Northwestern Medicine®

Mesulam Center for Cognitive Neurology and Alzheimer's Disease

25th Annual ALZHEIMER DAY

ABSTRACT BOOK

THURSDAY, MAY 9, 2019

WELCOME

Dear Friends and Colleagues:

It is my great pleasure to welcome you to the 25th annual Alzheimer Day at Northwestern. It is hard to believe that this tradition has been maintained year after year without interruption for a quarter century. This is also the first Alzheimer Day when I have the incredible privilege of addressing you as the Director of the recently renamed Mesulam Center for Cognitive Neurology and Alzheimer's Disease.

The fundraising campaign that led to this renaming also led to the building of beautiful and greatly expanded new space for our programs, the establishment of a professorial chair for research on Alzheimer's disease, and the activation of a much needed research endowment. These transformational developments will allow successful programs to grow and novel ones to be established.

None of this would have been possible without the inspired work of my colleagues on the Faculty of the Center and the generous philanthropy of our friends and Community Advisory Board members. Special recognition goes to the Davee Foundation and its Executive Administrator Mr. Craig Grannon for enabling this campaign to reach its goal in such a short time. The names of all those who have so generously sustained the work of our Center through major philanthropic gifts are listed on a plaque at the reception area of our new space on Tarry 8.

In view of the growth that lies ahead, I initiated changes of leadership. Emily Rogalski, PhD was recruited to serve as Associate Director of the Mesulam Center for Cognitive Neurology and Alzheimer's Disease. As you may know, a major component of the Mesulam Center is the NIH-funded Alzheimer's Disease Center (P30), which I established in 1996 and led until 2018. As of October 2019, Robert Vassar, PhD was recruited to serve as the Principal Investigator and Director of the P30 and will be assisted by Sandra Weintraub, PhD and John Disterhoft, PhD who agreed to serve as its Associate Directors. Additional noteworthy developments include the appointment of Tamar Gefen, PhD to serve as Assistant Clinical Core Leader for the P30, the appointment of Firas Wehbe, MD, PhD to lead our Data Management and Biostatistics programs and the appointment of Ian Grant, MD to lead our Clinical Trials programs. I also want to take this opportunity to express my profound gratitude to Fred Rademaker, PhD who just retired after dedicated and inspired leadership of biostatistics in our Center for the past 25 years.

It is no secret that experimental treatments of Alzheimer's disease keep failing. We are beginning to realize that reversal of established disease may be more difficult than anticipated and that the best hope lies in prevention. This will be the topic of this year's Mendelson Lecture by Eric M. Reiman, MD. Dr. Reiman is Executive Director of the Banner Alzheimer's Institute and Chief Executive Officer for Banner Research. He is Professor of Psychiatry at the University of Arizona, University Professor of Neuroscience at Arizona State University, Clinical Director of Neurogenomics at the Translational Genomics Research Institute (TGen) and Director of the Arizona Alzheimer's Consortium. He is a world-renowned leader and pioneer in the field of Alzheimer's Disease and also a superb lecturer. The annual Mendelson Lectureship and related educational programs at the Mesulam Center are generously supported by gifts from Mr. and Mrs. Robert and Linda Mendelson and Family.

Following the keynote presentation, and partly overlapping with lunch, we will have a poster session where clinicians and scientists affiliated with our Center will showcase their recent work in the areas of aging, dementia and Alzheimer's disease. The posters will cover topics ranging from basic science to patient care, from emerging medical treatments to behavioral interventions. In the afternoon, we will hold a program, featuring Borna Bonakdarpour, MD, focusing on the role of music and the arts for non-pharmacologic interventions. The psychosocial programs and life enrichment interventions for our patients and families are generously supported by gifts from The Glen and Wendy Miller Family Foundation.

Marsel Mesulam, MD
Ruth Dunbar Davee Professor of Neuroscience and Neurology
Director, Mesulam Center for Cognitive Neurology and Alzheimer's Disease

THANK YOU

The Mesulam Center for Cognitive Neurology and Alzheimer's Disease would like to thank the Mendelson Family for their generous support of this event.

In honor of Robert and Linda Mendelson's 50th wedding anniversary, David and Blythe Mendelson, Sharon and Scott Markman, and Debbie Mendelson Ponn established the Mendelson Lectureship, which brings a keynote speaker to the Mesulam Center's annual Alzheimer Day.

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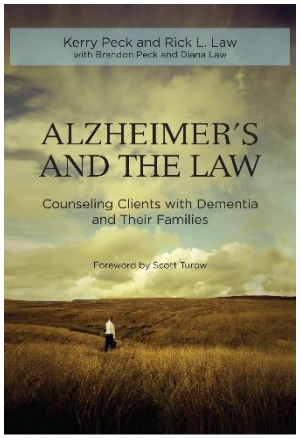

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SCHEDULE OF EVENTS

25TH ANNUAL ALZHEIMER DAY

Thursday, May 9, 2019

11:30 AM

Welcoming Remarks
M.-Marsel Mesulam, MD, Director, Mesulam Center for Cognitive Neurology and Alzheimer's Disease, and Ruth Dunbar Davee Professor of Neuroscience, Feinberg School of Medicine

Presentation of Marie and Carl Duncan Prize in Memory Research
John Disterhoft, PhD, Associate Director, Ernest J. and Hattie H. Magerstadt Memorial Research Professor in Physiology, Feinberg School of Medicine

12:00 PM

The Mendelson Lecture
"Preventing Alzheimer's"
Eric M. Reiman, MD, Executive Director, Banner Alzheimer's Institute and CEO, Banner Research Professor of Psychiatry, University of Arizona University Professor of Neuroscience, Arizona State University Clinical Director of Neurogenomics, Translational Genomics Research Institute Director of Arizona Alzheimer's Consortium

1:00 PM

Lunch and Scientific Poster Viewing

2:15 PM

Welcoming Remarks
Darby Morhardt, PhD, LCSW, Research Associate Professor, Mesulam Center for Cognitive Neurology and Alzheimer's Disease and Department of Preventive Medicine, Feinberg School of Medicine

"Alzheimer's and the Law"
Kerry Peck, Peck Ritchey, LLC

2:30 PM

The Miller Family Symposium
"Music, the Arts and Human Experience"
Borna Bonakdarpour, MD, Assistant Professor of Neurology at Feinberg School and pianist
Frank Babbitt, violist, Lyric Opera of Chicago Orchestra
Good Memories Choir - directed by Jonathan Miller
Arts for Brain Health Coalition - Scott Lundius
Caregiving Family Presentation

4:00 PM

Adjourn

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DARBY MORHARDT, DIRECTOR OF OUTREACH, RECRUITMENT AND EDUCATION

Thank you to all Mesulam Center staff and faculty who have made this day a success!

The Mesulam Center appreciates your dedication and commitment to making this day possible.

LIST OF VENDOR TABLES BY NUMBER

The numbers for each vendor correspond to the Map of Vendor Fair on Page 9.

1 Peck Ritchey, LLC
2 Silverado
3 Home Care Assistance
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8 Senior Living Experts
9 Dutton & Casey
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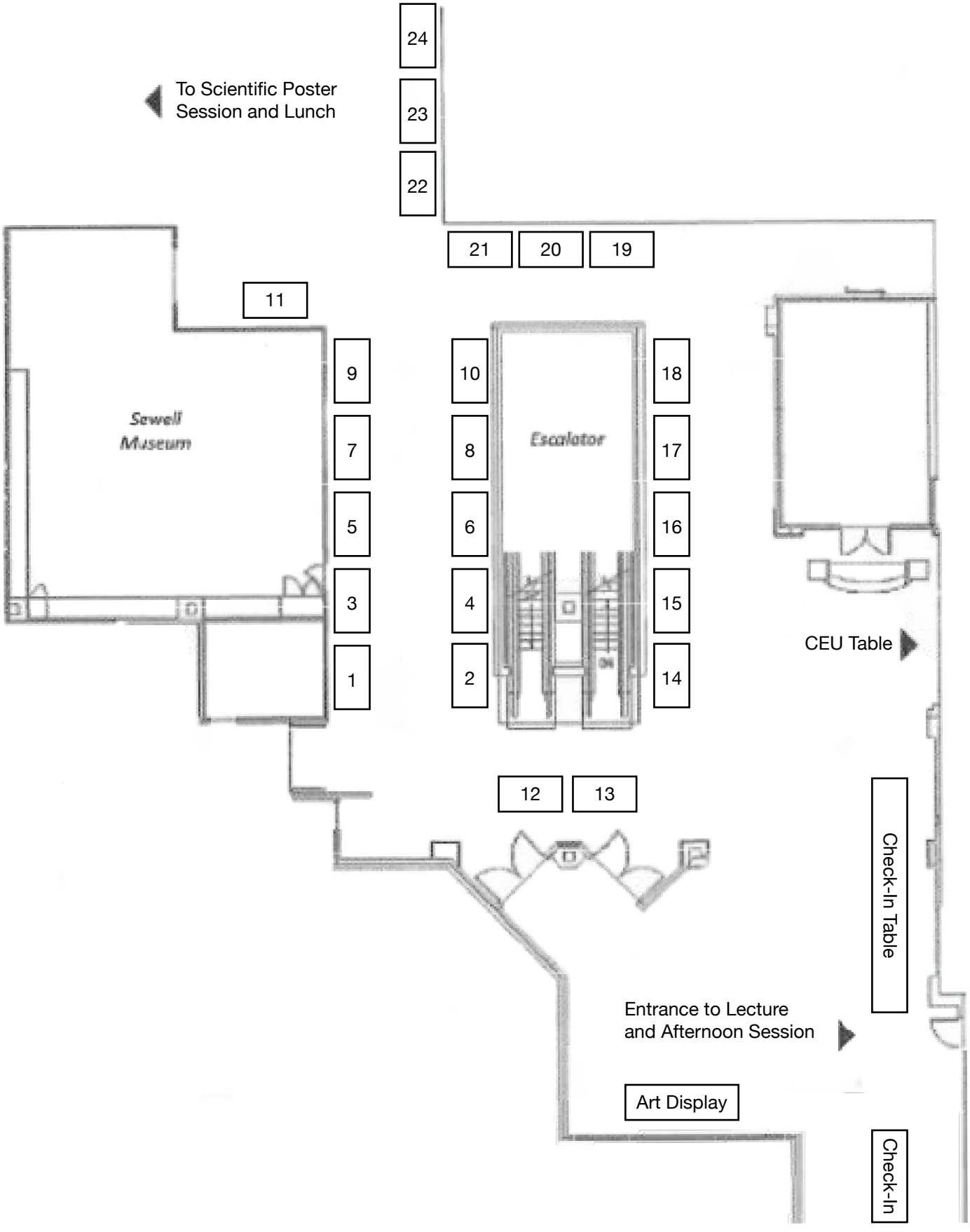
11 White Oaks at McHenry
12 Northwestern Mesulam Center for Cognitive Neurology and Alzheimer's Disease
13 Northwestern Mesulam Center Research
14 Elderwerks Educational Services
15 All Trust Home Care
16 Arden Courts
17 SeniorBridge
18 CJE SeniorLife
19 Gentle Home Services
20 Home Instead Senior Care
21 Gardant Management Solutions
22 Skyline Village
23 Geriatrics
24 Health Learning Center

MAP OF VENDOR FAIR



MORNING SESSION

Marsel Mesulam, MD

Marsel Mesulam is the Ruth Dunbar Davee Professor of Neuroscience, founder and Director Emeritus of the National Institutes of Health Alzheimer's Disease P30 Center at Northwestern University (established in 1996), and current Director of the Mesulam Center for Cognitive Neurology and Alzheimer's Disease Center. He served as president of the Organization for Human Brain Mapping, Vice President of the American Neurological Association, and Chair of the Medical Advisory Board of the Association for Frontotemporal Degeneration. His research has addressed the connectivity of the cerebral cortex in the primate brain, anatomy of human cholinergic pathways, representation of cognitive functions by large-scale networks, and neurobiology of dementias. He received the Potamkin Prize from the American Academy of Neurology, the Javits Award from the United States National Institutes of Health, the McKnight Foundation Director's Award, and the Bengt Winblad Life Achievement Award from the Alzheimer's Association. He held the Robert Wartenberg and Houston Merritt lectureships of the American Academy of Neurology. He served on the editorial boards of Brain and Annals of Neurology. His textbook, Principles of Behavioral and Cognitive Neurology, is used by multiple training programs. His current research focuses on the biology of neurocognitive networks and on the pathophysiology of focal dementias. His trainees in clinical, cognitive and basic neuroscience lead major research programs in the United States and abroad.

MENDELSON LECTURE
"PREVENTING ALZHEIMER'S"

Eric Reiman, MD

Dr. Reiman is Executive Director of the Banner Alzheimer's Institute, Chief Executive Officer of Banner Research, Professor of Psychiatry at the University of Arizona, University Professor of Neuroscience at Arizona State University, Clinical Director of Neurogenomics at the Translational Genomics Research Institute (TGen), and Director of the Arizona Alzheimer's Consortium.

He received his undergraduate and medical education at Duke University and his Psychiatry Residency Training at Duke and Washington University, and launched his career in brain imaging research under the mentorship of Marcus Raichle at Washington University in St. Louis. He has played leadership roles in brain imaging, brain mapping, and genomics research, the unusually early detection and tracking of Alzheimer's disease (AD), and the accelerated evaluation of Alzheimer's prevention therapies. He has also sought to advance new models of biomedical research collaboration and dementia care.

Dr. Reiman and his Banner Alzheimer's Institute colleagues established the Alzheimer's Prevention Initiative (API) to launch a new era in Alzheimer's prevention research. API includes public-private partnerships, prevention trials and biomarker development programs in cognitively unimpaired persons at high genetic and/or biomarker risk for AD, unusually large registries and innovative programs to support enrollment in these and other studies, precedent-setting trial data and biological sample sharing agreements, and other efforts to help find and support the approval, affordability and availability of prevention therapies as soon as possible.

Dr. Reiman is an author of more than 400 publications, a principal investigator of six current NIH grants, and a member of the National Advisory Council on Aging (NIA Council). He is a recipient of the Potamkin Prize for his pioneering contributions to the study of preclinical AD and the accelerated evaluation of AD prevention therapies.

MORNING SESSION

John Disterhoft, PhD

John Disterhoft and his laboratory group are studying the neurobiology of associative learning in the young and aging mammalian brain with in vivo and in vitro techniques using eyeblink conditioning, spatial learning and fear conditioning as behavioral model systems.

Many of their ongoing experiments focus on the hippocampus, a paleocortical region involved in transferring information during learning from short- to long-term memory storage. Single-neuron ensemble recording in the conscious animal is used to localize and functionally characterize the cell types involved in laying down the "memory trace" in the hippocampus and associated medial temporal lobe regions. In parallel experiments, biophysical measurements are made from brain slices taken from trained animals to define ionic mechanisms for the conditioning-specific alterations in postsynaptic intrinsic currents that have been observed. Synaptic alterations related to conditioning are also being explored in brain slices. Cellular and systems alterations in aging brain that may underlie learning deficits and agents which may be useful in enhancing learning rates in aging are being studied.

An overall goal of their studies is to understand both the mechanisms of learning and of memory storage. Hippocampus is especially involved in the initial acquisition of associative tasks. More permanent memory storage occurs in other brain regions after a process called memory consolidation. Some of their recent experiments are focusing on the manner that prefrontal, sensory and temporal lobe neocortical regions, and the caudate nucleus of the basal ganglia change during both initial learning and after longer term storage of the eyeblink conditioned response. After regions are defined that store memories of the conditioned response after consolidation, more focused cellular and molecular studies can be done to characterize how this storage occurs at the subcellular level.

The portion of Dr. Disterhoft's research program investigating slow outward currents during learning in aging has received two consecutive MERIT award designations from the National Institute on Aging. He also has funding from the NIA to investigate the synaptic changes occurring in aging hippocampus using cutting edge molecular and 2P imaging approaches. The other portion of his research program involves studying the activity of many single neurons and doing brain imaging in conscious animals during learning and memory consolidation. Dr. Disterhoft directs the Northwestern University NIA funded predoctoral and postdoctoral training program on Mechanisms of Aging and Dementia and the NU IN-PREP postbaccalaureate training program, is Associate Director of the Northwestern University Alzheimer's Disease Center and is Executive Director of the Northwestern University Behavioral Phenotyping Core.

THE MILLER FAMILY SYMPOSIUM
"MUSIC, THE ARTS, AND HUMAN EXPERIENCE"

Darby Morhardt PhD, LCSW

Darby Morhardt, PhD, LCSW is Associate Professor in the Mesulam Center for Cognitive Neurology and Alzheimer's Disease and Department of Preventive Medicine, Northwestern University Feinberg School of Medicine. She directs the Mesulam Center's Outreach, Recruitment and Education Core, the Miller Family Quality of Life Enrichment Programs, in addition to clinical social work services for the Northwestern Medicine Neurobehavior and Memory Clinic.

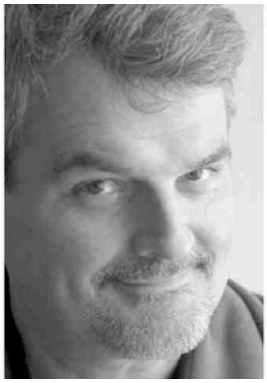
The focus of Dr. Morhardt's work has been on the impact of cognitive impairment on the individual, family and their social networks. Areas of clinical research include the experience of families living with dementia; the process of tailoring care to specific needs and symptoms; and the development and evaluation of quality-of-life enrichment programs, support groups and other therapeutic interventions. These interventions include the award-winning Buddy Program, a unique experience that pairs persons with dementia as mentors to first year medical students and is offered in other universities through the United States and Italy.

Dr. Morhardt is responsible for organizing the Mesulam Center's community engagement to increase dementia education, awareness, research participation and quality of life enhancing programs throughout Chicago especially in underrepresented groups. She is a leader in the Illinois Cognitive Resources Network, she has been involved in coordinating efforts of dementia friendly communities, particularly the collaborative initiative to position the Carter G Woodson library on Chicago's far south side as the city's first dementia friendly library.

Borna Bonakdarpour, MD, FAAN

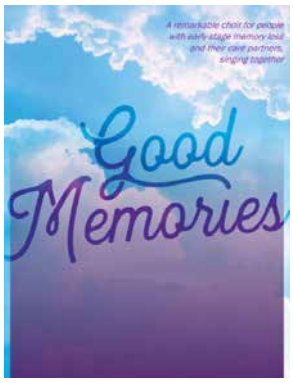
Dr. Bonakdarpour is a faculty member of the Northwestern Mesulam Center and an assistant professor of neurology at Northwestern Feinberg School of Medicine department of neurology. He received his medical degree from Tehran University of Medical Sciences with a minor in music and piano performance. His doctoral research on melodic intonation therapy for stroke patients received international attention and brought him to Northwestern University for his research fellowship in aphasia rehabilitation and neuroimaging of language. Following that, he finished his residency in neurology at The University of Arizona, and then completed the Florane and Jerome Rosenstone cognitive neurology fellowship at the Mesulam Center. He is board certified in neurology and behavioral neurology. His research is funded by a five year career development award from the NIH to study pathophysiology of primary progressive aphasia using functional and structural neuroimaging. Dr. Bonakdarpour is the principal investigator of Musical Bridges to Memory TM research project in collaboration with Institute for Therapy through the Arts and Silverado Memory Care. He has been an invited lecturer on the topic of music and medicine at many venues, including Chicago Symphony Orchestra's SoundPost and Shirley Ryan Ability Lab. As an accomplished pianist, he has been performing for fundraising and scientific events related to music and medicine in collaboration with eminent Chicago musicians.

THE MILLER FAMILY SYMPOSIUM
"MUSIC, THE ARTS, AND HUMAN EXPERIENCE"



Frank Babbitt

Frank Babbitt is a member of the Lyric Opera of Chicago Orchestra. He revived a BA in Music and Drama from Lawrence University and a Master of Music in Violin Performance from SUNY Stony Brook. He is a frequent performer with many local ensembles including the Grant Park Orchestra and the Chicago Philharmonic. He is a past member of the Chicago Symphony Chorus and has appeared in opera, oratorio and recital. He has performed a solo version of Dickens' "A Christmas Carol" each December since 2007, often as a benefit for arts organizations and educational and other not for profit groups. He is currently on the faculty at Loyola University of Chicago.



Good Memories Choir

Good Memories is a choir for people with early-stage memory loss, who sing along with their care partners. Dedicated singer volunteers help to create the unique community atmosphere of Good Memories, where everyone feels supported in dealing with a common struggle. A professional conductor and pianist lead rehearsals of 3-part music, usually arrangements of melodies that are familiar to the singers. People with memory loss and their care partners who sing in Good Memories enjoy doing something uplifting together; it's a place where laughter and joy happen every week. The rehearsals lead to a free public concert at Fourth Presbyterian Church. Especially where drug interventions have failed to make any impact on memory loss, Good Memories is a quality-of-life intervention that participants say is the high point of their week.

Good Memories is part of the larger organization of the Sounds Good! Choirs, co-founded by Sandy and Jonathan Miller in 2016. With 7 Sounds Good! Choirs and more than 400 singers rehearsing every week, Sounds Good! is the Chicago area's largest choral-music organization for older adults. Sandy Siegel Miller serves as program director of Good Memories, and Jonathan Miller is artistic director and CEO. More information is available at soundsgoodchoir.org or goodmemorieschoir.org.

Anna Brothers and Mary Blackwell

Anna Brothers and her mother Mary Blackwell are both retired school teachers. Ms. Blackwell is from Mississippi and Ms. Brothers is from Alabama. Both love to sew, knit, and crochet. Ms. Brothers is an accomplished gardener and baker and the owner of Sweet Lassteens Desserts for All Occasions.

THE MILLER FAMILY SYMPOSIUM
"MUSIC, THE ARTS, AND HUMAN EXPERIENCE"

Arts for Brain Health Coalition

Founded in 2016, Arts for Brain Health Coalition is a city-wide consortium of arts and healthcare leaders dedicated to supporting people with memory loss and those who care for them. The first Arts for Brain Health convening was held in the summer of 2017 where the original seven organizations combined their efforts to produce a half-day festival in Lincoln Square featuring workshops designed to creatively engage this population. Since this initial success, the Coalition has subsequently expanded to include additional partners in order to provide more opportunities for this work in communities throughout the city. In 2018, the Coalition launched its first events at Woodson Regional Library and the National Museum of Mexican Art in addition to a return to the North Side. Coalition members have included the Art Institute of Chicago, Chicago Dance Therapy, Good Memories Choir, Hubbard St. Dance Chicago, LaBrocha, Lookingglass Theatre, Loyola University Museum of Art, Mesulam Center for Cognitive Neurology and Alzheimer's Disease at Northwestern University Feinberg School of Medicine, Old Town School of Folk Music, and Rush University's Alzheimer's Disease Center. Arts for Brain Health Coalition convenes on a monthly basis throughout the year and is currently planning its programs for September 2019 and beyond.

Our mission statement reads: Arts for Brain Health Coalition activates collaboration between healthcare and arts providers to design and provide programs that use creative engagement to improve the lives of people with memory loss and those who care for them.

Scott Lundius is a co-founder of Arts for Brain Health Coalition and currently oversees organizational strategy and development efforts for The Legacy Project, a Chicago non-profit dedicated to preserving LGBT contributions to world history while inspiring an affirming and inclusive future. He has more than 30 years of experience leading educational initiatives and organizational development for groups including the Prospect Park Alliance, Taos Center for the Arts, Marwen and Old Town School of Folk Music.

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Professor of Psychiatry, Neurology, and Psychology

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The Mesulam Center Advisory Board was formed to increase public awareness and knowledge of the Center, and to help garner ongoing philanthropic support for the Mesulam Center's programs and facilities. The Board helps promote the Center both locally and nationally, and assists in securing the funding necessary to position the Center among the premier Alzheimer's research and patient care facilities in the United States.

If you are interested in learning more about the Mesulam Center Advisory Board, please contact Thongsy Singvongsa at 312-503-2832 or visit our website:
http://www.brain.northwestern.edu/about/giving.html

MARIE AND CARL DUNCAN PRIZE IN MEMORY DISORDERS RESEARCH

Professor Carl Duncan is widely regarded as the first to demonstrate the existence of memory consolidation, showing the vulnerability of recently stored memories. His landmark work is cited more than half a century later. Upon his passing in 1999, his wife, Dr. Marie Duncan, who received her medical degree from Northwestern, set up the Duncan Fund to encourage research and discussion on issues related to memory.

