24th Annual Alzheimer Day

Abstract Book
Thursday, May 10, 2018
Dear Friends and Colleagues:

It is my great pleasure to welcome you to our 2018 Annual Alzheimer Day.

This year’s Mendelson Lecture by Dr. Jeffrey Kaye will focus on revolutionary advances in technology to monitor health changes due to dementia and aging. Dr. Kaye has pioneered the development of unobtrusive sensors for the home-based quantitation of mobility, sleep, medication use, weight change and social engagement. These developments allow rapid interventions aiming to prevent avoidable health deterioration and loss of independence.

Following the keynote presentation, and partly overlapping with lunch, we will have a poster session where clinicians and scientists affiliated with the Northwestern Alzheimer’s Disease 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 focusing on creative use of technology for addressing the psychosocial and interpersonal aspects of dementia-related conditions.

It is becoming increasingly clear that Alzheimer’s disease comes in different clinical and biological forms. The most common form impairs memory but there are forms that impair word finding, behavior or spatial orientation rather than memory. When it comes to caring for patients, we need to pay attention to these differences so we can personalize interventions according to the principles of precision medicine. We are also realizing that brain aging takes different forms and that incapacitating memory loss is not a necessary part of growing old. Identifying the factors that promote the preservation of memory in advanced age will help us understand the factors that increase resistance to Alzheimer’s disease. These themes of heterogeneity in dementia and aging are being pursued through our Primary Progressive Aphasia and SuperAging research programs.

Our center reached a major milestone this year. A $10 million campaign launched by the Feinberg School of Medicine to double the space of the Cognitive Neurology and Alzheimer’s Disease Center (CNADC) and endow its research enterprises has been completed. We are scheduled to move to our new location by November 2018. The expansion and endowment will allow successful programs to grow and novel ones to be initiated. This great milestone would not have been reached without the generosity of our Community Advisory Board and especially the vision and dedication of the Davee Foundation and of Mr. Craig Grannon, who serves as co-chair of our Community Advisory Board. I am honored and humbled by the decision of the Feinberg School of Medicine to name the expanded CNADC as the Mesulam Center.

On March 21, 2018, on the first day of Spring, The United States Congress has included in the 2018 budget a bipartisan request to increase funding for research on Alzheimer’s Disease and related disorders (including Frontotemporal Dementia and Primary Progressive Aphasia) by $414 million. Through this appropriation, research funding in this area will reach $1.8 billion, still not enough but definitely a change in the right direction. As I hope you will see by attending the keynote lecture, the afternoon session and the research posters, there are many promising developments that could make excellent use of this increased funding.

Welcome and enjoy the day.

Marsel Mesulam, MD
Ruth Dunbar Davee Professor of Neuroscience and Neurology
Director, Cognitive Neurology and Alzheimer’s Disease Center
THANK YOU

The Cognitive Neurology and Alzheimer’s Disease Center 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 CNADC’s annual Alzheimer Day.

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Kerry R. Peck, Managing Partner, is active in the Alzheimer’s community as a member of the Alzheimer’s Association Greater Illinois Chapter Board of Directors and a frequent presenter at Alzheimer’s Association education seminars. His is also co-author of the American Bar Association published book, “Alzheimer’s and the Law”.

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**SCHEDULE OF EVENTS**

**24TH ANNUAL ALZHEIMER DAY**

*Thursday, May 10, 2018*

**11:30 AM**  
**Welcoming Remarks**  
M.-Marsel Mesulam, MD, Director, CNADC, and Ruth Dunbar Davee  
Professor of Neuroscience, Feinberg School of Medicine

Alan M. Krensky, MD, Northwestern Medicine Executive for Development, Vice Dean for Development and Alumni Relations, Office of Finance and Administration, 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**  
“Pervasive Computing in Dementia Research and Care”  
Jeffrey Kaye, MD, Director of Layton Aging and Alzheimer’s Disease Center, Director of Oregon Center for Aging and Technology, and Layton Professor of Neurology and Biomedical Engineering, Oregon Health and Science University

