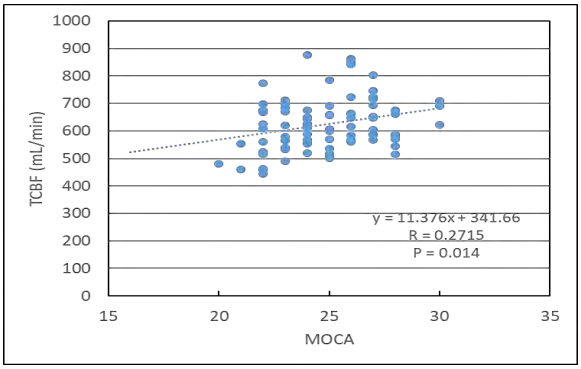
Drs. Bonnie Levin and **Katalina McInerney** remain actively involved and lead the MBAR behavioral studies by monitoring the quality control and accuracy of data entry into the REDCap database from all sites. They have been leaders in data analyses for preliminary and pilot results for presentations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

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

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

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





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

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

McKnight Brain Aging Registry (MBAR) Update Across Sites - Our mission is to establish and maintain the multi-institutional infrastructure to support and implement a Brain Aging Registry of the oldest old, which includes assessments of particular importance to the field of cognitive aging, including neuroimaging, extensive cognitive and functional assessments and blood-based biomarkers.

MBAR Scientific Progress

The principal investigators along with co-investigators and study coordinators involved in both the MBAR Neuroimaging and Cognitive Cores, have continued to work hard to advance the project and considerable progress has been made over the current reporting period. To date, we have enrolled 141 participants who have been recruited across the four MBI sites, approaching 75% of our targeted enrollment, and who have been fully engaged in the registry, providing clinical, neuropsychological and brain imaging data. It is anticipated that recruitment and assessments will be completed by the end of the next fiscal year with enrollment of the originally planned cohort of 200 MBAR oldest old participants.

We held additional regular bi-weekly conference calls, which were either focused on specific project-related discussions on neuroimaging and cognitive issues or were dedicated for our monthly MBAR Scientific Advisory Committee (SAC) call. The SAC is a representative committee of MBAR PIs and investigators fully familiar with the MBAR cohort and data collection, with approximately two representatives from each MBAR MBI participating site. The SAC calls

provide for discussions of broader issues related to the registry, including plans for new grant submissions, identifying priorities for data analyses and lead investigators for MBAR manuscripts, and plans for enhancing use and accessibility of the growing MBAR dataset.

With our MBAR database infrastructure established, the REDCap dataset continues to be fully operational and is actively being populated with data from each participant across all MBI sites. MRI data is uploaded from each site to the HiPerGator super-computer at UF, where it is pre-processed into a unified format enabling different imaging modalities to be more easily examined simultaneously. Blood specimens are sent to UF for storage in freezers located in the phlebotomy laboratory. The detailed report on MBAR for all sites has been submitted to the Trustees by the Inter-Institutional MBAR investigators. It is included in **Appendix I**.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

9.1.3. *Update on Other MBI Projects*

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

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

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

Dr. Tatjana Rundek is the Principal Investigator for the **Disparities in Stroke Outcomes and Care Delivery in Patients with Atrial Fibrillation: FLiPER-AF Study** which continued in 2019. This study examines race-ethnic and sex disparities in health care delivered to stroke patients with atrial fibrillation and their outcomes after acute stroke hospitalization. It is funded by ARISTA-USA.

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

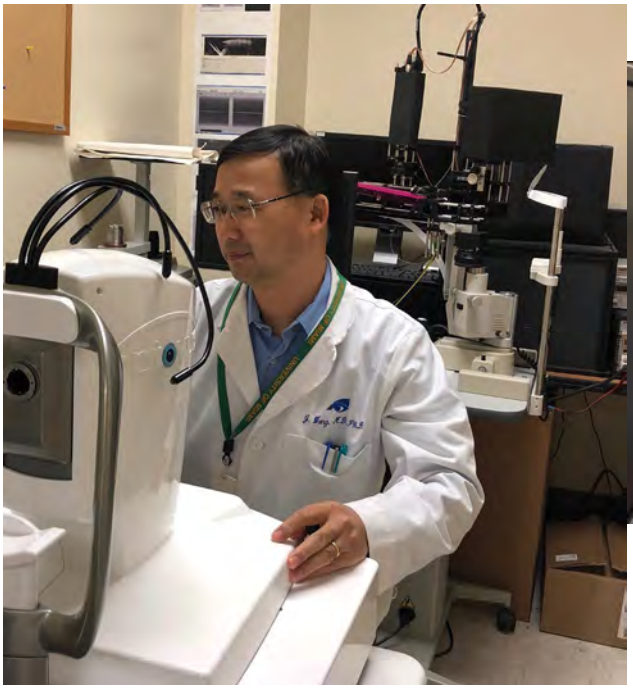
Dr. Tatjana Rundek is a Co-Investigator of the **Oral Infections, Carotid Atherosclerosis and Stroke (INVEST)** study, a study of a cohort study that examines the effect of chronic periodontal disease and inflammation as a risk factor for stroke and carotid atheroma progression at Columbia University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

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

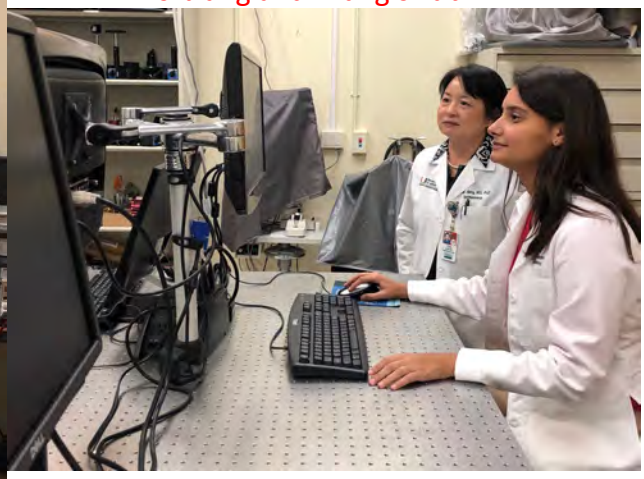
Brain Vascular Imaging Phenotypes (VIP) and cognitive and neurodegenerative profile (VIP study) - **Drs. Tatjana Rundek** and **David Loewenstein** completed their first year of work in 2019. This year was spent preparing MRI scans for the completion of their first aim. Dr. Tatjana Rundek and team have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

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

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



Drs. Jiang and Wang's Lab



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

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

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

Dr. Elizabeth Crocco, our collaborator, has been working on several research studies sponsored by state and federal funds and pharmaceutical sponsored clinical trials. These include: Treatment of Psychosis and Agitation in Alzheimer's Disease (Lithium Study), funded by the NIA (PI for UM Site); Novel Detection of Cognitive and Functional Impairment in the Elderly, funded by the NIA (Co-I); A Consortium to Study Precision-based Computerized Assessment for the Detection of Mild Cognitive Impairment in Older Adults, funded by the State of Florida Department of Health, Ed and Ethel Moore AD Research Program (Co-I); A Non-pharmacological intervention for Patients with Alzheimer's Disease and Family Caregivers, funded by the NIA (Co-I); Precision-based assessment for the Detection of Mild Cognitive Impairment in Older Adults, funded by the NIA (Co-I); Non-invasive Ocular Screening Approach to Identify Early Biomarkers in AD study, funded by the Alzheimer's Association (Co-I); A randomized double-blind, placebo controlled, parallel group study to evaluated the efficacy and safety ofCNP520 in participants at risk for the onset of clinical symptoms of Alzheimer's Disease, funded by Novartis (PI); A Randomized, Double-Blind, Parallel-Group, Placebo-Controlled, Dose-Rannfing study of Piromelatine in patients with mild dementia due to Alzheimer's disease, funded by Neurim Pharmaceuticals (PI); and A randomized, double-blind, placebo-controlled, two cohort parallel group study to evaluate the efficacy of CAD106 and CNP520 in participants at risk for the onset of clinical symptoms of Alzheimer's disease, funded by Novartis (PI).

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

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

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

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

Dr. Sacco and Dr. Levin's Team

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

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

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

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

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

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

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

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

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

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

Dr. Bonnie Levin and her team submitted and participated in the following grant proposals in 2019:

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

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

9.1.5. *Update on Neuroimaging MBI Core*

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

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

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

9.1.6. *Update on Other MBI Research Performed by Trainees*

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

- She has continued to make progress on her University of Miami Evelyn F. McKnight Pilot Grant. This project aims to examine the influence of a 4-week aerobic exercise regimen (moderate versus high intensity) on neurocognitive performance and neuroplasticity, or the brain's ability to adapt to changes imposed by experience, environment and aging itself. The study is ongoing with 12 participants having completed the program. Recruitment is anticipated to wrap up by the summer of 2020, with a goal of manuscript preparation for the Fall of 2020.

- In taking active steps toward examining dose-response relationships for exercise and cognition in aging adults, **Dr. Joyce Gomes-Osman** continues to make progress on the project that is part of her Career Development Award (KL2) by the Miami Clinical and Translational Science Institute. In this project, aging adults are participating in a 2-month exercise intervention, and she is examining neuroplasticity, neurocognitive performance, exercise capacity and genetic modification of response. Currently, 30 participants have enrolled, 16 have completed (with a goal of 80 total by December 2020.)

- **Dr. Joyce Gomes-Osman** was selected from a competitive pool of early career investigators at the University of Miami to be among the 4 participants at the prestigious *11th Annual International Certificate Course,* Eureka Institute for Translational Medicine that took place April 7th - 13th, 2019, in Syracusa, Italy. Eureka is a weeklong immersive program, that focuses on the fundamentals of translational medicine that trains scientists to be leaders in the translational medicine field through coaching, networking and mentorship opportunities. The Eureka Institute's vision is to develop translational medicine to address unmet needs. Its mission is to build and foster a global community of translational medicine professionals for the tangible benefit of patients and society as a whole. Its strategy is to catalyze, integrate and impact education, research and policy making in an international translational medicine ecosystem that benefits society.

- **Drs. Joyce Gomes-Osman** and **David Loewenstein** were selected as a model mentee-mentor pair to participate in an important research mentoring training and certification

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

- **Dr. Joyce Gomes-Osman** was invited to move her Neuromotor Plasticity Laboratory to the prestigious Miami Project to Cure Paralysis, at the Lois Pope Life Center. This move not only allowed more physical space for her team to conduct their research activities, but also many opportunities for collaboration and potential synergies with many other clinical and translational investigators.

- **Dr. Joyce Gomes-Osman** has been collaborating with **Dr. Tatjana Rundek** and the remainder of the University of Miami Bugher team investigating brain plasticity changes in individuals post-stroke who are undergoing combined exercise and cognitive training, exercise in isolation or stretching exercises. She is currently working on two manuscripts from this work to be submitted in 2020.

- **Dr. Joyce Gomes-Osman** is collaborating with the Alagoas State University for Health Sciences, in Brazil and is overseeing a study to evaluate the influence of an exercise literacy workshop to improve engagement in physical activity and cognitive performance in older adults. Thirty participants have completed the study and data analysis and manuscript preparation are underway.

Dr. Gomes-Osman's Team

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

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

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

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

9.1.7. *Update on Basic and Translational Science Research*

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

9.2. *Future Research Plans*

9.2.1. *Upcoming Clinical Translational and Population-Based Research*

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

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

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

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

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

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

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

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

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

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

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

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

9.2.2. *Upcoming Basic and Translational Science Research*

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

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

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

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

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

9.2.3. *Upcoming Education Program*

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

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

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

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

- Helping to coordinate and oversee in conjunction with **Dr. Barry Baumel** and **Dr. Tatjana Rundek**, an Individual Career Development Plan (IDP) consisting of clinical and research components that will be developed with our new **Cognitive Behavioral Fellow, Michelle Marrero**. It will focus on distinguishing the characteristics of normal aging and brain changes from those due to pathological etiologies. This will be key to understanding the challenges and thereby the precision needed for diagnoses in this patient population. She will learn how to design a research project and to submit it to the Institutional Review Board (IRB) and how to write grant proposals, abstracts and manuscripts. Lastly, her IDP will include forming collaborations with cross-disciplinary partners and learning principles of team science.

- Working with the Miami-Dade Mayor's office on the coordination of the "Miami-Dade Mayor's Initiative on Aging: Your Brain" seminar series that will take place again at a different location in the Miami-Dade area. Additionally, efforts will be made to conduct the series in Spanish.

- The McKnight Journal Clubs and Research Seminars which will be based on core topics and categories to focus more intently on specific areas of research. Additionally, an emphasis will be placed on mentor-mentee teams co-presenting. A "How to be a mentor" workshop will take place as well.

- Continuing the brain cutting sessions started this year, and plan for dissemination in partnership with the Research Component of our CTSI.

- Planning for a greater integration of our MBI trainees in CTSI research, education and training programs (through **Drs. Ralph Sacco** and **Tatjana Rundek's** roles in our CTSI). This will include applying for KL2, pilot and EUREKA awards, the Connection Club for research, and applying to our MS in Clinical Translational Investigation (MSCTI) directed by **Dr. Tatjana Rundek**.

- Integrating our trainees with other award educational/training opportunities such as AAN, NeuroNext/StrokeNet, NIH Clinical trial course, 1FL ADC and others.

- Branching out further than Miami-Dade County with our community education and outreach program by forming partnerships in Broward and/or Palm Beach Counties.

10. Technology Transfer

N/A

BUDGET UPDATE AND GROWTH POOL RESULTS

SECTION 11

McKnight Members Grants

Stroke Incidence and Risk Factors in a Tri-ethnic Region
Source: NIH, NINDS (R01 NS029993)
Principal Investigator: **Ralph Sacco**
2019 Budget: $1,731,055

Miami Clinical and Translational Science Institute
Source: NIH//NCRR/NIMHD
Principal Investigator: **Ralph Sacco**
2019 Budget: $3,549,587

Family Study of Stroke Risk and Carotid Atherosclerosis
Source: NIH/NINDS R01 NS040807
Principal Investigators: **Tatjana Rundek**
2019 Budget: $596,641

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
2019 Budget: $702,964

Disparities in Care Delivery in Patients with Atrial Fibrillation: FLiPER-AF Study
Source: ARISTA-USA CV185-564, Pfizer/BMS
Principal Investigators: **Tatjana Rundek**
2019 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**
2019 Budget: $237,500

University of Miami Memory Disorder Clinic
Source: State of Florida, Division of Elder Affairs
Co-Investigator: **Xiaoyan Sun**
2019 Budget: $167,100

The Effects of Cannabinoids on TBI
Source: Scythian Biosciences
Co-Investigator: **Bonnie Levin**
2019 Budget: $633,330

Red Blood Cell Microparticles (RMPs) to Reduce Bleeding Following Hemorrhagic Stroke
Source: NIH, NINDS (R2121 NS094896)
Principal Investigator: **Kunjan Dave**
2019 Budget: $412,594 (NCE)

Nicotine Exposure and Intracerebral Hemorrhage
Source: State of Florida, James and Esther King Biomedical Research Program, FDOH (9JK08)
Principal Investigator: **Kunjan Dave**
2019 Budget: $245,457

McKnight Members Grants *Continued*

Ischemic Preconditioning: Mechanisms of Neuroprotection
Source: NIH, NINDS (R01NS034773)
Principal Investigator: **Miguel Perez-Pinzon**
2019 Budget: $335,781

Metabolic Master Regulators for Ischemic Neuroprotection
Source: NIH/NINDS
Site Principal Investigator: **Miguel Perez-Pinzon**
2019 Budget: $335,781

Neuroprotective mechanisms regulating Nmnats by PKCε preconditioning
Source: AHA, Greater Southeast Affiliate Winter 2018 Predoctoral Fellowship (19PRE34400074)
Principal Investigator: **Jing Xu** (PhD student in **Perez-Pinzon** lab)
2019 Budget: $26,844

ORCATECH Collaborative Aging (in Place) Research Using Technology CART
Source: OHSU/NIA (5U2CAG054397-04)
Site PI: **David Loewenstein**
2019 Budget: $104,075

A non-pharmacological intervention for patients with Alzheimer's disease and family caregivers
Source: Cornell/NIA (7R01AG054009-04)
Site PI: **David Loewenstein**
2019 Budget: $297,529 (including carryover)

A Personalized Health Behavior System to Promote Health and Well-Being in Older Adults
Source: Cornell/NIA (7R01AG053163-04)
Site PI: **Daniel Jimenez**
2019 Budget: $231,694

Center for Research and Education for Aging and Technology Enhancement (CREATE IV)
Source: Cornell/NIA (5PO1AG0172-21)
Site PI's: **David Loewenstein/Joseph Sharit**
2019 Budget: $432,443