In addition to an annual lecture on fundamental research on memory in the name of Professor Duncan, the Duncan Fund inaugurated in 2006 the Marie and Carl Duncan Prize in Memory Disorders Research to award accomplishments in clinically relevant arenas of inquiry.

MARIE AND CARL DUNCAN AWARD WINNERS

2018
Melvin Thompson and Darby Morhardt
REACH to Faith 2.0: Building the Dementia Friendly Woodson Library

2017
Borna Bonakdarpour
Altered Language Network Connectivity in Primary Progressive Aphasia

2016
Ashlee E. Rubino
Internalized Tau_{45-230} Aggregates Can Spread Tau Pathology and Neuronal Degeneration in Alzheimer's Disease and Related Disorders

2015
Dina Simkin
Calbindin-D_{28K} Restores the Intrinsic Excitability Properties of Aged CA1 Pyramidal Neurons to Young-Like State

2014
Daniel M. Curlik II
Ameliorating Age-Related Cognitive Impairments by Reducing Expression of L-Type Calcium Channels in Area CA1 of the Hippocampus

2013
Diana Schwab Himmelstein
Characterization of the Oligomeric Form of Tau

2012
Tharinda Rajapaksha
The Alzheimer's β-Secretase Enzyme BACE1 is Required for Accurate Olfactory Sensory Neuron Axon Guidance and Normal Glomerulus Formation in the Olfactory Bulb

2011
Carmen Westerberg
Electrically Enhancing Memory Consolidation During Sleep: A Novel Method for Reducing Age-Related Memory Decline

2010
Nicolas Kanaan
Phosphorylation in the N-Terminal Region of Tau Can Regulate Tau-Mediated Inhibition of Anterograde Fast Axonal Transport in the Squid Axoplasm

2009
Katherine Sadleir
The Role of EIF2-α Phosphorylation in $Aβ_{42}$ Induced BACE1 Elevation

2008
Carmen Westerberg
Relationships Between Poor Sleep and Poor Memory in Mild Cognitive Impairment

Who We Are

MISSION

The Mesulam Center for Cognitive Neurology and Alzheimer's Disease (Mesulam Center) is a multidisciplinary organization dedicated to the following pursuits:

- Conducting research to discover how the brain coordinates cognitive functions such as memory, language, attention, and emotion.
- Discovering causes and treatments for diseases that disrupt these functions, such as Alzheimer's disease and related dementias.
- Transferring the benefits of this research to patients and their families.
- Training researchers and clinicians who want to work in this field.

RESEARCH AREAS

- Treatment and Prevention of Alzheimer's Disease
- Causes and Treatments of Primary Progressive Aphasia, Frontotemporal Degeneration, and other Younger Onset Dementias
- Nature of Cognitive and Behavioral Changes in Alzheimer's Disease
- Human Cognitive Brain Mapping
- Experimental Treatments
- Chemistry of Memory
- Maintenance of Cognitive Functions in Aging
- Genetics
- Impact of Non-Pharmacological Interventions on Quality of Life

Northwestern Medicine

The Mesulam Center has a number of research studies for which we are seeking volunteer participants. If you are interested in participating in memory research and/or would like to be placed on our mailing list, please contact us at 312-926-1851 or join a study at **brain.northwestern.edu/join**

300 E. SuperiorStreet
Tarry 8th Floor
Chicago, IL 60611
Phone: 312-908-9339
Fax: 312-908-8789
mesulam-center@northwestern.edu

Northwestern University Feinberg School of Medicine
Mesulam Center for Cognitive Neurology and Alzheimer's Disease
brain.northwestern.edu

Neurobehavior and Memory Clinic

CARE FOR PATIENTS AND FAMILIES

The Neurobehavior and Memory Clinic is designed to meet the needs of persons experiencing memory loss or other symptoms of dementia, and their families.

SERVICES INCLUDE

- Evaluation and follow-up care by behavioral neurologists who specialize in the diagnosis and treatment of dementia syndromes
- Evaluation of memory and other thinking abilities with the use of specialized tests given by a clinical neuropsychologist
- Management of medication for memory disorders
- The opportunity to participate in clinical research and clinical drug trials
- Psychiatric evaluation and treatment for mood and behavior disorders associated with neurological disease
- Education and counseling for patients and families
- Symptom specific interventions and strategies
- Information and referral to other supportive services

Our dedicated clinical team includes behavioral neurologists, a geriatrician, neuropsychiatrists, neuropsychologists, and social workers.

Call for an appointment:
312-695-9627

676 North St. Clair Street
Suite 945
Chicago, IL 60611
Phone: 312-695-9627
Fax: 312-695-6072

Northwestern Medicine

Northwestern University Feinberg School of Medicine
Mesulam Center for Cognitive Neurology and Alzheimer's Disease

brain.northwestern.edu/care-and-support

NEUROBEHAVIOR AND MEMORY CLINIC

A DEDICATED CLINICAL TEAM

BEHAVIORAL NEUROLOGISTS
M.-Marsel Mesulam, MD, Director
Borna Bonakdarpour, MD
Ian Grant, MD
Daniel Lee, MD

GERIATRICIAN
Fernanda Heitor, MD

NEUROPSYCHIATRISTS
Fred Ovsiew, MD
Deborah Reed, MD

NEUROPSYCHOLOGISTS
Tamar Gefen, PhD
Jana Wingo, PhD
Sandra Weintraub, PhD, ABPP-CN

SOCIAL WORKERS
Deborah Dyslin, AM, LSW
Paige Gesicki, MSW, LCSW
Rebecca Kilcoyne, AM, LSW
Darby Morhardt, PhD, LCSW
Kim Sangster, PhD, MDiv, LCSW

CLINIC MANAGER
Caren Rodriguez, BSN

FORMER CLINIC MANAGER
Megan Rising, MA

PSYCHOMETRIST
Nicole Wright, BA, CSP

PATIENT ACCESS REPRESENTATIVES
Kerry Boyle
Anthony Nowaske

WHY I PARTICIPATE IN RESEARCH

Responses from Mesulam Center for Cognitive Neurlogy and Alzheimer's Disease research participants and families.

"My family has a history with Alzheimer's Disease and I am willing to do whatever I can to further research to find a treatment or a cure."

"Participation in these studies is our way to help research in important scientific projects."

"I enjoy it. Also, I am happy improving the health/research for others as well as myself."

"A few years ago my wife lost her mother to Alzheimer's, we've been involved ever since."

"I love to do it. It makes me feel good. It gives me some confidence and makes me feel that I am being monitored."

"I believe research is vital to the human condition."

"To be challenged, evaluate myself, and ask questions."

"Because research is essential to understanding the world. One learns things from systematic analysis of data that cannot be learned from collecting anecdotes."

THE IMPORTANCE OF BRAIN DONATION

Please help us combat dementia.
To win the fight against Alzheimer's disease and other brain diseases that cause dementia we need more research. Brain donation at the time of death from individuals who have been well studied during life is one of the most important and generous gifts a patient who has lived with dementia and his/her family can make. Brain donations from older individuals who do not suffer from dementia are also critical for comparison and to learn why some people are able to withstand Alzheimer's and other dementias.

Brain donation is one of the most important contributions to research.
The study of brain tissue from individuals with and without disease who have been carefully studied during their lifetime allows scientists to understand the mechanisms of disease, and how those with and without disease differ in their genes and molecules. While major advances have already been made possible through the generosity of brain donation, there is still much more to be learned and a need for continued support.

Brain donation provides a valuable service to families.
A comprehensive autopsy is performed on the brain of donors. The family of the donor receives a full report detailing the neuropathologist's findings. At present, neurodegenerative diseases that cause dementia can only be diagnosed with 100% certainty through a brain autopsy, so families are provided with a definitive diagnosis. Such information is useful if other family members develop a dementia in the future or if there is a known strong family history. Making this generous donation provides the family with a way to potentially help others, which can create a sense of hope and power over the illness that affected their loved one.

Please consider that we are not able to accept every donation.
If someone interested in brain donation was never seen as part of research or for a clinical evaluation at Northwestern University's Alzheimer's Disease Center, we may not be able to accept the brain donation. We can determine on a case-by-case basis if the donation would be appropriate for our research.

Brain autopsy is a decision that individuals and their families can make only after thoughtful consideration. The decision has important emotional and practical implications.

Members of the professional staff at the Mesulam Center for Cognitive Neurology and Alzheimer's Disease at Northwestern are available to talk with you and answer your questions.
Phone: 312-926-1851
Email: memory-research@northwestern.edu

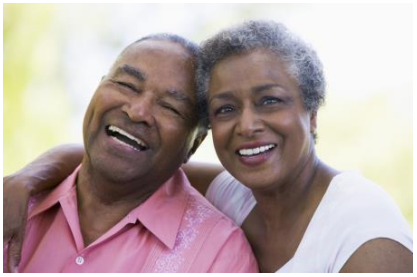
CORE CENTER RESEARCH STUDY

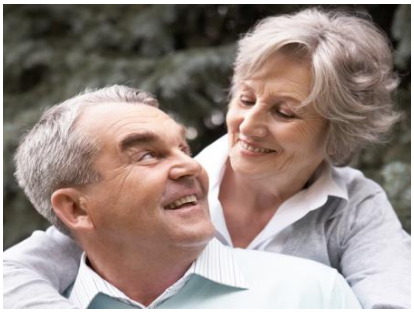
Goals

- Enroll individuals who have been diagnosed with Alzheimer's disease or a related disorder
- Enroll older healthy individuals without memory or other cognitive problems
- Identify a study partner who will be able to provide additional information about the participant
- Obtain information from participants that will support research studies of aging and memory in the larger NU community and the nation
- Understand needs of diagnosed individuals and their families
- Provide counseling, education, and referrals to community services as needed
- Encourage commitment to our brain donation program

Participants May Receive

- Participants receive annual evaluations of memory and other cognitive functions
- We will provide participants with information on the latest treatments and preventions of memory loss
- Participants will also receive our quarterly newsletter and other educational materials relevant to preserving memory health
- Social work advice is available to inform participants about community resources
- No cost for participation





Initial Research Visit Include

The enrollment visit takes approximately 2 hours. During this time:

- Demographic information and medical history is gathered from participants and their study partners
- Paper and pencil tests are given to evaluate memory and thinking skills
- A social worker meets with family members and/or care partners
- A blood sample is taken to test for genetic markers
- Participants are informed of our brain donation program

Annual Return Visits Include

The annual return visits take approximately 90 minutes. During this time:

- Information about the previous year is gathered from participants and their family members and/or care partners
- Paper and pencil tests are given to evaluate memory and thinking skills

Speak to a Research Coordinator: (312) 926-1851
www.brain.northwestern.edu

PI: Dr. Robert Vassar
STU#: STU00023196

ARMADA STUDY

JOIN THE EFFORT TO BETTER UNDERSTAND COGNITIVE DECLINE AND ALZHEIMER'S DISEASE

The ARMADA study is currently seeking participants in order to test a new set of measurements, the NIH Toolbox. Investigators are testing the NIH Toolbox's ability to detect early signs of cognitive decline and to differentiate normal and abnormal performance in older individuals.

Who Are You?

- At least 65 years old
- Native English speaker
- Cognitively healthy without memory problems
- Diagnosed with Mild Cognitive Impairment
- Diagnosed with early stage dementia due to Alzheimer's Disease
- Currently enrolled in Northwestern Alzheimer's Disease Center Core study or eligible to enroll

What Is Involved?

- One visit per year for up to three years
- Each visit is two hours long
- Complete a series of tests on an iPad related to thinking abilities, emotional, sensory, and motor functions

Am I Compensated?

- Each participant receives $100 Visa debit card for each visit
- Visa debit cards cover the cost of transportation

To learn more contact Michaela Riley at 312-503-5103 and michaela.riley@northwestern.edu or visit http://www.brain.northwestern.edu/

Advancing Reliable Measurement in Alzheimer's Disease and cognitive Aging (ARMADA)
STU00205290

SUPERAGING STUDY

-OVER 80 AND GOING STRONG-

Does this sound like you or someone you know?

If so, join our research study!

Who?

Adults over the age of 80 who remain actively engaged in life

Why?

To help us better understand and identify factors that contribute to SuperAging, the maintenance of cognitive functioning in old age

Where?

Northwestern University CNADC

300 E. Superior Street, Tarry Building, Chicago, IL

What is involved?

Participants in our study will visit our center in Chicago every 2 years for:

- **Cognitive testing**
- **An MRI brain scan**
- **Surveys and Questionnaires**

Compensation will be offered for your time

If interested, contact us for more information:

Phone: (312) 503-2716

Email: agingresearch@northwestern.edu

Website: www.brain.northwestern.edu

Study funded by: National Institute on Aging and The Davee Foundation
Grant #: 1R01AG045571-01, IRB#: STU00027225
Study Title: Super Aging study: Correlates of Active Engagement in Life in the Elderly

THE COMMUNICATION BRIDGE SPEECH THERAPY STUDY

Who?

Individuals with a diagnosis of Primary Progressive Aphasia and their Communication Partners

Why?

To help us better understand the effects of speech language therapy on communication abilities in individuals with PPA.

Where?

All components of the study take place remotely via video-conferencing.

Over the course of one year, participants in our study will be involved in:

- **5 Evaluations with a licensed speech language therapist**
- **15 Therapy Sessions with a licensed speech language therapist**
- **Exercises through our Web-Application**

There are no costs to participate in this study. Compensation will be provided

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If interested, contact us for more information:

Phone: (312) 503 – 4012

Email: communicationbridge@northwestern.edu

Website: www.brain.northwestern.edu

Study funded by: National Institute on Aging, IRB#: STU00206086, PI: Dr. Emily Rogalski
Study Title: Communication Bridge: Using Internet-Based Speech Therapy to Improve Quality of Life and Access to Care

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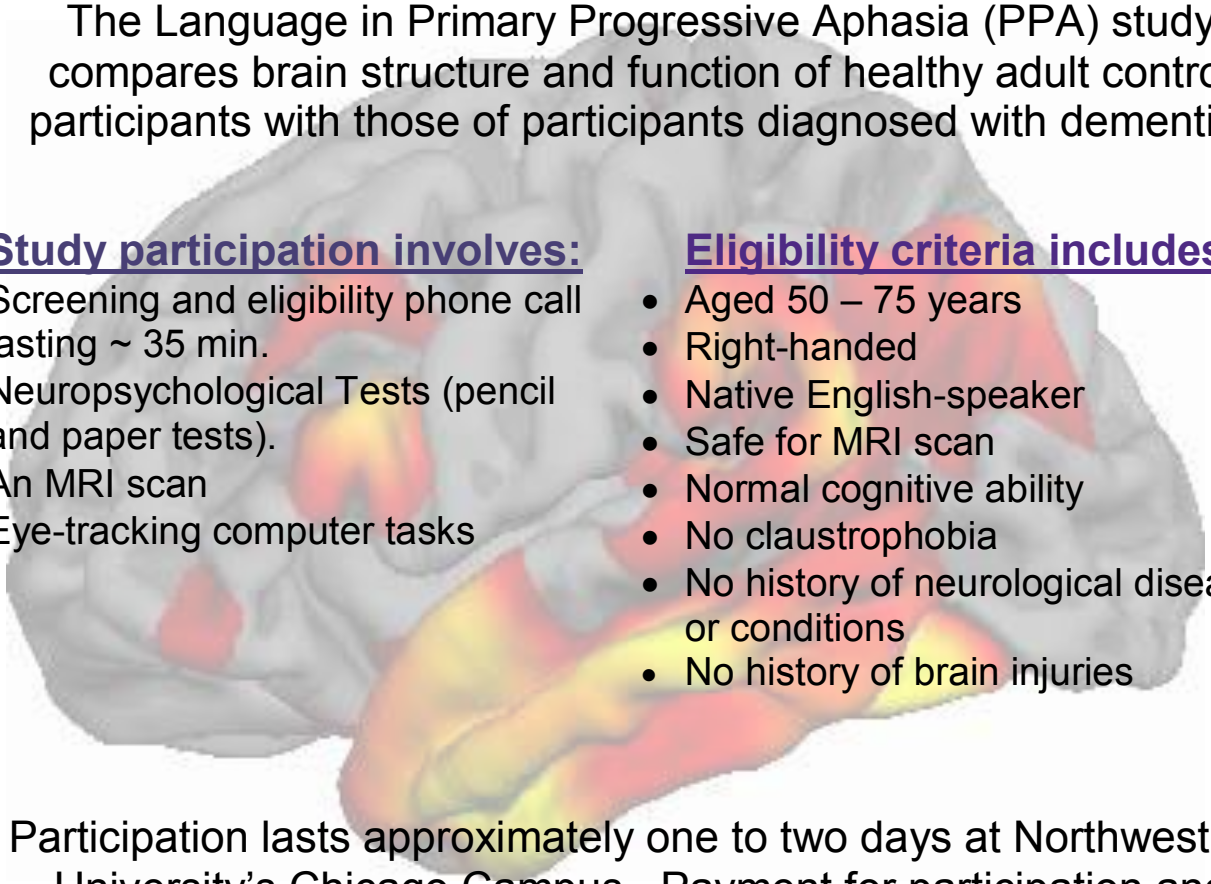
LANGUAGE IN PRIMARY PROGRESSIVE APHASIA RESEARCH STUDY, CONT.

Northwestern Medicine®
Feinberg School of Medicine

Healthy adults needed for research participation!

The Language in Primary Progressive Aphasia (PPA) study compares brain structure and function of healthy adult control participants with those of participants diagnosed with dementia.



Study participation involves:

Screening and eligibility phone call lasting ~ 35 min.
Neuropsychological Tests (pencil and paper tests).
An MRI scan
Eye-tracking computer tasks

Eligibility criteria includes:

- Aged 50 – 75 years
- Right-handed
- Native English-speaker
- Safe for MRI scan
- Normal cognitive ability
- No claustrophobia
- No history of neurological diseases or conditions
- No history of brain injuries

Participation lasts approximately one to two days at Northwestern University's Chicago Campus. Payment for participation and reimbursement for travel will be provided by mailed check.

Contact: ppa.research@northwestern.edu

CLINICAL TRIALS

T2 PROTECT AD

Troriluzole Trial (T2) for Alzheimer's Disease

The Troriluzole Trial in Alzheimer's Disease

The T2 Protect AD Study is a national multi-site clinical trial testing an investigational drug for people with mild to moderate Alzheimer's disease (AD). The trial is designed to determine if the study drug can protect against, or slow down, memory and thinking problems that increase as Alzheimer's disease progresses.

T2 Protect AD Basic Eligibility Criteria

- Women and men aged 50-85
- Diagnosed with mild to moderate Alzheimer's disease
- Taking Alzheimer's medication(s) for at least three months:
  - Donepezil/Aricept® or rivastigmine/Exelon® or galantamine/Razadyne®
  - With or without memantine/ Namenda®
- Living in the community (not in a residential nursing home)
- Participants must have a study partner who knows the participant well and can come to study visits.
- Willing to participate in the T2 Study for 48 weeks

What happens during the T2 Protect Study?

Participation in the study will take 48 weeks.A potential participant will first go through a screening process to see if they are eligible to take part in the clinical trial.

Screening includes:

- Memory and thinking tests
- EKGs (a look at your heart rhythms)
- MRI scans (a picture of your brain that shows changes related to Alzheimer's disease)

For more information or to volunteer, please contact:

Mesulam Cognitive Neurology and
Alzheimer's Disease Center
Northwestern University
IRB STUOO207754

Please call or email:

Jordan Robson
312-503-5212
jordan.robson@northwestern.edu

www.T2Protect.org

CLINICAL TRIALS

MIND

Memory Improvement Through Nicotine Dosing

Northwestern University CNADC
PI: Ian Grant, MD | STU00204222
Kristine Lipowski, Research Manager
Phone: 312-503-2486
Email: k-lipowski@northwestern.edu

The Memory Improvement Through Nicotine Dosing (MIND) study will determine whether daily transdermal nicotine will have a positive effect on early memory loss in people diagnosed with MCI.

We need your help.

If you are a healthy, non-smoking adult age 55+ and are interested in learning more about this study, please visit MINDstudy.org or call 866-MIND-150. There is no cost to participate.

This study is being conducted by Vanderbilt University and the University of Southern California Alzheimer's Therapeutic Research Institute and funded by the National Institute on Aging (NIA).

CLINICAL TRIALS

Did You Know You Can Help Make Alzheimer's History?

Join the ADNI Study

An Observational Study of Brain Aging

ADNI
Alzheimer's Disease Neuroimaging Initiative

ADNI is a historic study of brain aging which could help change the future of Alzheimer's disease.

We need your help.

ADNI is seeking people over age 55, who are healthy, as well as those with mild memory problems and those who have been diagnosed with mild dementia due to Alzheimer's. There is no experimental medication involved.

To learn more, please visit ADNI3.org or call:

1-888-2-ADNI-95
(1-888-223-6495)

Your local site is:

Kristine Lipowski, Research Project Manager
Phone: (312) 503-2486
Email: k-lipowski@northwestern.edu

Funded by the National Institutes of Health (NIH) and the Foundation for the National Institutes of Health (FNIH).

THE MILLER FAMILY QUALITY OF LIFE ENRICHMENT PROGRAMS

The Mesulam Center for Cognitive Neurology and Alzheimer's Disease provides a number of programs to help support the quality of life of persons living with memory loss, mild cognitive impairment, or other forms of dementia like Alzheimer's, frontotemporal degeneration, dementia with Lewy bodies and primary progressive aphasia.

If you would like to learn more about one of the following programs, please contact us at 312-908-9023 or visit www.brain.northwestern.edu

Support Groups

The Mesulam Center offers two support groups for families and care partners:

- *Frontotemporal Degeneration (FTD) & Primary Progressive Aphasia (PPA) Caregiver Support Group*
- *Younger Onset Caregiver Support Group (for care partners and families caring for persons diagnosed with dementia under 65)*

The Buddy Program

This unique program pairs first year students from Northwestern's Feinberg School of Medicine with persons in the early stages of cognitive decline providing an opportunity for persons living with dementia to mentor a medical student and the students a unique advantage of spending time with diagnosed individuals outside of a clinical setting.

The Memory Ensemble

A collaboration between the Mesulam Center and the Lookingglass Theatre Company, the Memory Ensemble is an improvisational theatre experience for persons in the early stages of memory loss. Program participants learn to use their instincts, creativity, and spontaneity as they explore and create together.

Storytelling Workshop

This workshop offers individuals in the early stages of cognitive decline and their partners an opportunity to develop and write a shared story from their lives through reminiscence and exploration of the impact dementia has had on their lives. The program seeks to preserve relationships and decrease social isolation.

SEED

The Support and Education for Early Dementia (SEED) program gives newly diagnosed individuals and families the opportunity to learn and connect with others. Educational presentations help participants learn about dementia, community resources, adjusting to changes, research opportunities, practical interventions, and legal and financial considerations. Facilitated support groups provide the opportunity to share experiences and helpful resources.

Memory Café

The Chicago Memory Café is an engaging monthly social gathering for persons living with dementia and their family, friends, and care partners to attend together.

Art in the Moment

A collaboration with the Art Institute of Chicago, Art in the Moment engages participants in creative dialogue and a positive experience through discussion of art in the museum galleries and artistic expression in a studio activity. The program serves as a vehicle for intellectual stimulation, creative expression, social engagement and personal validation.

The Miller Family Quality of Life Enrichment Programs are made possible by a grant from the Glen and Wendy Miller Family Foundation.

SEED: SUPPORT & EDUCATION FOR EARLY DEMENTIA

An 8-week program for individuals recently diagnosed with Alzheimer's dementia or related disorders and their care partners.