**1:00 PM**  
**Lunch and Scientific Poster Viewing**

**2:30 PM**  
**“The Tele-Savvy Program and Other Technological Approaches to Care: One Size Does Not Fit All”**  
Fayron Epps, PhD, RN, Assistant Professor, Byrdine F. Lewis College of Nursing and Health Professions, Georgia State University

**Panel Discussion with Northwestern Clinicians, Researchers, Persons with Dementia, and Family Caregivers**  
Moderated by Lauren Dowden, MSW, LCSW

**4:00 PM**  
**Adjourn**

*Disclaimer: The advertisements published are not an endorsement of services, nor do they represent the recommendations, opinions, or views of the Northwestern University Cognitive Neurology and Alzheimer’s Disease Center.*
MAP OF VENDOR FAIR

Entrance to Lecture and Afternoon Session

To Scientific Poster Session and Lunch

Sewell Museum

Registration Table

CEU Table

18 17
16 15
14
12 13

Entrance to Lecture and Afternoon Session

7
LIST OF VENDOR TABLES BY NUMBER

The numbers for each vendor correspond to the Map of Vendor Fair on Page 7.

1  Peck Ritchey, LLC
2  Artis Senior Living
3  Terra Vista
4  Dutton, Casey, & Mesoloras
5  SeniorBridge
6  Health Learning Center
7  Home Instead Senior Care
8  Renewal Care Partners
9  Alzheimer’s Association
10 Belmont Village
11 The Alden Network
12 Northwestern Cognitive Neurology and Alzheimer’s Disease Center (CNADC)
13 Northwestern CNADC Research
14 BrightStar Care
15 AMITA Health Neurosciences Clinical Research
16 JourneyCare
17 Northbrook Inn Memory Care Community
18 Senior Living Experts
19 All Trust Home Care
20 Elderwerks Educational Services
21 CJE SeniorLife
22 Good Memories Chorale
23 Institute for Therapy through the Arts (ITA)
24 Northwestern Geriatric Medicine
25 Skyline Village
THANK YOU

We would like to thank our Silver Sponsors and Bronze Sponsors for their support of this event.

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THE 24TH ANNUAL ALZHEIMER DAY PLANNING TEAM

LAUREN DOWDEN
THERESE NELSON
KRISTINE ZACHRICH
DARBY MORHARDT, DIRECTOR OF EDUCATION

Thank you to all CNADC staff and faculty who have made this day a success!
The CNADC appreciates your dedication and commitment to making this day possible.
Marsel Mesulam, MD

Marsel Mesulam is the Ruth Dunbar Davee Professor of Neuroscience and Director of the Cognitive Neurology and Alzheimer’s Disease Center at Northwestern University. 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 founded the Behavioral Neurology Unit at the Beth Israel Hospital of Harvard Medical School and the Cognitive Neurology and Alzheimer’s Disease Center at Northwestern University. He has 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.
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.
Jeffrey Kaye, MD

Dr. Jeffrey Kaye is the Layton Endowed Professor of Neurology and Biomedical Engineering at Oregon Health & Science University. He is the Director of the Oregon Center for Aging and Technology (ORCATECH) and Director of the Oregon ADC – known as the Layton Aging and Alzheimer's Disease Center.

Over the past two decades, Dr. Kaye’s research has focused on understanding healthy aging using a variety of approaches ranging across the fields of genetics, neuroimaging, physiology and continuous activity monitoring. He leads several ongoing longitudinal studies of aging including the Oregon Brain Aging Study and the ORCATECH Life Laboratory which uses pervasive computing technologies for continuous assessment of health and function among the aging in their homes.
AFTERNOON SESSION
“THE TELE-SAVVY PROGRAM AND OTHER TECHNOLOGICAL APPROACHES TO CARE: ONE SIZE DOES NOT FIT ALL”

Fayron Epps, PhD, RN

Dr. Fayron Epps has over 15 years of nursing experience. She is currently serving as an Assistant Professor at Georgia State University Byrdine F. Lewis College of Nursing and Health Professions and as an affiliate faculty with the Gerontology Institute and Partnership for Urban Health Research. Dr. Epps received her BSN from Tuskegee University, MSN in Health Care Systems Management from Loyola University New Orleans, and a PhD in Nursing from Southern University and A & M College. In 2015, she completed her postdoctoral fellowship with the National Hartford Center of Gerontological Nursing Excellence. She recently received the “E. Louise Grant Award” for excellence in leadership in the areas of teaching, scholarship, and service from Georgia State University, School of Nursing.