Novel Detection of Early Cognitive and Functional Impairment in the Elderly
Source: NIA (5R01AG047649-05)
Principal Investigator: **David Loewenstein**
2019 Budget: $510,809

A Novel Computerized Cognitive Stress Test Designed for Clinical Trials in Early Alzheimer's: Relationship with Multimodal Imaging Biomarkers in Diverse Cultural Groups.
Source: NIA (5R01AG061106-02)
Principal Investigator: **David Loewenstein**
2019 Budget: $657,827

Middle-Aged Offspring of Late Alzheimer's Probands: Novel Cognitive and Biomarker Assessment
Source: FSDH (9AZ24)
Principal Investigator: **David Loewenstein**
2019 Budget: $117,763

McKnight Members Grants *Continued*

The Relationships between Multimodal Neuroimaging Biomarkers and Novel Cognitive Stress Test Among Ethnically Diverse Older Adults
Source: FSDH (8AZ23)
Principal Investigator: **David Loewenstein**
2019 Budget: $254,936

University of Florida – Mt. Sinai Medical Center AD Research Center
Source: UF/NIA (5P50AG047266-05)
Site PI: **David Loewenstein**
2019 Budget: $116,917.31

Understanding Factors Influencing Financial Exploitation Among Diverse Samples of Older Adults
Source: UPitt/NIA (5R01AG055511-03)
Site PI: **David Loewenstein**
2019 Budget: $18,773

The Role of Retinal Microvascular Impairment on Neurodegeneration
Source: National Multiple Sclerosis Society
Principal Investigator: **Hong Jiang**
2018 Budget: N/A (NCE)

Imaging of Conjunctival Microvasculature During Contact Lens Wear
Source: Johnson and Johnson contact lens study
Principal Investigator: **Hong Jiang**
2018 Budget: N/A (NCE)

Exploring Sleep in Neurocognitive Aging and Alzheimer's Research (eSANAR)
Source: NIH/NIA (1R21AG056952)
Principal Investigator: **Alberto Ramos**
2019 Budget: $63,965

Elucidating the link between sleep apnea and dementia using multimodal MRI and cognitive testing.
Source: Scientific Advisory Committee Pilot Study Award, Miller School of Medicine, University of Miami
Principal Investigator: **Alberto Ramos**
2019 Budget: $39,028

Arrhythmia Detection In Obstructive Sleep apnea (ADIOS)
Source: Boehringer Ingelheim
Principal Investigator: **Seemant Chaturvedi/Alberto Ramos**
2019 Budget: $47,142

McKnight - FY20 - Budget Actual
June 1, 2019 - May 31, 2020

Endowment - McKnight Project			Budget Actual Summary
Revenue			**698,076.48**
Personnel			
Faculty	***Role In Project***	***Effort***	
Tatjana Rundek, MD (supplement 85K and 7% Shoninger Professorship)	Scientific Director	36%	
Ralph Sacco, MD (5% for cost sharing - Shoninger Professorship)	Executive Director	5%	
Xiaojan Sun, MD (20% Shoninger Professorship)	Educational Director	20%	
TBA Cognitive Chief ((20% Shoninger Professorship) - start date 9/1/2019	Research for Age-related Cognitive Disorder	20%	
Bonnie Levin, PhD	Neuropsychology	17%	
Kunjan Dave (5% McK and 5% Deptm admin)	Neurology - Basic Science	5%	
Chuanhui Dong, PhD - MRI	Neurology -Statistician	5%	
Noam Alperin, MD - (Main 10%, Shoninger 10%)	Radiology	10%	
Jiang Hong, MD	Neurologist	5%	
Roger C McIntosh, PhD (reduced Marti to save to be able to cover him)	Neurology (part time)	3%	
Subtotal Faculty Salary and CFB			***298,325.04***
Staff	***Role in Project***	***Effort***	
Stacy Merritt	McKnight Project Manager	100%	
Sang Lee (10% MBAR)	Radiology	10%	
Digna Cabral	Neurology	7%	
Marti Flothmann	Clinical Research Coordinator	70%	
MD-PhD Student	MD/PhD Student - Neuro	100%	
TBA volunteer	Bugher volunteer	50%	
Isabel Saul	Research Support Specialist-Basic Science	15%	
Anita Saporta	Neuropsychology	50%	
Susan Fox Rosellini	Neuropsychology	75%	
NeuroPsych 1	Neuropsychology	100%	
NeuroPsych 2	Neuropsychology	25%	
NeuroPsych 3	Neuropsychology	25%	
NeuroPsych 4	Neuropsychology	25%	
NeuroPsych 5		25%	
Subtotal Staff and CFB			***369,169.56***
Total Personnel			***667,494.60***
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, Reception - Annual retreat			
SC08852 - Monthly - Lines & Sets & SC08858 - Monthly - Voice Mail			
SC08103 - Advertising - Other			
SC08024 - Interdepartmental / Intercompany - Service Other - pilot awards			
SC08235 - Computer Hardware & Software Non-Capital			
SC08218 - Clerical Supplies			
SC08229 - Photocopy, Publishing, & Printing Supplies			
SC08200 - Chemicals			
SC08011 - Interdepartmental / Intercompany - Animal Care Services - Internal			
SC08225 - Technical Supplies - Other			
SC09301 Cost share Rundek- Tidemark budgeted under SC08811			
SC08751 - Research participant payments			
Total Non Personnel Expenses			***30,581.82***
Grand Total Expenses			***698,076.42***

McKnight - FY21 - Budget Proposal
June 1, 2020 - May 31, 2021

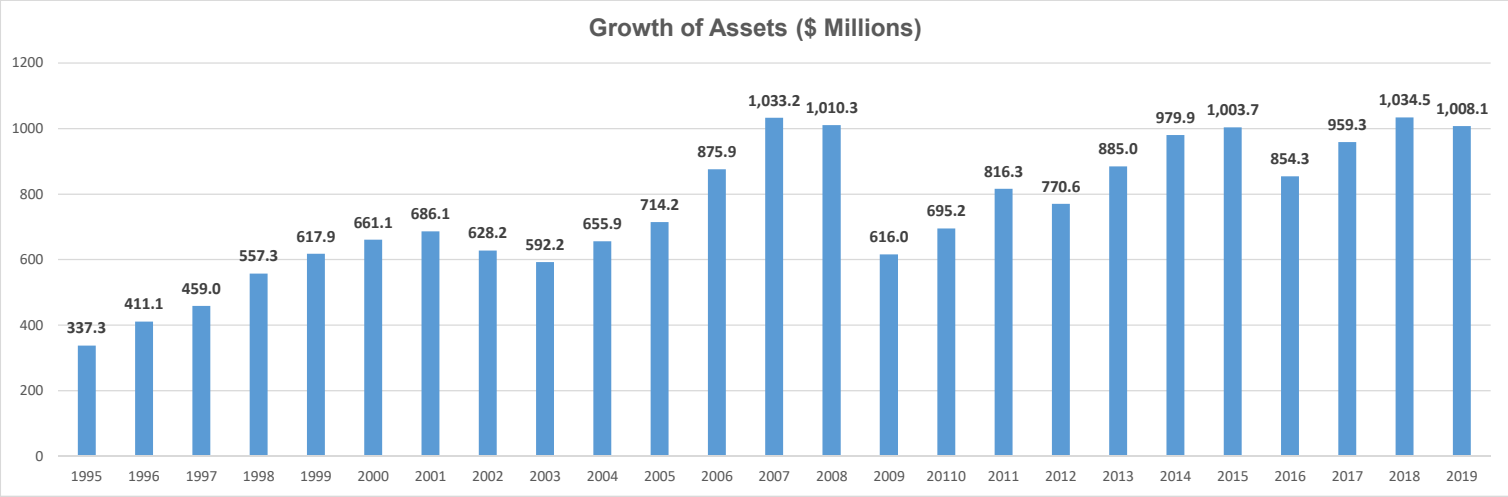
Endowment - McKnight Project				Budget Summary
Revenue Based on FY20 Endowment				**689,000.00**
Personnel				
Faculty	***Role In Project***	***Effort***		
Tatjana Rundek, MD (supplement 100K Chair -75%)	Scientific Director	75%		
Tatjana Rundek, MD (supplement 100K Main - 25%)	Scientific Director	25%		
Ralph Sacco, MD (only cost share)	Executive Director	5%		
Xiaojan Sun, MD (12% Shoninger Professorship - after covering Isaacson)	Educational Director	10%		
TBA Cognitive Chief (20% Shoninger Professorship) -Richard Isaacson 6/1/2020	Research for Age-related Cognitive Disorder	20%		
Bonnie Levin, PhD (15% Schoninger Neuro Psych)	Neuropsychology	15%		
Bonnie Levin, PhD (15% Schoninger Neuro Psych)	Neuropsychology	5%		
Kunjan Dave (5% McK and 5% Deptm admin)	Neurology - Basic Science	5%		
Chuanhui Dong, PhD - MRI	Neurology -Statistician	5%		
Noam Alperin, MD - (Main ?)	Radiology	10%		
Jiang Hong, MD	Neurologist	5%		
McKnight Fellow (7/1/2020)	Neurology	100%		
Sarah Getz (carry forward 40K given in FY20)	Neuropsychology	8%		
Sonya Kaur	Neuropsychology	8%		
Subtotal Faculty Salary and CFB				***299,473.23***
Staff	***Role in Project***	***Effort***		
Stacy Merritt (reduced fte to .80)	McKnight Project Manager	100%		
Sang Lee (10% MBAR)	Radiology	10%		
Marti Flothmann	Clinical Research Coordinator	100%		
MD-PhD Student	MD/PhD Student - Neuro	100%		
Isabel Saul	Research Support Specialist-Basic Science	15%		
Anita Saporta	Neuropsychology	50%		
Susan Fox Rosellini	Admin	30%		
Susan Fox Rosellini	Admin	10%		
NeuroPsych 1	Neuropsychology	50%		
NeuroPsych 2	Neuropsychology	25%		
NeuroPsych 3	Neuropsychology	25%		
NeuroPsych 4	Neuropsychology	25%		
NeuroPsych 5	Neuropsychology	25%		
Subtotal Staff and CFB				**372,288.58**
Total Personnel				***671,761.81***
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, Reception - Annual retreat				
SC08852 - Monthly - Lines & Sets & SC08858 - Monthly - Voice Mail				
SC08103 - Advertising - Other				
SC08024 - Interdepartmental / Intercompany - Service Other - pilot awards				
SC08235 - Computer Hardware & Software Non-Capital				
SC08218 - Clerical Supplies				
SC08219 - Instructional supplies				
SC08229 - Photocopy, Publishing, & Printing Supplies				
SC08200 - Chemicals/blood samples storage/shipping and handling				
Total Non Personnel Expenses				***17,238.19***
Grand Total Expenses				**689,000.00**

University of Miami - All Managed Assets
Performance Periods Ending: May 31, 2019

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	0.0	7.5	4.2	7.1	8.1
Growth Pool Market Benchmark**	12/31/1990	-0.1	7.6	4.8	8.1	8.6
Value (+/-)		0.1	-0.1	-0.6	-1.0	-0.5

15 Year Growth Pool Risk/Return as of May 31, 2019		
Growth Pool	**15 Year Return**	**5 Year Standard Deviatio**
Growth Pool Total Composite	5.8	9.7
Growth Pool Market Benchmark	5.9	10.8

*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



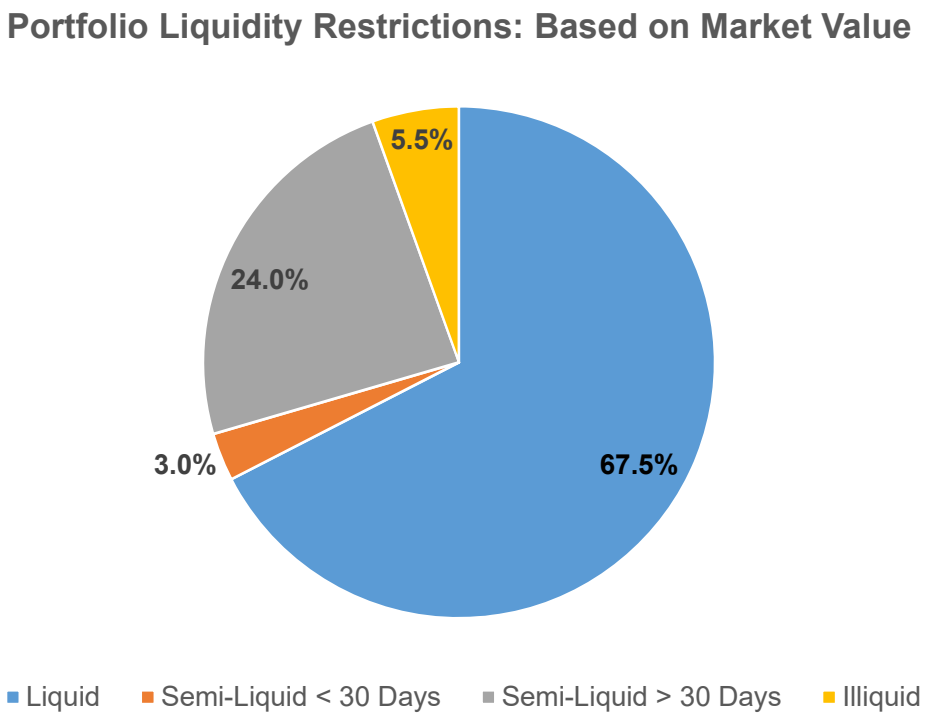
UNIVERSITY OF MIAMI - GROWTH POOL
Manager Structure - Market Values and Allocations
As of May 31, 2019

			Growth Pool
Manager	Asset Class	Market Value ($)	% of Total Fund
Large/Mid/All Cap Equity		340,860,114	33.8%
Vanguard Institutional Index (10/31/14)	US Large Cap Core Equit	149,658,590	14.8%
Adage Capital Mgmt (6/30/04)	US Large Cap Core Equit	90,045,185	8.9%
Columbia Dividend Income (2/2/17)	US Large Cap Core Equit	18,509,993	1.8%
Loomis Large Cap Growth (2/2/17)	US Large Cap Growth Eq	20,916,927	2.1%
MFS Large Cap Value (2/2/17)	US Large Cap Value Equi	17,029,740	1.7%
Earnest Partners Mid Cap (8/31/2018)	US Midcap Value Equity	14,710,491	1.5%
Janus Enterprise Mid Cap Growth (2/2/17)	US Midcap Growth Equity	10,482,806	1.0%
Vanguard Mid Cap (2/2/17)	US Midcap Core Equity	19,506,382	1.9%
Small Cap Equity		51,936,092	5.2%
Ariel Small Cap (8/31/2018)	US Small Cap Value Equi	12,780,024	1.3%
Vanguard Small Cap (2/2/17)	US Small Cap Equity	39,156,068	3.9%
International Equity		241,726,447	24.0%
Developed International Equity		163,357,115	16.2%
Silchester International (6/30/05)	Non-US DM/EM Value Eq	59,569,875	5.9%
Vanguard Developed Markets (2/2/17)	Non-US DM Core Equity	103,786,397	10.3%
Schroders International Growth (2/2/17)	Non-US DM Core Equity	843	0.0%
Emerging Markets		78,369,332	7.8%
Neuberger Berman (9/30/2018)	Non-US EM Equity	29,579,754	2.9%
Vanguard FTSE Emerging Markets (2/2/17)	Non-US EM Equity	26,587,841	2.6%
WGI Emerging Markets (10/31/08)	Non-US EM Equity	22,201,737	2.2%
Total Alternative Investments		161,114,734	16.0%
Credit Strategies		27,851,503	2.8%
Davidson Kempner (10/01/93)	Credit Strategy	15,032,625	1.5%
Watershed Capital (1/01/08)	Credit Strategy	328,483	0.0%
Regiment Capital (6/30/07)	Credit Strategy	912,348	0.1%
Octagon CLO III (1/31/2019)	Credit Strategy	1,252,715	0.1%
Shenkman Opp Crd (8/31/2018)	Credit Strategy	10,325,332	1.0%