Week 1

Brain Health Practices

Week 2

The Basics of Dementia

Week 3

Maintaining Your Relationships and Discussing the Diagnosis with Others

Week 4

Practical and Functional Interventions

Week 5

Supportive Community Resources

Week 6

Research Opportunities

Week 7

Legal and Financial Considerations

Week 8

Life after SEED

Spring, Summer, and Fall Sessions Offered

Interview required to participate | $150 per person per 8 week session | Scholarships are available

For further information contact:

Debbie Dyslin, AM, LSW

deborah.dyslin@northwestern.edu

312-503-5559

Tele-Savvy Clinical Trial

Dementia Caregiver Research Participants Needed

Site Investigator: Darby Morhardt, PhD, LCSW

Northwestern University, Feinberg School of Medicine, Mesulam Center for Cognitive Neurology and Alzheimer's Disease

Principal Investigator: Kenneth Hepburn, PhD

Emory University, Schools of Nursing and Medicine & Alzheimer's Disease Research Center

Study Details

Participants will be randomly assigned to one of three groups

- Tele-Savvy Group—Immediately receives the Tele-Savvy Education Program
- Healthy Living Education Group—Immediately receives 6 weeks of education on healthy lifestyle choices, and receives the Tele-Savvy Education Program after 6 months
- Usual Care Group—Continuing with your existing care routine, and the receive Tele-Savvy after 6 months

All participants will receive the Tele-Savvy Education Program prior to the end of the study.

Who may participate?

Informal caregivers of dementia patients.

Is there a cost to participate?

No, participation is completely free.

Will I be compensated for my participation?

Yes, compensation will be provided for completing study-related interviews.

What is the Tele-Savvy Study?

A clinical trial of an on-line education program for dementia caregivers.

Caregiver Training

During the program, you will receive caregiver training in the following areas:

- Dementing Illnesses
  - Stages
  - Causes
  - Signs and Symptoms
  - Disease Management
- Environmental changes to enhance quality of life for you as a caregiver and your person living with dementia
- Caregiving Strategies
- Self-Care for the Caregiver

Why Tele-Savvy?

Caregiving is a demanding and stressful role. Caregivers need training to optimize their person's and their personal quality of life.

Many skills can be learned to decrease caregiver burden, stress, and the severity of dementia symptoms experienced by their person.

This program is conveniently offered online on weekdays and weekends.

We make it easy to participate with life tech support at every step of the program.

Sessions in the program are designed and led by experts in dementing illnesses

You will be meeting with other dementia caregivers throughout your time in the program.

What will I do as a participant?

You will participate in a 6-week online program that includes weekly video conferences and online video lessons.

You will complete up to 6 interviews over the course of 12 months. These interviews are focused on understanding your caregiving experience.

How much time do I need to commit to participating?

Weekly teleconferences—Up to 90 minutes on a regularly scheduled day of the week (weekday or weekend).

Daily Video Lessons—Up to 15 minutes daily. These videos will be emailed to you and may be watched on your own schedule as time permits.

Interviews—Study related interviews will be conducted up to 6 times throughout the program. They are scheduled roughly every 3 months and will be limited to 60 minutes.

What do I need to participate?

You will need a computer or mobile device with internet. Webcams may be provided if needed.

New to videoconferencing?

Program uses a simple, introductory level program for video conferences.

Research assistants will be available for help at all stages.

What if I start and cannot finish?

This is a voluntary study. You can stop at any time. There are no penalties for discontinuing participation.

I'm Interested! Now what?!

Contact

Kim Sangster, Site Coordinator

312-503-0604

kimberly.sangster@northwestern.edu

COUNSELING, EDUCATION, & SUPPORT

Clinical Social Work Consultation:

A Customized Approach to Care

The Northwestern Neurobehavior and Memory Clinic offers a multidisciplinary team approach. Your care team includes neurologists, psychiatrists, neuropsychologists and social workers. Clinical social workers are available to discuss your questions and work with you to develop a personal and customized approach to care. Following are some questions you may have:

- **"Do I understand the diagnosis?"**

  Your social worker will:

  - Review the diagnosis and provide the opportunity to ask questions and get up-to-date disease information.
  - Discuss changing behaviors and other diagnosis-related symptoms, and offer helpful communication strategies.

- **"How do I cope with this now and as it progresses?"**

  Your social worker can:

  - Provide counseling regarding changing roles as the disease progresses.
  - Help you to assure your own self-care and to strengthen your support network.
  - Provide referrals for individual, couples, and/or family counseling.

- **"How can I plan for future care?"**

  Your social worker can:

  - Connect you to trusted elder law attorneys for estate planning and to establish powers of attorney for health care and finances.
  - Provide counseling regarding advance directives.
  - Help you to explore long-term care options and funding sources.

- **"What services are available at Northwestern or in my own neighborhood?"**

  Your social worker can guide you to:

  - Specialized support and education groups for newly diagnosed individuals and families.
  - Quality-of-life programs designed to offer meaningful and purposeful activity.
  - Other community programs in which you can find enriching opportunities.

Please call the Northwestern Neurobehavior and Memory Clinic,
312-695-9627 or ask your doctor for a referral for a clinical social work consultation.

Become a Dementia Friend

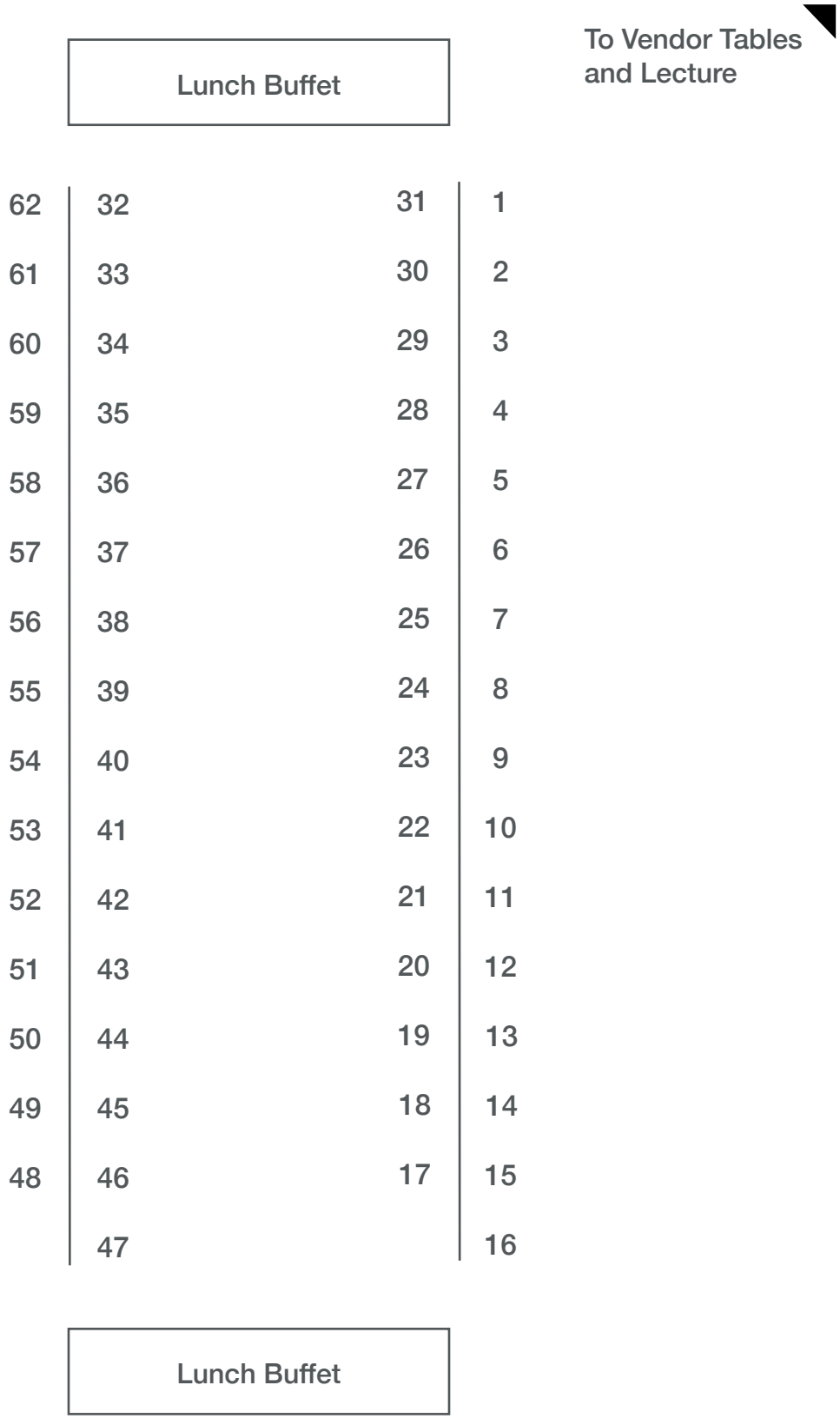
Dementia Friendly America, a national collaborative just launched the Dementia Friends program in the United States. Dementia Friends is a global initiative that began in the United Kingdom and aims to empower and educate individuals about dementia.

Dementia Friends is designed to raise awareness about dementia and educate individuals and communities about how they can best support and interact with people living with dementia.

The program accomplishes this via an online training that includes a series of short videos and encourages people to commit to take action.

Become a Dementia Friend by going to www.DementiaFriendsUSA.org. From there you can become a Dementia Friend by committing to an activity that will help someone in your community with dementia.

MAP OF POSTER SESSION



POSTER SESSION

CELL & MOLECULAR BIOLOGY

1 **Neuronal Apolipoprotein E4 increases cell death and p-tau release in stem cell-derived neurons from AD patients**
Anil R. Wadhwani, Amira Affaneh, Stephanie VanGulden, John A. Kessler

2 **Creating a Tool Kit for the Structural Characterization of Neurotoxic Amyloid Beta Oligomers in Alzheimer's disease**
Anthea Weng, Erika Cline, Claudia Casula, Maira Bicca, Andre Bitencourt, Adriano Sebolla, William Klein

3 **Role of Unc5c, an Alzheimer's Risk Gene in Late-Onset Alzheimer's Disease in a Novel Mouse Model**
Devi Krishna Priya Karunakaran, Becky Wang, Katherine Sadleir, Ammaarah Khatri, Jelena Popovic, Ryan J Watts, Jasvinder K Atwal, Robert J Vassar

4 **The Role of CRAC Channels in Neuritic Dystrophy in Alzheimer's Disease**
Katherine R .Sadleir, Jelena Popovic, Agila Somasundaram, Murali Prakriya, Robert Vassar

5 **Impaired Turnover of Synaptic Vesicle Machinery Contributes to Amyloid Pathology in Mouse Models of Alzheimer's Disease**
Timothy J. Hark, Ewa Bomba-Warczak, Samual N. Smukowski, Laith Ali, Nalini Rao, Huan Bao, Edwin Chapman, Jeffrey N. Savas

CLINICOPATHOLOGIC STUDIES

6 **ApoE4 is Not a Risk Factor for Alzheimer's Disease Pathology in PPA, Irrespective of Clinical Subtype**
Sandra Weintraub, Merilee Teylan, Ben Rader, Mark Bollenbeck, Emily Rogalski, Eileen Bigio, M.-Marsel Mesulam

7 **A Highly Sensitive Sandwich ELISA to Detect CSF Progranulin, a Potential Biomarker for CNS Disorders**
Xiaojing Zheng, Emily J. Rogalski, Haibin Xia, Eileen H. Bigio, Qinwen Mao

8 **Behavioral and Psychological Symptoms of Dementia (BPSD) in Alzheimer's Disease: Antemortem Clinical Assessment and Postmortem RNA-sequencing Analysis**
Rachel M. Keszycki, Daniel W. Fisher, David A. Bennett, Robert S. Wilson, Hongxin Dong

POSTER SESSION

HEALTH SERVICES

9 **Detecting Cognitive Impairment and Dementia and Primary Care: Current Practices and Feasibility of the MyCog Detection Paradigm**
Rachel O'Conor, Julia Yoshino Benavente, Laura M. Curtis, Marina Arvanitis, Richard C. Gershon, Michael S. Wolf

NEUROANATOMY

10 **Cortical Thickness as a Predictor of Memory Change in Aging Populations**
Lagoutina, Y., Nilakantan, Voss, J., Wang, L., Heywood, A.

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POSTER 1

NEURONAL APOLIPOPROTEIN E4 INCREASES CELL DEATH AND P-TAU RELEASE IN STEM CELL-DERIVED NEURONS FROM AD PATIENTS

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Objective: The apolipoprotein E (APOE) E4 isoform is the strongest genetic risk factor for sporadic Alzheimer's disease (AD). While APOE is predominantly expressed by astrocytes in the central nervous system, neuronal expression of APOE is of increasing interest in age-related cognitive impairment, neurological injury, and neurodegeneration. Here we show that endogenous expression of E4 in stem cell-derived neurons predisposes them to injury and promotes the release of phosphorylated tau.

Methods: Induced pluripotent stem cells from two unrelated Alzheimer's disease patients carrying the E4 allele were corrected to the E3/E3 genotype with the CRISPR/Cas9 system and differentiated into pure cultures of forebrain excitatory neurons without contamination from other cells types.

Results: Compared to unedited E4 neurons, E3 neurons were less susceptible to ionomycin-induced cytotoxicity. Biochemically, E4 cells exhibited increased tau phosphorylation and ERK1/2 phosphoactivation. Moreover, E4 neurons released increased amounts of phosphorylated tau extracellularly in an isoform dependent manner by a heparin sulfate proteoglycan-dependent mechanism.

Interpretation: Our results demonstrate that endogenous expression of E4 by stem cell-derived forebrain excitatory neurons predisposes neurons to calcium dysregulation, and ultimately, cell death. This change is associated with increased cellular tau phosphorylation and markedly enhanced release of phosphorylated tau. Importantly, these effects are independent of glial APOE. These findings suggest that E4 accelerates spreading of tau pathology and neuron death in part by neuron-specific, glia-independent mechanisms.

POSTER 2

CREATING A TOOL KIT FOR THE STRUCTURAL CHARACTERIZATION OF NEUROTOXIC AMYLOID BETA OLIGOMERS IN ALZHEIMER'S DISEASE

Anthea Weng[1], Erika Cline[1], Claudia Casula[2], Maira Bicca[1], Andre Bitencourt[3], Adriano Sebolla[3], William Klein[1]

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Alzheimer's disease (AD) is a progressive, neurodegenerative disease and is the sixth leading cause of death in the U.S. Amyloid beta oligomers (AβOs) are neurotoxins that contribute to AD pathogenesis and cause pathologies like synapse loss and neuronal death. However, it has been difficult to structurally characterize AβOs as they are unstable and tend to aggregate in low abundances in the human AD brain. In this project, various methodologies were used to separate and stabilize neurotoxic AβO populations to aid in the structural characterization of AβOs.

In order to pull out AD-relevant AβO subpopulations, the AβO-specific antibody NUsc1 was used. Through multiple techniques, NUsc1 was found to bind a AβO subpopulation > 50 kDa. To test if this AβO population was neurotoxic, experiments were conducted in vitro as well as in vivo. When mice were injected with NUsc1-depleted fractions, they didn't have memory deficits. This suggests that the AβO > 50 kDa population is neurotoxic and causes AD pathologies.

The NUsc1 data indicates that >50 kDa targeted subpopulation is complex so I proposed to decrease sample complexity by decreasing starting Aβ concentration through SEC analysis. As the starting Aβ concentration decreased, the sample molecular weight (MW) range decreased. At the lowest concentration, only one molecular weight (~100 kDa) was targeted. This illustrated that low Aβ concentrations could be utilized to target MW-specific AβO subpopulations.

We also have started to use NUsc1 to investigate the structure & stability toxic AβOs in the brain of an AD mouse model. Preliminary data indicates there may be stable AβO >250 kDa populations already existing in the AD brain. This population appears stable as the addition of AβO-stabilizing DFDNB didn't affect the detected AβO signal.

By using these tools together, it will allow for structure-function analysis of AD-relevant AβOs, which can be applied to the development of AD therapeutics/diagnostics.

POSTER 3

ROLE OF UNC5C, AN ALZHEIMER'S RISK GENE IN LATE-ONSET ALZHEIMER'S DISEASE IN A NOVEL MOUSE MODEL

Devi Krishna Priya Karunakaran[1], Becky Wang[1], Katherine Sadleir[1], Ammaarah Khatri[1], Jelena Popovic[1], Ryan J Watts[2,3], Jasvinder K Atwal[2], Robert J Vassar[1]

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Purpose: Alzheimer's disease (AD) is characterized by amyloid plaques, neurofibrillary tangles, and synaptic and neuronal loss. Since memory loss is one of the debilitating symptoms of AD, understanding how neuronal cell loss occurs is crucial. However, the mechanism of neuronal cell death in AD remains under explored. Recently, a rare autosomal dominant coding mutation, T835M, was discovered in the Un-coordinated 5c (Unc5c) netrin receptor gene that segregated with late-onset AD (LOAD). Unc5c is a netrin1 receptor and is involved in axon guidance during development. The T835M mutation leads to cell death in HEK-293T cells and reduces survival in the presence of neurotoxic stimuli in cultured primary neurons. Combining this result with the robust expression of Unc5c in hippocampus, we hypothesize that UNC5C T835M mutation predisposes to LOAD by making neurons more vulnerable to cell death induced by pathogenic Aβ and Tau and Unc5c death domain activation.

Methods: We employed the mouse knock in (KI) model of Unc5c T835M that were crossed with 5XFAD amyloid mouse model. Brain sections obtained from Unc5cKI/KI;5XFAD mice and littermate controls were imaged by immunofluorescence confocal microscopy for neurons (NeuN), Aβ deposits (Thiazine Red, Aβ42, Aβtotal), apoptosis (TUNEL), astrocytes (GFAP), and microglia (Iba1) and immunoblot of cortices and hippocampi. We also employed unbiased proteomics and stereology to understand the proteome changes and to obtain the neuron count, respectively. In vitro studies using primary neuronal culture obtained from KI and wildtype (WT) control mice were also employed to study the effects of various stressors including Aβ42, staurosporine and glutamate.

Results: Overall, our studies show that homozygous KI mice are very similar to WT littermate controls in terms of the histology, protein and RNA expression or in cell death. However, Primary KI neurons showed an increased cell death in the presence of cytotoxic stressors. Additionally, proteomics analysis of KI and wildtype (WT) mice brains showed upregulation of apoptotic proteins and down-regulation of neuronal proteins, which was supported by immunoblot analysis of some of these proteins. Most of these neuronal proteins were synaptic and vesicular proteins suggesting that the mutation might affect the synaptic connectivity.

Significance: Since Unc5c is highly expressed in hippocampus and cortex and that we see downregulation of synaptic proteins suggest that this mutation cause neuron loss, thereby affecting memory. We anticipate that our study will lead to a greater understanding of the underlying molecular pathway involved in AD-related neuron loss and how Unc5c mediates AD risk. Our study also aim at identifying novel therapeutic targets for reducing neuron loss in AD and potentially other neurodegenerative diseases.

POSTER 4

THE ROLE OF CRAC CHANNELS IN NEURITIC DYSTROPHY IN ALZHEIMER'S DISEASE

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Practical implications: The area right around the amyloid plaques is very inflammatory and toxic to the neurons. We are investigating ways to block the toxic effect of the plaque, even if the plaque is not removed to see if this could help the neurons function better and in this way treat Alzheimer's disease.

Background: BACE1 is the β-secretase enzyme that initiates Aβ production and is a prime therapeutic target for Alzheimer's disease (AD). Drugs that inhibit BACE1 enzyme activity are in clinical trials for AD, but early termination of a recent trial raise concerns regarding safety and efficacy of these agents. Animal studies suggest that BACE1 inhibition may cause multiple neurological side effects. Thus, it is crucial to develop alternative therapeutic strategies that reduce BACE1 cleavage of APP without impairing essential BACE1 functions. We have shown that global BACE1 protein levels are markedly elevated in APP transgenic mouse and AD brains. Elevated BACE1 is concentrated within dystrophic axons and terminals surrounding amyloid plaques and is associated with increased generation of BACE1-cleaved APP fragments and Aβ42. Our preliminary results show that Aβ elevates resting [Ca2+]i in primary neurons via Ca2+ release-activated (CRAC) Ca2+ channels. Moreover, we observe that axons of Aβ-treated primary neurons exhibit disrupted microtubules and impaired BACE1 axon transport. Peri-plaque dystrophic axons in 5XFAD mice also show elevated resting [Ca2+]i and disrupted microtubules. We hypothesize a feed-forward mechanism in which plaque-associated Aβ causes axonal dystrophy, BACE1 accumulation, and accelerated Aβ generation that drives amyloid progression.

Purpose: The purpose of this experiment is to determine whether the CRAC channels play a role in elevated calcium and dystrophic neurite formation near amyloid plaques in a mouse model of amyloidopathy.

Methodology: To test the role of CRAC channels in dystrophic neurite formation, BACE1 accumulation and amyloid generation, we have generated a cohort 5XFAD mice with or without the conditional deletion of Orai1, the pore forming subunit of the CRAC channel, in the excitatory neurons of the forebrain using an iCre transgene driven by the CaMKII promoter. At six months of age, brains from 5XFAD Orai1 flox/flox CaMKII iCre and 5XFAD Orai1 flox/flox control mice are stained with Lamp1 and BACE1 to mark dystrophic neurites, and thiazine red to mark plaques. In addition, immunoblotting is used to quantify BACE1, LAMP1, LC3B and Aβ in the cortex and hippocampi of these mice.

Findings: We hypothesized that the 5XFAD Orai1 flox/flox CaMKII iCre mice will have reduced peri-plaque dystrophic neurites, reduced BACE1, and lowered resting calcium compared to 5XFAD Orai1 flox/flox control mice. In fact, we observed that BACE1, LC3B, LAMP1 and amyloid levels are unchanged in the 5XFAD Orai1 flox/flox CaMKII iCre mice compared to 5XFAD Orai1 flox/flox control mice, indicating that Orai1 does not play a large role in dystrophic neurite formation, or that there is compensation by other Orai family members.

POSTER 5

IMPAIRED TURNOVER OF SYNAPTIC VESICLE MACHINERY CONTRIBUTES TO AMYLOID PATHOLOGY IN MOUSE MODELS OF ALZHEIMER'S DISEASE

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Alzheimer's Disease (AD) is the most prominent neurodegenerative disorder, affecting over 40 million people worldwide. Behaviorally, symptoms of AD include a gradual decline in short-term memory, reasoning skills, and executive functioning. However, these behavioral symptoms manifest many years after irreversible synapse loss and neurodegeneration, thus it is our goal to understand the earliest mechanisms of AD pathology. Molecularly, AD is characterized by misfolding and aggregation of proteins, especially amyloid beta (Aβ). Aβ accumulation occurs gradually and well before any other dysfunction takes place and this accumulation likely triggers subsequent toxic events. However, how accumulating Aβ confers toxicity to neurons in the brain remains poorly understood. One hypothesis is that Aβ impairs normal protein degradation causing certain proteins to persist in the brain for longer periods and disrupt healthy cellular functions. Our project aims to identify proteins that persist in the brain due to Aβ accumulation and to determine if they contribute to AD etiology or pathology.

To investigate protein degradation dynamics, we utilized a novel metabolic pulse-chase stable isotope labeling method in AD model mice with quantitative mass spectrometry (MS)-based proteomic analysis. Mice receive chow containing exclusively heavy isotopes, then "chased" with light isotopes, and proteins that have not been degraded remain labeled with the heavy isotopes while newly synthesized or turned over proteins incorporate the light isotopes. MS is able to detect both the heavy and light isotopes, allowing determination of proteins with altered degradation following Aβ accumulation. We utilize a recently developed mouse model of AD. This mouse model expresses endogenous levels of a humanized Amyloid Precursor Protein (APP), coupled with mutations common to familial cases of AD. APP is the precursor to Aβ, and the mutations cause increased levels of Aβ, which recapitulate aspects of AD. Using this model coupled with pulse-chase labeling and MS, we determined which proteins are abnormally persisting in the brain.

In these experiments, we quantified thousands of proteins and determined which proteins have protracted lifetimes following pathology. After GO term analysis, we found that the proteins persisting in pathogenic mice were significantly enriched for presynaptic proteins, particularly proteins associated with synaptic vesicle cycling. These proteins had impaired degradation in the cortex and hippocampus, but not the cerebellum, where Aβ42 pathology only occurs at late stages of AD, supporting an Aβ42 dependent effect. This is interesting since we already know that Aβ is released at synapses in an activity dependent manner. We are now using biochemical assays and microscopy to investigate why these presynaptic proteins are perturbed in response to AD-like pathology. Preliminary data suggests that these proteins and possibly whole presynaptic terminals are nearby or associated with deposition of Aβ oligomers or nascent plaques. Together, these experiments suggest presynaptic proteins are among the earliest perturbed in AD-like pathology potentially due to their close association with Aβ42's processing, release, and aggregation. These perturbed proteins and protein networks may critically contribute to mechanisms of early AD pathology and further inform our understanding of this debilitating disease.