Dr. Epps is an active member of numerous professional organizations, including the Gerontological Society of America, Southern Gerontological Society, and International Dementia Scholars Collaborative. She currently serves on the Board of Directors for the National Hartford Center of Gerontological Nursing Excellence. Dr. Epps is also an active volunteer with the Alzheimer’s Association. She has several publications that can be found in the Journal of Religion, Spirituality & Aging, Geriatric Nursing, Journal of Gerontological Nursing, Research in Gerontological Nursing, Research in Nursing and Health, and Issues in Mental Health Nursing. She also serves as a peer reviewer for several journals. Dr. Epps has disseminated her research findings through numerous venues at state, regional, and national levels.

Her career goal as a nurse scholar is to promote health across the life span by increasing the quality of life for family caregivers and recognizing the multidimensional complexities of supporting older adults through nursing research, education and service. Her program of research involves evidence-based practices for promoting quality of life for African Americans with dementia and their family caregivers.
AFTERNOON SESSION
“The Tele-Savvy Program and Other Technological Approaches to Care: One Size Does Not Fit All”

Lauren Dowden, MSW, LCSW
Lauren Dowden is a clinical social worker at the Cognitive Neurology and Alzheimer’s Disease Center at Northwestern University, where she works closely with individuals and families, who are living with a dementia diagnosis or other cognitive impairment. She holds a Masters in Social Work from Loyola University Chicago, is a Second City alum [Las Vegas] and is an instructor of medical improvisation for medical students at Northwestern University Feinberg School of Medicine. Ms. Dowden co-facilitates The Memory Ensemble and co-created and facilitates a storytelling workshop for families facing a dementia diagnosis at the CNADC, which has been featured by the TODAY Show and The New York Times.

Marcia Festen
Marcia Festen’s spouse was diagnosed with Alzheimer’s just over a year ago, at age 56. She has two children, ages 12 and 14. Marcia runs a philanthropic consulting firm, which she founded in 1999. She works with foundations of all sizes to help them direct and evaluate their charitable giving. She is an avid painter and spends all her free time in her studio, or with her dog. Marcia is a Chicago native.

Ian Grant, MD
Dr. Ian Grant attended Indiana University School of Medicine where he earned his MD as well as a master’s degree in bioethics. He completed residency training in neurology at Northwestern University and is currently completing an advanced training fellowship in cognitive/behavioral neurology. He is involved in clinical care of patients at Northwestern’s Neurobehavior and Memory Clinic as well as overseeing several clinical trials here at Northwestern.

Becky Khayum, MS, CCC-SLP
Becky Khayum is co-founder and president of MemoryCare Corporation, a company specializing in non-pharmacological cognitive-communication interventions for people with neurodegenerative conditions. She holds an adjunct faculty position at Northwestern University where she collaborates on research initiatives in the area of person-centered interventions for people with Primary Progressive Aphasia. Khayum’s clinical expertise focuses upon the use of functional treatment approaches and technology integration to increase life participation for individuals with aphasia and cognitive deficits.