			Growth Pool
Manager	Asset Class	Market Value ($)	% of Total Fund
Equity Long/Short		45,417,205	4.5%
Viking Global Equities III (11/30/10)	Equity Long/Short	23,365,541	2.3%
Renaissance Institutional (8/31/17)	Equity Long/Short	21,736,562	2.2%
Glenview Capital Management (2/01/06)	Equity Long/Short	315,102	0.0%
Multi-Strategy		87,846,026	8.7%
AQR Delta XN Offshore (1/31/17)	Multi-Strategy	14,613,159	1.4%
AQR Risk Parity (2/21/17)	Multi-Strategy	57,310,722	5.7%
AQR Style Premia (12/14/16)	Multi-Strategy	15,922,145	1.6%
Private Equity		39,635,606	3.9%
TIFF Partners IV (01/31/01)	Private Equity	924,080	0.1%
TIFF Partners V (04/30/04)	Private Equity	192,315	0.0%
TIFF Partners 2006 (04/30/06)	Private Equity	750,772	0.1%
TIFF Partners 2007 (01/31/07)	Private Equity	1,855,509	0.2%
TIFF Partners 2008 (01/31/08)	Private Equity	8,813,600	0.9%
OCM Principal Opportunities IV (12/31/06)	Private Equity	137,868	0.0%
Denham Commodity Fund V (6/30/08)	Private Equity	1,497,924	0.1%
Clayton, Dubilier & Rice Fund IX (5/31/2014)	Private Equity	10,548,332	1.0%
Carlyle Strategic IV (11/30/16)	Private Equity	2,776,836	0.3%
KKR Americas XII (9/30/16)	Private Equity	4,275,440	0.4%
HIG Advantage Buyout (4/30/18)	Private Equity	690,594	0.1%
Carlyle Partners VII (12/31/2018)	Private Equity	1,143,318	0.1%
Apollo Investment Fund IX (3/15/2019)	Private Equity	635,372	0.1%
Silver Lake Partners (6/30/2018)	Private Equity	4,227,182	0.4%
Vista Equity Partners (6/30/2018)	Private Equity	1,166,464	0.1%
Private Real Assets		23,219,566	2.3%
WCP Real Estate Strategies Fund (7/31/06)	Private Real Assets		0.0%
Parmenter Realty Fund III (04/30/06)	Private Real Assets	-	0.0%
WCP Real Estate Fund I (7/31/06)	Private Real Assets	137,682	0.0%
WCP Real Estate Fund II (11/30/08)	Private Real Assets	1,405,401	0.1%
Metropolitan Real Estate Fund (9/30/06)	Private Real Assets	183	0.0%
SRI Nine REIT (3/31/08)	Private Real Assets	1,147,913	0.1%
LBA Realty IV (10/31/09)	Private Real Assets	1,247,012	0.1%
Warburg Energy (5/31/14)	Private Real Assets	7,902,961	0.8%
Ishares Inf. Global ETF (6/30/2018)	Public Real Assets	10,415,587	1.0%
GS Renew PWR LLC (8/31/2018)	Private Real Assets	962,827	0.1%

			Growth Pool
Manager	Asset Class	Market Value ($)	% of Total Fund
Total Fixed		144,061,848	14.3%
Vanguard Total Bond Fd (10/30/14)	Aggregate Bonds	22,591,047	2.2%
CIFC Sr. Secured Corp Fund (8/31/2018)	Corporate Bonds	25,687,658	2.5%
PIMCO Income Fund (7/24/17)	Aggregate Bonds	27,073,359	2.7%
Vanguard Short-Term Bond Fd (04/03/19)	Short Duration Bonds	48,968,643	4.9%
Prudential US High Yield (2/2/17)	High Yield Bonds	19,741,141	2.0%
Cash		5,552,841	0.6%
Total Managed Assets		1,008,107,248	100.0%

Allocation to Index or Enhanced Index Strategies	
	Growth Pool
% of Total:	40.7%



UNIVERSITY OF MIAMI - GROWTH POOL
Inception to Date Performance vs. Relevant Benchmark(s)
Periods ending - May 31, 2019
Net of Fees

Total Returns (%) - Annualized if Greater than 1 Year	ROR	Value Added (+/-)	Years
Large/Mid/All Cap Equity			
Vanguard Institutional Index (9/30/14)	9.05	-0.59	4.7
S&P 500	9.64		4.7
Adage Capital Mgmt (6/30/04)	11.17	2.72	14.9
S&P 500	8.45		14.9
Earnest Partners Mid Cap (8/31/2018)	-1.94	2.52	0.7
Russell Midcap	-4.46		0.7
Columbia Dividend Income (2/2/17)	10.88	0.42	2.3
Russell 1000 Value	10.46		2.3
Loomis Large Cap Growth (2/2/17)	17.10	1.27	2.3
Russell 1000 Growth	15.83		2.3
MFS Large Cap Value (2/2/17)	7.15	2.03	2.3
Russell 1000 Value	5.12		2.3
Janus Enterprise Mid Cap Growth (2/2/17)	17.37	3.24	2.3
Russell Midcap Growth	14.13		2.3
Vanguard Mid Cap (2/2/17)	7.98	-0.07	2.3
CRSP MidCap Index	8.05		2.3
Small Cap Equity			
Ariel Small Cap (8/31/2018)	-14.81	0.58	0.7
Russell 2000 Value	-15.39		0.7
Vanguard Small Cap (2/2/17)	6.63	0.09	2.3
CRSP US Small Cap TR Index	6.54		2.3
Developed International Equity			
Silchester International (6/30/05)	7.41	4.03	13.9
MSCI EAFE Value ND	3.38		13.9
Vanguard Developed Markets (10/31/2014)	2.99	-0.35	4.6

Total Returns (%) - Annualized if Greater than 1 Year	ROR	Value Added (+/-)	Years
FTSE Dev All Cap ex US	3.34		4.6
Emerging Markets			
Neuberger Berman (9/30/2018)	-1.40	2.05	0.7
MSCI Emerging Markets ND	-3.45		0.7
Vanguard FTSE Emerging Markets (2/2/17)	5.33	-0.86	2.3
MSCI Emerging Markets ND	6.19		2.3
WGI Emerging Markets (10/31/08)	9.62	6.83	0.6
MSCI Emerging Markets ND	2.79		0.6
Credit Strategies			
Davidson Kempner (10/01/93)	8.95	-0.31	25.7
HFR Event-Driven	9.26		25.7
Shenkman Opp Crd (8/31/2018)	2.33	3.13	0.7
HFRI ED: DIST RS (USD)	-0.80		0.7
Equity Long/Short			
Viking Global Equities III (11/30/10)	9.78	1.02	8.5
MSCI World Index	8.76		8.5
Renaissance Institutional (8/31/17)	4.87	1.21	1.7
MSCI ACWI ND	3.66		1.7
Multi-Strategy			
AQR Delta XN Offshore (1/31/17)	-8.48	-11.45	2.3
HFRI Fund of Funds Composite	2.97		2.3
AQR Risk Parity (2/21/17)	4.99		2.3
60 MSCI AC WORLD/40 BB Barclays U.S. Aggregate	5.55		2.3
AQR Style Premia (12/14/16)	-3.77	-5.31	2.5
ICE ML 3M US Treasury Bill	1.54		2.5
Fixed Income			
Vanguard Total Bond Fd (10/30/14)	2.62	-0.23	4.6
BB Barclays U.S. Aggregate	2.85		4.6
Pimco Income Fund (7/24/17)	4.13	1.18	1.9
BB Barclays U.S. Aggregate	2.95		1.9

Total Returns (%) - Annualized if Greater than 1 Year	ROR	Value Added (+/-)	Years
Prudential US High Yield (2/2/17)	5.39	0.67	2.3
BB Barclays U.S. Corporate High Yield	4.72		2.3
CIFC Sr. Secured Corp Fund (8/31/2018)	2.75	0.21	0.7
S&P/LTSA Lev Loan Index	2.54		0.7
Vanguard Short-Term Bond Fd (04/03/19)	2.41	-1.45	0.2
BB Barc US Gov/Credit 1-5 Years	3.86		0.2

McKnight053119

Summary

Evelyn F. McKnight Brain Institute's Endowments
at the Miller School of Medicine
Market Value Analysis
05/31/2019

2002 Gift & Match

McKnight Contribution	$5,000,000
UM Match	5,050,913
Transfers from Other University Funds	1,362,153
Investment Return	6,317,842
Distributions for Spending	(6,086,198)
05/31/19 Endowment Balance	$11,644,710
Unmatched Balance	$0

2014 Gift & Match

McKnight Contribution	$2,000,000
UM Match	2,000,000
Transfers from Other University Funds	0
Investment Return	856,138
Distributions for Spending	(578,628)
05/31/19 Endowment Balance	$4,277,510
McKnight Foundation Pledge Balance	$0

McKnight053119
Annual

University of Miami
Evelyn F. McKnight Brain Institute's Endowments
Summary Analysis at Market Value
June 1, 2018 - May 31, 2019

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, 6/1/18	$7,412,186	$1,146,735	$1,041,231	$2,603,076	$0	$12,203,228
Investment Return	(24,589)	(3,804)	(3,454)	(8,636)		(40,483)
Distributions for Spending	(314,652)	(48,680)	(44,201)	(110,502)		(518,035)
Transfers from other University funds						0
Matching gifts						0
Ending Balance at Market, 05/31/19	$7,072,945	$1,094,251	$993,576	$2,483,938	$0	$11,644,710

2014 Gift & Match

	Schoninger Professor in Memory Disorders 262471	Evelyn F. McKnight Endowed Chair 262490				Total
Beginning Balance at Market, 6/1/18	$2,132,248	$2,350,425	$0	$0	$0	$4,482,673
Investment Return	(7,074)	(7,797)				(14,871)
Distributions for Spending	(90,515)	(99,777)				(190,292)
Transfers from other University funds						0
Matching gifts						0
McKnight Foundation gifts						0
Ending Balance at Market, 05/31/19	$2,034,659	$2,242,851	$0	$0	$0	$4,277,510

EDUCATIONAL PROGRAMS

SECTION 12

12. Educational Programs Focusing on Age-Related Memory Loss

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

12.1. *General Education Program (Community Outreach)*

Evelyn F. McKnight Brain Institute Community Educational Program

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

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

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

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

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

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

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

Evelyn F. McKnight Brain Institute Fellows

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

Evelyn F. McKnight Research Fellow

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

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

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

Dr. Anita Saporta also works on the **McKnight Frailty Project** under **Drs. Bonnie Levin** and **Katalina McInerney** conducting medical chart reviews.

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

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

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

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

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

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

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

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

- **Our Special Invited Speaker Dr. Ron Lazar, PhD, FAHA, FAAN** University of Alabama, Birmingham joined us on June 7th to present "Vascular Cognitive Impairment: Insights from Vascular Interventions." He is the Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging and the Director of the Evelyn F. McKnight Brain Institute at UAB. As part of our commitment to partner with our Inter-Institutional McKnight colleagues, **Dr. Lazar** met with faculty from our department as well as with cross-disciplinary faculty to discuss future research and collaborations with emphases on reversible causes of cognitive decline, risk-factor modification to promote cognitive resiliency and recovery after stroke.

- **Our Special Invited Speaker Dr. Vladimir Hachinski, CM, MD**, University of Toronto, DSc, FRCPC, FRSC joined us on June 26th to present "Origin, Status and Future of the Hachinski Ischemic Score" which was followed by a lucrative roundtable discussion in which future collaborations with our McKnight members, collaborators and trainees were discussed. **Dr. Hachinski** has transformed the understanding, diagnosis, treatment and prevention of the two greatest threats to the brain: stroke and dementia. He co-discovered a link between Alzheimer's and stroke and introduced new concepts and a new clinical diagnosis tool; the Hachinski Ischemic Score for identifying the treatable components of dementia. He co-founded the world's first successful acute stroke unit, now the standard of care. Dr. Hachinski was Editor-in-Chief of *Stroke*, the leading publication in the field for an unprecedented 10 years (2000-2010).

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

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

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

Mentoring, Training and Teaching by UM McKnight Members and Collaborators

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

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

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

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

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

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

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

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

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

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

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

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

Dr. David Loewenstein's mentors these dissertation students.

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

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

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

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

Dr. Ami Raval taught the following courses this year.

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

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

- Qismat Niazi
- Sonya Patel
- Verun Reddy

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

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

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

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

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

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

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

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

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

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

COLLABORATIONS

SECTIONS 13-14

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

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

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

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

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

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

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

young investigators to engage in clinical studies relevant to age-related cognitive decline and memory loss. The award also recognizes the importance of rigorous training in clinical research and encourages young investigators in seeking opportunities to establish future careers in the area of human cognitive aging.

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

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

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

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

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

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

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

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

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

WHATS IN THE FUTURE?

RESEARCH AND CLINICAL INITIATIVES

SECTION 15

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

Upcoming Clinical Translational and Population-Based Research

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

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

Upcoming Basic and Translational Science Research

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

Upcoming Education Program

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

Upcoming Plans for the McKnight Scientific Advisory Board

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

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

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

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

No funds were used for prohibited purposes.

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

No.

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

Yes.

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

None

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

N/A

ACHIEVEMENTS OF THE YEAR

SECTION 22

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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January 14th, 2020

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

Date

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

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December 1, 2019

McKnight Brain Aging Registry: Neuroimaging and Cognitive Cores
Progress Report to the Trustees of the Evelyn F. McKnight Brain Research Foundation

Dear Trustees,

We are pleased to provide an update on our progress in establishing the McKnight Brain Aging Registry (MBAR) and its Neuroimaging and Cognitive Cores. This initiative has a primary goal of facilitating cross-institute collaborations across the four McKnight Brain Institutes, while advancing the collective mission of enhancing our understanding of cognitive and brain aging to support the development of interventions for age-related cognitive decline. Despite experiencing some significant challenges during the early start-up phases of the project, we have continued to make considerable progress over the last reporting period, and data collection continues to be fully underway. In this report, we summarize our ongoing scientific progress and plans for the coming year. Consistent with our last progress report, we have combined our reports on the Neuroimaging and Cognitive Cores, as the activities of these cores have been integrated to accomplish the collaborative MBAR mission. To the extent there are activities specifically related to one of the two cores, we have indicated this in the report.

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

Sincerely,

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McKnight Brain Aging Registry Update: Neuroimaging and Cognitive Cores

Vision

A Successful Aging Research Network that will facilitate multi-institutional collaborations across the McKnight Brain Institutes (MBI) to enhance our understanding of cognitive and brain aging and to identify intervention targets to ameliorate age-related cognitive decline.

Mission

Establish and maintain the necessary multi-institutional infrastructure to support and implement a Brain Aging Registry of the oldest old, which includes assessments of particular importance to the field of cognitive aging, including neuroimaging, extensive cognitive and functional assessments, and blood-based biomarkers.

Scientific Progress

The principal investigators, along with co-investigators and study coordinators involved in both the MBAR Neuroimaging and Cognitive Cores have continued to work hard to advance the project and considerable progress has been made over the current reporting period. To date, we have enrolled 141 participants who have been recruited across the four MBI sites, approaching 75% of our targeted enrollment, and who have been fully engaged in the registry, providing clinical, neuropsychological, and brain imaging data. It is anticipated that recruitment and assessments will be completed by the end of the next fiscal year with enrollment of the originally planned cohort of 200 MBAR oldest old participants.

Since the MBAR and neuroimaging cores were approved by the MBRF and funding began in January 2015, weekly conference calls have been held to discuss and implement the comprehensive assessments for collection of multi-modal neuroimaging, cognitive, and functional data from older adults over the age of 85 years who have been screened to exclude those with MCI or dementia and are showing evidence of successful cognitive aging. Over the last reporting period, the MBAR research activities have been mainly focused on our ongoing recruitment, execution of the data acquisition protocols, database modifications and data entry, and conducting interim data analyses for meeting presentations and development of submissions for publication. Weekly conference calls were held to discuss MBAR related issues. These were organized to include bi-weekly conference calls, attended by the PIs along with the study coordinators and MR physicists at each site. These calls focused on resolving any logistical, procedural, and data management issues or questions that may have arisen. A great deal of effort has been directed to insure harmonization of acquisition methods and data across sites to optimize quality assurance and quality control procedures. On alternate weeks, we held additional regular conference calls which were either focused on specific project-related discussions on neuroimaging and cognitive issues or were dedicated for our monthly MBAR Scientific Advisory Committee (SAC) call. The SAC is a representative committee of MBAR PIs and investigators, fully familiar with the MBAR cohort and data collection, with approximately two representatives from each MBAR MBI participating site. The SAC calls provide for discussions of broader issues related to the registry, including plans for new grant

submissions, identifying priorities for data analyses and lead investigators for MBAR manuscripts, and plans for enhancing use and accessibility of the growing MBAR dataset.

With our MBAR database infrastructure established, the REDCAP dataset continues to be fully operational and is actively being populated with data from each participant across all MBI sites. MRI data is uploaded from each site to the HiPerGator super-computer at UF, where it is pre-processed into a unified format enabling different imaging modalities to be more easily examined simultaneously. Cognitive and clinical data are uploaded to UM, where it is double entered into REDCAP with ongoing reliability checks. Data from the physical activity actigraph recordings are sent to Dr. Alexander at UA for processing and analyses. Blood specimens are sent to UF for storage in freezers located in the phlebotomy laboratory. All study coordinators have been trained in use of the database, including how to enter test scores and other clinical information. Several of the tests that are being employed require processing of scores and formatting prior to data entry. We have devoted effort in the last reporting period to further develop these tools for automatic data processing. All data is double entered into the REDCAP database, and quality control checks are conducted on a regular basis. Data sharing agreements and coordinated IRB approvals have been previously obtained for each site to support sharing data across MBI sites. In the sections below, additional progress relative to each core and component of the MBAR project are described.