POSTER 6

APOE4 IS NOT A RISK FACTOR FOR ALZHEIMER'S DISEASE PATHOLOGY IN PPA, IRRESPECTIVE OF CLINICAL SUBTYPE

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Background: AD neuropathology can give rise to non-amnestic dementias, including selective aphasic, visuospatial or behavioral phenotypes, with ages of onset in mid rather than late life [1]. Primary progressive aphasia (PPA), one of the best-studied non-amnestic forms of AD [2], demonstrates an atypical neuroanatomic distribution whereby neurofibrillary tangles can display asymmetric aggregation in the left hemisphere, with a 'hippocampal sparing' pattern [3]. We previously reported that the e4 allele of ApoE, a major risk factor for typical amnestic AD, did not show this association with PPA with AD (PPA/AD) [4]. In that study, the amnestic AD subjects were significantly older and lacked post-mortem verification of AD. These are potential limitations since amnestic dementias can be caused by non-AD pathologies and since the role of e4 as a major risk factor for AD could be age-dependent. The current study was undertaken to address these two limitations.

Method: Thirty-four longitudinally studied cases with a clinical diagnosis of PPA and neuropathologic diagnosis of AD from the Northwestern brain bank were compared to thirty-four individuals matched to the PPA group for age-at-onset and sex with a clinical diagnosis of amnestic dementia and neuropathologic diagnosis of AD (AmD/AD) and to thirty-four cognitively healthy controls (NC) matched for sex and age at study entry from the National Alzheimer Coordinating Center database. The frequency of the e4 allele (≥ 1 vs none) was compared between the groups.

Results: ApoE e4 allele frequency was greater in the amnestic AmD/AD than in the PPA/AD group (82% vs 47%, p=.03). PPA/AD and NC (35%) groups did not differ in e4 allele frequency (p=.33). Of interest, only one PPA case and one healthy control case possessed 2 e4 alleles compared with 8 of the amnestic AD cases.

Conclusion: In two groups with autopsy-confirmed AD matched for age of disease onset, the e4 allele is not a risk factor for AD pathology in aphasic dementia. Therefore, the e4 allele is not a universal risk factor for AD but for the type of AD that selectively undermines episodic memory, probably by targeting medial temporal limbic networks of the brain[5].

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POSTER 7

A HIGHLY SENSITIVE SANDWICH ELISA TO DETECT CSF PROGRANULIN, A POTENTIAL BIOMARKER FOR CNS DISORDERS

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Progranulin (PGRN) plays critical roles in inflammation, tumorigenesis and neurodegeneration. PGRN levels in blood and cerebrospinal fluid (CSF) are being increasingly investigated as potential biomarkers for these disorders. However, the value of CSF PGRN as a biomarker has been limited because currently available commercial enzyme-linked immunosorbent assay (ELISA) kits have suboptimal sensitivity for detecting CSF PGRN. In this study, pairs of monoclonal antibodies were first screened from 11 monoclonal anti-PGRN antibodies using indirect ELISA, then a sandwich ELISA was established using the two optimized monoclonal antibodies. This system displayed high sensitivity, with a lower limit of detection of 60.0 pg/ml and a lower limit of quantification of 150 pg/ml. By using this ELISA system, we showed varied CSF PGRN levels in different brain disorders. For example, as compared with the normal controls, patients with Alzheimer disease or multiple sclerosis showed mildly increased CSF PGRN; those with aseptic encephalitis or neuropsychiatric systemic lupus erythematosus showed moderately increased CSF PGRN; those with bacterial leptomeningitis showed severely increased CSF PGRN. Additionally, determining CSF PGRN levels could monitor CNS metastasis and CSF seeding of carcinomas. These results indicate that this system can be valuable in studying the diagnostic and prognostic value of CSF PGRN in brain disorders.

POSTER 8

BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA (BPSD) IN ALZHEIMER'S DISEASE: ANTEMORTEM CLINICAL ASSESSMENT AND POSTMORTEM RNA-SEQUENCING ANALYSIS

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By 2050, the global number of patients with dementia is expected to rise to 115.4 million people of which 60-80% will carry a diagnosis of Alzheimer's disease (AD) specifically. Among these millions of individuals, the vast majority of them will experience changes in their perceptions, thoughts, emotions, and behaviors that interfere with their daily functioning. These changes are broadly referred to as behavioral and psychological symptoms of dementia (BPSD) and evidently represent a critical worldwide healthcare issue. Clinical presentations among those with BPSD vary widely, making BPSD as a whole too broad of a target for intervention. Targeting individual symptoms is also likely ineffective because patients tend to experience symptoms in clusters rather than in isolation. Thus, has long been contended that BPSD should be categorized into domains based on these clusters because this could lead to the discovery of common underlying etiology and thus of effective treatment targets. The purpose of this study was to choose a select group of AD patients who were either highly affected or unaffected-to-mildlyaffected on particular BPSD domains. Based on previous research findings, we hypothesized that patients' symptoms would cluster into four major domains: affective symptoms (depression and anxiety), apathy, hyperactivity (irritability, disinhibition, aggression, and aberrant motor behavior), and psychosis (delusions and hallucinations). We performed factor analysis on 660 antemortem behavioral interviews with patients who had a dementia diagnosis, revealing four factors that were similar to yet different from those we had hypothesized. In accordance with our hypothesis, we obtained apathy and affective domains. Regarding psychosis, delusions did not load well onto any of our factors, and aberrant motor behavior loaded strongest with hallucinations. Although the behavioral interviews did not address disinhibition or irritability directly, a number of aggression questions specifically inquired about impulsive aggression. As such, aggressive symptoms alone constituted our last factor. We obtained severity scores for all patients on these four domains who had an AD diagnosis and a behavioral interview within two years before death (n = 100). Within a particular domain, we designated those in the top 70% as "cases" and those in the bottom 30% as "controls." We selected 55 patients using these cutoffs and gender counter-balancing across all domains' cases and controls. In the near future, we plan to perform RNA sequencing analysis on several postmortem brain regions from these additional patients. Previously, we conducted preliminary RNA-sequencing analysis on 17 patients' postmortem anterior cingulate tissues according to the four domains we had hypothesized. This analysis revealed 57 differentially expressed genes for the affective domain, 44 for the hyperactivity domain, 34 for the psychosis domain, and 20 for the apathy domain. We propose that we will find differentially expressed genes across our adjusted BPSD domains and additional brain regions as well. Future research into BPSD should consider how epigenetic and environmental interventions upregulating or downregulating these domain-related genes may be helpful in developing treatment strategies to alleviate corresponding symptoms.

POSTER 9

DETECTING COGNITIVE IMPAIRMENT AND DEMENTIA AND PRIMARY CARE: CURRENT PRACTICES AND FEASIBILITY OF THE MYCOG DETECTION PARADIGM

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Background: As the age of the US population increases, so does cognitive impairment (CI); therefore early detection of CI is critical for ensuring its appropriate management. As part of a NINDS Consortium to detect CI and dementia in primary care (DetectCID), we are implementing and evaluating a brief 2-step CI detection paradigm (MyCog), that can be delivered in clinics with diverse populations via the electronic health record (step 1) and iPad (step 2). We sought feedback from primary care practices to inform the implementation of our CI detection paradigm.

Methods: We conducted focus groups with 25 clinicians and administrative leaders from academic and community primary care practices to 1) understand how CI is being assessed, and 2) evaluate the feasibility of implementing the MyCog paradigm into existing primary care workflows. The research team took detailed notes during the discussion groups and reviewed them for common themes across participants.

Results: No proactive detection strategy for CI was regularly used outside of the Medicare Annual Wellness Visits (AWV); variable assessments including the Minicog, MoCA, or MMSE were used to fulfill the AWV requirement. Regarding the feasibility of our MyCog Paradigm, our 2-step process was positively received, with the brief case-finding step 1 satisfying AWV requirements and replacing the longer assessments currently being used. Clinicians preferred that step 2 be self-administered due to limited clinician time for wellness visits, and highlighted logistical challenges such as room availability and storage and maintenance of the iPad. Overall, clinicians felt that the identification of CI was valuable and supported standardization, but indicated regular case finding was unlikely without clear guidance on clinical decision-making.

Conclusions and Practical Implications: CI is not routinely detected in primary care outside of the Medicare AWV. Our 2-step MyCog paradigm was positively received by clinicians, but the need for additional guidance on subsequent care planning following the detection of CI is necessary to promote uptake.

POSTER 10

CORTICAL THICKNESS AS A PREDICTOR OF MEMORY CHANGE IN AGING POPULATIONS

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Changes in cortical thickness are a well-known neuroanatomical correlate of aging. The present project investigated the role of age-related cortical atrophy in post-TMS memory change by comparing cortical thickness in younger and older participant samples. Using regression analysis of MRI data, a set of regions of interest showing the most significant amount of cortical loss was identified, effectively constituting the 'aging signature' network. Age-related hippocampal volume atrophy was also evaluated as a predictive factor in post-TMS memory change in an older participant sample. Overall, the present study provided a significant contribution to the current understanding of how neuroanatomical changes in aging populations affect individual ability to benefit from TMS.

POSTER 11

TOWARD AN OLFACTORY IMAGING BIOMARKER FOR EARLY-STAGE NEURODEGENERATIVE DISEASE

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The sense of smell plays a fundamental role in human cognition, and olfactory perceptual performance has been indicated as a potential biomarker for early-stage neurodegenerative diseases. In fact, olfactory dysfunction is present in 90% of early-stage Parkinson's disease (PD) cases, a higher prevalence than many cardinal motor signs. Despite its importance, the structure and function of the olfactory system in humans is poorly understood. These areas have proven difficult to characterize with dMRI methods, since they contain small and crossing white matter fibers that are not visible when using the traditional diffusion tensor model. These areas are also particularly prone to signal attenuation and imaging artifacts because of their proximity to the sinuses. In the present project, we will apply novel diffusion magnetic resonance imaging (dMRI) techniques to measure human olfactory white matter pathways in vivo. We will then develop an olfactory pathway template that can be used as a reference for future PD biomarker development.

Pilot subjects (n=5) underwent a multi-shot echo planar imaging (MS-EPI) dMRI sequence with 1.5 mm isotropic resolution, used to reduce imaging artifacts common in olfactory regions. Subjects wore custom 3D-milled helmets to prevent head movement. A constrained spherical deconvolution (CSD) model was fit, capable of resolving small crossing and curving white matter pathways. White matter tractography was performed using MRtrix2. Olfactory perceptual data were collected on two separate days from each subject.

Based on anatomical studies in rodents and primates, we hypothesize that primary olfactory cortical regions will show structural connectivity with limbic regions, including the amygdala, hippocampus, entorhinal cortex, and ventral striatum; motor areas including the basal ganglia and primary motor cortex; and higher-order cortical areas including the orbitofrontal cortex, ventromedial prefrontal cortex, and anterior temporal cortex.
Understanding the anatomy of the human olfactory system and its shared connectivity with diverse brain areas is a critical first step in understanding its relationship with neurodegenerative disorders that affect these areas and their function. Structural differences in olfactory areas may prove to be key biomarkers in diagnosing these disorders, and may help to inform future research on the mechanisms of disease-onset.

POSTER 12

MICROGLIAL SUBTYPES DIFFERENTIALLY RELATE TO NEURONAL DENSITIES AND IN VIVO CORTICAL ATROPHY IN PRIMARY PROGRESSIVE APHASIA CAUSED BY ALZHEIMER'S DISEASE

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Primary progressive aphasia (PPA) is a language-based dementia syndrome associated with multiple pathologies including Alzheimer's disease (AD). The cellular basis of in vivo cortical atrophy in PPA remains poorly understood. The current study determined how measures of cortical atrophy related to densities of activated microglia and neurons in five PPA participants with AD neuropathology (PPA-AD) and structural MRI scans within 2.5 years of death. All in vivo and ex vivo data were collected with anatomic correspondence between MRI and postmortem brain sections in the same 14 regions per case, which included five language and two non-language regions in the left hemisphere, along with their contralateral homologues. Regional cortical thickness was measured with FreeSurfer software and then converted to metrics of atrophy by deriving z-scores based on a healthy control group. Postmortem tissue was immunohistochemically processed with NeuN and HLA-DR antibodies to visualize neurons and activated microglia, respectively. All cell types were quantified using unbiased stereology, with hypertrophic microglia (HM) and ramified microglia (RM) counted separately due to the former's association with inflammation and neurotoxicity. Linear mixed models accounting for repeated measures were used for all analyses investigating the relationships between cortical atrophy and cell densities. Cortical atrophy was negatively related to RM ($p<0.01$). However, cortical atrophy had a positive relationship with HM and a negative relationship with neurons that did not reach statistical significance. HM and RM displayed an inverse relationship ($p<0.01$). Neurons were negatively related to HM ($p<0.01$) and positively related to RM ($p<0.01$). Therefore, RM might represent a class of HLA-DR-positive microglia less involved in neurodegenerative processes in PPA-AD. In contrast, more HM in areas with fewer neurons suggests microglia-mediated neuroinflammation might have a role in neurodegenerative processes that lead to cortical atrophy in PPA-AD.

POSTER 13

STRAIN-SPECIFIC EXPRESSION AND ACCUMULATION OF HUMAN TRANSGENIC TDP-43 IN A MOUSE MODEL OF FRONTOTEMPORAL LOBAR DEGENERATION

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Accumulation of TDP-43 in inclusions is one of the pathological hallmarks of frontotemporal lobar degeneration (FTLD). Mouse models have shown that overexpression of wild-type or mutant human TDP-43 (hTDP-43) results in the formation of inclusions and neuronal loss. To investigate the temporal sequence of inclusion formation and degeneration, we employed a conditional transgenic mouse model expressing hTDP-43 under the control of tetracycline operator sequences. Past studies have shown that in certain strains of mice, tetracycline transactivator (tTA) possesses toxicity independent of hTDP-43, which was rescuable by moving the transgene onto a congenic C57BL/6 background (B6). Brains of TDP conditional transgenic mice were harvested and immunohistochemically stained using antibodies against phosphorylated TDP-43 (pTDP-43) and hTDP-43. The number of TDP-43-positive inclusions were quantified in the frontal, temporal and parietal cortices after 5 and 14 days, as well as 4, 8, and 24 weeks of transgene expression. TTA and hTDP-43 transgenic mice were bred on 129SVE and FVB backgrounds respectively, which are among the mouse strains susceptible to neurodegeneration from tTA. To avoid tTA-specific degeneration, we backcrossed hTDP-43 overexpressing mice with B6 mice for 5 generations and bred animals with B6 mice expressing the tTA transgene. Pups were weaned, and brains examined after 14 and 28 days, as well as 8, 15, and 24 weeks of TDP expression. Brains were cut and stained for pTDP-43 and hTDP-43. Double transgenic mice on the 129SVE/ FVB background showed inclusions as early as 5 days after TDP-43 expression, followed by a gradual increase in the number of inclusions, peaking at14 days of post-weaning expression. After 8 and 24 weeks of transgene expression, inclusions were rarely encountered, but the brains showed the most severe degeneration. Transgenic mice on the B6 background showed a decrease in hTDP expression and in the size and number of inclusions, as well as a delay in their formation. Staining for human TDP-43 confirmed that although double transgenic B6 mice overexpress TDP-43, there is a significant reduction in hTDP-43 immunoreactivity compared to the original 129SVE/ FVB mice. These observations suggest that after prolonged transgene expression, TDP-43 inclusions disappear as neurons are lost. They also indicate that backcrossing hTDP-43 overexpressing mice onto a B6 background decreases the expression of TDP and delays inclusion formation. Our TDP-43 mouse model serves as a valuable tool in examining the temporal sequence of TDP-43 inclusion formation and its association with neuronal degeneration.

POSTER 14

MORPHOLOGY AND DISTRIBUTION OF TDP-43 PRE-INCLUSIONS IN PRIMARY PROGRESSIVE APHASIA

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Diffusely stained phosphorylated 43-kDa TAR DNA-binding protein (TDP-43)-positive "pre-inclusions" have been described. This experiment investigated morphological subtypes of pre-inclusions and their relationship with TDP-43 inclusions in primary progressive aphasia (PPA), a dementia characterized by gradual dissolution of language. Brain sections from five PPA participants with post-mortem diagnoses of frontotemporal lobar degeneration with TDP-43 pathology (FTLD-TDP) were immunohistochemically stained using an antibody to phosphorylated TDP-43, and quantitatively examined for regional and hemispheric distribution using unbiased stereology. Cortical TDP-43 pre-inclusions included smooth, granular/dot-like, or fibrillar staining with localization to the nucleus, cytoplasm, or both. Mature- and pre-inclusions were quantified in a region with high and a region with low mature inclusion density, and contralateral homologues. Regions with lower mature inclusions were characterized by higher densities of pre-inclusions, while increasing burden of inclusions corresponded to lower densities of pre-inclusions ($p<0.05$). Mature inclusions showed significant asymmetry that favored the language-dominant hemisphere ($p<0.01$), while pre-inclusions displayed the opposite pattern ($p<0.01$). Granular-type pre-inclusions were more abundant ($p<0.05$), and drove the hemispheric and regional differences ($p<0.02$). These results suggest that pre-inclusions are present in greater abundance prior to the formation of mature TDP-43 inclusions, and appear to develop through progressive stages into mature intracytoplasmic, or intranuclear aggregates.

POSTER 15

THE USE OF SUCROSE AS A CRYOPROTECTANT FOR FIXED HUMAN TISSUE

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The Mesulam Center for Cognitive Neurology and Alzheimer's Disease conducts and facilitates research for neurodegenerative diseases such as Alzheimer's disease, frontotemporal lobar degeneration, and vascular disease. The brain bank at the Mesulam Center is responsible for housing over 900 human brains. Human tissue is ideal for researching neurodegenerative diseases. To ensure adequate preservation of these precious tissues, brains are fixed with either paraformaldehyde (PFA) or neutral buffered formalin (NBF) and stored in an increasing gradient of sucrose ranging from a 10% to 40% concentration, acting as a cryoprotectant. During a brain bank relocation process, the cold room, where brains are stored, malfunctioned. This triggered the temperature to decrease from 4°C to -11°C, causing the sucrose and tissue to freeze. Without the cryoprotectant, this would pose a threat to the tissue because damage caused by ice crystals, known as freezing artifact, produce micro-tears in the tissue. The specimens impacted by the freeze were examined through morphological staining and immunohistochemistry by experienced neuropathologists to determine the resulting integrity of the brain tissue. Lower percentages of sucrose have a higher concentration of water, and therefore have a higher freezing point. This explains why tissue stored in 10% sucrose were more affected by freezing artifacts, and tissue stored in 20% or higher were relatively unaltered. However, procedurally it is important to begin storage at a lower concentration of 10% and gradually bring it to 40%. Immediately immersing specimens in the highest concentration of sucrose would be too harsh on the tissue. Although some damage occurred for brains stored in 10% sucrose, the neuropathologists determined that the human brain samples are still valid due to the Center's methods of storage and preservation.

POSTER 16

IMAGING CORE AT THE NORTHWESTERN ALZHEIMER'S DISEASE CENTER

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The Imaging Core at the Mesulam Center for Cognitive Neurology and Alzheimer's Disease aims to enhance research activities on aging and dementia within and outside of Northwestern University. Neuroimaging is focused on the spectrum of extraordinary cognitive aging to dementia, including the FTD-spectrum of disorders. The Imaging Core contains multimodal data from scans that provide optimal quantitative information on brain structure (MPRAGE MRI), white matter properties (FLAIR MRI), axonal pathways (diffusion MRI), resting state hemodynamic fluctuations for establishing functional connectivity (rsfMRI), cerebral blood flow (ASL MRI), amyloid (18F-Florbetaben PET) & tau (18FFlortaucipir PET) binding and glucose (18F-FDG PET) uptake. Neuroimaging data are available to enhance diagnostic characterization of the participants and to enrich projects of our collaborators. This poster will highlight the neuroimaging data available and some of the recent findings from studies using neuroimaging data from Clinical Core participants in the Mesulam Center.

POSTER 17

FAM76B MODULATES MICROGLIA ACTIVATION AND NEUROINFLAMMATION IN NEURODEGENERATIVE DISEASES

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Neuroinflammation is implicated in numerous brain disorders, including ischemic injury, traumatic brain injury and neurodegeneration. However, the molecular mechanisms by which neuroinflammation contributes to these diseases remains unknown. We previously found that FAM76B could suppress inflammation mediated by macrophages. In this study, we successfully produced FAM76B knockout (KO) mice, which showed activation of macrophages in bone marrow and of microglia in the hippocampus and thalamus. After lipopolysaccharide (LPS) challenge to induce local inflammation, FAM76B-deficient mice had significantly increased tingible body macrophages in the white pulp of spleen, and prominent microglial activation in the brain. Furthermore, we found that the response of FAM76B-positive microglia showed unique patterns in neurodegenerative diseases. FAM76B-positive microglia showed minimal response to tangles and plaques in brain tissue with Alzheimer's disease (AD) pathology without hippocampal sclerosis (HS), while having a prominent response to hippocampal sclerosis in both AD and frontotemporal lobar degeneration with TDP-43 proteinopathy (FTLD-TDP). This responsive pattern was not seen in the general microglial population labeled by IBA-1. This study suggests that FAM76B's biological function is that of a modulator of neuroinflammation, and that it may have a role in the pathogenesis of hippocampal sclerosis in neurodegeneration.

POSTER 18

SEX DIFFERENCES IN THE RELATIONSHIP BETWEEN CORTICAL NEURODEGENERATION AND FDG-PET HYPOMETABOLISM IN AD AND PROGRESSIVE-MCI

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Background: To better understand the relationship between cortical thinning (neurodegeneration) and cortical glucose hypometabolism throughout disease progression and across genders, the correlation between measures was compared in individuals with Alzheimer's Disease (AD, n = 223), Mild Cognitive Impairment (MCI, n= 261) who convert to AD, MCI who remain stable (n = 370), and normal controls (n = 282).

Method: All T1-MPRAGE and FDG-PET scans were downloaded from the Alzheimer's Disease Neuroimaging Initiative website (cohorts ADNI-1&2) and underwent further processing. MPRAGE scans underwent FreeSurfer processing, correcting for geometric inaccuracies or topological defects. PET data were projected onto the FreeSurfer cortical white surface. These processing steps resulted in vectors of cortical GM thickness and cortical GM FDG-PET uptake data, correspondingly indexed over the FreeSurfer template white surface and smoothed to the same degree across all subjects. Individual Pearson correlation coefficients were computed to assess subject-wise concordance of cortical thickness and cortical FDG-PET uptake measures. Linear mixed effects models assessing the effects of time, gender, diagnostic category on correlations while accounting for age, education and APOE-4 status were examined.

Result: Linear mixed-effects models revealed significant effect of time on the correlation between cortical thickness and cortical FDG-PET uptake, such that concordance between measures decreased across all time points ($p<.001$). Female participants had increased correlations across all time points ($p<.05$), and showed higher concordance than males at worsening disease-states (Females > Males at pMCI & AD, $p<.05$).

Conclusion: Our findings highlight differing profiles of the correlation in metabolic-structural neurodegeneration in males and females across diagnostic categories and time, suggesting possible differences in the pathological mechanisms, temporal sequence of mechanisms or overall disease burden across genders.