Darby Morhardt, PhD, LCSW
Dr. Darby Morhardt is Research Associate Professor for the Cognitive Neurology and Alzheimer’s Disease Center (CNADC) and Department of Preventive Medicine, Northwestern University Feinberg School of Medicine. She leads the CNADC’s Outreach and Recruitment, the Miller Alzheimer Family Support Program, in addition to social work services for the Northwestern Medicine Neurobehavior and Memory Clinic.
Emily Rogalski, PhD
Dr. Emily Rogalski is a neuroscientist and Associate Professor at Northwestern University’s Feinberg School of Medicine. She currently serves as Associate Director of the Northwestern’s NIA-funded Alzheimer Disease Center and Director of Neuroimaging. Her research falls under the broad umbrella of aging and dementia and uses a multimodal approach to investigate two aging perspectives: primary progressive aphasia (PPA) in which neurodegenerative disease invades the language network and SuperAging in which individuals are seemingly resistant to the deleterious changes in memory associated with “normal” or more typical cognitive aging. Her investigations assist in defining the clinical and anatomical features of different dementia syndromes over the course of disease as well as identifying genetic and other risk factors. She has also developed educational programs, support groups and Communication Bridge, a telemedicine person-centered intervention to maximize quality of life for individuals with dementia. She receives research support from the National Institutes of Health and other philanthropic sources.
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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

2017
Borna Bonakdarpour, MD
Altered Language Network Connectivity in Primary Progressive Aphasia

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

2015
Dina Simkin, PhD
Calbindin-D\textsubscript{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\textsubscript{42} Induced BACE1 Elevation

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

COGNITIVE NEUROLOGY AND ALZHEIMER’S DISEASE CENTER
NORTHWESTERN UNIVERSITY FEINBERG SCHOOL OF MEDICINE

MISSION
The Cognitive Neurology and Alzheimer’s Disease Center (CNADC) 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
• Impacts of Non-Pharmacological Interventions on Quality of Life

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

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• Symptom specific interventions and strategies
• Information and referral to other supportive services

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Research Professor
Cognitive Neurology and Alzheimer’s Disease Center
ADVISORY BOARD

We would like to graciously thank our Advisory Board, founded and led from 1998 to 2008 by the late Jerome Rosenstone.

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Craig C. Grannon, Co-Chair
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Gloria LaGrassa

The CNADC Advisory Board was formed to increase public awareness and knowledge of the Center, and to help garner ongoing philanthropic support for the CNADC’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 CNADC Advisory Board, please contact Thongsy Singvongsa at 312-503-2832 or visit our website:
http://www.brain.northwestern.edu/about/giving.html
WHY I PARTICIPATE IN RESEARCH

Responses from CNADC 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 Cognitive Neurology and Alzheimer’s Disease Center at Northwestern are available to talk with you and answer your questions.
Phone: 312-926-1851
Email: memory-research@northwestern.edu
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
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/
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
320 E. Superior Street, Searle 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

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
INFORMATION ABOUT THE STUDY

The study lasts four days in total, for about seven hours each day, including breaks and lunch. On days one through three, you will be in Chicago where you will participate in a battery of neuropsychological tests. Neuropsychological tests are paper and pencil tasks that evaluate your language, memory and other areas of cognition. Also during the first three days, you will have a magnetic resonance imaging (MRI) scan and participate in an eye tracking task. On the fourth day, you will travel to Northwestern’s main campus in Evanston, IL (about 15 miles north) and participate in a variety of language and naming experiments, some that involve voice recording.

250 people with PPA and 150 age-matched controls will participate in this study. Participants will be asked to return two years later to compare changes between the two visits. Participants with PPA are asked to choose a study partner to accompany them on their visits. This can be a spouse, partner, family member or friend.

Participants must be:
- Diagnosed with PPA
- Right-handed
- Not claustrophobic
- Safe for an MRI
- Free of any illness or condition other than PPA that would affect their ability to participate now or in the future.

Individuals not seen at the Northwestern Cognitive Neurology and Alzheimer’s Disease Center will need to send records (neurology, neuropsychology and imaging reports) and have a phone interview before being approved by the study director to participate.

GOALS OF THE STUDY

The materials collected from your participation in the research study will be used to investigate a variety of topics. The information that we obtain in four days from you and other participants could lead to exciting developments in the knowledge and treatment of Primary Progressive Aphasia (PPA).