Neuroimaging Core Progress

1) The MBAR neuroimaging protocol is fully operational. As described previously, we are collecting multimodal structural, functional, and metabolic neuroimaging data that includes: T1 images for cortical and subcortical volumetric and thickness measures; FLAIR-white matter hyperintensity lesion load; Diffusion Tensor Imaging for white matter integrity and tractography; MRS for cerebral metabolite concentrations, including GABA and glutamate; resting state fMRI functional brain activity at rest to measure functional connectivity; and MRI phase contrast scans for measures of cerebral vascular pulsation and blood flow analyses.
2) MR standardization: This has been accomplished and continues with all sites following standard procedures for the MRI protocols and order of administration.
3) MRI quality control: Each site sent data from pilot participants for each imaging modality to assess any scanner specific sources of artifact and to ensure that all metrics being obtained were consistent across sites. This involved each site processing a particular modality of data. For example, MRS data from each site was processed at UF, while resting state fMRI was processed at UAB. Considerable effort was directed at specific neuroimaging data types with novel applications for cognitive aging (see MRS below).
4) MRS spectroscopy: We have successfully implemented megapress MRS across sites, and have overcome technical challenges that occurred at certain sites. Dr. Porges has been conducting ongoing quality control of the GABA and other metabolite measures that have been obtained. Data quality has been excellent.
5) Time constraints: The neuroimaging protocol can typically be executed with acquisition within 60 minutes. We have not encountered complaints from the participants about the length of the MRI scan. For the most part they do not report finding this assessment burdensome nor do they describe significant discomfort. We believe this protocol

provides the opportunity for innovative and cutting-edge measures of brain structure, function, network connectivity, and neurometabolic and cerebral hemodynamic health.

6) Neuroimaging data collection continues to be well underway and imaging quality assurance across the sites is ongoing.
7) The neuroimaging data being acquired in the MBAR project is unique for the field of cognitive aging. There have not been other studies of people over the age of 85 that have assessed participants with such an extensive multimodal MRI scan battery.

Cognitive Core Progress

The Cognitive Core has continued to integrate their conference calls into the regular weekly calls described above to facilitate group communication across the cores and MBI sites. Most discussions have focused on resolving any data entry and analytic questions, as well as occasional queries from the study coordinators regarding minor procedural and scoring questions. However, most of the focus has been on strategic planning regarding the sequence of analyses to be conducted. There have also been ongoing discussions to consider adding a few additional cognitive measures or rating scales that might provide added valued for the cognitive assessments. During the past year we achieved numerous objectives in this core as outlined below:

1) Identified cognitive parameters: We have continued to implement the battery of cognitive tests to address assessment of the proposed cognitive domains.
2) Battery refinement: We have continued to use our finalized main cognitive and clinical assessment battery.
3) Standardization of cognitive and clinical assessment procedures: We continued to use our training manuals, training videos that include test administration and scoring, and other tools to insure consistency of the assessment approach across sites and testers. Examples of the manuals and videos we created can be accessed at: https://labs.uab.edu/visscher/2-uncategorised/48-mbarresearchtraining
4) Certification program: Study coordinators have been certified to insure standardization. To achieve this standardization, we set up a procedure whereby one person (e.g., research associate) at each site is certified for cognitive and clinical test administration and scoring. This, in addition to ongoing oversight by investigators, gives us confidence that the study protocol is implemented in a systematic and uniform manner across sites.
5) NIH-Toolbox expanded domains: These measures continue to be collected, including measures from the motor and sensory domains.
6) Expanded memory assessment: The Face-Name Association Test and the Mnemonic Similarities Test continue to be implemented with data being collected on an ongoing basis at all sites.
7) Actigraphy: We continue to implement the use of Actigraph actigraphy watches to assess physical activity in our oldest old cohort for a 7-day period, consistent with the Center for Disease Control (CDC) standard research protocol. Processing and analysis software have been developed and applied at the UA with preliminary testing completed and initial results presented at the 2019 SFN McKnight Reception (see below).
8) NACC battery: Measures developed and employed by National Alzheimer's Coordinating Centers (NACC) continue to be collected following standardized procedures for all participants and are being used for clinical screening and adjudication

of cases with questionable MCI. This data will enable future harmonization with data collected in the NIA Alzheimer's Disease Centers and memory disorder programs at the MBI sites.

Laboratory Measures: Blood Biobanking

The MBAR is also collecting blood samples from participants. These samples are obtained using standard protocols and procedures across sites and are stored for future use for genetic, metabolic, and other analyses.

1) Blood samples from participants are being drawn on most participants across the MBI sites. These samples are centrifuged, frozen, and then sent to UF for central storage in the CAM freezers.

We have continued to make great progress over the past year. The time and effort directed at the MBAR project has resulted in the collection of important clinical, cognitive and neuroimaging data that should make a significant contribution to the clinical neuroscience of cognitive and brain aging. With the accumulation of the MBAR data, we are planning initial interim manuscripts for submission as we continue to approach our target sample size of 200 participants. We further expect that a greater number of analyses and manuscripts will be developed towards the end of the next fiscal year using data from the fully recruited cohort.

Deliverables

Leveraging the infrastructure and opportunities for inter-institutional collaborations provided by the MBAR over the past year, the MBAR leadership and investigators have had a number of achievements, including collaborative grant awards, manuscript publications, presentations at scientific meetings, and the roll out of a MBRF pilot project program. In addition, please note that many MBAR investigators from each of the MBI sites have benefited from the inter-institutional interactions facilitated by the MBAR effort, leading to numerous grant submissions and manuscripts that are not reflected by the cross-institutional grants and papers listed below. The specific deliverables showing cross-institutional collaboration are described below:

***Frontiers in Aging Neuroscience* Special Edition**: The core and affiliated faculty of the four MBIs have generated a special edition, with additional articles submitted for publication in the last year, of the journal focusing on the use of neuroimaging for the study and assessment of cognitive and brain aging. The editors for this special edition include several PIs and investigators for MBAR (Cohen, Alexander, Visscher, Wright, Woods). All but one of the manuscripts planned for this special edition have already been published. An additional overview article by the special edition editors is in preparation.

Augmenting Cognitive Training in Older Adults (ACT) Project Update: This five-year, $5.7M NIA-funded, R01 multicenter Phase III RCT continues to be actively recruiting the planned 360 healthy older adults between the ages of 69-90 years. This project utilizes the infrastructure created by MBAR for this multisite trial between the MBIs at UF and UA (MPIs: Cohen, Marsiske, Woods; UA Site PI: Alexander). The effects of transcranial direct current stimulation (tDCS) given in conjunction with cognitive training is being examined to determine if

tDCS increases neuroplasticity (as measured using neuroimaging methods) and ultimately whether it leads to improved cognitive outcomes as measured by the NIH-Toolbox. This study is the largest tDCS study of its kind ever conducted or supported by NIH. This study fits fully with the MBAR mission and the MBRF more broadly, and is a direct byproduct of the inter-institute collaborative work initiated within the MBAR. It is a major deliverable resulting from this inter-institute collaboration. A manuscript describing this cross-institutional, collaborative RCT protocol has been published (Woods et al., 2018; see below). In addition, collaborative manuscripts for journal publication (Hausman et al., submitted; Kraft et al., submitted) and presentations at the International Neuropsychological Society meeting (Boutzoukas et al., January, 2020; Evangelista et al., January, 2020; Hardcastle et al., January, 2020; Hausman et al., January, 2020; Kraft et al., January, 2020), using the baseline assessment and neuroimaging data, have been submitted (see references below).

Near Infrared Brain Stimulation Study: A new $3.8M NIA R01 RCT grant proposal was awarded in August, 2019 to examine the effects of near infrared brain stimulation on cognitive and brain function in older adults to determine its ability to augment cognition during aging. This highly innovative multisite proposal between UF and UA (MPIs: Woods, Alexander, Bowers) directly utilizes the collaborative, multi-institutional infrastructure created by MBAR and represents the largest study to apply this novel method to enhance brain and cognitive performance during aging.

Vagal Nerve Stimulation Study: As part of the McKnight Interventions Core, a pilot study was awarded in October, 2019 by the MBRF to investigate the potential for using vagal nerve stimulation to enhance cognitive function in healthy older adults. This work directly leverages the infrastructure established as part of the MBAR with UF (Williamson (PI), Cohen, Woods, Lamb, Porges) and UA (Alexander) MBI teams, to support the investigation of this novel intervention pilot study. With the essential pilot data from this study, we would plan to pursue a larger scale subsequent NIA grant submission.

MBI Inter-Institute MBAR Grant Initiative: The MBI sites are discussing plans for new grant proposals to NIA that will expand on findings from MBAR. Following discussions and recommendations from NIA program, the MBAR PIs have been working to establish access to PET imaging and neuropathology follow-up across MBI sites to enhance this proposal effort. We are planning to develop this initiative into one or more NIA grant submissions in the coming year.

Manuscripts: With the MBAR sample now reaching well over 100 participants, we are currently also planning two manuscripts for publication from the MBAR data. One manuscript will be led by Dr. Alexander and his team on the physical activity data using actigraphy in relationship to cognitive and brain aging. A second analysis is underway examining the initial GABA MRS data in this cohort. Additionally, a graduate student working with Dr. Visscher is planning her dissertation research with the MBAR data, which is expected to lead to three new manuscripts for publication. We anticipate a series of additional manuscripts based on data from the registry to be developed in the coming year.

Figure 1. Brain regions showing greater medial frontal cortical volume with greater exercise in the MBAR cohort.

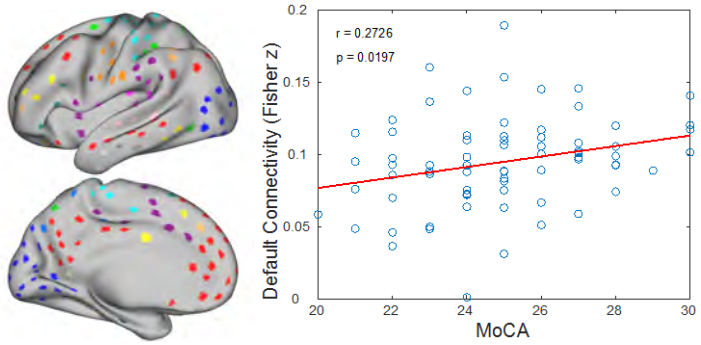

Figure 2. Left shows, in red, cortical regions that are part of the Default Mode Network. Plot on the right shows that the strength of functional connectivity of those Default Mode regions correlates with performance on MoCA, a test of cognitive function.

Meeting Presentations: Progress for the MBAR was presented at the 2019 McKnight Inter-institutional meeting at UF with slide presentations by Drs. Alexander (UA), Porges (UF), and Visscher (UAB), reporting recent efforts and progress in the recruitment and acquisition of neuroimaging and cognitive data for the registry cohort. Posters with research findings were presented during the 2019 SFN McKnight Reception meeting in Chicago, IL with interim results on actigraphy measures of moderate to vigorous exercise in relation to regional cortical thickness, area, and volume maps from structural MRI scans, on magnetic resonance spectroscopy findings, and on resting state functional connectivity analyses in the MBAR oldest old cohort. This work showed support for increased engagement in aerobic activity associated greater cortical volume in regions of medial frontal cortex in oldest-old individuals from the MBAR cohort (Raichlen et al., November, 2019; see Figure 1). Additionally, posters were presented showing analyses with resting state functional connectivity scans (Visscher et al., November, 2019; see Figure 2) and magnetic resonance spectroscopy data (Porges et al., November, 2019) in the MBAR cohort, supporting these novel brain imaging measures in the evaluation of successful cognitive aging.

Challenges and Barriers

While we have been quite productive and achieved many of our MBAR goals for the past year, we have had to overcome several challenges and barriers that impeded our progress in the early stages of the project. However, we believe the study is well underway and continues to run efficiently, and we are on target to reach our original goal of 200 MBAR participants in the coming year. To reach this goal and to maintain our throughput of new potential recruits of cognitively unimpaired oldest old adults, we have collectively continued to enhance our community outreach, use newspaper ads, and use population databases in the public domain (e.g., voter registration rolls) or other sources for targeted mailings. Going forward we plan to leverage the data collected to support new publications that will contribute to the scientific literature, will advance translation and implementation of the assessments for clinical use, and will support the development of multiple inter-institute grant proposals that capitalize on the unique McKnight dataset of successful aging oldest old adults.

Summary

Despite past challenges, the MBAR continues to be fully operational with recruitment ongoing and data for the registry continues to be actively collected. We fully expect that our substantial progress will continue over the coming year. To support our goals and plans for the MBAR cohort, we are kindly requesting a no cost extension for the combined Neuroimaging and Cognitive Cores through the next fiscal year, so we can continue our MBAR progress to reach our original target enrollment goal at no additional cost through December 31, 2020. During this time, we will also continue to examine in conjunction with the Clinical Interventions Core, opportunities for new and emerging studies, manuscripts, and grant proposals that fully leverage the collaborative inter-institutional infrastructure and expertise created by the MBAR.

Cited References

Boutzoukas EM, O'Shea A, Evangelista ND, Hausman HK, Kraft JN, Porges E, Hishaw GA, Wu S, DeKosky S, Alexander G, Marsiske M, Cohen R, Woods AJ. (January, 2020) Contribution of region specific white-matter hyperintensities in cognitive aging. Abstract for presentation at the International Neuropsychological Society meeting, Denver, CO.

Evangelista ND, O'Shea A, Kraft JN, Hausman HK, Boutzoukas E, Hardcastle C, Porges E, Alexander GE, Marsiske M, Cohen R, Woods AJ. (January, 2020) Independent contributions of dorsolateral prefrontal structure and function to working memory in older adults. Abstract forpresentation at the International Neuropsychological Society meeting, Denver, CO.

Hardcastle C, O'Shea A, Kraft JN, Hausman HN, Evangelista ND, Boutzoukas EM, Porges E, Alexander GE, Marsiske M, Cohen R, Woods AJ. (January, 2020) Lateralized hippocampal contributions to cognition in healthy older adults. Abstract for presentation at the International Neuropsychological Society meeting, Denver, CO.

Hausman HK, O'Shea A, Kraft JN, Boutzoukas EM, Evangelista ND, Van Etten EJ, Bharadwaj PK, Smith SG, Porges E, Hishaw GA, Wu S, DeKosky S, Alexander GE, Marsiske M, Cohen R, Woods AJ. (January, 2020) The role of resting-state network functional connectivity in cognitive aging. Abstract for presentation at the International Neuropsychological Society meeting, Denver, CO.

Hausman HK, O'Shea A, Kraft JN, Boutzoukas EM, Evangelista ND, Van Etten EJ, Bharadwaj PK, Smith SG, Porges E, Hishaw GA, Wu S, DeKosky S, Alexander GE, Marsiske M, Cohen R, Woods AJ. The role of resting-state network functional connectivity in cognitive aging. Manuscript Submitted.

Kraft JN, O'Shea A, Albizu A, Evangelista ND, Hausman HK, Boutzoukas E, Porges E, Alexander GE, Marsiske M, Cohen R, Woods AJ. (January, 2020) Structural neural correlates of speed of processing. Abstract for presentation at the International Neuropsychological Society meeting, Denver, CO.

Kraft JN, O'Shea A, Albizu A, Evangelista ND, Hausman HK, Boutzoukas E, Nissim NR, Van Etten EJ, Bharadwaj PK, Song H, Smith SG, Porges E, DeKosky S, Hishaw GA, Wu SS, Marsiske M, Cohen R, Alexander GE, Woods AJ. Structural neural correlates of speed of processing. Manuscript Submitted.

Raichlen DA, Bharadwadj PK, Franchetti MK, Sims SA, Rezaei RF, Merritt SS, Jessup CJ, Porges EC, Geldmacher D, Hishaw GA, Alperin N, Trouard TP, Wadley VG, Levin BE, Woods AJ, Rundek T, Visscher KM, Cohen RA, Alexander GE. (November, 2019) Relation of daily activity patterns to cortical gray matter maps in the healthy oldest old: Findings from the McKnight Brain Aging Registry. Abstract presented at the Society for Neuroscience meeting, Chicago, IL.

Porges EC, Bharadwaj PK, Franchetti MK, Sims SA, Rezaei RF, Forbes MA, Merritt SS, Jessup CJ, Raichlen DA, Geldmacher D, Hishaw GA, Alperin N, Trouard TP, Wadley VG, Levin BE, Woods AJ, Rundek T, Visscher KM, Cohen RA, Alexander GA, Jensen G, Foster B, Puts NAJ. (November, 2019) Age-related decreases in cortical GABA concentrations assessed over the lifespan abate in cognitively intact adults over 85 years of age. Abstract presented at the Society for Neuroscience meeting, Chicago, IL.