POSTER 19

CALCIUM BINDING PROTEIN IMMUNOREACTIVITIES ARE VIRTUALLY ABSENT FROM HUMAN LOCUS COERULEUS NORADRENERGIC NEURONS

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A G_4C_2 hexanucleotide repeat expansion (HRE) in the first intron of the *C9orf72* gene (C9) is the most significant genetic driver of amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). Recent findings identified a novel pathogenic mechanism wherein the C9 mutation disrupts nucleocytoplasmic transport. Accordingly, we developed a C9-HRE expression system and utilized biochemical subcellular fractionation coupled to mass spectrometry (MS)-based quantitative proteomics to identify proteins that demonstrate altered subcellular distribution in C9-HRE-expressing cells compared to controls. We found that the proteome shifted to a higher level of cytosolic accumulation in cells expressing the C9-HRE. Further, we identified 126 proteins that demonstrate a significantly altered nuclear to cytoplasmic ratio. The majority of proteins that showed a bidirectional change, shifted localization from the nucleus to the cytosol. Gene ontology analysis revealed a striking enrichment for proteins involved in RNA metabolism, proteostasis, nucleocytoplasmic transport, and protein translation. We validated that these changes correspond to functional pathways in patient-derived motor neurons (MNs) by analyzing *de novo* protein translation and found it was significantly reduced in C9 patient-derived MNs. Finally, we validated that one identified protein, eukaryotic termination factor 1 (ETF1), is enriched in the nuclear fraction of C9 patient-derived MNs and are pursuing downstream consequences of this particular mislocalized protein.

POSTER 20

HIPPOCAMPAL EPILEPTIC ACTIVITY DURING SLEEP DISRUPTS MEMORY CONSOLIDATION

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Memory consolidation may depend on temporal coordination among cortical slow-oscillations, sleep-spindles, and hippocampal-ripples during slow-wave sleep. This proposed mechanism may be dysfunctional in certain neurological groups. Some patients with epilepsy, for example, experience “accelerated long-term forgetting,” in that forgetting becomes excessive only with some delay after initial learning. This pattern, with normal memory after shorter delays, has been difficult to explain given conventional conceptions of memory. We propose that abnormal electrical activity in the hippocampus due to a seizure disorder could disrupt memory storage. Here, we analyzed relationships between seizure activity during sleep and memory consolidation. Our strategy was to use targeted memory reactivation (TMR) by presenting learning-associated sounds during sleep, with a within-subject design that avoided the interpretive challenges of comparing retention intervals with sleep versus wake. Patients diagnosed with temporal-lobe epilepsy performed a spatial memory task before and after nocturnal sleep. Five patients without seizure activity overnight remembered cued object-locations better in the morning compared to uncued object-locations (as do healthy individuals). In contrast, forgetting in four patients with seizure activity was increased for cued object-locations. Because memory was preferentially influenced for cued object-locations, rather than defective for all object-locations that had been learned, we suggest that overnight seizures specifically accelerated forgetting for exogenously reactivated memories. Given that this seizure activity was apparent unilaterally in the hippocampus, but not at the scalp, we speculate that this problem may impact patients with epilepsy even when standard scalp EEG recordings during sleep appear normal.

POSTER 21

CHARACTERIZATION OF THE FUNCTION OF THE HNK-1 CARBOHYDRATE EPITOPE IN ALZHEIMER'S DISEASE

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Glycosylation is a common but complex post-translational modification that is estimated to occur in over half of all proteins. This process adds both structural and functional diversity to proteins and deficits in glycosylation can lead to protein misfolding and destabilization. Despite its critical role in protein structure and function, changes in glycosylation in the development of Alzheimer's disease (AD) remain elusive. The Human Natural Killer-1 (HNK-1) carbohydrate epitope, a sulfated trisaccharide synthesized in the Golgi apparatus, is highly expressed in the hippocampus and is required for learning and memory. Prior studies report a widespread reduction of HNK-1 in the AD brain. Accordingly, the purpose of this research is to further characterize the function of HNK-1 in AD through an immunohistochemical analysis of HNK-1 expression in different brain areas. We find an upregulation of HNK-1 expressed in microglia that surround amyloid plaques in the AD brain. We hope to eventually identify the specific proteins to which HNK-1 is attached in order to determine widespread changes in glycosylation in AD and their corresponding functional consequences. This research will lead to a better understanding of the role of oligosaccharides conjugated to membrane glycoproteins in transducing cellular processes leading to cognitive decline in AD. Furthermore, our finding that HNK-1 is expressed in microglia alludes to a possible function of HNK-1 in the AD immune response.

POSTER 22

SEX DIFFERENCES OF THE PHOSPHOPROTEOMIC PROFILES IN APP/PS1 MICE AFTER CHRONIC UNPREDICTABLE MILD STRESS

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Of the 5.4 million Americans suffering from Alzheimer's Disease (AD), roughly two-thirds are women. While women's longer average lifespan is a plausible explanation for the prevalence gap in AD diagnosis, increasing evidence suggests that there remains an age- and risk factor-matched enhanced risk for AD in women. The biological mechanisms underlying this sex divergence in the prevalence of AD, however, remains unknown. Previous research has shown sex-specific biochemical differences in central stress responses that bias female mice towards pro-AD signaling on the phosphoproteomic level via Corticotropin Releasing Factor (CRF) Receptor 1 activation after CRF overexpression. In this study, we aimed to determine if these findings could similarly be reproduced under physiological CRF expression following chronic stress. We stressed APP/PS1 mice using a Chronic Unpredictable Mild Stress (CUMS) paradigm for 1 month. CUMS is commonly used in animal models to mimic the daily life stress of humans. In our model, we used a variety of mild to moderate stressors including wet bedding, cage tilt, and acute restraint at differing times of the day. Following CUMS and behavioral assessments, we collected brain tissue and identified and quantified whole protein and phosphoprotein levels in the cortex of the stressed and non-stress APP/PS1 mice using MaxQuant. While there were no significant differences at the total protein and peptide levels, we found 909 statistically significant phosphopeptides between stressed and unstressed females and 841 statistically significant phosphopeptides between stressed and unstressed males using a False Discovery Rate of 5%. Of these significant phosphopeptides, only 301 were the same in males and females. These results indicate that while both males and females undergo protein phosphorylation changes following stress, the peptides that are phosphorylated differ between sexes. We then compared these significant phosphopeptides using Metacore analysis to determine which biological pathways were affected. We found that several pathways were changed differently between male and female mice including NMDA receptor trafficking, cytoskeleton organization, and Tau pathology. Our next step will be to confirm such changes in the statistically significant pathways of interest, specifically those associated with AD-related neuropathogenesis. The differing biological pathways affected between males and females in response to chronic stress may help us to better understand why women are at a higher risk of AD and what may be causing the link between female-biased, stress associated neuropsychiatric disorders such as major depression disorder with AD.

POSTER 23

ROLE OF HIPPOCAMPAL NEUROGENESIS AND BMP SIGNALING ON AGING RELATED CHANGES IN COGNITION AND AFFECT

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Global population aging makes the maintenance of cognitive and coping abilities throughout life a crucial public health concern, yet little is known about the mechanisms of healthy cognitive and affective function in later life. Regular exercise or exposure to an enriched environment supports adaptive abilities in old age and can partially restore age-related decline in cognitive functions. These improvements are shown to be associated with increased neurogenesis in the hippocampus. However, the mechanisms underlying the increased neurogenesis and the relationship to the changes in cognition are unclear. We found that bone morphogenetic protein (BMP) signaling increases greatly during aging in both mouse and human hippocampus. Inhibition of BMP signaling in the hippocampus of aging mice enhances neurogenesis and prevents hippocampus-dependent cognitive decline. Furthermore, cognitive decline during aging is associated with an increased risk of depression/anxiety, and inhibition of BMP signaling in the hippocampus also improves affective behavior. This observation is consistent with numerous studies that have correlated decreased neurogenesis and cognition with depression-like behavior. Thus, BMP signaling represents a key mechanism supporting adaptive cognitive and affective capacities, as well as neurogenesis in late adulthood. Nevertheless, while changes in neurogenesis and behavior occur in parallel after inhibition of BMP signaling in neural stem/progenitor cells, at present this is just a correlation. To address the question of causality, I had to develop a tool, I chose DREADD technology and conditional expression of the mutant G protein-coupled receptors, hM4Di and hM3Dq, which are exclusively activated by exogenous otherwise inert ligand CNO. First of all, I produced double transgenic mice, Ascl1-CreERT2; R26LSL-hM4Di, which allowed me conditional expression of HA-tagged hM4Di and yellow fluorescent protein (YFP) in Ascl1-expressing cells, which includes intermediate neural progenitor cells as well as a small subset of actively dividing neural stem cells in the dentate gyrus of the hippocampus. Electrophysiological characterization of these YFP-expressing newborn granule neurons on hippocampal slices showed that CNO substantially decreased the number of action potentials elicited by depolarizing current injection in hM4Di-expressing neurons, demonstrating that CNO mediated activation of hM4Di had a potent effect on the excitability of the neurons. Next, I tested the behavioral effects of this selective inhibition. To start with, I chose fluoxetine treatment to modulate the number of newborn neurons, because we have already shown that fluoxetine treatment is an effective and efficient way to increase neurogenesis and it would be suitable during the process of establishing this new DREADD method. Adult Ascl1-CreERT2; R26LSL-hM4Di mice received fluoxetine or saline together with CNO or vehicle supplementation for 3 weeks. By this way, newborn neurons were silenced during the entire period of fluoxetine treatment. At the end of the 3rd week, behavioral assessment showed that fluoxetine treatment alone improved the behavioral phenotype in parallel to increased neurogenesis and neuronal activity in the DG. However, CNO supplementation together with fluoxetine treatment blocked the ameliorative effects of the antidepressant on both behavioral and molecular phenotypes. Additionally, CNO treatment of hM4Di animals in the absence of fluoxetine reduced the neuronal activity below baseline levels correlating with the behavioral findings. CNO supplementation in the absence of hM4Di and hM4Di expression in the absence of CNO did not alter measured phenotypes. Taken together, these findings indicate that the activity of newly generated neurons in the DG exerts profound effects on behavior and by using DREADD technology I can manipulate it. Right now, I am aging these double transgenic animals to examine their performance later. As the main goal of my project is to dissect out the role of BMP signaling on neurogenesis and cognitive/affective phenotypes during aging, I have produced triple transgenic mice, Ascl1-CreERT2; RIIflx/flx; R26LSL-hM4Di. These mice express HA-tagged hM4Di in neural stem/progenitor cells and their progeny simultaneously with the deletion of BMP type II receptor (BMPRII) after the administration of tamoxifen. By this

way, I can increase the number of newborn neurons by inhibiting BMP signaling and silence specifically these newborn neurons by using CNO supplementation. I used a similar experimental design to examine the effects of BMP signaling inhibition on behavioral phenotypes, neurogenesis and neuronal activity. After tamoxifen injection, adult Ascl1-CreERT2; RIIflx/flx; R26LSL-hM4Di mice received CNO or vehicle supplementation for 3 weeks. At the end of the 3rd week, behavioral assessment showed that inhibition of BMP signaling by deleting BMPRII improved the behavioral phenotypes, while CNO supplementation blocked this effect, similar to above described fluoxetine study. Immunohistological analyses of these samples are ongoing to determine whether CNO treatment affected the proliferation of the DG cells and/or reduced activation of hM4Di-expressing neurons. Once I have the molecular results, I will start the experiments to determine whether increased neurogenesis, resulting from the inhibition of BMP signaling, is causal to long-term enhancements of hippocampus-dependent cognition and anxiety/depression-like behaviors in aged mice by using DREADD/CNO-based method.

POSTER 24

NEUROPLASTICITY OF LANGUAGE NETWORKS IN PRIMARY PROGRESSIVE APHASIA: EVIDENCE FROM A PATIENT WITH AGRAMMATIC VARIANT OF PPA

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Introduction: Studies focused on the neural reorganization of language networks associated with treatment have been conducted primarily with stroke-induced aphasic individuals (Hartwigsen & Saur, 2017; Kiran & Thompson, 2019). A small but emerging body of literature suggests that treatment can improve language in primary progressive aphasia (PPA) as well. However, few studies have reported neural changes associated with treatment. One study found increased activation in left dorsal prefrontal regions following training of word-retrieval (Beeson et al., 2011) and another reported increased resting-state connectivity in left temporo-parietal and right frontoinsular regions following speech production script training (Bonakdarpour et al., 2018). The present study examined the neurocognitive effects of a sentence production/comprehension treatment in one participant (DK) with agrammatic PPA (PPA-G) by investigating changes in on-line sentence processing and neural activation using eye-tracking and fMRI, respectively, and their relation to atrophy patterns. We predicted that improvement in offline sentence processing (as measured by behavioral tasks) would be mirrored by changes in online processing strategies and shifts in neural activation, similar to recent findings on language recovery in stroke agrammatism (Barbieri et al., under revision; Mack, Nerantzini, & Thompson, 2017; Mack & Thompson, 2017). Such findings would serve to inform clinicians about approaches for treatment of PPA-G.

Methods: DK, a 70-year-old right-handed man, was diagnosed with PPA-G based on language and cognitive testing and neurological examination. At the time of enrollment in the study, he was three years post symptom-onset and presented with difficulties in sentence production and verb morphology, in the presence of unimpaired single word comprehension and semantic knowledge, and high average performance on measures of memory, attention, abstract reasoning and executive function. DK underwent Treatment of Underlying Forms (TUF; Thompson & Shapiro, 2005), using a longitudinal single-subject multiple probe design to train passive sentences (e.g., the boy was shaved by the man in the barbershop) in the first phase and object-cleft sentences (e.g., it was the boy who the man shaved) in the second phase. Treatment was provided for 3 months for each structure, with weekly testing of trained and untrained sentences. Immediately before, after, and 3-months following each treatment phase offline sentence comprehension and production probes, eyetracking using sentence-picture matching and sentence production priming tasks1 and an fMRI sentence verification task were administered to test trained and untrained sentence structures. Structural MR scans also were acquired before and after each treatment phase to map changes in cortical atrophy throughout the study, using voxel based morphology (VBM). In total, the study spanned 15 months.

Results: Production of passive and object-cleft sentences improved during the first and the second treatment phase, respectively. Whereas, comprehension of passive sentences was relatively unimpaired before, and remained so, during passive treatment, comprehension of object-cleft sentences was low, and unchanged during this period, but improved during object-cleft treatment (see Figure 1). Generalization of treatment gains to untrained simpler, linguistically-related structures and changes in eye movements were noted following both treatment phases. Eye movement shifts occurred following Phase 1 treatment on the sentence production priming task, with post-

treatment patterns reflecting use of an incremental processing strategy seen in healthy older adults (Mack et al., 2017); after Phase 2 treatment, eye-movements on the sentence-picture matching task showed emergence of timely thematic prediction, also in line with healthy participants' patterns (Mack & Thompson, 2017), but no change in thematic integration was noted. Improvements in language test scores, including those derived from the Northwestern Assessment of Verbs and Sentences (NAVS: Thompson, 2011), also were found following passive treatment, but declines were noted prior to object cleft treatment, with further declines following treatment. Performance on tests of cognitive function, however, remained relatively unchanged through the study. Neural activation patterns shifted following both treatment phases in non-atrophied regions of the brain. Prior to Phase 1, atrophy was constrained to the left hemisphere, in the hippocampus and orbitofrontal region, which spread to include the anterior parahippocampus, subcallosal cortex and caudate nucleus following treatment. FMRI results showed post-passive treatment upregulation of neural activation in both left and right hemisphere regions in the superior, middle, and inferior frontal gyri (SFG, MFG, IFG, respectively), and inferior parietal lobe (IPL), regions activated in healthy individuals for sentence processing (Europa et al., 2019; Walenski et al., 2019). Prior to Phase 2, atrophy had spread to include the right hippocampus and caudate nucleus and, at post-treatment, greater atrophy in these regions in the both hemispheres were found. Nevertheless, upregulation in the left frontal pole and IFG, and right IPL was found following Phase 2 treatment (see Figure 2).

Discussion: The study provides compelling evidence for treatment-induced neuroplasticity in the presence of neurodegenerative disease and lends support for the implementation of linguistically-based sentence processing treatment for patients with PPA-G. Similar to patterns seen in post-stroke aphasia, DK showed behavioral improvements in sentence comprehension and production, mirrored by changes in processing strategies (as shown by eye-tracking), indicating a shift toward normal-like eye movement patterns. Changes in off-line and on-line measures also were associated with recruitment of brain regions, bilaterally, that are activated by healthy participants and engaged for recovery of sentence processing in stroke-agrammatic aphasia.

POSTER 25

KLOTHO IMPACT ON ALZHEIMER'S DISEASE PATHOGENESIS THROUGH TRPC CHANNEL MODULATION

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Klotho is a single-pass transmembrane anti-aging protein that significantly enhances cognitive function. Recent studies indicate that Klotho -/- mice demonstrate accelerated development of aging-like phenotypes including stunted growth, thin and atrophic skin and cognitive deficits. It was observed that administration of a α-klotho protein fragment (αKL-F) peripherally induced cognitive enhancement in mice. Despite Klotho's ability to mitigate cognitive decline, whether Klotho also affects the neuropathogenesis of AD is still unknown. Klotho by its β-glucuronidase activity acts as a mediator of transient receptor potential (TRP) cation TRPV5 channel trafficking. Interestingly, it was shown that one of the TRP family, TRPC6 interacts with APP leading to inhibition of its cleavage by γ-secretase and, thus, a reduction in Aβ production. Therefore, we hypothesize that Klotho may impact on AD neuropathgenesis through the regulation of the TRPC channels function. In this study, using bioinformatic approach, we analyzed brain-specific AD and control transcriptome sequence datasets (HISAT2, STRINGTIE, and DESeq2 packages) from whole brain, frontal and temporal lobes to determine gene profiles and differential gene expression in AD subjects compared to controls. We focused mainly on Klotho, TRPCs genes as considering their role in Alzheimer's disease pathogenesis and progression. We found that the TRPC1, TRPC3, TRPC5, as well TRPC6 were down-regulated >3-fold in the cortex of AD subjects. Additionally, Klotho gene was also down regulated by 3-fold in the same areas. Protein-protein interaction network analysis of Klotho and TRPC6 and their interacting partners shows that Klotho, beta-Klotho, TRPC6 along with Phospholipase C Gamma 1(PLCG1) had higher between-ness centrality in the network. In AD subjects Klotho was down regulated along with its known interacting partner TRPC genes. The co-downregulation of Klotho and TRPC genes, especially TRPC6 gene and their link in the network suggesting a possible direct or indirect interaction among the proteins. Our biochemical studies by western blot analysis demonstrated that Klotho and TRPC1, TRPC5 and TRPC6 were significantly downregulated in the cortical tissues of AD post-mortem brain and the brains of AD mouse models, suggesting that these molecules may be instrumental in AD pathogenesis. Klotho and TRPC6 co-localize in cortical neuronal membrane in the 13-month old AD knock-in mouse brains (APPNL-G-F) further supporting that Klotho may impact on AD through TRPC6 channels trafficking and influence γ-secretase-mediated cleavage in the AD. To confirm this link, next we will conduct the chromatin immunoprecipitation (ChIP) assay for Klotho-TRPC6 on γ-secretase gene promoter, and through overexpression of Klotho by viral vector mediated genome editing approach, in AD mice to improve the entrapment of TRPC channels in the plasma membrane and decrease Aβ production. Our work may open a novel avenue to develop a new target for therapeutic potential for treatment of AD.

POSTER 26

THE EFFECTS OF LEARNING AND AGING ON FUNCTIONAL CHARACTERISTICS OF LAYER V PYRAMIDAL NEURONS OF THE LATERAL ENTORHINAL CORTEX

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Increased human longevity has caused a steady rise in the prevalence of aging-related health issues, most notably age-related cognitive decline, including forms of dementia, such as Alzheimer's disease (AD). While many aged individuals experience some level of cognitive impairment (age impaired, AI), there are other individuals, 'super-agers' (age unimpaired, AU), that maintain cognitive performance similar to that of younger adults (Y). The lateral entorhinal cortex (LEC) is known to be vitally important for temporal associative learning, and is among the first areas of the brain to exhibit AD pathologies prior to the observation of behavioral deficits. One of the prominent features of layer V LEC pyramidal neurons is their ability to exhibit a graded persistent firing activity, a cholinergic dependent property that is a potential mechanism underlying associative learning and memory. Cholinergic activity is reduced in aging and AD, which could reduce cellular excitability and negatively impact persistent firing throughout the LEC. The LEC is thus a rich potential target in which to study memory and age-related changes in cognition.

This project utilizes whole-cell patch clamp electrophysiology to evaluate age-related changes in the intrinsic excitability of layer V pyramidal neurons of the LEC. All recordings were derived from young adult (3-6 month) or aged (28-31 month) hybrid Fisher 344 x Brown Norway rats. To incorporate behavioral changes in learning and memory, I used trace eye blink conditioning (tEBC) to separate aged individuals into AU or AI cohorts.
I analyzed postburst AHP to investigate changes in intrinsic excitability. Results from recordings taken 24 hours after the final training session indicate that the slow AHP (sAHP) is reduced in young and AU rats that underwent tEBC, when compared to young pseudoconditioned and AI rats. Data indicates there is no difference between sAHP of young and AU rats. However, one month after the final training session, AU rats exhibit a sAHP similar to that seen in AI rats, indicating that the decrease in sAHP seen at the 24hr time point is transient in nature.

While it is currently unknown how cholinergic tone within deep layers of LEC is affected with age, one component of AD pathology is the degradation of cholinergic neurons and receptors. By applying the muscarinic receptor agonist carbachol I can elicit persistent firing in layer V LEC pyramidal neurons. Results indicate that persistent firing is less robust in aged tissue, potentially stemming from a loss of cholinergic tone. Combined, the observations from this study are among the first to reveal how aging and learning affect the cellular physiology of the LEC.

POSTER 27

GENE EXPRESSION REVEALS MOLECULAR INSIGHT FOR SELECTIVE VULNERABILITY IN ALZHEIMER'S DISEASE

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The hippocampus is known for its complexity and function in learning, memory, and spatial navigation. The structure of hippocampus consists of several divisions, which include subiculum, the four cornu ammonis (CA) sectors, and the dentate gyrus. Each region is known for its unique function and connectivity. Interestingly, in diseases not all areas of the hippocampus is equally affected in patients. In an effort to build effective treatment strategies, we need to understand the molecular basis of their identification, connectivity and vulnerability in diseases. We hypothesize that even though all neurons have access to the same genetic material, not all neurons express the same genes. The choice they make and the genes they decide to express implement their identity, shape their connectivity and at times of diseases determine their vulnerability. Therefore, we think that gene expression profiles in distinct areas of the hippocampus help bring a mechanistic insight for the cellular events that are primarily important for their function, and could indeed be the causes of their vulnerability when perturbed. We investigated the expression profile of 2342 genes and grouped them based on the location they are primarily expressed. We found that 74 genes are primarily expressed in the dentate gyrus, 41 genes in the CA3 region, 29 in the CA1-2 region of the hippocampus. When the canonical pathways the proteins encoded by these genes are involved in are investigated by large-data management tool boxes, distinct cellular events are suggested to be more important in different parts of the hippocampus. In addition, some key proteins, with involvement in numerous cellular events, also became evident. These studies suggest that one of the reasons for selective vulnerability is their inability to maintain homeostasis for the canonical pathways that are critically important for their function. Understanding those canonical pathways and key converging domains would help develop effective treatment strategies.

POSTER 28

PRIMARY PROGRESSIVE APHASIA RESEARCH PROGRAM AT THE MESULAM CENTER FOR COGNITIVE NEUROLOGY AND ALZHEIMER DISEASE

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Primary progressive aphasia (PPA) is a neurodegenerative dementia syndrome characterized by a progressive loss of language function. PPA has a low prevalence in clinical practice compared to Alzheimer's dementia. In the absence of medical treatment, the Mesulam Center for Cognitive Neurology and Alzheimer's Disease seeks to advance PPA research through a collaborative program aimed at studying, educating, and improving treatment for individuals living with PPA and their families.

Over the past decade, more than 250 participants from 35 US states, Canada, Singapore, and Spain have enrolled in PPA studies at the Mesulam Center. Participants visit Chicago every 1-2 years to complete neuropsychological assessments that precisely measure language, memory, and cognition, as well as experimental studies of language processing using eye tracking technology. Additionally, participants undergo multiple brain imaging examinations with MRI and PET scanners in our state-of-the-art imaging facilities. Researchers combine neuropsychological testing with these advanced neuroimaging techniques to better understand the underlying mechanisms of language decline in the PPA brain.

Some participants also take part in the Mesulam Center's web-based speech/language therapy and educational research programs, which are tailored to the needs of people living with PPA. These life-enrichment interventions use innovative technology to improve access to specialized care. In addition to several multi-day visits throughout the disease course, most Mesulam Center PPA research participants agree to take part in our brain donation program to allow for further scientific investigation of the neuropathologic causes of the illness. These studies allow us to improve the diagnosis, prognosis, and quality of life for individuals living with PPA, as well as understand the biological basis of language in the brain.