Specifically, the goals of this study are:
- To characterize individuals with PPA using neuropsychological testing and brain imaging.
- To investigate naming and word processing problems in PPA and see how they relate to brain changes.
- To increase awareness of PPA, educate others about this unique disorder and encourage more research to eventually develop a treatment.
ABOUT MRI

MRI, or magnetic resonance imaging, is a special technique that researchers and clinicians use to see the tissues inside the body. For this study, we will be looking at the brain.

The MRI portion of the study takes about forty-five minutes. You will change into a hospital gown and remove all metallic objects (jewelry, hearing aids, etc.). You will be asked to lie still on your back on a table with a specifically designed headrest. This will help keep you from moving your head. After you are positioned, the table will slide into the enclosed portion of the scanner.

The MRI scanner is loud and you may feel a small vibration, but this is normal. To communicate with the staff through an intercom system and to protect you from the noise, you will be wearing headphones specifically designed for MRI scanners. You will have constant contact with the researchers while you are in the scanner.

The images obtained will be used to compare with other participants, learn more about the brains of people with PPA, and examine the relationship between brain changes and test performance.

ABOUT EYE TRACKING

The eye tracking device uses infrared light and an infrared reflective mirror to track eye movements. This data provides researchers with a novel tool to understand the way language is processed in the brain for someone with PPA.

In this experiment, you will be asked to wear contacts or glasses if you need them for reading. You will then rest your chin on a platform within the eye tracker, as shown on the left. You will be asked to perform a variety of tasks with pictures and words while the camera records your eye movements. The experiment will last approximately 1 hour and 30 minutes.

COMPENSATION

TRAVEL | Out of town participants and study partners will have air travel and accommodations paid for and booked in advance by the research study. Local participants will have travel expenses reimbursed.

MEALS | Participants and study partners who are from out of town will be reimbursed for three meals a day; local participants will be reimbursed for lunches.

COMPENSATION | In addition to travel and meal costs, participants will be paid $100 per day, up to $400.

PAYMENT | Participation compensation and meal and travel reimbursement will be paid in the form of a check. The check should arrive to the subject’s home 30-60 days after the receipts are received.

FOR MORE INFORMATION, PLEASE CONTACT:

Benjamin Rader
PPA.Research@Northwestern.edu; (312) 908-9681
Northwestern University CNADC
320 E Superior Street, Searle 11 579
Chicago, IL 60611
Worrying About Your Memory?

Join the MIND Study
A Treatment Study for Mild Cognitive Impairment (MCI)

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).
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

We are funded by the National Institutes of Health (NIH) and the Foundation for the National Institutes of Health (FNIH).
The Northwestern University Cognitive Neurology and Alzheimer’s Disease Center (CNADC) 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 disease.

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 CNADC offers two support groups for patients and families:
- Frontotemporal Degeneration (FTD) & Primary Progressive Aphasia (PPA) Caregiver Support Group
- Younger Onset Support & Education Group (for persons living with Alzheimer’s disease under the age of 65 and their families)

**The Buddy Program**
This unique program matches first year students from Northwestern’s Feinberg School of Medicine with persons in the early stages of cognitive decline. The Buddy Program provides an opportunity for persons with Alzheimer’s disease and related dementias to mentor a medical student and gives medical students the unique advantage of spending time with diagnosed individuals at an early stage of illness and outside of the clinical setting.

**The Memory Ensemble**
A collaboration between the CNADC 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. During this 8-week program, benefits of this non-pharmacological intervention are investigated.

**iLUMAnations**
Designed as a program for people with memory loss and their care partners, the primary goal of iLUMAnations is to spark creative dialogue and foster meaningful exchange around art in a supportive environment. With the guidance of specially trained docents, participants tour exhibits at the Loyola University Museum of Art.