Visscher KM, Stewart P, Sims SA, Bharadwaj PK, Franchetti MK, Rezaei RF, Merritt S, Jessup CJ, Raichlen DA, Porges EC, Geldmacher D, Hishaw GA, Trouard TP, Alperin N, Wadley VG, Levin BE, Woods AJ, Rundek T, Cohen RA, Alexander GE. (November, 2019) Functional connectivity in the healthy oldest old: Findings from the McKnight Brain Aging Registry. Abstract presented at the Society for Neuroscience meeting, Chicago, IL.

Woods AJ, Cohen R, Marsiske M, Alexander GE, Czaja SJ, Wu S. (2018) Augmenting cognitive training in older adults (The ACT Study): Design and methods. Contemporary Clinical Trials, 65, 19-32.

Budget Expenditures

For expenses from November 1, 2018—September 30, 2019

University of Arizona Expenditures

Personnel:	
Co-Investigator	$ 315
Research Coordinator	$ 4,855
Research Assistant	$ 4,316
Graduate Research Assistant	$ 2,859
Other:	
Research Supplies	$ 517
Advertising & Mailing	$ 786
MRI & Blood Collection	$ 23,466
Subject Pay & Parking	$ 3,295

University of Arizona total expenditures this period: $40,409

For expenses from November 1, 2018—September 30, 2019

University of Alabama at Birmingham Expenditures

Personnel:	
Co-Investigator	$ 7,379.65
Neurologist	$ 17,153.36
Research Coordinator	$ 7,346.48
Graduate Research Assistant	$ 34,578.13
Other:	
Research Supplies	$ 1,511.55
Mailing	$ 835.82
Copying and Printing	$141.34
MRI & Blood Collection	$3,125 *paid by an internal UAB CCTS grant obtained
Subject Pay & Parking	$2,770.48
Staff Travel	$633.91
Phone Service	$77.13

University of Alabama at Birmingham total expenditures this period: $ 75,552.85

For expenses from November 1, 2018—September 30, 2019

University of Florida Expenditures

Personnel:	
Co-Investigator	$ 00,000.00
Neurologist	$ 00,000.00
Research Coordinator	$ 53,913.86
Research Assistant	$ 20,588.32
Test Development Research Assistant	$ 00,000.00
Graduate Research Assistant	$ 00,000.00
Other:	
Research Supplies	$ 2,441.25
Advertising	$ 606.91
Mailing	$ 193.23
MRI & Blood Collection	$ 10,500.00
Subject Pay & Parking	$ 2640.00

University of Florida total expenditures to date: $ 90,883.57

For expenses from November 1, 2018—September 30, 2019

University of Miami Expenditures

Given the University of Miami MBAR funds have been expended, all MBAR efforts for this budget period were completely covered by complementary UM institutional funds. Of course, please note that we are fully committed to continuing to support our UM MBAR efforts with our UM institutional funds to complete the originally planned target enrollment.

Appendix II - UM McKnight Brain Institute Strategic Plan

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

Our **Mission** and **Vision** are:

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

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

Our major **Goals** are:

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

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

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

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

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

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 at 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 Principle 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 1st and 3rd in a list of top 20 articles in this domain published since 2013 and another article featured by AJNR news digest. Our first contribution employed our lamped parameter modeling of the cranio-spinal system to document reduced spinal canal compliance in IIH, which likely explains the associated with obesity through increased abdominal pressure (a). The following paper provided evidence for impaired CSF homeostasis and the involvement of the extra cranial venous drainage in the etiology of IIH (b). We documented increased intracranial CSF volume in the extra-ventricular spaces in IIH, consistent with the reduced ability of the spinal canal to accommodate the increased CSF volume. We made an important contribution by developing an automated method for quantitation of the eye globe deformation in IIH that provide quantitative measures of the optic nerve protrusion and posterior sclera flattening (c). Using these novel quantitative measures we found that the degree of papilledema severity is proportional to the nerve protrusion length, an observation that favors a "mechanical" over a "vascular cause of papilledema. We then correlated MRI and Optical coherence tomography (OCT) imaging of the globe and were able to translated the method to measured nerve protrusion with OCT, which is a more widely used imaging modality for the eye globes.

a. Tain RW, Bagci AM, Lam BL, Sklar EM, Ertl-Wagner B, Alperin N. (2011). Determination of cranio-spinal canal compliance distribution by MRI: Methodology and early application in idiopathic intracranial hypertension. Jour. Magn. Reson. Imag. 34:1397-404.

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

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

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

NNX16AG96G Alperin (PI) 03/01/16-09/28/17
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 intracranial pressure syndrome in astronauts

NNX14AB51G Alperin (PI) 08/01/14-06/31/17
Analyses of MR Imaging of CSF flow dynamics Pre and Post Space Flights
The goal of this directive contract from NASA is to identify hydrodynamic measures that are associated with developing elevated ICP in microgravity.
Role: PI

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: Brown, Scott Charles, Ph.D.

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

POSITION TITLE: Research Associate Professor of Public Health 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
West Virginia University; with honors	BA	1992	Psychology
University of Toronto, Canada	MA	1995	Psychology
University of Toronto, Canada	PhD	2000	Psychology

A. Personal Statement

I am a Research Associate Professor in the Department of Public Health Sciences at the University of Miami (UM) Miller School of Medicine, with a joint appointment in the UM School of Architecture. I have collaborated in research with the UM Built Environment, Behavior, and Health Group for 16 years. As a public-health researcher examining community environmental determinants of health on funded studies (NIH, HUD, RWJF), I have the expertise in research methodology and in assessing social determinants, including built environmental policies and initiatives in relation to populations' health. As PI on a federally-funded (HUD) research grant of neighborhood built-environment determinants of obesity and related chronic disease among Miami Medicare beneficiaries, I identified the role of greenery in diabetes, cardiovascular disease (CVD), depression and Alzheimer's disease (AD) among ~250,000 Miami Medicare beneficiaries. I am currently PI on three grants (Robert Wood Johnson Foundation Evidence for Action; Ed & Ethel Moore Alzheimer's Research Grant; Sylvester Center Pilot Grant) evaluating impacts of greenness and greening initiatives (tree planting) on health outcomes (CVD; AD; and cancer) in Medicare beneficiaries residing in low-income Miami neighborhoods. I participated in 3 NIH grants and 2 foundation grants (as Co-I, Project Director or Investigator) examining impacts of the built environment (e.g., mixed-land use such as stores near homes; "eyes on the street" such as porches) on health in Hispanics (NIH Grants DK-74687; AG-027527 & MH-63709; RWJ Grant No. 037377; PI: Szapocznik). I was Co-I on two foundation-funded research projects (IAC Foundation Research Grant; PI: Rundek) examining the relationship between the health-care built-environment (regional variation in vascular and echocardiography testing accreditation) and Medicare beneficiaries' cardiovascular outcomes. My interdisciplinary research team includes architecture, biostatistics, epidemiology, exercise physiology, geography, medicine, nutrition, public health, and urban planning. I provide expertise in science leadership, project management and analyses of "big data" to conduct cross-sectoral, cross-disciplinary research to understand those initiatives and strategies that best enhance the health outcomes for residents, particularly those at risk for obesity, CVD, stroke, AD, cognitive decline, physical inactivity, and social isolation. The overarching goal of my program of research is to inform policies at the local, regional and national levels that best promote health in underserved populations and communities. My most relevant publications are:

a. Wang, K., Lombard, J., Rundek, T., Dong, C., Gutierrez, C. M., Byrne, M. M., Toro, M., Nardi, M. I., Kardys, J., Yi, L., Szapocznik, J., & **Brown, S. C.** (2019). The relationship of neighborhood greenness to heart disease in 249,405 U.S. Medicare beneficiaries. *Journal of the American Heart Association, 8:*e010258. DOI: 10.1161/JAHA.118.010258.
b. **Brown, S. C.,** Perrino, T., Lombard, J., Wang, K., Toro, M., Rundek, T., Gutierrez, C. M., Dong, C., Plater-Zyberk, E., Nardi, M. I., Kardys, J., & Szapocznik, J. (2018). Health disparities in the relationship of neighborhood greenness to mental health outcomes in 249,405 Medicare beneficiaries. *Int J Environ Res Public Health,* 15:430.

c. **Brown, S. C.,** Lombard, J., Wang, K., Byrne, M., Toro, M., Plater-Zyberk, E., Feaster, D. J., Kardys, J., Nardi, M., Perez-Gomez, G., Pantin, H., & Szapocznik, J. (2016). Neighborhood greenness and chronic health conditions in Medicare beneficiaries. *American Journal of Preventive Medicine,* 58(1), 78-89. http://www.sciencedirect.com/science/article/pii/S0749379716000659. DOI:10.1016/j.amepre.2016.02.008.

d. **Brown, S. C.,** Lombard, J., Toro, M., Huang, S., Perrino, T., Perez-Gomez, G., Plater-Zyberk, E., Pantin, H., Affuso, O., Kumar, N., Wang, K., & Szapocznik, J. (2014). Walking and proximity to the urban growth boundary and central business district. *American Journal of Preventive Medicine, 47*(4), 481-486.

e. **Brown, S.C.,** Mason, C.A., Perrino, T., Lombard, J., Martinez, F., Plater-Zyberk, E., Spokane, A.R., & Szapocznik, J. (2008). Built environment and physical functioning in Hispanic elders: The role of "eyes on the street". *Environmental Health Perspectives,* 116 (110), 1300-1307.

B. Positions and Honors

Positions & Employment

1993-1999 Teaching Assistant, Department of Psychology, University of Toronto

1996-1998 Instructor, Department of Psychology, University of Toronto

1999-2002 Postdoctoral Fellow and Dissemination Team Leader, Center on Aging and Cognition: Health, Education, and Training (CACHET), Institute for Social Research, University of Michigan

2002-2003 Postdoctoral Fellow, Division of Rheumatology, University of Michigan Medical Center

2003-2007 Research Assistant Professor, Center for Family Studies, Department of Psychiatry and Behavioral Sciences, University of Miami Miller School of Medicine

2008-5/2018 Research Assistant Professor of Public Health Sciences (primary appointment), University of Miami School of Medicine

2011-Present Affiliated Faculty Member, Urban Studies Program, University of Miami College of Arts and Sciences

2012--Present Research Assistant Professor of Architecture (secondary appointment), University of Miami School of Architecture

6/2018-Present Research Associate Professor of Public Health Sciences and Architecture, University of Miami

8/2019-Present Invited Member, Faculty Advisory Committee, Abess Center for Ecosystem Science & Policy, University of Miami

Other Experience:

2010-Present Honorary Editorial Board Member, *Journal of Psychosocial Intervention (Intervención Psicosocial)* (new peer-reviewed international journal, to publish papers in both Spanish and English; Editor: Enrique Gracia, Universidad de Valencia, Spain)

2000-Present Ad-hoc invited reviewer for: *Acta Tropica; BMJ Open; Circulation: Cardiovascular Quality and Outcomes; Stroke; American Journal of Epidemiology; American Journal of Preventive Medicine; American Journal of Public Health; Preventive Medicine; PLoS ONE; Environment and Behavior; Environment & Planning B: Planning & Design; Health and Place; Landscape and Urban Planning; Sustainability; Health Environments Research & Design (HERD) Journal; Urban Studies; The Gerontologist; Journal of Gerontology: Social Sciences; Journal of Gerontology: Psychological Sciences; Gerontechnology; Journal of Aging and Health; International Journal of Aging and Human Development; Drugs and Aging; Journal of International Neuropsychological Society; Journal of Psychosomatic Research;* and, *Behaviour Research and Therapy.*

Honors

1991 Psi Chi, Psychology Honorary

1992 Graduated *summa cum laude,* West Virginia University

1993 Phi Beta Kappa

1996 Second Prize, Ontario Psychological Association's Thesis Awards, Master's Division

1993-1996 Connaught Fellowship, University of Toronto

1996-1998 Open Doctoral Fellowship, University of Toronto

1997-1998 Wilfred George Scott Fellowship in Gerontology, University of Toronto

2003 American Pain Society Citation Poster Award

2014-Present American Institute of Architects (AIA) Design & Health Research Consortium, Charter Member (One of 11 university teams (with Professor Lombard) selected nationwide to address cross-cutting issues in design & public health, and in 2017, was renewed for 3+ years, 2018-2020.)

C. Contributions to Science

1. ***Built environment, behavior and health.*** Our highly interdisciplinary team of behavioral scientists, physicians, methodologists and architects extended research on built environment-behavior-health to Hispanics; I conducted research on a sample that minimized the confound of choice on walkability; used a nationally available walkability measure to facilitate national replications, and established the role of greenery on weight-related disease (e.g., diabetes) among Medicare beneficiaries.
   a. **Brown, S. C.,** Lombard, J., Wang, K., Byrne, M., Toro, M., Plater-Zyberk, E., Feaster, D. J., Kardys, J., Nardi, M., Perez-Gomez, G., Pantin, H., & Szapocznik, J. (2016). Neighborhood greenness and chronic health conditions in Medicare beneficiaries. *American Journal of Preventive Medicine,* 58(1), 78-89. DOI: 10.1016/j.amepre.2016.02.008.
   b. **Brown, S. C.,** Lombard, J., Toro, M., Huang, S., Perrino, T., Perez-Gomez, G., Plater-Zyberk, E., Pantin, H., Affuso, O., Kumar, N., Wang, K., & Szapocznik, J. (2014). Walking and proximity to the urban growth boundary and central business district. *American Journal of Preventive Medicine, 47*(4), 481-486.
   c. **Brown, S.C.,** Mason, C.A., Perrino, T., Lombard, J., Martinez, F., Plater-Zyberk, E., Spokane, A.R., & Szapocznik, J. (2008). Built environment and physical functioning in Hispanic elders: The role of "eyes on the street". *Environmental Health Perspectives,* 116 (110), 1300-1307.
   d. Szapocznik, J., Lombard, J., Martinez, F., Mason, C.A., Gorman-Smith, D., Plater-Zyberk, E., **Brown, S.C.,** & Spokane, A. (2006). The impact of the built environment on children's school grades: The role of diversity of use in a Hispanic neighborhood. *American Journal of Community Psychology*, 38, 299-310.

2. ***Social environments, behavior and health.*** I led the first studies examining the relationship of the neighborhood social climate (a new construct encompassing multiple aspects of social life within neighborhoods, including supportive acts of neighboring, informal social ties, a lack of neighbor annoyance, and a sense of attachment to the neighborhood) -- to Hispanics' health outcomes, including cognitive and affective functioning, and walking. I was a contributing author on a paper examining neighborhood socioeconomic environment and physical activity in recent Hispanic immigrants.
   a. Affuso, O., Singleton, C. R., **Brown, S. C.,** Perrino, T., Huang, S., & Szapocznik, J. Associations between neighborhood socioeconomic environment and physical activity in Cuban immigrants. (2016). *Social Science & Medicine (SSM) – Population Health, 2,* 130-135. DOI: dx.doi.org/10.1016/j.ssmph.2016.02.010.
   b. **Brown, S. C.,** Huang, S., Perrino, T., Surio, P., Borges-Garcia, R., Flavin, K., Brown, C. H., Pantin, H., & Szapocznik, J. (2011). The relationship of the perceived neighborhood social climate to walking in Hispanic older adults: A longitudinal, cross-lagged panel analysis. *Journal of Aging & Health*, *23*(8), 1325-51, 2011. Epub 2011 Sep 1.
   c. **Brown, S.C.,** Mason, C. A., Perrino, T., Hirama, I., Verdeja, R., Spokane, A. R., Cruza-Guet, M. C., Lopez, B., Pantin, H., & Szapocznik, J. (2009). Longitudinal relationships between neighboring behavior and depressive symptoms in Hispanic older adults in Miami, Florida. *Journal of Community Psychology, 37*(5), 618-634.
   d. **Brown, S.C.,** Mason, C. A., Spokane, A. R., Cruza-Guet, M. C., Lopez, B., & Szapocznik, J. (2009). The relationship of neighborhood climate to perceived social support and mental health in older Hispanic immigrants in Miami, Florida. *Journal of Aging and Health, 21*(3), 431-459.