Funding from the National Institutes of Health, Illinois Department of Public Health, Run4Papa campaign, Association for Frontotemporal Degeneration, and generous personal donations have provided the opportunity for the Mesulam Center to research novel diagnostic and therapeutic initiatives in PPA. Through its multidisciplinary approach to both research and patient care, Northwestern University's Mesulam Center remains one of the top referral centers in the world for PPA. We are grateful for the time and dedication of our research participants.

POSTER 29

ELEVATION OF NEWLY GENERATED SOLUBLE AMYLOID PRECURSOR PROTEIN-B IN CEREBROSPINAL FLUID OF HUMANS WITH AMYLOID DEPOSITION

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Background: The amyloid hypothesis proposes that increased production and/or decreased clearance of amyloid-beta (Aβ) leads to higher order amyloid structures that initiate a cascade of events, culminating in neuronal death that manifests as Alzheimer's disease (AD). Sequential cleavage of Amyloid Precursor Protein (APP) generates Aβ. APP may be processed in one of at least two pathways, initially being cleaved by either α- or β-secretase (BACE1). α-secretase cleavage of APP precludes Aβ formation and produces soluble APP-α (sAPPα). Alternatively, BACE1 cleavage of APP releases soluble APP-β (sAPPβ) and subsequent cleavage by γ-secretase produces Aβ. Therefore, while sAPPβ is a direct product of BACE1 cleavage of APP, Aβ is an indirect product of BACE1 processing that also requires γ-secretase activity. Nevertheless, BACE1 processing of APP is an obligate initial step in Aβ production, and sAPPβ is a surrogate marker of BACE1 activity. In some studies BACE1 and sAPPβ are increased in cerebrospinal fluid (CSF) and post-mortem AD brain. Our previous data demonstrate an increase in CSF sAPPβ: sAPPα ratio in AD subjects versus age-matched controls, indicating a pathophysiological shift toward BACE1 processing of APP. Further, sAPPβ and Aβ concentrations are highly positively correlated in human CSF, but sAPPα and Aβ correlate less well, which suggests BACE1 activity mediates both sAPPβ and Aβ differences among people. In brains of postmortem AD and amyloid mouse models, we have shown that BACE1 levels are dramatically increased in dystrophic neurites surrounding amyloid plaques, which exhibit increased BACE1 cleavage of APP and the generation of both sAPPβ and Aβ. Recently it was shown that CSF Aβ38 and Aβ40, as surrogate markers of Aβ production, were elevated in humans with amyloid deposition. Moreover, the correlation between Aβ38 and Aβ40 and amyloid load was most pronounced in subjects negative for ApoE4. Since ApoE4 reduces Aβ clearance, the correlation between Aβ38 and Aβ40 and amyloid load in ApoE4 negative subjects indicates a subgroup of individuals in which the mechanism of Aβ accumulation is not simply due to decreased clearance. Together these findings suggest increased BACE1 activity may cause increased Aβ in an AD subpopulation, but has not been directly assessed until now.

Methods: Using highly sensitive stable isotope labeling kinetics (SILK)/immunoprecipitation (IP)/liquid chromatography-tandem mass spectrometry (LC-MS/MS) methods, we quantified sAPPβ and sAPPα in CSF from human AD subjects and controls to determine β- and α-secretase activity in human CNS. In this pilot study, newly generated sAPPβ and sAPPα were measured in eleven elderly human subjects who had undergone [U-13C6] leucine labeling and hourly CSF collection over 36 hours. Three of the subjects had brain amyloidosis (Amyloid+), and the remaining eight were free of amyloid (Amyloid-). Serially-sampled CSF underwent sequential IP to isolate sAPPβ (using a neo-epitope sAPPβ-specific antibody-bead complex) and then sAPPα (using a W02-antibody bead complex). Peptides resulting from tryptic digest of the purified sAPPβ or sAPPα were quantified by LC-MS/MS using the Dionex UltiMate 3000/TSQ Quantum Ultra system. To determine kinetic behavior of APP metabolites, the fraction of the metabolite derived from de novo synthesis was measured by calculating hourly sAPPβ and sAPPα mole fraction labeled (MFL), normalized to plasma leucine enrichment, over 36 hours. In order to determine each subject's newly generated APP metabolites by absolute quantitation, normalized sAPPβ or sAPPα MFL was multiplied by the absolute concentration of sAPPβ or sAPPα, respectively. Absolute concentrations were previously determined by sAPPβ and sAPPα specific ELISAs.

Results: Both sAPPβ and sAPPα turnover rates were slower in Amyloid+ subjects. There was a slight upslope of the ratio of newly generated sAPPβ:sAPPα in the Amyloid+ subjects (slope, m=0.019) which was significantly higher than the Amyloid- group (m=0.013; p=0.013); both slopes were significantly non-zero ($p<0.0001$). This indicates that sAPPβ turnover rate is marginally slower than sAPPα, and this difference is accentuated in the setting of amyloid deposition. Newly generated sAPPβ, as well as the absolute ratio of newly generated sAPPβ:sAPPα, were significantly elevated in Amyloid+ subjects ($p<0.0001$). In contrast, newly generated sAPPα was not significantly different between groups. Importantly, these results strongly suggest increased processing of APP by BACE1 in the subjects with brain amyloid deposition.

Conclusion: We will next expand this pilot study to include a larger sample size of 46 subjects. We hypothesize that most AD patients overproduce Aβ due to increased BACE1 activity as measured by increased absolute production of sAPPβ. By directly measuring the kinetics and newly generated sAPPβ in vivo, we are determining if, and by how much, BACE1 activity is increased in AD subjects. These results would allow for characterization of AD subpopulations most likely to benefit from BACE1 inhibitors. Outcomes will elucidate human CNS APP physiology and AD pathophysiology and also prove useful for measuring pharmacodynamic effects of candidate therapeutics. BACE1 is currently a high priority target for AD, thus results of altered BACE1 activity in AD are critical for understanding AD pathophysiology and development of disease modifying therapeutics.

POSTER 30

THE ROLE OF ASTROCYTE CALCIUM SIGNALS IN THE PRODUCTION OF INFLAMMATORY FACTORS AND MODULATION OF SYNAPTIC FUNCTION

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Astrocytes play a central role in inflammation by releasing inflammatory factors such as cytokines. These cytokines are elevated in a growing list of pathologies, including Alzheimer's Disease (AD), that exhibit altered synaptic function. Currently, it is unclear how these cytokines are produced and how they contribute to synaptic dysfunction. However, cytokine production has been linked to extended intracellular calcium elevations, which requires store operated calcium entry (SOCE) in many non-excitable cells. In astrocytes, SOCE is mediated by the channel protein, Orai1, and a calcium sensor, Stim1. The goal of my project is to understand how cytokines regulated by astrocytic SOCE affect synaptic function. My results show that astrocytes rely on SOCE to produce multiple cytokines. Orai1 KO astrocytes have impaired activation of transcription factors NFAT and NFκB, indicating that SOCE may regulate cytokine production through these transcription factors. The effects of these cytokines on neuronal function is being tested through glutamate uncaging on single dendritic spines and calcium imaging with gCaMP6f to measure the synaptic responses. My preliminary results indicate that conditioned media from thrombin-stimulated astrocytes induces an increased glutamate response in spines. Taken together, these studies examine the role of astrocytic SOCE in inflammation, providing a framework for understanding how astrocytes modulate neuronal function in health and in inflammatory diseases like Alzheimer's Disease.

POSTER 31

EXAMINING PATHOLOGICAL HETEROGENEITY OF A-SYNUCLEIN IN LEWY BODY DISORDERS WITH COMORBID Aβ AND TAU PATHOLOGY

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Purpose: Pathological and clinical heterogeneity has been well established in neurodegenerative disorders, however there is no mechanistic explanation for this phenomenon. In Parkinson's disease (PD) and diffuse Lewy body disease (DLBD), aggregates of alpha-synuclein (α-syn) comprise Lewy body inclusions that characterize the disease. However, a significant portion of patients also develop Alzheimer's disease (AD) pathology including amyloid-beta containing plaques, and tau-containing neurofibrillary tangles. In this study we examined the post-mortem brains of patients with Lewy bodies that have low vs. high AD pathology to determine if differences in biochemical features of a-syn exist in the brain. These studies may begin to provide insight into the mechanisms of disease comorbidity in PD and other Lewy body disorders.

Methodology: To distinguish between pathological α-syn from physiological conformers in human brain, we performed sequential extraction of post-mortem frontal cortex brain samples from the Northwestern Alzheimer's disease pathology core, including 4 controls, 6 DLBD, and 6 DLBD-AD. We employed a 5-step extraction protocol of high salt buffer, 1% Triton X-100, 1% Triton+30% sucrose, 1% sarkosyl, and sarkosyl insoluble extracts. The sarkosyl insoluble fractions from DLBD and DLBD+AD samples were subjected to limited proteinase K digestion then analyzed by western blotting to determine the differences in proteinase K (PK) sensitivity.

Findings: Analysis of different fractions from sequential extractions by western blotting using LB509 antibody revealed an accumulation of pathological α-syn in the 1% sarkosyl and sarkosyl insoluble fractions. Further, analysis of total α-syn levels in the sarkosyl insoluble fraction between DLBD and DLBD-AD samples revealed no difference in the overall abundance of α-syn when comparing DLBD and DLBD+AD. Digesting equal amounts of α-syn-containing lysates with increasing PK concentrations revealed increased PK resistance in AD samples, indicating the presence of a more stable form of α-syn. We also found differences in the immunoreactivity of distinct α-syn fragments after PK digestion using different amino or carboxy-terminal α-syn antibodies. Future experiments involving epitope mapping and seeding ability of distinct conformers from DLBD and DLBD+AD will aid in understanding the development and progression of α-Synucleinopathies, and may facilitate the design of new therapies.

POSTER 32

ALTERED BASAL GANGLIA AND LANGUAGE NETWORK CONNECTIVITY IN PRIMARY PROGRESSIVE APHASIA

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Backgrounds: Primary progressive aphasia (PPA) is a syndrome of progressive language impairment secondary to neurodegenerative disease. Connectivity between language regions within the brain cortex is decreased in PPA. Cortical language regions are interconnected with deeper regions of the brain including the basal ganglia. Neuropathologic studies have shown abnormal pathology within the basal ganglia in PPA. However, the effect of these changes on resting connectivity between the basal ganglia and language regions has not been well investigated. In this study, using resting state functional magnetic resonance imaging (rsfMRI), we investigated the status of resting connectivity between basal ganglia structures and the language network.

Methods: We analyzed rsfMRI scans of 73 PPA patients and 33 healthy controls. Using REST-PLUS software, connectivity between three known language network regions (inferior frontal gyrus [IFG], middle frontal gyrus [MTG], and anterior temporal lobe [ATL] and the basal ganglia was evaluated and compared to the control group. We also evaluated whether changes in connectivity would correlate with measures of naming, word comprehension, grammar, and repetition.

Results: Comparison with the control group showed consistently decreased connectivity between the left IFG and clusters within the left caudate head and left putamen across all subtypes of PPA. The left caudate cluster showed a positive correlation with Boston Naming Test (BNT) scores. A median split based on BNT scores across all PPA patients showed a positive correlation between naming and IFG-caudate connectivity ($r = 0.457$, $p = 0.004$). These results continued to be significant when the role of cortical regions underlying naming were factored out.

Discussion: In this study we showed decreased connectivity between the IFG region and the head of caudate across all subtypes of PPA. We also demonstrated that such change is correlated with patients' naming scores. Until now most studies have focused on cortical connectivity. The role of caudate nucleus in naming has been shown in few studies healthy and stroke induced aphasic individuals (Mendez et al., 1989; Abdullaev et al, 1997). This study provides more insights into the neural correlates of naming and its disruption in PPA.

POSTER 33

AGING RELATED CHANGES IN BONE MORPHOGENETIC PROTEIN SIGNALING IN HIPPOCAMPAL NEUROGENESIS

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As the world's population ages, maintenance of cognitive and coping abilities throughout life is a crucial public health concern, yet little is known about the mechanisms promoting healthy cognitive and affective function in later life. In particular, hippocampal function declines with age, but the physiologic and anatomic changes underlying the age-associated impairment of hippocampal function are not fully understood. It has been shown that processes which increase hippocampal neurogenesis, such as exercise and enrichment, can improve memory and cognitive function. However, the mechanisms underlying the increased neurogenesis and its relationship to the changes in cognition are unclear. Prior work from our lab, and others, has shown that bone morphogenetic protein (BMP) signaling increases greatly during aging in both mouse and human hippocampus (HIP) and that inhibition of BMP signaling in the adult HIP enhances both neurogenesis and HIP-dependent function. This project serves to extend our understanding of the relationship between BMP mediated signaling, cognitive function, and HIP neurogenesis through two main approaches. First, we will use cre-mediated ablation of type II BMP receptor in various neural stem and progenitor cell populations to test the hypothesis that inhibition of BMP signaling increases neurogenesis by activating quiescent neural stem/progenitor cells in aged mice. Secondly, we will take advantage of an animal model in which we can spatially and temporally control the electrophysiological activity of newly generated neurons using Designer Receptors Exclusively Activated by Designer Drugs (DREADD) technology. These DREADD mice will be used to examine the behavioral effects of silencing the activity of newly generated HIP neurons following BMPRII ablation, thus increasing neurogenesis, or of activating them in the absence of increased neurogenesis. Excitingly, the cell autonomous restriction of our experimental manipulations exclusively to the progenitor cell population makes this an ideal system that will allow us to definitively show whether there is a causal link between neurogenesis and cognitive functions.

POSTER 34

UNCOVERING THE MOLECULAR AND CIRCUIT MECHANISMS OF β-AMYLOID TOXICITY ON SLEEP AND CIRCADIAN RHYTHMS IN A DROSOPHILA MODEL OF ALZHEIMER'S DISEASE

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Alzheimer's disease is associated with accumulation of pathogenic β-amyloid peptides in the brain. Growing evidence has demonstrated a disease link between sleep, circadian rhythms, and Alzheimer's disease, where impaired sleep/rhythms are prodromal symptoms of the disease. In this study, we are trying to understand the molecular basis behind how Alzheimer's disease impacts sleep and circadian rhythms. Pan-neuronal expression of toxic β-amyloid peptides using the pan-neuronal ELAV-Gal4 driver in Drosophila melanogaster reduces and fragments sleep and loss of circadian rhythms. A GAL4 screen of 400+ drivers expressing wild-type β-amyloid in different regions and cellular subtypes of the brain identified specific cellular subsets that are susceptible to β-amyloid induced changes in sleep and circadian rhythms, including mushroom body, antennal lobe, and dopaminergic receptor expressing neurons. We are currently conducting genetic screens to identify genes that either suppress or enhance these sleep and circadian phenotypes in our Drosophila AD model. These identified brain regions and gene candidates could not only reveal molecular mechanisms that link sleep/circadian rhythms and neurodegenerative disease, but may also provide potential targets for novel therapies.

POSTER 35

DECREASED RESTING CONNECTIVITY OF LANGUAGE NETWORK WITH EXTRASYLVIAN REGIONS DISTINGUISHES NEURAL DISRUPTION IN SUBTYPES OF PRIMARY PROGRESSIVE APHASIA

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Background: Primary progressive aphasia (PPA) is a syndrome of language impairment due to underlying neurodegenerative disease. In our previous research we demonstrated decreased resting state connectivity within 3 regions of the language network. That approach differentiated semantic (PPA-S) and non-semantic subtypes of PPA, but not the two non-semantic subtypes (i.e. the logopenic [PPA-L] and agrammatic [PPA-G]). In this study we investigated whether including additional of perisylvian and extrasylvian regions would better distinguish network disruptions in different PPA subtypes.

Methods: We performed pairwise resting connectivity analysis on different PPA subtypes using resting state functional magnetic resonance imaging. Interconnectivity of 8 left hemisphere regions were evaluated: the inferior frontal gyrus pars triangularis (IFGt), medial temporal gyrus (MTG), and anterior temporal lobe (ATL) which we had identified previously; we also discovered extrasylvian regions connected to but outside the above three regions using a whole-brain seed-based connectivity mapping: superior frontal gyrus (SFG), pre-motor cortex (PM), and angular gyrus (AG). Additional regions were posterior superior temporal gyrus (STG), and pars opercularis of IFG (IFGo). These latter regions are known to contribute to language processing but were not included in our triangular model. The results were then corrected for multiple comparisons.

Results: All PPA patients showed decreased connectivity between IFGtg-MTG, MTG-SFG, and PM-IFGtg. The PPA-L group showed specific decreased connectivity between IFGtg-AG. The PPA-G group showed decreased specific decrease connectivity between the IFGtg-SFG. The PPA-S group showed unique decreased connectivity between MTG-ATL.

Discussion: In this study we found decreased connectivity between IFGtg-SFG, IFGtg-AG, and MTG-ATL that are unique to PPA-G, PPA-L and PPA-S respectively. Decreased IFGtg-SFG in PPA-G is in line with disruption in the Aslant tract which affects fluency. In PPA-L, decreased connectivity between IFGtg-AG is most likely related to dysfunction within AG as it is one of the common regions affected by neurodegenerative pathology in PPA-L. Finally, decreased MTG-ATL connectivity is consistent with our previous findings and in line with impairment in the ventral language pathway in PPA-S. Our findings suggests that evaluation of connectivity between a combination of perisylvian and extra-sylvian regions reveals network anomalies that are unique to each subtype of PPA.

POSTER 36

SUPERAGING STUDY: CORRELATES OF ACTIVE ENGAGEMENT IN LIFE IN THE ELDERLY

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Many individuals have come to expect that memory and thinking abilities will begin to deteriorate with advancing age. Though such decline is common, the SuperAging Project at the Northwestern University Mesulam Center for Cognitive Neurology and Alzheimer's Disease has found that some individuals are able to maintain high levels of cognitive function as they age. The Northwestern SuperAging Project, has identified a group of individuals over the age of 80 with exceptional episodic memory ability that is at least as good as that of individuals 20-30 years their junior. The study seeks to identify factors that help an individual avoid age-related cognitive decline and memory loss.

To qualify as a SuperAger, individuals must perform at or above average normative values for individuals in their 50s and 60s on tests of episodic memory, and at least within the average range for their age and education on non-memory cognitive domains according to published normative values.

Participants visit our center every two years for a comprehensive cognitive evaluation, structural and functional MRI scans, and blood collection for genetic testing. SuperAgers also complete questionnaires investigating personality, family history, and daily health habits. All participants are invited to take part in our Center's brain donation program, providing researchers the opportunity to further investigate the biological mechanisms behind SuperAging.

Since its inception, the SuperAging Project has used a multidisciplinary approach to study successful cognitive aging. Findings suggest that SuperAgers resist the cortical atrophy that is typically thought to be associated with normal aging. Additionally, SuperAgers display a higher density of von Economo neurons, a specialized neuronal population implicated in social intelligence, in the anterior cingulate. The study has wide ranging implications and may ultimately provide clues on how to slow or avoid age-related cognitive decline. Moving forward, the study will continue to use cognitive, structural, genetic, and histopathologic markers to identify factors that promote resistance to age-related changes in the brain and allow individuals to maintain high memory capacity in old age.

POSTER 37

NUCLEOCYTOPLASMIC PROTEOMIC ANALYSIS UNCOVERS ETF1 AND NONSENSE MEDIATED DECAY AS MODIFIERS OF ALS *C9ORF72* TOXICITY

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The most common genetic cause of amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD) is a hexanucleotide repeat expansion in C9orf72 (C9-HRE). While RNA and dipeptide repeats produced by the C9-HRE disrupt nucleocytoplasmic transport, the proteins that become redistributed remain unknown. Here, we utilized biochemical subcellular fractionation coupled with tandem mass spectrometry and identified 126 proteins, enriched for protein translation and RNA metabolism pathways, which collectively drive a shift towards a more cytosolic proteome in C9-HRE cells. Amongst these was ETF1, which regulates translation termination and nonsense-mediated decay (NMD). ETF1 accumulates within elaborate nuclear envelope invaginations in iPSC-patient neurons and postmortem tissue. It mediates a protective shift from protein translation to NMD-dependent mRNA degradation, while overexpression of the NMD-driver UPF1 ameliorates C9-HRE toxicity in vivo. Our findings provide a resource for proteome-wide nucleocytoplasmic alterations across neurodegeneration-associated repeat expansion mutations and highlight ETF1 and NMD as therapeutic targets in C9orf72-associated ALS/FTD. learning, and memory function. The study will enroll 300 participants for 2 years.

POSTER 38

METHODS FOR EXAMINING DENDRITIC CALCIUM EVENTS AND AGING

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In age related cognitive decline and dementias such as Alzheimer's disease, the loss of normal memory function is a major reason patients lose the ability to live independently. Hippocampal place cells fire when an animal visits specific locations in an environment, known as the place field. When young animals are exposed to a room for the first time, a process called "global remapping" occurs, where some cells cease to fire, others start to fire, and the locations of the firing fields shift around the environment. The process of building this firing pattern as a result of experience is an example of memory encoding, and the steps in this process are unclear. Many physiological changes occur in the hippocampus of aged animals. CA1 cells become less excitable increase cellular calcium buffering. Together, these changes are likely to result in a marked decrease in dendritic excitability and calcium. When aged animals are exposed to novel environments, there is a greater overlap between the ensemble of place cells in the novel and familiar environments: the new map is less specific. This has been proposed to reflect problems in memory encoding in aged animals. Notably, previous work from our lab using two-photon imaging in virtual reality has correlated regenerative dendritic calcium events to both novel map formation and familiar map stability. This implicates dendritic calcium events as a possible major player in dysfunction during aging. Here, we discuss methods we are developing to study these events during the context of remapping and during aging. Novel two-photon techniques using a Gauss-Bessel beam will allow us to access a much larger range of the dendritic arbor, and a spatially guided operant behavioral task will allow us to correlate age related physiological changes with memory performance.

POSTER 39

DENDRITIC HCN CHANNELOPATHY IN THE VENTRAL HIPPOCAMPUS OF ALZHEIMER'S MOUSE MODELS

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Background: Voltage-gated ion channels mediate important processes, such as action potential propagation and dendritic integration, which makes them critical to proper neuronal function. However, pathological insults and genetic mutations are known to disrupt the proper function and expression of these channels, causing conditions referred to as a channelopathies. Previously, our laboratory identified a channelopathy in the dorsal hippocampus of transgenic mouse models of Alzheimer's disease (AD). Specifically, CA1 pyramidal neurons of transgenic AD mice were shown to exhibit mis-localization and altered functional expression of hyperpolarization-activated cyclic-nucleotide gated (HCN) channels. In the present study, we investigated the possibility that this channelopathy may also occur in ventral CA1 pyramidal neurons.

Method: A combination of 5xFAD and 3xTg mouse models was utilized for the present study. Using electron microscopy, localization and membrane expression of HCN channels was assessed by quantification of gold particles in the dendrites of CA1 pyramidal neurons. The functional consequences of altered HCN channel expression were assessed by whole cell current clamp. Depolarizing current injections were used to assess cellular excitability, while hyperpolarizing current injections were employed to examine subthreshold voltage signatures of HCN channel function. Additionally, pharmacological agents known to induce rapid expression of HCN channels were applied to slices during recording sessions to determine if the channelopathy could be pharmacologically rescued in transgenic AD mice.

Results: Ventral CA1 pyramidal neurons from transgenic AD mice exhibited decreased HCN expression in the distal dendrites, which are typically rich in HCN channels. Additionally, changes to subthreshold HCN voltage signatures were observed in ventral neurons, similar to those seen in the dorsal hippocampus. These deficits could be rescued pharmacologically by the administration of drugs that have been shown to rapidly induce HCN membrane expression wild type mice. Interestingly, while exacerbated accommodation of action potential firing was observed in dorsal CA1 pyramidal neurons of AD mice, this was not seen in ventral neurons.

Conclusion: Overall, our data implicate a specific means by which neurons may become dysfunctional in response to AD pathology. Specifically, the results suggest that changes to HCN channel expression during AD pathogenesis may cause functional alterations in neurons that deviate from normal. This likely has large effects on how neurons process electrical inputs, and thus communicate with one another. However, our findings also support the idea that these changes can be rescued pharmacologically, providing a potential target for therapeutics.