3. ***Psychosocial determinants of Hispanic older adults' health.*** I co-authored papers examining the psychosocial determinants of Hispanics' health. The four papers listed below examined a population-based cohort of urban Hispanic older adults in Miami, FL, for an NIH-funded study on which I was Project Director for seven years (MH-63709; AG-27527). We found that high levels of depressive symptoms may be associated with lower levels of walking over time in Hispanic older adults (paper 3b); however, too much social support may be detrimental for mental and physical functioning in this population (papers 3a & 3d). Additionally, low levels of cognitive functioning may presage depressive symptomatology, rather than vice versa, in Hispanic elders over time (paper 3c).
   a. Perrino, T., **Brown, S.C.,** Huang, S., Brown, C.H., Perez Gomez, G., Pantin, H., & Szapocznik, J. (2011). Depressive symptoms, social support, and walking among Hispanic older adults. *Journal of Aging & Health*, 23(6), 974-973. doi: 10.1177/0898264311404235.

b. Perrino, T., Mason, C. A., **Brown, S. C.,** & Szapocznik, J. (2010). The relationship between depressive symptoms and walking among Hispanic older adults: A longitudinal, cross-lagged panel analysis. *Aging and Mental Health, 14*(2), 211-219.
c. Perrino, T., Mason, C. A., **Brown, S. C.,** Spokane, A.R., & Szapocznik, J. (2008). Longitudinal relationships between cognitive functioning and depressive symptoms among Hispanic older adults. *Journal of Gerontology: Psychological Sciences*, *63B*(5), P309-P317.
d. Cruza-Guet, M.C., Spokane, A.R., Caskie, G. I. L., **Brown, S. C.,** & Szapocznik, J. (2008). The relationship between social support and psychological distress among Hispanic elders in Miami, Florida. *Journal of Counseling Psychology*, *55*(4), 427-441.

4. ***Behavioral health in patient populations.*** As a postdoctoral fellow, I conducted studies examining behavioral health in patient populations, including the role that age-related cognitive changes may play in older adults' processing of health information (papers 4a and 4c). In other research in behavioral rheumatology, I examined the relationship of chronic pain to behavioral health, including the impacts of arthritis pain on affective and cognitive functioning (paper 4b), and the relationship of environmental stressors to symptomatology in patients with chronic pain and fatigue (paper 4d).
    a. **Brown, S. C.**, & Park, D. C. (2003). Theoretical models of cognitive aging and implications for translational research in medicine. *The Gerontologist, Special Issue I:* 57-67, 2003.
    b. **Brown, S. C.**, Glass, J. M., & Park, D. C. (2002). The relationship of pain and depression to cognitive function in rheumatoid arthritis patients. *Pain, 96*(3):279-284.
    c. **Brown, S. C.**, & Park, D. C. (2002). Roles of age and familiarity in learning health information. *Educational Gerontology, 28*(8):695-710.
    d. Williams, D. A., **Brown, S. C.**, Clauw, D. J., & Gendreau, R. M. (2003). Self-reported symptoms before and after September 11 in patients with fibromyalgia. *Journal of the American Medical Association, 289*(13):1637-1638, 2003.

5. ***Broader environmental influences on public health and health-care.*** I examined the broader role of the built environment on public health and health-care, including in integrated vector management (paper 5a). I identified aspects of the health-care built environment that may impact quality of care and patient outcomes: Accreditation of vascular testing laboratories appears to be low nationally, particularly in regions with the highest prevalence of mortality from cardiovascular disease, including stroke (paper 5b). Other ongoing work suggests a hospital built environment intervention system (a change from private vs. semi-private rooms in a health-care system with the same health-care staff) may be linked to better patient outcomes among patients undergoing hip replacement surgery.
    a. Lizzi, K., Qualls, W., **Brown, S. C.,** & J. Beier. Expanding integrated vector management to promote healthy environments. (2014). *Trends in Parasitology,* 30*(8),* 394-400. Manuscript published online, August 2014. DOI: 10.1016/j.pt.2014.06.001.
    b. Rundek, T., **Brown, S.C.,** Wang, K., Dong, C., Farrell, M.B., Heller, G.V., Gornik, H.L., Hutchisson, M., Needleman, L., Benenati, J.F., Jaff, M.R., Meier, G.H., Perese, S., Bendick, P., Hamburg, N.M., Lohr, J.M., LaPerna, L., Leers, S.A., Lilly, M.P., Tegeler, C., Alexandrov, A V., & Katanick, S.L. (2014). Accreditation status and geographic location of outpatient vascular testing facilities among Medicare beneficiaries: The VALUE (Vascular Accreditation, Location & Utilization Evaluation) Study. *Vascular Medicine,* 2014. DOI: 10.1177/1358863X14547561.

Complete List of Published Work on ResearchGate:
https://www.researchgate.net/profile/Scott_Brown15

D. Additional Information: Research Support and/or Scholastic Performance
Ongoing Research Support:
Robert Wood Johnson Evidence for Action (RWJ E4A) Brown (Lead PI) & Szapocznik (PI) 2018-2021
Impacts of Greening on Cardiovascular Disease (CVD) in Low-Income Miami Neighborhoods
Addressing health disparities in access to greenery in lower socioeconomic status neighborhoods, which may be a risk/protective factor for obesity-related chronic diseases, this prospective longitudinal study will evaluate impacts of neighborhood greenness and greening interventions on a global cardiovascular index in 20,000 low-income Medicare beneficiaries, in 3,000 lower-income blocks of Miami-Dade County, Florida.
Role: Contact PI

Ed & Ethel Moore Alzheimer's Research Grant (FL-Dept. of Health) Brown (PI) 2019-2021
Impacts of Neighborhood Greenness & Greening Initiatives on Alzheimer's Disease in Medicare Beneficiaries
This prospective longitudinal study will evaluate impacts of neighborhood greenness/ greening interventions on Alzheimer's disease in 20,000 Medicare beneficiaries in 3,000 low-income blocks in Miami-Dade, FL.
Role: Principal Investigator

Sylvester Cancer Center Pilot Research Grant Brown (Lead PI) & Szapocznik (PI) 2019-2020
Neighborhood Greenness and Cancer Risk in Medicare Beneficiaries in Miami-Dade County, FL
This Sylvester Cancer Center pilot grant will evaluate the association of neighborhood greenness to 5 cancer diagnoses (breast, colorectal, endometrial, lung and prostate cancer) in ~250,000 Medicare beneficiaries.
Role: Contact PI

Centers for Disease Control & Prevention (CDC) Beier; Cummings; Dame; et al.(PIs) 2017-2022
Southeast Regional Center of Excellence in Vector-Born Disease (VBD): The Gateway Program
The Center uses current outbreaks of Zika & Dengue as a proving ground to develop innovative surveillance-response packages and decision-making tools. The aims are to 1) understand vector ecology, including built/social environments, in arbovirus infectious rates to optimize mosquito control; 2) break transmission of mosquito-borne arboviruses; 3) develop ecological models for vector-borne disease in Florida & the US.
Role: Investigator

Completed Research Support:

University of Miami U-LINK Phase I Grant Shearer (PI) 2019
Leveraging Untapped Opportunities in Place and Time: A Community-Based Child Well-Being Collaborative
The aims are: (1) build an interdisciplinary research team to examine individual child- and neighborhood-level factors on children's educational/health outcomes; (2) construct cross-disciplinary data integration tool and process for stakeholder input; (3) develop visioning process for long-term integrated data system infrastructure.
Role: Co-Investigator

CDC Partners In Community Health (PICH) Rivera (PI; Brown/Lombard/Nardi, Co-Is) 2015-2017
CDC Partnerships to Improve Community Health (PICH) Grant, Miami-Dade County
This was a follow-up to the CDC Communities Putting Prevention to Work Grant. Aims were to: 1) increase access to physical activity opportunities via healthy park-related policies and health messaging (Parks 305 web application); 2) monitor parks utilization/access before vs. after buildout of greenways in Miami-Dade County.
Role: PI of the University of Miami subcontract

Intersocietal Accreditation Commission (IAC) Rundek PI (Brown, Co-I) 2015-2016
Accreditation & Utilization of Cardiac Echo Laboratories in Medicare Beneficiaries: The VALUE-Echo Study
This research proposal investigated the proportion of IAC-accredited vascular testing facilities that perform echocardiographic diagnostic testing, identifying that almost all (>99%) echo testing facilities utilized by Medicare beneficiaries in the US were accredited, suggesting a uniformly high quality of testing nationwide.
Role: Co-Investigator

HUD H-21620-RG Brown & Plater-Zyberk (PIs) 2011-2015
Health Impacts of the Built-Environment among Miami Medicare Beneficiaries
This study investigated the health impact of the built-environment on ~250,000 Medicare beneficiaries in Miami-Dade County. Results revealed that comparing individuals living in addresses with +1 vs -1 SD from the mean on Normalized Difference Vegetation Index (NDVI) predicted reductions of: 10% in hyperlipidemia, 13% hypertension and 14% in diabetes. The results were strongest for lower SES Census blocks.
Role: PI

R01 DK 74687 Szapocznik (PI; Brown, Investigator) 2007-2013
Hispanics, Built Environment and Metabolic Syndrome
This prospective study examined effects of built environment walkability on physical activity and biomedical factors of 391 30-45 year-old, recent Cuban immigrants. Over 24 months, results revealed that - controlling for age, gender and dietary intake - built-environment walkability predicts the trajectory of physical activity, which is related to the trajectory of insulin resistance, which in turn is related to metabolic syndrome indicators.
Role: Investigator & Project Director

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- Director, Memory Disorder Center, Center for Cognitive Neuroscience and Aging, Department of Psychiatry and Behavioral Sciences,
Miller School of Medicine at University of Miami, FL
2009- Division Chief, Geriatric Psychiatry, Department of Psychiatry and Behavioral Sciences, Miller School of Medicine at University of Miami, Miami, FL
2015- Associate Clinical Professor, Department of Psychiatry and Behavioral Sciences, University of Miami Miller School of Medicine, Miami, FL

Other Experience and Professional Memberships

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

Honors

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

C. Contribution to Science

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

   a. **Crocco, E.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

   b. **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.

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

   d. Loewenstein, 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 not well understood. I have published several journal articles related to cognition and dementia in the elderly. This includes a widely cited meta-analysis and meta regression analysis relating early depression as a risk factor for Alzheimer's disease (AD). I have also published on the relationship of depression and other psychiatric symptoms in MCI and cognitive changes related to geriatric depression in general.

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

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

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

d. Duara, R, Loewenstein, 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:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1Pg52WCUHj95C/bibliography/47914940/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

XZ703 (Crocco, Elizabeth-PI) 07/01/2018-06/30/2019
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

5R01AG047649-04 (Loewenstein, David-PI) 02/01/2015-01/31/2020
NIH/NIA
Novel Detection of Cognitive and Functional Impairment in the Elderly
The role of the Co-investigator is to examine the utility of a unique set of neuropsychological and daily functioning tests in individuals ranging from cognitively normal (NC) to those with preclinical mild cognitive impairment (preMCI) and those with amnestic mild cognitive impairment (aMCI), in combination with select diagnostic biomarkers and tests such as atrophy on structural MRI, amyloid, tau and phosphorylated tau biomarkers in CSF and in predicting rate of cognitive decline.
Role: Co-investigator

7AZ14 (Curiel, Rosie-PI) 02/23/2017-03/31/2019
Florida Department of Health
A Consortium to Study Precision-based Computerized Assessment for the Detection of Mild Cognitive Impairment in Older Adults
The role of the Co-investigator is to measure for early detection of cognitive impairment of Hispanic and non-Hispanic elderly persons by administering three novel computerized tests to 120 older adults 40 normal elderly,

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

1R01AG055638-01A1 (Curiel, Rosie-PI) 04/01/2018-01/31/2023
NIH/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

5R014G047146-05 (Devanand, Davangere-PI) 03/01/2015-01/31/2019
NIH/NIA
Treatment of Psychosis and Agitation in Alzheimer's Disease
I am a Co PI with a subcontract involved in this study that compare changes in agitation/aggression with or without psychosis in patients with AD who receive 12 weeks of randomized, double-blind treatment with lithium or placebo.
Role: Co-investigator

AARGD-17-531255 (Cabrera, Delia-PI) 12/01/2017-02/28/2020
Alzheimer's Association
Non-invasive Ocular Screening Approach to Identify Early Biomarkers in AD
The Co-Investigator will advise on all work outlined in the proposal and in protocol refinement, manuscript preparation and dissemination of data. She will recruit appropriate patients, oversee safety issues, periodically review experimental data and statistical analysis regarding integrating the experimental findings. She will meet any clinical administrative requirements including compliance with the IRB. She will also advise on the overall perspective and direction of the study.
Role: Co-investigator

CAPI015A2201J (Crocco, Elizabeth-PI) 11/17/2016-08/31/2024
Novartis Pharmaceuticals
A randomized, double-blind, placebo-controlled, two cohort parallel group study to evaluate the efficacy of CAD106 and CNP520 in participants at risk for the onset of clinical symptoms of Alzheimer's disease.

CAPI015A2201J (Crocco, Elizabeth-PI) 11/17/2016-08/31/2021
Novartis Pharmaceuticals
A randomized, double-blind, placebo-controlled, two-cohort parallel group study to evaluate the efficacy of CAD106 and CNP520 in participants at risk for the onset of clinical symptoms of Alzheimer's disease

NEUP11AD2 (Crocco, Elizabeth-PI) 08/19/2016-08/18/2020
Neurim Pharmaceuticals
A randomized, Double-Blind, Parallel-Group, Placebo-Controlled, Dose-Rannfing study of Piromelatine in patients with mild dementia due to 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: 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: 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 first year as an Instructor at the University of Miami Miller School of Medicine. My research interests as a graduate student at Princeton University focused 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 and the development the "Assessment of Situational Judgement" questionnaire. 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 Principle 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. **Getz, S. J.**, & Levin, B. (2017). Cognitive and neuropsychiatric features of early Parkinson's disease. Archives of Clinical Neuropsychology, 32(7), 769-785.
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.

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. 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., Lloyd, K., Lai, V., Grilli, M.D., Wilson, R.C. (In preparation). LabPHIT: A novel laboratory assessment of phishing emails correlates with real-world phishing efficacy.

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

<u>Ongoing Research Support</u>

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 research that harnesses neuroplasticity through interventions such as neuromodulation and exercise to promote functional and cognitive improvements in different neurologic populations. I am the Director of the Neuromotor Plasticity Laboratory, and an Assistant Professor of Clinical Physical Therapy and Neurology at the University of Miami Miller School of Medicine (UMMSM). Additionally, I am Faculty at the Transcranial Magnetic Stimulation Intensive Course, Berenson-Allen Center for Non-invasive Brain Stimulation, Beth Israel Deaconess Medical Center, Harvard Medical School. My early clinical studies have been directed at using transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) to characterize neuroplasticity and to augment rehabilitation targeting functional hand use after spinal cord injury. In addition to my interest in physical health, my work in recent years has focused on better understanding how to use exercise to promote neuroplasticity for improving cognitive brain health for aging individuals. The research study proposed in this KL2 application will investigate the mechanisms underlying cognitive benefits after an 8-week aerobic exercise intervention in adults aged 55+ years by combining the use of a non-invasive assessment of synaptic neuroplasticity by TMS and the examination of potential effect modifications by genetic factors. In addition, this KL2 Award will allow me to me to advance my academic career by obtaining training and mentorship from a distinct and cross-disciplinary group of established researchers at UMMSM and Harvard, combining the fields of clinical and translational research in older adults, genetics, neurophysiology and cognition. The successful completion of the research and training aims will allow me to approach my long-term goal of developing exercise interventions that can be individually tailored to promote cognitive brain health in aging adults, which will be the focus of a future K or R proposal. 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 KL2 award.

B. Positions and Honors

Positions and Employment

2017- 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

2018 Dr. Gomes-Osman was selected to participate in the prestigious Training for Grantsmaship in Rehabilitation Research (TIGRR) that took place January 9 to 13, 2017 at the Wild Dunes Resort in Charleston (Isle of Palms) South Carolina, hosted by the Medical University of South Carolina. The TIGRR Workshop is funded by NIH/NICHD grant number T15HD074546.
2007 Humberto de Castro Lima Award by the Bahiana School of Medicine and Public Health-Salvador, Brazil as Outstanding Student in the year of 2007.
2005 Fundacao de Amparo a Pesquisa do Estado da Bahia (FAPESB) Scholarship for Young Scientists. First non-MD student to be awarded this scholarship by the State of Bahia [Brazil] Foundation for Research

Other Experience and Professional Memberships

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. Furthermore, I found that while the majority of available evidence supports aerobic exercise, other exercise types such as resistance training and low-intensity yoga were also seen to improve cognitive performance in older adults. This study advances the field by producing practical, evidence-based dose parameters of exercise to improve cognitive function. I served as primary and corresponding author on this publications, which 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.

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. 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.

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 (single-pulse TMS, paired-pulse TMS, TMS Plasticity), and determine the minimum number of pulses to achieve an accurate estimation of the mean and 95% confidence interval for these measures. This work adds to the literature by providing guidelines to achieve reliable measurements using TMS, and has the potential to decrease the variability often seen with TMS measures across the literature. I served as a co-author in this study.

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.

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.

C5. **Characterizing the influence of neuromodulation on neuroplasticity after acute peripheral nerve injury.** My pre-doctoral work measured neuroplasticity in the form of axonal sprouting in a mouse model of sciatic crush lesion. I contributed to the validation of the sciatic static index for mice, a widely used and highly cited functional measure of sciatic nerve injury. In addition, I contributed to studies demonstrating that clinically available neurostimulation approaches such as TENS and low-frequency pulsed electromagnetic fields impair peripheral regeneration when applied in the cute stage after a crush lesion to the sciatic nerve in mice. I served as a co-author in these studies.

1. Baptista AF, Goes BT, Menezes D, Gomes FC, Zugaib J, Stipursky J, **Gomes JR**, Oliveira JT, Vannier-Santos MA, Martinez AM; PEMF fails to enhance nerve regeneration after sciatic nerve crush lesion. ***Journal of the Peripheral Nervous System***; 2009; 285-293.
2. 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.
3. 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.

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

1. 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; in press.
2. **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.
3. **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.
4. 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.
5. **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.
6. **Gomes-Osman J**, Tibbett JA, Poe BP, Field-Fote E. Priming for Improved Hand Strength in Persons with Chronic Tetraplegia: A Comparison of Priming-augmented Functional Task Practice, Priming Alone, and Conventional Exercise Training. ***Frontiers in Neurology***; 2016; 1-13.
7. 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.
8. Chang WH, Fried PJ, Saxena S, Jannati A, **Gomes-Osman J**, Kim YH, Pascual-Leone A; Optimal number of pulses as outcome measures of neuronavigated transcranial magnetic stimulation; ***Clinical Neurophysiology***; 2016; 2892-2897.
9. **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.

10. **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.
11. **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.
12. **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.
13. 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.
14. 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.
15. 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.

D. Research Support

Current

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 will investigate mechanisms underlying cognitive benefits after an 8-week exercise intervention in sedentary adults over 55 years of age. In this study, I will combine the use of a non-invasive assessment of synaptic neuroplasticity by Transcranial Magnetic Stimulation (TMS), neuropsychological outcome measures, and examine potential effect modifications by genetic brain-derived neurotrophic factor (BDNF) and and apolipoprotein E (APOE) factors. Role: Principal Investigator. Grant amount: 75% of current salary plus $32,500 per year for the award period.

2017 **National Institutes of Health (NIH) R01 5R01AG053163-02.** A personalized health behavior system to promote well-being in older adults. This project consists in adapting an existing mobile application to promote increased participation in physical exercise, from middle-aged adults to the older adult population. **Role: Consultant (Exercise intervention development).** Grant amount $579,139.

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.

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

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

BIOGRAPHICAL SKETCH

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

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

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

POSITION TITLE: Clinical 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: 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, 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 direct the Schoninger Neuropsychology and Clinical Neuroscience Teaching Program. I supervise the clinical and research activities of PhD graduate students, interns and post doctoral fellows in the Division of Neuropsychology. I have taught the graduate level course, Foundations of Neuropsychology, for over 30 years. I work collaboratively with research teams in Neurology,Neurosurgery, 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. I am a co-investigator on the Bugher AHA grant and a Dept of Defense study examining brain metabolites underlying pain associated with traumatic injury. Also, I am the director of clinical outcomes on the Scythian Bioscience Project, a study examining the role of cannabinoids in mild traumatic injury. 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. 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

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 behavioral and cognitive decline in normal aging and neurodegenerative disease. As the Schoninger Professor or Neurology, I oversee the Division of Neuropsychology, a major training and research site that evaluates over 300 patients a year examining age related cognitive change as well as pathological behavioral alterations associated with degenerative disease. I have published extensively on cognitive change across the lifespan.

1. Kelley, R.E., Chang, JY, Scheinman, NJ, **Levin, BE**, Duncan, RC, Shih-Chang, L: Transcranial doppler ultrasonographic assessment of cerebral artery flow velocity during cognitive activity. Stroke, 1992; 23:9-14.
2. Tomer, R**, Levin, BE**, Differential affects of aging in two verbal fluency tasks. Perceptual and Motor Skills, 1993; 76: 465-466
3. **Levin, BE**, Katzen, H.L., Klein, B., Llabre, M. Cognitive decline affects subject attrition in longitudinal research. Journal of Clinical and Experimental Neuropsychology. 2000, 22 (5), 580-586.
4. Geldmacher, DS, **Levin BE**, Wright CB. Characterizing healthy samples for studies of normal cognitive aging. Front. Ag. Neurosci., 2012, 4:6

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 Eecutive 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

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
(B. Levin 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.

Scythian Bioscience 08/01/2016-7/30/2021
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

7 R01 NS 029993 (PI, Sacco) NIH/NINDS 02/01/03-03/31/21
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

National 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 DIT . I am Co-Leader of the Clinical Core for the 1Florida, Alzheimer's Disease Research Center (ADRC) as well Director of Scientific Project 2. 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. I have been leader of Biostatistics Cores for a number of NIH funded program project grants.

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);
Associate Editor, Journal of Alzheimer's Disease
Triage Editor, American Journal of Geriatric Psychiatry; Member Institute of Medicine Subcommittee for Determining Functional Capacity and the Need for Representative Payees (2015);
American Psychological Association (Division 40: Neuropsychology; Division 20: Aging; National Academy of Neuropsychology)

C. Contributions to Science (185 Peer Reviewed Journal Articles)

1. Development of tests for early detection of neurodegenerative diseases. I am the author of 185 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 (Selected Ongoing)

1R01AG061106-01 (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 - 01/31/2020
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: 7AZ18 State of Florida Ed and Ethel Moore Grant
PI: David Loewenstein PhD Project Title: Brain Amyloid Load and Novel Cognitive Measures in Diverse Ethnic Groups 2/2017- 2/2020 This project will examine amyloid load and its relation to structural MRI and novel cognitive stress tests in African American and Hispanic Elderly at Risk for AD. .6 CM

1P50AG047266-OA1 (NIA/NIH) Todd E Golde (PI) 08/15/2015 – 05/31/2020
Project II University of Florida – Mt. Sinai Medical Center AD Research Center
Core B will provide baseline clinical and imaging biomarker studies and longitudinal evaluations of 490 study participants, of which at least 50% will be Hispanic.
Role: (Loewenstein, PI) / Clinical Core (Co-Leader, Investigator) 1.2 CM

2PO1AG017211-16 (NIA/NIH) Czaja, Sara J (PI) 07/01/2015 - 03/31/2020
Data Management: Center on Research and Education for Aging and Technology Enhancement (CREATE IV)
CREATE is a highly successful, productive, and cohesive multidisciplinary Center for research and education on aging and technology.
Role: Project Leader .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: Roger Christopher McIntosh, Ph.D.

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

POSITION TITLE: Assistant Professor

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
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	Post-doc	07/2014	Psychoneuroimmunology CV Behavioral Medicine

A. Personal Statement

My program of research broadly examines the effects of aging and disease on neuropsycholgical outcomes in ethnically-diverse persons living the Human Immunodeficiency Virus (HIV). My particular focus is the manifestation of cardio-autonomic and inflammatory-immune dysregulation on the central nervous system (CNS) via biobehavioral pathways. My approach to examining these CNS manifestations include the use of electroencephalography, structural and functional neuroimaging. This data is collected and analyzed in conjunction with neuroendocrine and inflammatory-immune biomarkers to elucidate biobehavioral risk for neuropsychological impairment in persons living with chromic cardiovascular and HIV disease. Moreover, this research is conducted in ethno-racially diverse community samples of predominately low socioeconomic status with the aims of (1) elucidating ethno-racial disparities in these biobehavioral risk factors for neuropsychological impairment and (2) increasing community awareness and participation in health and cognitive aging research. My work is currently funded by an NHLBI-funded mentored K01 award to increase diversity in biomedical research. Through this award mechanism my current work examines how the manifestation of peripheral cardiovascular disease and HIV-related immunosuppression contributes to disease of the central nervous system, within the context of culturally specific psychosocial stressors. This work is of importance based upon the disproportionate burden of neuropsychiatric impairment, cardiovascular disease, and chronic inflammation commonly observed in African American (AA) adults living with HIV. As a member of the ORE core my role will be to develop strategies and work with community partners in order to enhance recruitment, retention and community engagement of AA with Alzheimer's research initiatives in South Florida.

B. Positions and Honors

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 Membership

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. Contributions to Science

Contribution #1 HIV+ women have blunted psychophysiological reactivity to emotional stimuli.

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

Contribution #2 The neurocognitive bases of emotion dysregulation and its contribution to HIV disease progression.

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 there to be a cognitive vulnerability for depression in persons with HIV

Dementia (6). Furthermore, we have linked executive dysfunction to alexithymia, i.e., difficulty identifying and describing feelings in long-term survivors with HIV (7). This study noted cross-sectional associations between the alexithymia trait and poorer neuroendocrine, psychological and HIV disease outcomes. Our longitudinal research further shows longitudinal associations between trait alexithymia and viral load that was mediated by increases in stress, anxiety and depression (8).

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- 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

8- 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

Contribution #3 Behavioral, immune, and autonomic risk factors for cardiovascular disease (CVD) in HIV

Persons living with HIV are at an increased risk for CVD comorbidity. My work to this point has focused on behavioral, immune and autonomic phenotypes in HIV that may pose an increased risk for CVD. Anger and hostility are associated with an increased risk for CVD. HIV is also known as an inflammatory disease and many have looked at inflammation as a risk factor for atherosclerosis. We have reviewed literature showing an inverse relationship between markers of chronic inflammation and cardioautonomic functioning in persons living with HIV/AIDS and shown that despite advancements in the medication HIV patients show a deficit in heart rate variability (HRV) in the era of anti-retroviral therapy and that this reduction in HRV is skewed towards greater vagal withdrawal, compared to healthy controls, resulting in elevated sympathetic arousal (9). Most recently, we captured neural correlates of the symptom burden of inflammation and depression (10) in addition to cardio-autonomic dysfunction in ethnically-diverse older adult women living with HIV and/or hypertension (11, 12).

9-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

10- 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

11- 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

12- 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

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

Ongoing Research Support

K01 HL139722-01 McIntosh (PI) 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: 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
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 Peritz Scheinberg's Cerebral Vascular Disease Research Laboratories 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 Peritz Scheinberg Endowed Professor in 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) and over the last 5 years, we have been investigating the role of Physical Exercise in improving cognitive function following cerebral ischemia. 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.

My lab has a long track record of training undergraduate and graduate students and many postdoctoral trainees. Most of my trainees have secured fellowships and have been exceptionally productive during their years of training in my lab and have continued to excellent postdoctoral positions, or faculty or pharmaceutical positions.

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. A major area of research in my group is to define the pathological mechanisms in the brain that ensue following cardiac arrest. We have targeted multiple aspects of the pathology that include synaptic dysfunction, cognitive impairments and cerebral blood flow derangements. We have shown that PKCε activation provides neuroprotection while activation of PKCδ 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.

- Stradecki-Cohan, H. M., Youbi, M., Cohan, C. H., Saul, I., Garvin, A. A., Perez, E., Dave, K. R., Wright, C. B., Sacco, R. L. & Perez-Pinzon, M. A. Physical Exercise Improves Cognitive Outcomes in 2 Models of Transient Cerebral Ischemia. *Stroke* 48, 2306-2309, (2017). PMID:28663509
- 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
- 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
- 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

2. 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.

   - 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
   - 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
   - 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
   - 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.
   - 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
   - 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
   - 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
   - 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

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/pubmed/?term=perez-pinzon

D. Research Support.

Active
R01 NS34773-15 **Perez-Pinzon (PI)** 6/1/15-5/31/20
NIH/NINDS
Ischemic Preconditioning: Mechanisms of Neuroprotection
The major goal of this project is to study the signaling pathways that lead to ischemic preconditioning neuroprotection.

R01 NS34773-15 **Perez-Pinzon (PI)** 6/1/17-5/31/22
NIH/NINDS
Metabolic master regulators for ischemic neuroprotection
The main goals were the elucidation of signaling pathways involved in the fate of brain mitochondria following cerebral ischemia.
R01 NS45676-08 **Perez-Pinzon (PI)** 6/1/07-5/31/17
NIH/NINDS

Mechanisms of Neuroprotection against Cardiac Arrest
The major goal of this project is to study the mechanisms of synaptic and vascular dysfunction and putative neuroprotective agents following cardiac arrest.
Pending

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.

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

BIOGRAPHICAL SKETCH

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 under mentorship of Dr. Miguel A. Perez-Pinzon. Since joining CVDRC I have participated in several projects studying different aspects of cerebral ischemia which resulted in several peer-reviewed publications. Presently, my laboratory works on research projects with ultimate goal of lowering the incidence and severity of cerebral ischemia. One of the projects is focused on improving neurological health of diabetics by decreasing the severity and incidence of cerebral ischemia in diabetics as cerebral ischemia and heart disease are the most serious complications of diabetes, accounting for more than 84% of the mortality among diabetics. My lab also evaluates efficacy of red blood cell microparticles (RMPs) in preventing hematoma growth following experimental sICH in rats. In this collaborative project, with Dr. Perez-Pinzon and colleagues, we propose to determine importance of metabolic signaling pathways involved in cerebral protection ischemia. Following qualifications makes me well-suited as a collaborator on this grant: (1) Experience of my laboratory on models of cerebral ischemia. (2) Track record on studies evaluating effects of cardiac arrest on outcomes and ischemia protection. And (3) Presently, I have ongoing collaborations with Dr. Perez-Pinzon. Based on my past training and experience in the field of cerebral ischemia and neuroprotection, I believe that I am uniquely qualified to participate in this project and I also trust that I will be able complete my part in this project with utmost competence.

B. Positions and Honors

Professional experience:

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

Scholarship / Award:

- Stanley J. Glaser Foundation biomedical research award, University of Miami Miller School of Medicine 2007 - 2008.
- Recipient of award of Bursaries for young scientists to attend Brain'05 conference (Amsterdam, The Netherlands, June 2005) organized by the International Society for Cerebral Blood Flow and Metabolism.
- Received "Hari Ohm Ashram Prerit Shri Bhaikaka Inter-University Smarak Trust" Award, Sardar Patel University, Vallabh Vidyanagar, Gujarat, India for two research papers in year 1999-2000.
- Recipient of award of The Lady Tata Memorial Trust Research Scholarship, Mumbai (Bombay), India for years 1996-98.
- Recipient of Scholarship from Higher Education Commissioner, Government of Gujarat, India for year 1996.

Membership in Professional Societies:

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

Role as a reviewer:

- AHA Brain 5 Study section Spring 2013, Spring 2014, Spring 2015
- AHA Brain 1 study section Fall 2013
- Bando Giovani Ricercatori "Alessandro Liberati" 2013 (Italian funding agency)
- Abstract reviewer, International Stroke Conference 2014, 2015, 2016
- AHA Innovative Research Grant Study section Fall 2014, Fall 2015, Fall 2016
- Croatian Science Foundation 2014
- Abstract reviewer Brain 2015, Brain 2017 (International symposium on Cerebral blood flow, metabolism and function)
- AHA Cardiac Arrest Resuscitation Basic Study section; Spring 2015, Spring 2016
- AHA Cardiac Arrest Resus CL/Pop Merge with Basic Science Study section; Fall 2015
- AHA scientific sessions abstracts June 2016
- NIH- Acute Neural Injury and Epilepsy Study Section (ANIE) 6/2015, 10/2015, 2/2016, 6/2016, 10/2016, 2/2017, 10/2017, 6/2018, 10/2018, 2/2019, 6/2019
- AHA Brain 3 Study section Spring 2016, Fall 2016, Spring 2017
- Co-Chair AHA Brain 3 Study section Spring 2017
- Chair and Reviewer, AHA Brain 2 Study section; Fall 2018
- Reviewer, AHA Allen Brain Health Phase 1 review committee, Fall 2018
- Reviewer, AHA Allen Brain Health Phase 2 review committee, Fall 2018
- Reviewer, FWF Austrian Science Fund, Fall 2018

C. Contribution to Science

1. Cerebral ischemia and heart disease are the most serious complications of diabetes, accounting for more than 84% of the mortality among diabetics. Epidemiological studies of cerebral ischemia suggest that diabetes increases both the risk of incidence and exacerbates the consequences of cerebral ischemia. Hyperglycemia is one of the contributing factors. In clinical studies, intensive anti-diabetic therapy was able to delay the onset and slow the progression of secondary complications of diabetes. The major side-effect of intensive diabetic therapy is hypoglycemia. Using the streptozotocin-diabetic rat, we observed that recurrent hypoglycemia (RH) renders the insulin-treated diabetic (ITD) rat brain more sensitive to global cerebral ischemia and results in greater brain damage. Presently, we are investigating the mechanism by which RH increases ischemic damage in ITD.
    a. Dave K. R., Pileggi A., Raval A. P. Recurrent hypoglycemia increases oxygen glucose deprivation-induced damage in hippocampal organotypic slices. Neurosci Lett. 496:25-9, 2011.

b. Dave K. R., Tamariz J, Desai KM, Brand FJ, Liu A, Saul I, Bhattacharya SK, Pileggi A. Recurrent hypoglycemia exacerbates cerebral ischemic damage in streptozotocin-induced diabetic rats. Stroke. 42:1404-11, 2011.
c. Rehni A. K., Nautiyal N., Perez-Pinzon M. A., Dave K.R. Hyperglycemia / hypoglycemia-induced mitochondrial dysfunction and cerebral ischemic damage in diabetics. Metab Brain Dis. 2014 (In press)

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

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

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

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

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

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

D. Research Support

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

R21NS094896 (IGNITE mechanism) Dr. Dave, P.I. R21 phase: 2/1/2016 – 1/31/2017
NIH/NINDS R33 phase: 2/1/2017 – 1/31/2020
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

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

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
• University of Miami, Miller School of Medicine, Miami, USA	Postdoc	04/2015	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: 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 and PI of present application, laid a strong foundation for me in the basics essential for understanding ischemic neurodegeneration. I continued to study the mechanism of neuronal death following cerebral ischemia that is a consequence of cardiac arrest or stroke, and I am well versed in various *in vivo* and *in vitro* models of cerebral ischemia as well as in imaging, electrophysiology, and behavior and molecular biology techniques. Our most relevent initial publication using model of cardiac arrest are listed below. 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.