POSTER 40

SPEECH AND LANGUAGE PRESENTATIONS OF FTLD-TDP, TYPE B NEUROPATHOLOGY

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We present four right-handed patients with primary progressive aphasia (PPA) and transactive response DNA binding protein (TDP), Type B pathology. In all four, there were neither comportment changes nor motor findings at presentation. In two cases, left anterior temporal lobe (ATL) atrophy was marked, despite the clinical absence of semantic loss. While TDP-43, Type B pathology is commonly associated with motor neuron disease (MND) and behavioral variant frontotemporal dementia, it is less recognized as a pathologic correlate of PPA. These cases, taken together, contribute to the growing heterogeneity in clinical presentations associated with TDP pathology. Regarding the two in our series with left ATL atrophy and preserved word comprehension, we appeal to a recently proposed hypothesis that questions received lesion-deficit notions associated with left ATL.

POSTER 41

LONGITUDINAL EARLY-ONSET ALZHEIMER'S DISEASE STUDY (LEADS)

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The Longitudinal Early-onset Alzheimer's disease Study (LEADS) is a 2-year natural history, non-treatment study designed to look at disease progression in individuals with early onset Alzheimer's disease. Clinical/cognitive, imaging, biomarker, and genetic characteristics will be assessed across two cohorts: (1) individuals with Early-onset Alzheimer's disease (EOAD) and (2) cognitively normal (CN) control participants.
Cognitively normal volunteers will be enrolled for only 1 year. At least 400 AD participants and 100 cognitively normal participants will be enrolled at approximately 15 sites in the United States. Early-onset Alzheimer's disease participants will be followed for 2 years.
Participants will undergo longitudinal clinical and cognitive assessments, computerized cognitive batteries, biomarker and genetic tests, brain imaging scans (including PET and MRI), and cerebral spinal fluid analysis. Researchers will compare data from cognitively normal participants with early-onset Alzheimer's disease to study different elements of disease progression.

POSTER 42

T2 PROTECT AD STUDY

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The T2 Protect AD study is a national multi-site clinical trial testing an investigational drug for people with mild to moderate Alzheimer's disease (AD). T2 Protect AD is a clinical trial that examines the safety, tolerability, and effectiveness of the investigational drug, troriluzole, in people with mild to moderate Alzheimer's disease (AD). T2 Protect AD is taking place at dozens of sites across the United States.

The study is designed to determine whether troriluzole can protect against, slow down, and/or potentially improve memory and thinking problems associated with Alzheimer's disease progression.

Participation will include 9 study visits over a period of approximately 1 year.

POSTER 43

CURRENT CLINICAL TRIALS AT THE MESULAM CENTER

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The treatment of Alzheimer's disease (AD) is a central aim for the Mesulam Center for Cognitive Neurology and Alzheimer's Disease. In response to promising new treatments and efforts to design biomarkers for AD and other forms of dementia, the Mesulam Center is collaborating with the Alzheimer's Therapeutic Research Institute (ATRI) and the Alzheimer's Disease Cooperative Study (ADCS) to sponsor clinical trials for individuals with AD and other forms of dementia.

Emerging clinical trials and research studies are reviewed and approved by the Executive Committee of the Mesulam Center. Eligible individuals are received via the Clinical Core of the Mesulam Center, response to advertisements in the Chicago area community, Northwestern Medicine Enterprise Data Warehouse (NMEDW), and aging registries throughout Northwestern Medical Group. Recruitment efforts have continued to emphasize the inclusion of participants from minority groups and otherwise underserved communities.

Current trials are as follows:
1) Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease (A4) Study: The A4 study is a prevention trial aimed at treating amyloid-positive but otherwise healthy individuals (aged 65-85) at risk for developing Alzheimer's disease (AD). Cognitively-normal individuals were screened for amyloid burden in their brains (via PET scan). Those with positive amyloid PET scans were enrolled into the study and are currently being treated with an anti-amyloid antibody (Solanezumab) or placebo.

2) Longitudinal Evaluation of Amyloid Risk and Neurodegeneration (LEARN): The goal of this trial is to evaluate the rate of cognitive change in individuals without an amyloid burden (i.e., amyloid-negative PET scans). This observational study runs in parallel to the A4 Study, and there is no drug treatment.

3) Alzheimer's Disease Neuroimaging Initiative – 3 (ADNI3): The ADNI3 study is designed to identify biomarkers that may be useful in the diagnosis of early AD. The ADNI3 study will use annual cognitive assessments, blood and cerebrospinal fluid samples, MRI, and PET scans to evaluate biomarkers that may be useful in disease prediction.

4) Memory Improvement through Nicotine Dosing (MIND): The MIND study will determine if a daily nicotine patch is able to produce a significant cognitive, clinical, and functional improvement in participants with memory complaints or participants diagnosed with Mild Cognitive Impairment (MCI). Neuronal nicotinic receptors have long been known to play a critical role in memory function, attention, and learning. Participants enrolled in this study received either the nicotine patch, titrated to 21mg/day, or a placebo skin patch.

5) Longitudinal Early-onset Alzheimer's Disease Study (LEADS): The LEADS study examines disease progression in adults with early-onset Alzheimer's disease. Participants undergo longitudinal clinical and cognitive assessments, biomarker and genetic tests, brain imaging scans (including PET and MRI), and cerebral spinal fluid collection. Researchers will compare data between cognitively normal participants and late-onset AD participants to study different elements of disease progression.

6) T2 Protect AD (T2): The T2 Protect AD tests the investigational drug, troriluzole, in people with mild to moderate Alzheimer's disease. The study is designed to determine whether troriluzole can protect against, slow down, and/or potentially improve memory and thinking problems associated with AD progression.

POSTER 44

VULNERABILITIES OF BASAL FOREBRAIN CHOLINERGIC PROJECTION NEURONS

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The most common causes of dementia, Alzheimer's disease (AD) and secondarily Dementia with Lewy bodies (DLB) are characterized by age-related degeneration of cholinergic projection neurons (ChNs) in the substantia innominata/nucleus basalis magnocellularis (SI/nbM), a region of the basal forebrain (BF) providing a rich cholinergic innervation to cortical regions implicated in cognition.
Surprisingly, little is known about ChNs susceptibility in AD and DLB. These neurons possess extensive axonal arborizations and likely rely heavily on mitochondrial energy to maintain function and structural integrity. Moreover, we found that ChNs exhibit large, activity-dependent fluctuations in cytosolic Ca2+ concentration triggered by opening of plasma membrane Cav1 channels. These fluctuations could determine a feed-forward stimulation of mitochondrial oxidative phosphorylation (OXPHOS), increasing mitochondrial exposure to oxidative stress. Remarkably, these features altogether can indeed represent an exceptional bioenergetic and proteostatic challenge for the cell.

Lewy Body Dementias (LBDs) are characterized by intracellular proteinaceous inclusions containing misfolded, aggregated forms of α-synuclein (α-syn). The effect of α-syn inclusions on the physiology of nbM-ChNs is not known. However previous work has shown that α-syn preformed fibrils (PFFs) can increase both cytosolic and mitochondrial oxidant stress, spiking activity, and alter intracellular Ca2+ signaling.

Using a combination of 2-photon laser scanning microscopy (2-PLSM) and genetically encoded fluorescent probes we found that the basal relative oxidation of SI/nbM-ChNs mitochondria is high in control mice. Importantly, this effect is reversed by blocking Cav1 channels, indicating that ChNs rely on a Ca2+-dependent feed-forward mechanism to drive OXPHOS. Finally, preliminary data from our laboratory show that PFFs directly injected in the pedunculopontine nucleus (PPN) are taken up preferentially by ChNs, but not neighboring glutamatergic or GABAergic neurons. As similar experiments are ongoing and will clarify if this is the case also for SI/nbM-ChNs, using conventional electrophysiology we found that PFFs directly injected in SI/nbM doubled ChNs basal firing rate. An effect that could lead to increased Cav1 opening likely worsening oxidative stress.

The unique make-up of nbM-ChNs physiology creates a 'perfect storm' for mitochondrial dysfunction that might become particularly severe in the presence of synuclein pathology. We believe that our research will unveil peculiar "weaknesses" in ChNs design that render them more susceptible to the alterations seen in varies forms of dementia (including AD and LBDs).

POSTER 45

MONTREAL COGNITIVE ASSESSMENT (MOCA) PERFORMANCE AND DOMAIN-SPECIFIC INDEX SCORES IN AMNESTIC VERSUS APHASIC DEMENTIA

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Objective: The Montreal Cognitive Assessment (MoCA) is a screening tool for detecting cognitive impairment in older individuals. The MoCA yields a total score to represent general level of cognitive ability. The total score contains items that can generate index scores within each of the following six domains: 1) Memory; 2) Executive; 3) Attention; 4) Language; 5) Visuospatial; and 6) Orientation. It remains unclear whether MoCA Index scores differentiate among distinct clinical dementia syndromes. The current study compared MoCA Index scores between normal controls, patients with clinically diagnosed mild Dementia of the Alzheimer's Type (DAT, amnestic) or with primary progressive aphasia (PPA, aphasic).

Participants and Methods: Total MoCA scores (maximum = 30) and domain-specific Index scores were calculated from initial administration of the MoCA in patients followed longitudinally at the Northwestern Alzheimer's Disease Center. Groups included those with mild DAT (N = 33), PPA (N = 37), and cognitively normal control subjects (N = 83). ANOVAs adjusted for age followed by posthoc pairwise comparisons with Bonferroni corrections were used to compare MoCA total and Index scores among the three groups.

Results: MoCA total scores were significantly lower for each patient group compared to the control group (mean = 26.08; SD = 1.93; $p < 0.001$), but not for the DAT (mean = 18.94; SD = 3.32) compared with the PPA group (mean = 20.97; SD = 3.59). DAT patients scored significantly lower on Memory and Orientation Index scores compared to normal controls and PPA patients ($p < 0.001$), whereas PPA patients scored significantly lower in Language and Attention Index scores compared to both other groups ($p < 0.001$).

Conclusions: MoCA Index scores can distinguish between amnestic and aphasic dementia phenotypes despite no difference in total score.

Practical Implications: The MoCA is a widely used neuropsychological short screener for detecting dementia. These findings suggest that practitioners can gain further insight into the results by calculating domain-specific Index scores in order to assist in diagnosis and help guide patients into appropriate clinical trials or treatments as they become available.

POSTER 46

LEAF (LIFE ENHANCING ACTIVITIES FOR FAMILY CAREGIVERS): A POSITIVE EMOTION REGULATION INTERVENTION

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Purpose: The stress of dementia caregiving is associated with a range of physical and psychological health problems. Interventions for dementia caregivers have primarily focused on education and skills training with the goal of reducing negative emotions and burden. However, over the past few decades, it has become clear that positive emotions are uniquely related to better psychological and physical well-being, independent of the effects of negative emotion, suggesting that an intervention that specifically targets positive emotion holds promise for improving caregiver well-being.

Methods: A randomized controlled trial (N = 170) compared LEAF (N=86) to an emotion reporting/waitlist condition (N = 84) in dementia caregivers. LEAF was delivered live by trained facilitators via the internet on study-supplied tablet computers. The intervention condition consisted of 6 sessions in which a facilitator taught participants a set of eight emotion regulation skills intended to increase positive emotion. Participants in the control condition completed daily online emotion reports, then crossed over into the intervention condition after 6 weeks.

Results: Analyses of difference in change from baseline to 6 weeks demonstrated significantly greater decreases in PROMIS depression, ($d = -.25$; $p = .02$) and NeuroQOL anxiety ($d = -.33$; $p < .01$), and improvements in PROMIS physical health ($d = .24$; $p = .02$) in the intervention condition compared to the emotion reporting/waitlist control. The intervention also showed greater improvements in positive emotion ($d = .58$; $p < .01$) and positive aspects of caregiving ($d = .36$; $p < .01$). Additionally, effects on caregiving burden ($d = -.16$; $p = .07$) and perceived stress ($d = -.20$; $p=.10$) were in the hypothesized direction but did not reach statistical significance. Increases in positive emotion significantly mediated the effect of LEAF on depression over time.

Conclusions and Impact: The present randomized controlled trial in dementia caregivers showed that, compared to an emotion reporting control condition, the LEAF positive emotion regulation intervention led to significantly greater increases in the primary outcome of interest, positive emotion, as well as improvements on secondary outcomes including increases in positive aspects of caregiving, decreases in depression and anxiety, and improvements in self-reported physical health. These results show promise for remotely delivered programs to improve psychological well-being in caregivers of people with dementia.

POSTER 47

COMMUNICATION BRIDGE: A PERSON-CENTERED INTERNET-BASED INTERVENTION FOR INDIVIDUALS WITH PRIMARY PROGRESSIVE APHASIA

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The diagnosis of primary progressive aphasia (PPA) is made when a relatively isolated progressive impairment of language occurs as a result of neurodegenerative disease. Although there are no pharmacological treatments for PPA, speech-language therapy (SLT) is an intervention that can offer individuals with PPA a means to compensate for their communication difficulties. Unfortunately, individuals with PPA are under-referred for SLT treatment. Other barriers individuals with PPA may face in receiving care include limited availability of speech-language pathologists (SLPs) who specialize in PPA, and limited insurance coverage of SLT. In hopes of circumventing these barriers, the Communication Bridge study provides web-based SLT to individuals with PPA and their care partners residing both nationally and internationally. The study aims to understand SLT effects on communication abilities in people living with PPA and to determine optimal intervention strategies for this population.

Results from a pilot study of 57 participants with PPA demonstrated that functional gains and increased confidence in communication after eight weeks of SLT were maintained for the following four months. The next phase of Communication Bridge is currently underway in a randomized controlled trial that delivers web-based SLT to individuals with PPA and their communication partners. Participants will be in the study for approximately one year and take part in 15 SLT sessions, five SLP evaluations, and exercises to support communication through a custom web-application on a computer provided for the length of the study.

Enrollment began in May 2018; there are currently 22 individuals with mild PPA and their communication partners enrolled in the study. Planned enrollment will add an additional 68 participants over the next three years. Current participants come from 15 states, two Canadian provinces, and England. Interest in the study has been extremely high. To enroll in the study, participants must be English speaking, be in the mild stages of PPA, have adequate experience with computers and have a communication partner who is willing to participate.

POSTER 48

SENTENCE PROCESSING IMPAIRMENTS IN PRIMARY PROGRESSIVE APHASIA: PRELIMINARY FINDINGS

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Introduction: Primary Progressive Aphasia (PPA) is a neurodegenerative disease in which language deteriorates while other cognitive functions remain largely intact1-4. Current diagnostic criteria divide PPA into three subtypes: PPA-G, the agrammatic variant who show grammatical deficits in production; PPA-S, the semantic variant who display severe naming deficits and difficulties with single-word comprehension; and PPA-L, the logopenic variant who have word finding and repetition deficits. This study focuses on three components of sentence processing: verb comprehension and production, thematic mapping, and grammatical morphology that have been shown to be impaired in PPA4-8. Though impairments in sentence processing are primarily impacted in PPA-G, they have been found in other PPA subtypes as well. The current (ongoing) study uses online eye-tracking and offline production tasks to examine processing in each of these domains in patients with PPA to identify patterns of impairment across domains and how they relate to clinical PPA subtypes.

Methods: Two groups of healthy individuals (younger: 18-31 years (n=21); older: 53-73 years (n=21)) and a group of 18 PPA patients (56-77 years) have completed the study, requiring completion of comprehension and production tasks testing three components of sentence processing (verbs, thematic mapping, and verb morphology). Eye movements were recorded during comprehension tasks and accuracy and reaction time (RT) were recorded for production tasks. For the verb comprehension task, participants listened to a verb (transitive or intransitive) while viewing pictures of the target verb, and three distractors. On half the trials, one distractor was semantically-related to the target. Verb production involved naming action pictures. Thematic mapping comprehension involved listening to a sentence in which the last word was missing. Participants viewed four pictures and had to select the one that best completed the picture. Sentences contained either restrictive or unrestrictive verbs (e.g., Tomorrow, Susan will open/break the…), where restrictive verbs (i.e., open) could only be completed by one of the four pictures (i.e., jar, but not plate, stick, or pencil), all of which complete the unrestrictive verbs (i.e., break). Production was assessed with the production of sentences containing 1-, 2-, and 3-place verbs in the Argument Structure Production Test (ASPT) of the Northwestern Assessment of Verbs and Sentences (NAVS)9. Morphosyntactic comprehension was assessed with an adaptation of the Test for Assessing the Reference of Time10, where participants saw two pictures of the same event, one that was completed and one that was ongoing. They listened to a sentence in either the past or present tense and had to match it to the corresponding picture. Tenses were either finite (simple present, simple past) or non-finite (present continuous, present perfect). Production of finite and non-finite verbs was assessed with the Northwestern Assessment of Verb Inflection (NAVI)11.

Results: For verb comprehension, patients were less accurate than controls overall, and showed a transitivity effect wherein they were less accurate and slower on transitive than intransitive verbs. Eye movements for both verb types were reduced and delayed compared to age-matched controls. Patients' verb naming was less accurate and slower than controls, but showed no effect of transitivity. Thematic mapping comprehension showed an effect of verb subcategorization where patients were less accurate on restrictive verbs, and showed reduced looks to the target object. Production showed an effect of verb argument structure complexity where performance was impaired on 2- and 3-place verbs, but not 1-place verbs. Finally, morphosyntactic comprehension showed an

emerging finiteness effect where finite verbs were less accurate than non-finite verbs. Eye movements were reduced compared to controls. Production of finite, but not non-finite verbs was impaired in patients.

Discussion: Across these sentence processing tasks, the PPA patients as a group were less accurate and more slowly on behavioral measures and showed reduced and delayed eye movements as compared to both age-matched and young normal participants. Several of our preliminary findings are in line with processing deficits for patients with PPA-G: the transitivity effect found for verb comprehension and thematic mapping production and comprehension, and the finiteness effect in production of grammatical morphology. However, these effects were not found for verb naming and comprehension of verb morphology, likely reflecting the constellation of PPA patients (which included patients of all PPA subtypes). Future analysis will include greater numbers of participants and allow examination of the relation between sentence processing deficits and PPA subtype. In addition, analysis will examine individual variability and the interrelation between processing on each task, providing an experimental perspective of sentence processing to augment the clinical diagnosis of PPA subtypes.

POSTER 49

PRIMARY PROGRESSIVE APHASIA AND TECHNOLOGY: CREATIVE "APP"LICATIONS TO PROMOTE INCREASED LIFE PARTICIPATION

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The use of technology may be an effective way to support the life participation approach for people living with primary progressive aphasia (PPA). We recognize that technology is not a single entity but instead can be used both directly and indirectly to enhance communication through (1) increasing access to care through telemedicine; (2) facilitating practice of personalized impairment-based word exercises; (3) facilitating use of compensatory approaches (low-tech or high-tech communication aids); and (4) supporting participation in leisure activities. This poster will demonstrate the potential benefits of utilizing technology to optimize evidence-based and person-centered interventions for individuals with progressive communication impairments.

Feasibility evidence will be provided from two technology-based research projects (Communication Bridge and CoChat) that were designed for individuals living with PPA. In the Communication Bridge feasibility study, the care model focuses upon a person-centered, multicomponent, dyadic approach that includes disease education and counseling, with individualized impairment- and compensatory-based communication strategy training. Technology is integrated to apply this approach in a telemedicine platform with a custom web application. The web application includes many components to promote a life participation approach throughout the course of treatment, including: personalized lexical retrieval and pronunciation exercises that integrate participants' own pictures, personalized script practice exercises, and educational videos discussing communication strategies. CoChat is a research application developed for the iOS platform that generates lexical displays on a tablet based on user-captured photos and related comments that are obtained by real-time use of a social network for word suggestions. CoChat was presented to six individuals with PPA in an effort to improve lexical retrieval during spontaneous conversation.

Both the Communication Bridge and CoChat studies help show that technology-based solutions can be implemented across service delivery models (e.g., aphasia centers, private practice, home care) to better meet the needs of individuals with PPA and their families.

POSTER 50

EVALUATING CONTRIBUTING FACTORS IN SPEECH LANGUAGE THERAPY EFFECTIVENESS FOR INDIVIDUALS LIVING WITH PRIMARY PROGRESSIVE APHASIA

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Primary Progressive Aphasia (PPA) is a clinical neurodegenerative dementia syndrome characterized by deficits in spoken and written language and language use. Currently, there are no effective treatments to reverse or halt the underlying disease process. Speech-language therapy (SLT) may be helpful; however, it can be difficult to find local speech-language pathologists (SLP) with dementia treatment experience. We previously established the feasibility of a telehealth model for delivering SLT, via Internet videoconferencing, which connects individuals with PPA to an expert SLP for treatment. This study examined feasibility of our telehealth intervention in a larger participant group (n=48) and examined two potential treatment-design mediators of communication confidence outcomes: monthly post-therapy 'check-in' sessions and care partner engagement. All participants received an initial evaluation, eight person-centered Internet-based SLT sessions, and two post-therapy evaluations. Half of the participants were randomized to receive three additional monthly post-therapy 'check-in' sessions, which were used to reinforce skills acquired during the initial eight sessions. Care partner engagement was rated by the SLP on a five point scale. The primary outcome was the Communication Confidence Rating Scale for Aphasia (CCRSA), which was completed by the PPA participants at baseline, two and six months. Participants enrolled from four countries. CCRSA ratings improved at the two month evaluation and showed no significant decline at the six month evaluation, independent of check-in SLT visit group status. However, PPA participants who had more engaged care partners tended to have higher CCRSA ratings both post-treatment and at six months. Consistent with our previous study, Internet-based person-centered intervention demonstrates promise as a model for delivering SLT to individuals with PPA. Here, care partner engagement appears to be a more robust mediator of communication confidence outcomes than number of maintenance sessions.

POSTER 51

THE SEED PROGRAM: EVALUATION OF AN 8-WEEK PSYCHOEDUCATION AND SUPPORT PROGRAM FOR PERSONS LIVING WITH EARLY DEMENTIA AND THEIR FAMILIES

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Introduction: The early stage of dementia presents a unique opportunity wherein the person who had been diagnosed retains the insight and cognitive awareness to consider the progression of their disease. They may find themselves yearning for more information about their disease as well as desiring connection to others who are similarly situated. Previous research has demonstrated that early-stage support and education benefit both the diagnosed person, as well as their care partners, as seen through improved quality of life, more motivated and goal-focused care planning, improved psychological wellbeing, and the preservation of hope through stronger social connections.

Methods: The Support and Education for Early Dementia (SEED Program) is an 8-week psychoeducational program for those with early stage dementia and their care partners. The program is organized by topic and begins with a lecture from a guest presenter with professional expertise including neuropsychologists, speech language pathologists, and social workers. After a short break, the second half of the 2.5 hour program is devoted to support groups separated into persons with diagnosis in one room and their care partners in another. Facilitated by licensed social workers, these groups offer participants the opportunity to discuss the morning's educational program, how the diagnosis has impacted functioning and quality of life, and, give and receive support from one another.

After the SEED program had demonstrated feasibility after several years of success since its inception, focus groups were conducted in two separate cohorts. The focus groups were transcribed and coded for emerging themes. In total, these groups were comprised of 45 people between ages 47 and 87 with an overall average age of 67. In the first cohort, there were eight people with dementia and 11care partners, as well as one peer mentor for each support group. In the second cohort, there were 11 people with dementia, 13 care partners and no peer mentors.

Preliminary Results: The following themes emerged through data analysis: decreased feeling of isolation and improved connection to others, empowerment through understanding the diagnosis, feeling strengthened by available resources, empowerment to take action, and a sense of community and desire to maintain relationships after the formal program ended. At the end of the fall 2018 SEED program, the participants reserved a room in a local library and hired a group facilitator to continue meeting in their separate, concurrent support groups. They continue to meet regularly. This is just one example that illustrates the strength of an empowered group of people who decided to extend the benefits they felt from the SEED program, even after the formal programming concluded.

Conclusion: SEED continues to fulfill a need for persons living with early-stage dementia by offering a supportive, educational program for both care partners and the person with the diagnosis. The SEED program facilitates strong group cohesion, providing the framework to extend the benefits of the program beyond its formal completion. Further coding will be completed to expand on the evident themes, with a particular focus of narrowing and operationalizing the definition of "quality of life."

POSTER 52

ATTITUDES ABOUT BRAIN DONATION AMONG AFRICAN AMERICAN RESEARCH PARTICIPANTS

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Introduction: African Americans carry a disproportionate biomedical and economic burden of Alzheimer's and other dementias. The participation of African Americans in research is thus essential in the ongoing quest for effective cures, treatments, therapies, and means of prevention. Brain donation, a crucial part of ongoing research on Alzheimer's and other dementias, is less common among African American research participants than White research participants at Alzheimer's Disease Centers (ADCs) located across the US and internationally. Existing literature on brain donation, among African Americans in particular, suggest three main categories of factors which contribute to decisions about brain donation: experience, knowledge, and concerns about participating in research and brain donation; religious practice, beliefs, and funeral arrangements; and family participation in decision making and support for brain donation. Existing knowledge about potential interventions is limited.

Methods: The Mesulam Center is currently conducting seven focus groups to accommodate approximately 45 research participants who had either agreed to or were considering brain donation as a part of Alzheimer's research. Each focus group consists of 6-12 participants, plus 2-4 study personnel. A total of four focus groups are being held at the Southeast (Atlas) Regional Senior Center and a total of three focus groups are being held at the Northwestern University Chicago campus. Based on the number of eligible participants, five focus groups will be conducted among participants with normal cognitive status, one focus group will be conducted among participants with mild cognitive impairment or mild dementia (CDR score of 0.5 or 1), and one focus group will be conducted among study partners and/or family members of Alzheimer's research participants with moderate or advanced dementia (CDR score of greater than 1). Focus groups are co-facilitated by Northwestern social workers, a Northwestern neuroscience PhD student, and a social work intern at the regional senior center. The focus group discussions are being audio recorded, transcribed and coded for emerging themes.

Preliminary Results: By the time of this submission, 17 people have participated in three of seven focus groups. Twenty-six individuals intend to participate in the remaining four focus groups. The majority of eligible participants responded to recruitment with appreciation for the opportunity and eagerness to participate. Emerging themes that appear to impact the decision for or against brain donation include: knowing someone with memory loss or dementia; the desire to help create a better future; spirituality/religion; financial costs; historical and current racism in health care and scientific research; importance of trust; representation of women and African Americans in research; discussion in family and community settings; community education and awareness of available research opportunities.

Conclusion: Preliminary results indicate that African American research participants are open to sharing thoughts on brain donation. We expect results will inform future interventions.

POSTER 53

PROSOCIAL AND NEUROPSYCHIATRIC BENEFITS OF A MUSIC INTERVENTION FOR PEOPLE WITH DEMENTIA AND THEIR CAREGIVERS

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Background: There is increasing need for the use of nonpharmaceutical interventions to improve quality of life, and manage neuropsychiatric symptoms in people with moderate-severe dementia (PWD). The current pilot study determines efficacy of a 12-week music intervention for PWD for improving social engagement and decreasing caregiver distress. In contrast to previous music intervention programs, the Musical Bridges to Memory (MBM) provides dyadic participant-caregiver involvement including perceptive (i.e., listening) and expressive (e.g., dancing, singing, playing percussion) participation and caregiver training to elicit better communication.

Methods: PWD from two assisted living communities were invited to participate in the MBM with their caregiver. Ten-minute video segments were recorded at baseline and post- intervention for coding behavioral observations. PWD (n=23, 11 and 12 in intervention and control groups respectively) were at least 55 years of age and had a diagnosis of dementia (Mini Mental Status Exam; MMSE < 20). Weekly live concerts based on PWD's musical preferences, were held for the experimental group PWD and caregivers. Sociable and unsociable behaviors were coded using the Verbal-Nonverbal Communication Scale (VNVIS-CR). Psychiatric symptoms were evaluated using the Neuropsychiatric Inventory (NPI). Relationship satisfaction was assessed via questionnaire, completed by caregivers. Significance was set at $p<.05$.

Results: At baseline, experimental and control PWDs did not differ on MMSE, NPI severity, NPI distress and VNVIS-CR subscales. Seven and 8 PWDs completed the intervention and control video evaluations respectively at baseline and post-intervention. ANOVAs controlling for respective baseline VNVIS-CR scores revealed that post-intervention the experimental group PWDs had greater VNVIS-CR sociable verbal and nonverbal behaviors and less unsociable nonverbal behaviors compared to the control group PWDs. ANOVAs controlling for baseline relationship satisfaction indicated greater post-intervention relationship satisfaction in the experimental group compared to controls. The experimental group declined in average NPI severity (M=22.00 vs. M=14.86), though these changes were not significant ($p = .31$). An ANOVA controlling for baseline NPI severity indicated that the experimental group was less severe at post-intervention than the control group. This effect was present at the trend level ($p = .084$).

Discussion: This pilot study of MBM provides evidence PWD engage in more sociable verbal and nonverbal behaviors and less unsociable nonverbal behaviors with their caregiver following a dyadic music intervention. Caregiver satisfaction also increased for those whose loved ones were enrolled in the MBM intervention. Neuropsychiatric symptoms appeared to decrease in severity, however a larger sample may be necessary to detect significance. Future work will examine social engagement and psychiatric effects in a larger sample and will examine predictors of efficacy.

POSTER 54

UNDERSTANDING THE LIVED EXPERIENCE OF THE FRONTOTEMPORAL DEMENTIA FAMILY CAREGIVER

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Caregivers of persons with frontotemporal disorders (FTD) have unique challenges and needs. They show higher levels of stress, depression and burden than those caring for persons with Alzheimer's disease. The clinical profiles and pathologies associated with FTD are heterogeneous and characterized by two main phenotypes: a progressive deterioration in behavior, emotion, and interpersonal conduct known as behavioral variant FTD (bvFTD); and a decline in language skills; known as primary progressive aphasia (PPA). While there is an abundant literature regarding the experience of caregiving for persons with AD, there are very few studies examining the experience of caring for persons with FTD and none that have compared behavior and language variant caregivers.

Caregivers of persons with FTDbv (Indiana University) and PPA (Northwestern University) were invited to participate in in-depth individual interviews to understand the nature of living with FTD from early symptoms to diagnosis and caregiving over time. 10 caregivers (5 bvFTD and 5 PPA) were interviewed. Interviews were recorded and transcribed. Transcripts underwent content analysis for emerging themes within the same profile and then discussed among authors for similarities and differences between profiles. Analysis revealed the following resulting themes: 1) Obtaining an accurate diagnosis was a difficult and lengthy process; 2) Finding lack of available information and misunderstanding the diagnosis; 3) Adapting to changing roles; 3) Experiencing significant financial and legal challenges; 4) Grieving losses, particularly developmentally non-normative losses due to younger age of onset; 5) Finding lack of disease specific services and knowledgeable providers; and 6) Receiving support in disease specific programs. Within these common general themes, there were differences in how disease presentations impacted functioning and challenged relationships. The findings from these interviews illuminate the need for greater attention and support for FTD caregivers by knowledgeable care providers.

POSTER 55

LIVING WITH KNOWLEDGE OF THE FUTURE: AN EXPLORATORY QUALITATIVE CASE STUDY OF THE IMPACT OF A DIAGNOSIS OF MILD COGNITIVE IMPAIRMENT WITH ALZHEIMER DISEASE BIOMARKERS

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Introduction: A diagnosis of Mild Cognitive Impairment (MCI) is warranted when a person exhibits mild decline in either single or multiple cognitive domains such as memory, attention, language, visuospatial, or executive functioning abilities. In recent years, the use of cerebrospinal fluid (CSF) biomarkers in clinical practice has significantly advanced the understanding of disease trajectory for people living with MCI. As a result, individuals learn that they possess a high likelihood of developing Alzheimer Disease (AD), perhaps years before the onset of clinical presentation. It is unclear, however, how individuals and families are impacted by this knowledge. How might the family system be shaped by an awareness that the person living with MCI will eventually develop a terminal and stigmatized illness?

Methods: This research project, which serves as an exploratory qualitative case study, is in process. The purpose is to understand how a diagnosis of MCI with CSF biomarkers that indicate AD pathology impacts an individual and their family. Approximately two to three dyads will participate. Each dyad includes a primary care partner and a person with a diagnosis of MCI with CSF biomarkers that indicate AD pathology. Firstly, the person living with MCI and the care partner participate in a joint interview that explores the impact of the illness upon the couple and family. Upon conclusion of a joint interview, participants complete a separate individual interview that focuses on personal experiences within their respective roles. All interviews, which are facilitated with the use of a structured interview guide, will be audio recorded, transcribed, and coded for emerging themes.

Preliminary Results: To date, one dyad has participated in the study. Emerging themes include the ambiguity of diagnosis and disease trajectory, an impact on various relationships within the family system, a sense of loss regarding future experiences, an increase in present-focused living resulting from the recognition of a shortened lifespan, the role of hope and acceptance as bulwark against fear of the future, and a greater appreciation for current functioning in the context of progressive illness.

Conclusion: This study, upon completion, will contribute to increased understanding of the unique lived experience of people who are living with MCI with AD biomarkers.

POSTER 56

NORTHWESTERN ALZHEIMER'S DISEASE CENTER OUTREACH, RECRUITMENT AND EDUCATION CORE (ORE CORE) 2018-19

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Introduction: The Northwestern Alzheimer's Disease Center's Outreach, Recruitment and Education Core provides outreach and educational programs for the recruitment of underrepresented groups, novel non-pharmacological interventions for persons living with dementia and their families and public education programs in conjunction with city, state and national entities. We recognize and support the psychosocial needs of research participants and families with innovative programs that support their strength and resilience. Community education and training is aligned with city, state and national goals and objectives.

Methods/Results: The outreach, recruitment and education efforts have been based on the principles of community engaged research which requires that academic members become part of the community and community members become part of the research team. Community engagement relies on successful partnerships which take time, skill and mutual respect. Highlights of the past year include: 1) Partnership with the Endeleo Institute in its 5th year – REACH to Faith 2.0: Building community capacity to disseminate and implement culturally appropriate dementia friendly resources, research evidence and program interventions in the Woodson Library. 2) Partnerships with Chicago Department of Family and Support Services: Age Friendly Chicago Commission, Atlas Regional Senior Center and Renaissance Court, 3) Dementia Friendly Illinois community initiatives, 4) Primary care physician practice education, 5) Coordination of the Mesulam Center Bureau of Sages.

Specially trained social workers attend to the psychosocial needs of research participants and their families. The 8-week Support and Education for Early Dementia (SEED) program is offered to newly diagnosed patients and families along with The Memory Ensemble, an improvisational theatre project, Art in the Moment, an art-based project to stimulate creative dialogue, and The Buddy Program now in its 22nd year and replicated at 15 different universities. Two monthly caregiver support groups are offered for Frontotemporal/Primary Progressive Aphasia and Younger Onset Dementia.

Alzheimer Disease Seminar Series in addition to Alzheimer Day continue to bring together clinicians, scientists and the community to learn from each other and to foster collaborations. Training grants and fellowships supplement the training of scientists and clinicians.

Conclusion: The ORE Core continues to increase public awareness of dementia and treatment using community outreach, the training of scientists and clinicians, the provision of programs and support services for diagnosed persons and families and engagement in community-based research.

POSTER 57

THE LATINO ALZHEIMER'S CAREGIVER UNIQUE RESPONSIBILITIES ASSESSMENT (LA CURA): THE LIVED EXPERIENCE CARING FOR A FAMILY MEMBER WITH DEMENTIA

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Introduction: Alzheimer dementia (AD) is the most common type of dementia among individuals 65 and older. There are more than 5 million diagnosed in the US alone and this number is expected to triple by 2050. Several reports indicate that AD is more prevalent among Blacks and Latinos for reasons that continue to be poorly understood. As the country's fastest, largest-growing minority, Latinos may have more risk factors for developing dementia than any other demographic, and they appear to be showing symptoms of dementia earlier. Latinos historically have lower education and socioeconomic status than their White and Asian counterparts and have less propensity to seek external professional support. While it is known that caregivers of persons living with AD experience serious mental, emotional, psychological, and physical stress, the degree and manner in which this affects Latino families, needs further exploration. The aim of this study was to supplement the limited existing literature with the perspectives of Latino family caregivers of persons living with Alzheimer dementia.

Methods: Participants were recruited through the Northwestern Alzheimer's Disease Center Clinical Core. Two individual family caregivers were interviewed; one a 73 year old male, caring for his wife of 48 years; the other a 78 year old mother of her daughter with AD (in addition to multiple family members with Alzheimer dementia over the past 20 years). Through a semi-structured interview format, questions explored conceptualization of dementia, challenges to getting a diagnosis, ways of coping, impact on family, and service needs. Interviews were audio-recorded and coded for emerging themes.

Results: Preliminary results revealed that these caregivers are: 1) Desiring more disease education, 2) Not knowing where to go for help and support, 3) Feeling isolated, 4) Desiring more help from family, 5) Finding lack of services for younger onset dementia.

Conclusion: More research is needed to understand the experience and needs of Latino caregivers of persons with dementia and to identify the interventions to best meet these needs.

POSTER 58

CATCH-ON ADRD UPDATE: DELIVERING DEMENTIA EDUCATION TO ENHANCE THE WORKFORCE

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Purpose: As the older adult population and persons living with dementia continues to increase, the need for specialized healthcare providers is of national significance. Collaborative Action Team training for Community Health – Older adult Network (CATCH-ON) is one of 44 Geriatric Workforce Enhancement Programs (GWEP) in the United States charged with developing a health care workforce that maximizes patient and family engagement and improves health outcomes for older adults. CATCH-ON focuses on the critical need to enhance the geriatric workforce capable of managing multiple chronic conditions, including ADRD.

Methodology: The ADRD team is a subcomponent of the CATCH-ON grant. The CATCH-ON ADRD team is comprised of committed, multi-disciplinary expert partners across the state. During this past year and through regular meetings, the ADRD team continued to provide input on the development of interactive educational materials and resources. Additional dementia and delirium modules were added.

Results: Four CATCH-ON ADRD workshops were held over this past year to multidisciplinary statewide audiences. These sessions incorporated feedback from previous presentations and lessons learned. Online modules focusing on the basics of evaluating memory concerns and other symptoms of cognitive impairment, person-centered dementia care, and treatment of behavioral changes were included. A training on dementia using CATCH-ON materials was provided to the Illinois Aging Network (N=85) and primary care provider training was delivered to Lawndale Christian Health Center (N=38), a CATCH-ON physician practice partner and federally qualified health center. Additionally, Equip the Trainer sessions, day-long workshops for interprofessional groups, were delivered to the Loyola University School of Social Work (N=35) and to the Southern Illinois Pioneer Coalition (N=73). Evaluations revealed high levels of satisfaction and increased self-efficacy in training others at their organizations.

Conclusion: CATCH-ON ADRD continues to provide accessible, interactive resources and materials to facilitate ADRD education.

POSTER 59

SAGES IN EVERY SETTING: INCLUDING THE VOICE OF PEOPLE LIVING WITH EARLY-STAGE DEMENTIA IN RESEARCH

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Background: CJE SeniorLife is an organization that provides a variety of services for older adults in the Chicagoland area. Several years ago, the organization initiated a group, Bureau of Sages, which explored how to incorporate the experiential voice of older adults into research. A research advisory board composed of nursing home residents and homebound older adults was trained to provide input to relevant researchers and clinicians, suggesting outcomes they felt researchers should study based on their personal healthcare experiences.

Goals: Following the success of the Bureau of Sages, CJE SeniorLife initiated the Sages in Every Setting program to expand this model to different populations and settings. One objective of this project was to recruit a group of individuals with early-stage dementia living in the community and train them as a new research advisory group.

Methods: The board was created as an eight-week discussion section that provided research training to seven volunteer members, preparing them to provide input to researchers. The curriculum included training on basic research concepts, generating a list of important health outcomes to recommend researchers study, creating an original comparative-effectiveness study, and providing input to a geriatric health researcher who presented his study during the final session.

Findings/Lessons Learned: Members showed enthusiasm during participation in this curriculum, expressing especially strong interest and engagement in the sessions that required using creativity and applied knowledge (e.g. creating the original study design and providing input to the geriatric health researcher). This project demonstrated that older adults living with dementia are both capable of and motivated to complete a research training program and provide meaningful input to research design.

Conclusions/Next Steps: Older adults living with dementia are very capable of and also enthusiastic to advise research. Their input should be utilized to help researchers design studies that will best improve health and quality of life outcomes. This model should be expanded to additional populations as well, so that researchers of diverse domains will have the opportunity to learn from research advisory groups and design studies that adequately address the needs of their target population.

Practical implications of findings: This project demonstrated that older adults with dementia are both capable of and motivated to complete a research training program and provide meaningful input to research design. These training programs should be expanded to additional groups, so that more researchers can receive input that helps them best design research to improve health and quality of life for the people they are studying.

POSTER 60

NORTHWESTERN ALZHEIMER'S DISEASE CENTER (NADC) CLINICAL AND DATA MANAGEMENT AND BIOSTATISTICS CORES

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Introduction: The Northwestern Alzheimer's Disease Center (NADC) is entering its 24th year of funding from the National Institute on Aging (NIA). The goals are to: (1) provide state-of-the-art care to patients with Alzheimer's disease and related disorders, and (2) support clinical and basic research on memory and aging through the collection, storage and dissemination of clinical data and brain tissue from research participants. Resources support local, national and international collaborations. The NADC is comprised of five Cores: Clinical, Administrative, Neuropathology, Data Management and Biostatistics, and Outreach, Recruitment and Education. Over the past year, the Clinical and Data Cores have worked closely with the Education, Neuropathology, and Imaging Cores to recruit and enroll subjects, facilitate brain donations, obtain Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) scans, and educate the public on effectively coping with cognitive aging and dementia.

Methods: The Clinical Core recruits cognitively healthy individuals and patients with different forms of dementia (e.g. AD, PPA, FTD) and cognitive impairment. Participants are followed annually according to the methods of the Uniform Data Set (UDS) of the NIA ADC program, many for the remainder of their lifetime, after which brain donation provides tissue for investigators studying Alzheimer's disease and related disorders. The Data Core compiles all data obtained and makes it available to approved studies, and also to the National Alzheimer's Coordinating Center (NACC) database.

Results: From 1996-2019 the Clinical Core has enrolled more than 2,202 participants, and the current active cohort is 540. 61% of the cohort has been followed in the research study for 5 or more years. In the past year, the Clinical Core supported over 18 different investigators and 23 studies being conducted in the areas of cognitive neuroscience, clinical trials, neuroimaging and neuropsychology. A total of 20 original publications, 9 published/online abstracts, and 3 book chapters have been supported over the past year and new funding has been generated with the use of Clinical Core resources.

Conclusion: The Clinical and Data Management/Biostatistics Cores of the NADC together have facilitated research on Alzheimer's disease, frontemporal dementia, primary progressive aphasia and age-related cognitive change and have promoted collaborative efforts nationally and internationally.

POSTER 61

BUILDING THE CAPACITY OF THE CARTER G WOODSON REGIONAL LIBRARY TO DELIVER A DEMENTIA FRIENDLY LIBRARY PROGRAM

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Introduction: The African American population represents roughly 39% of the local Chicago population aged 65 and older. African American adults are more likely than other racial/ethnic groups to be diagnosed with Alzheimer's disease. By 2050, 20% of persons living with dementia will be African American. Similarly, the number of family caregivers will grow rapidly over the next 20 years.

Methods: This is the 2nd year for this community engagement collaborative partnership between the Endeleo Institute, Northwestern University and the Carter G Woodson Regional Library. Initially conceived of by a three-person community-campus partnership we have scaled up to become a multi-stakeholder collaborative advisory board that continues to guide the newly refurbished Woodson library with the goal of implementing dementia-friendly programs, practices and interventions. Operationalizing the broader scope and community impact has included: 1) identifying board priorities using dementia friendly guidelines; 2) scaling up to intentionally include community priorities through the design, development and delivery of a Town Hall meeting; and 3) designing and developing shared operational strategies and the delivery of a series of programs.

Results: Six advisory board meetings have been held with two active sub-committees formed, the program committee and the funding/sustainability committee. Steering committee members meet monthly. Sixty-nine people attended the Town Hall meeting and polling illustrated the range of community participation by dementia services they currently use, prioritization of program topics, and reasons why they like the library. A key result noted by board members is that participants actively requested learning more about research opportunities and research findings. The first program, Alzheimer's 101 was offered in March 2019 and delivered by advisory board member, Dr. Lisa Barnes.

Conclusion: Reciprocal relations between campus, community and city entities need careful and strategic planning. Collaborative sharing of knowledge along with community appreciation of participating in programs and library patrons' deep commitment to a public space like a library fostered the capacity for this dementia-friendly initiative. Lessons learned include the need to develop shared processes for marketing events, hosting events and data collection and sharing.

Longer-term goals include creating a sustainability plan for the dementia friendly Woodson library, to evaluate the impact of participation on older adult and caregiver health outcomes, and to enable all sectors of Washington Heights to become dementia-friendly*.

*Dementia Friendly Illinois was formed in 2017 and efforts to build dementia friendly communities through various sectors of society have been implemented since then.

Dementia Friendly Woodson Library project was started with seed funding from the Northwestern University Alliance for Research in Chicagoland Communities at the Center for Community Health.

POSTER 62

HISTORY OF THE NORTHWESTERN COGNITIVE NEUROLOGY AND ALZHEIMER'S DISEASE CENTER (CNADC, 1994-2018)

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The CNADC was established in 1994 by Drs. Marsel Mesulam and Sandra Weintraub when they were recruited to Northwestern to begin a program in Alzheimer's Disease and other forms of dementia. In addition to laying the foundation for research programs in cognitive aging and dementia, Dr. Mesulam also founded the Cognitive Brain Mapping Group, the first gathering of Northwestern faculty interested in imaging and brain function. The CNADC expanded and was awarded an Alzheimer's Disease Core Center grant (P30), funded by the National Institute on Aging (NIA) in 1996. The P30 has been continuously funded for 23 years and obtained perfect scores in two reviews during that time. The CNADC pioneered accredited training programs at Northwestern in Cognitive Neurology, Neuropsychiatry and Clinical Neuropsychology. With the support of a community advisory board that included many devoted individuals, the center continued to grow and developed independent programs in atypical forms of dementia, such as Primary Progressive Aphasia and Frontotemporal Dementia. In addition, Northwestern coined the term "SuperAger" to define a group of individuals over age 80 with memory capacity at the level of individuals much younger. The SuperAging study has also been funded by the NIA and is providing novel insights into the preservation of memory into advanced old age. Structural and functional brain imaging studies have made innovative contributions to the localization of language in the brain The CNADC also has been recognized for its unique quality of life programs, such as the Buddy Program, that pairs individuals in early stages of dementia with medical students. The Buddy Program has been replicated by 15 universities globally since its inception in 1997. In 2018, in recognition of its international reputation and impact on science, the CNADC moved to new, larger space and was renamed the Mesulam Center for Cognitive Neurology and Alzheimer's Disease.

POSTER 63

KETAMINE RESTORES ESCAPE BEHAVIOR BY RE-ENGAGING DOPAMINE SYSTEMS TO DRIVE CORTICAL SPINOGENESIS

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Escaping aversive stimuli is essential for complex organisms, but prolonged exposure to stress leads to maladaptive learning. Stress alters neuronal activity in distributed networks, plasticity, and neuromodulatory signaling; yet, the field lacks a unifying framework for its variegated sequelae. Here we build this framework using learned helplessness paradigm, where ketamine restores escape behavior after aversive learning. Low-dimensional optical readout of dopamine (DA) neuron activity across learning predicts acute behavioral responses, transitions through learning phases, and future sensitivity to ketamine treatment. Ketamine's effects are blocked by chemogenetic inhibition of DA signaling and mimicked by optogenetic activation. We use 2-photon glutamate uncaging/imaging to interrogate structural plasticity in medial prefrontal cortex, revealing that dendritic spinogenesis on pyramidal neurons is regulated by aversive experience and recovered by ketamine in a DA-dependent manner. Together, these data describe recurrent circuits that causally link neuromodulatory dynamics, aversive learning, and plasticity enhancements driven by a therapeutically promising anti-depressant.

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