Dr. Bramlett (Co-PI of current project) and I are longtime collaborators and currently Co-PIs on an ongoing study to determine efficacy of whole body vibration intervention for stroke recovery in nicotine-exposed rats supported by Florida Department of Health. 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.

a. **Raval AP**, Schatz M, Bhattacharya P, d'Adesky N, Rundek T, Dietrich WD, Bramlett HM. Whole body vibration therapy after ischemia reduces brain damage in reproductively senescent female rats. Int J Mol Sci 2018 Sep 13; 19(9). pii:E2749. Doi: 10.3390/ij,s19092749. PMID: 30217051.

b. **Raval, A**., Dave, K.R, Saul, I., Gonzalez, G.J. and Diaz, F. (2012) Synergistic inhibitory effect of nicotine plus oral contraceptive on mitochondrial complex-IV is mediated by estrogen receptor-ß in female rats. *J Neurochem.* 121:157-167. PMCID: PMID: 22248091

c. **Raval AP**, Borges-Garcia R, Diaz F, Sick TJ and Bramlett H. (2013) Oral contraceptives and nicotine synergistically exacerbate cerebral ischemic injury in the female brain. *Translational Stroke Research 4:402-412.*

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
- 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
- American Heart Association (AHA)- Innovative grant reviewer Fall 2014 - 2017
- American Heart Association- Brain 2 study section reviewer Spring 2015 – 2017
- American Heart Association- Career Development Award Committee Fall 2017 - Present
- NIH-NNRS Study Section Spring 2017 Ad-hoc
- AHA- Transformational Project Award Organ Sciences reviewer 2018 Spring
- VA- Rehabilitation Research and Development grant reviewer Fall 2019

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 = 25

1. Studies form my laboratory simulating the conditions of nicotine exposure produced by cigarette smoking and the oral contraceptive (OC) regimen of women in female rats provides evidence that the severity of ischemic hippocampal damage is far greater in female rats simultaneously exposed to OC

than to nicotine alone. These studies also demonstrated that the concurrent exposure of OC and nicotine reduces endogenous 17β-estradiol levels and inhibits ER-β signaling in the brains of female rats. My study demonstrated that concurrent exposure to nicotine and OC impaired ER-β-mediate mitochondrial respiration at the complex-IV level due to lower protein levels of its catalytic subunits in the hippocampus of female rats.

a. **Raval AP****, Dave KR, Saul I, Gonzalez GJ, Diaz F. Synergistic inhibitory effect of nicotine plus oral contraceptive on mitochondrial complex-IV is mediated by estrogen receptor-β in female rats. J Neurochemistry 2012; 121(1):157-67.
b. **Raval AP****, Borges-Garcia R, Diaz F, Sick TJ and Bramlett H. Oral contraceptives and nicotine synergistically exacerbate cerebral ischemic injury in the female brain. Translational Stroke Research 2013 4:402–412
c. **Raval AP****, Sick JT, Gonzalez GJ, Defazio RA, Dong C and Sick TJ. Chronic nicotine exposure inhibits estrogen-mediated synaptic functions in hippocampus of female rats. Neuroscience Letters 2012; 517(1):41-6
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. 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.

a. **Raval AP****, Borges-Garcia R, Moreno WJ, Perez-Pinzon MA and Bramlett H.Periodic 17β-estradiol pretreatment protects rat brain from cerebral ischemic damage via estrogen receptor-β. Plos One 2013;8(4):e60716
b. **Raval AP****, Saul I, Dave KR, DeFazio1 RA, Perez-Pinzon MA, Bramlett H. Pretreatment with a single estradiol-17β bolus activates CREB and protects CA1 neurons against global cerebral ischemia. Neuroscience. 2009; 160:307–18. (PMCID: 2711690)
c. **Raval AP****, Bramlett H, Perez-Pinzon MA. Estrogen preconditioning protects the hippocampal CA1 against ischemia. Neuroscience. 2006; 141(4):1721-30.
d. de Rivero Vaccari JP**,** Bramlett HB, Perez-Pinzon MA, **Raval AP****.** Estrogen preconditioning: a promising strategy to reduce inflammation in the ischemic brain Conditioning Medicine, 2019, 2(3): 106-113.

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

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

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. On the contrary, nicotine exposure exacerbates post-ischemic inflammation and injury in female rats. Furthermore, microglia -the primary immune cells of the brain- play a crucial role in progression and resolution of the neuroinflammatory response. Our research also focused to identify the role that microglia play in the sexual dimorphism that exists in the response to central nervous system (CNS) injury.

a. 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)
b. 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.
c. Kerr N, Dietrich WD, Bramlett HM, **Raval AP*** Sexually dimorphic microglia and ischemic stroke. CNS Neuroscience & Therapeutics 2019 (in press)

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

D. Active Support

Florida Department of Heath#7JK01 03/01/2017- 02/29/2020
Whole body vibrations improves stroke outcome in nicotine-exposed rats
These proposed studies aim to identify mechanisms by which WBV reduces frailty and improves stroke outcomes, and provide a basis for future targeted interventions to enhance recovery and ameliorate cognitive deficits after stroke in women smokers.
Principal Investigator: Dr. Helen Bramlett
Role: Co-PI (35% efforts)

NIH-NINDS 01/08/2017- 07/31/ 2022
Mitochondria and cerebral ischemia: Intracellular Signaling
Principal Investigator: Dr. Pérez-Pinzón
Role: Co-investigator (15% efforts)

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)

Completed Research Support:

American Heart Association- Grant-in-aid
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

Department of Neurology's 2016 Pilot Research Support Program 01/1/16-6/31/17
Mechanism of neuroprotection against cerebral ischemia
Role: PI

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, MD PhD**

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

POSITION TITLE: Professor of Neurology and Public Health Sciences, Scientific Director, McKnight Brain institute, Director of Clinical Translational Research Division, University of Miami Miller School of Medicine

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

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

A. Personal Statement

I have served as Scientific Director of The Miami Evelyn F. McKnight Brain Institute for the past 2 years. I also serve as PI of the Miami MBAR (McKnight Brain Aging Registry) and lead MBRF Inter-Institutional Interventional Cognitive Core that awards 2 pilot awards annually. As Scientific Director of the McKnight Brain institute (MBI), I am involved in cognitive and neuroimaging studies for age-related cognitive decline, MRI imaging phenotypes of neurodegeneration and cognitive and imaging analytical quantitative methods. I am a neurologist, neuroscientist and epidemiologist by training with an extensive experience in vascular 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 in neurology. 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 at the Miami CTSI (Clinical Translational Science Institute). I have a 25+year track record of NIH funding as PI, collaborative investigator, and research and career development mentor. I have been conducting cross-disciplinary research in aging brain health and disease for the past 20 years using clinical, genetics and neuroimaging approaches. I have been a productive investigator with over 400 publications in the area of brain atherosclerosis and cognitive decline in aging populations. I am a true collaborative clinical researcher with established extensive collaborations on the large NIH-funded studies at Columbia University (NOMAS, INVEST and U01 eMERGE), at Albert Einstein in the Bronx (Einstein Aging Study), and national and international consortia (NINDS SiGN, ISGC). My current clinical translation research focuses on age-related memory loss, genetic and epigenetic determinants of cognitive performance and multi-modal interventions against age-related cognitive decline, cognitive impairment and dementia.

These four peer reviewed publications highlight my relevant experience:

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 ;61(4):519-24. 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. Della-Morte D, Ricordi C, Rundek T. The fountain of youth: role of sirtuins in aging and regenerative medicine. Regen Med. 2013; 8(6):681-3. PMC24147522
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,Vascular 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 Division	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	Miller School of Medicine, Univ. of Miami, Miami, FL
2018-	Scientific Director, McKnight Brain Institute	Miller School of Medicine, Univ. of Miami, Miami, FL

Honors

1995	Humbolt Award, Neurosonology Laboratory, University of Ulm, Germany
1996	George Soros Scholarship, Neurology Seminars, University of Krems, Austria
1997-99	Fulbright Award and Scholarship, Neurological Institute, Columbia University, New York, NY
2006-	Nassau Women Physicians Foundation Award for Stroke Research in Women; Long Island, NY
2009-14	President, the Neurosonology Community of Practice, American Institute of Ultrasound in Medicine
2012-	Member, the Board of the Directors, Intersocietal Accreditation Committee (IAC)-Vascular
2012-	Consulting Editor of *Stroke*
2013-	Editorial Board Member of *Neurology, Cerebrovascular Disease, Journal of Ultrasound in Medicine*
2014-	Member, the Clinical Standards Committee, American Institute of Ultrasound in Medicine (AIUM)
2015-	Secretary, the Executive Committee, Intersocietal Accreditation Committee (IAC)-Vascular
2015-	Reviewer, NIH section ZHL1 CT-K (C1)1 – LRP
2015	The American Heart Association Core Vitae Award for Stroke
2018	The Evelyn F. McKnight Chair for Learning and Memory in Aging

C. Contribution to Science

1. Extracranial and intracranial imaging markers of carotid disease. Vascular imaging has been my primary tool to investigate atherosclerosis. I have been in the field of ultrasound for over 25 years. I was trained in ultrasound technologies by the inventor of transcranial Doppler (TCD) Dr. Rune Aaslid in early 80's and have been a part of an international brain hemodynamic research group since. I coauthored the first consensus document on carotid ultrasound imaging. I have been a part of large international collaborations on the progression of subclinical atherosclerosis (PROG-IMT, USE-IMT). I have applied arterial vessel wall principles to improve arterial compliance using a new technique of integrated power Doppler and changes of vessel wall diameter during cardiac cycle. In addition, I have helped advancing the field of brain circulation investigations using TCD to 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 the past 10 years as PI of 2 NINDS R01 grants and a NINDS K24 award, investigator 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, Jood K, Laurie CC, Lee JM, Lindgren A, Markus HS, McArdle PF, McClure LA, Mitchell BD, Schmidt R, Rexrode KM, Rich SS, 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 (from over 390 publications):
https://www.ncbi.nlm.nih.gov/myncbi/collections/bibliography/40707409/

D. Research Support

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.

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

U54TR002736-01/1KL2TR002737 Sacco (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 culturalize health sciences.
Role: Director of KL2 and Translational Workforce Development

NIH/NIDCR R01 DE 13094 Desvarieux (PI) 06/15/06-05/31/23
Oral Infections, Carotid Atherosclerosis and Stroke (INVEST)
This cohort study will examine the effect of chronic periodontal disease and inflammation as a risk factor for stroke and carotid atheroma progression.
Role: Co-Investigator

NIH/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 (PIs) 09/30/11-08/31/23
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 (PIs) 07/1/11-06/30/20
The Albert Einstein Study Program Project in Aging
This is a Cerebral Hemodynamics Study of Aging of the AES program project aimed to study the vascular mechanisms of normal aging, MCI and dementia using TCD challenge test.
Role: PI of TCD Core

NIH/NINDS U10 NS086528 Romano (PI) 09/30/13-07/31/23
Miami Regional Coordinating Center for NINDS Stroke Trials Network
PI: J Romano; T. Rundek, Training Director
The major goal of this award is to function effectively as a Regional Coordinating Center for the NINDS stroke trials and to enhance quality and efficiency of NINDS stroke trial implementation at the Miami site.
Role: Training Director

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

NIH/NHLBI N01-HC65234 Schneiderman (PI) 06/01/14-05/31/23
Hispanic Community Health Study-Study of Latinos (HCHS-SOL) Miami Field Center

The HCHS/SOL is a multi-center epidemiologic study designed to determine the role of acculturation in disease prevalence and to identify health risk factors in Hispanics/Latinos.
Role: Adjudication Core investigator

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

NIH/NIDA R01DA034589 Kumar (PI) 09/15/14-08/31/19
Predictive Biomarkers of CVD Risk in Diverse HIV-1+ Cocaine Abusers
This project will investigate risk factors for CVD in the target population (e.g. HIV-1 infected and cocaine abusers) and evaluate the impact of traditional CVD risk intervention on biomarkers and carotid IMT.
Role: Co-Investigator

NIH/NGRI Columba GENIE (GENomic Integration with EHR) Weng (PI) 09/01/15-05/31/19
This project addresses the needs of patients and clinicians for using genomic knowledge for disease prevention. We will develop scalable methods for next generation phenotyping using EHR data.
Role: Co-Investigator

Prior Research Support

NIH/NINDS U54 NINDS SPIRP U54NS081763 Sacco (PI) 01/01/13-12/31/18
Stroke Prevention/Intervention Research Program in Hispanics
The goal is to develop high-impact stroke disparities interventions with the ability to reduce stroke disparities in distinct Hispanic groups in Miami and Puerto Rico using effective and culturally appropriate methods.
Role: PI of Core C and PI of Supplement- Stroke Outcome in Women

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

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

NIH/NINDS R01 NS 065114 Rundek (PI) 07/01/10-06/30/17
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.

NIH/NINDS K24 NS 062737 Rundek (PI) 09/30/09-08/31/17
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.

NIH/NINDS U01 U01 NS 069208 Kittner (PI) 04/01/10-3/31/16
The NINDS International Stroke Genetics Consortium Study: Ischemic Stroke Genetics
PI: S. Kittner, U Maryland; T. Rundek, Site PI
This was a GWAS that established a large 11-study collaboration of unique scale to bring together the world's leading clinician-scientists in stroke genetics.
Role: Site 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: 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. I am fully committed to a clinical translational research agenda within my department and institution and have enhanced this mission through recruitments of academic faculty and the support of research infrastructure for training the next generation of translational scientists. As former president of the American Heart Association and immediate past president of the American Academy of Neurology, I am fully committed to advancing scientific collaborations and building partnerships for clinical and translational brain research.

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 Sacco (Director) 07/01/19-06/31/20
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) 01/01/93-07/31/20
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

U54 (NS 081763) (NCE) Sacco (PI) 01/01/13-03/31/19
Hispanic Stroke Prevention Intervention Research Program
Aims: The major goals of this project are to create the Florida Puerto Rico Stroke Registry to identify and reduce stroke disparities in acute stroke and secondary prevention
Role: PI

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

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. A large fraction of these patients has dementia disorders including Dementia with Lewy body and Parkinson's disease dementia. 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-present	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	Co-director of Brain Endowment Bank, University of Miami

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. 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

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

a. **Sun X ***, Beglopoulos V*, Mattson M, Shen J. Hippocampal Spatial Memory Impairments Caused by the Familial Alzheimer's Disease-linked Presenilin 1 M146V Mutation *Neurodegenerative Dis* 2005; 2:6-15
b. **Sun X.**, Steffens D.C., AU R., Folstein M., Summergrad P., Yee J., Rosenberg I., Mwamburi D.M., Qiu W.Q.. Amyloid-associated depression: a prodromal depression of Alzheimer disease? *Arch Gen Psych* 2008, 65: 542-50
c. **Sun X.;** Dong C. Levin B., Crocco E., Loewenstein D., Zetterberg H., Blennow K., Wright C. APOE ε4 carriers may undergo synaptic damage conferring risk of Alzheimer's disease. *Alzheimers & Dement:* 2016 Nov;12(11):1159-116
d. Headley A, De Leon-Benedetti A, Dong C, Levin B, Loewenstein D, Camargo C, Rundek T, Zetterberg H, Kaj Blennow K, Wright C**, Sun X,** and on the behalf of the Alzheimer's Disease Neuroimaging Initiative. *Neurology*, 2017 (in press)

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

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

4. **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) 09/1/13-8/31/21 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) 08/01/2019-07/31/2020 1.8 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

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

XZ703.A1 Crocco, Elizabeth (PI) 07/01/2018-6/30/2020 0.60 calendar
Florida Department of Elder Affairs $212,191
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 $418,549
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

McKnight Brain Institute, University of Miami Miller School of Medicine

Toyama (clinical trial) PI: Barry Baumel 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.

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