**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 couplehood and decrease social isolation.
This research program is an 8-week group for individuals with Alzheimer’s disease or related disorders and their families. Group sessions will provide:

- Education and resources from professionals
- Coping strategies
- Discussion
- Emotional support

**Fall and Spring Sessions Offered**

**WEEK #1**  
Welcome and Introductions

**WEEK #2**  
The Basics of Dementia

**WEEK #3**  
Coping with Changes: Practical and Functional Interventions

**WEEK #4**  
Coping with Changes: Maintaining Your Relationships and Disclosing the Diagnosis with Others

**WEEK #5**  
Coping with Changes: Supportive Community Resources & Interventions

**WEEK #6**  
Research Update and Opportunities

**WEEK #7**  
Legal & Financial Considerations

**WEEK #8**  
Life After SEED: Creative & Supportive Interventions and Q &A with Families Living with a Diagnosis  
[Schedule is subject to change.]

**INTERVIEW REQUIRED TO PARTICIPATE**
Discount parking will be provided.  
Please contact facilitators with any questions:

Lauren Dowden, MSW, LCSW  
lauren.dowden1@northwestern.edu  
312.503.0604

Darby Morhardt, PhD, LCSW  
d-morhardt@northwestern.edu  
312.908.9432

Therese Nelson, AM, LCW  
therese.nelson@northwestern.edu  
312.503.5767
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.
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.
Our Experience is Rooted in Memory Care... And Growing Every Day
At Arden Courts, our Memory Care roots run deep from over 20 years of experience caring for persons living with memory loss.

In the forest of memory care options, turn to Arden Courts to find strength and wisdom.

**Contact Arden Courts to arrange for your personal tour and for more information about our educational and support group events.**

Elk Grove
(847) 534-8815

Geneva
(630) 262-3900

Glen Ellyn
(630) 469-5500

Northbrook
(847) 795-9000

Palos Heights
(708) 361-8070

South Holland
(708) 895-1600

arden-courts.com

Arden Courts
Memory Care Community
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## POSTER SESSION

### CELL & MOLECULAR BIOLOGY

1. **Determining and Characterizing Substrates of Protein Degradation Impairments in Models of Alzheimer’s Disease**  
   Timothy J. Hark, Ewa Bomba-Warczak, Samuel N. Smukowski, Laith Ali, Jeffrey N. Savas

2. **Role of Unc5c, an Alzheimer’s Risk Gene in Late-Onset Alzheimer’s Disease in a Novel Mouse Model**  
   Devi Krishna Priya Karunakaran, Ryan J. Watts, Jasvinder K. Atwal, Robert J. Vassar

3. **Axonal Organization Defects in the Hippocampus of Adult Conditional BACE1 Knockout Mice**  
   Ming-Hsuan Ou-Yang, Jonathan E. Kurz, Toshihiro Nomura, Jelena Popovic, Tharinda W. Rajapaksha, Hongxin Dong, Anis Contractor, Dane M. Chetkovich, Warren G. Tourtellotte, Robert Vassar

4. **Role of Hippocampal Neurogenesis on Aging Related Changes in Cognition and Affect**  
   Elif Tunc-Ozcan, Yiwen Zhu, Chian-Yu Peng, Anis Contractor, John A. Kessler

### CLINICOPATHOLOGIC STUDIES

5. **Sleep Talking and Primary Progressive Aphasia: Report of a Case of Primary Progressive Aphasia with Overlapping Dementia with Lewy Bodies**  
   Alexandra Apple, Qinwen Mao, Eileen Bigio, Borna Bonakdarpour

6. **Challenges in Diagnosis of Primary Progressive Aphasia: Report of Two Cases**  
   Ellen Fitzmorris Clarke, Borna Bonakdarpour

7. **Von Economo Neurons in the Human Anterior Cingulate Cortex: Age-Related Changes and Vulnerability to Alzheimer’s Disease**  
   Tamar Gefen, Steven T. Papastefan, Eileen H. Bigio, Sandra Weintraub, Emily Rogalski, M.-Marsel Mesulam, Changiz Geula

8. **Trans-Synaptic Propagation of TDP-43 in Primary Progressive Aphasia**  
   Pouya Jamshidi, Garam Kim, Kabriya Bolbolan, Eileen H. Bigio, Marek-Marsel Mesulam, Changiz Geula

9. **Neurofibrillary Tangle and Amyloid-Plaque Burden in the Oldest-Old with Superior Memory and the Full Range of Alzheimer Pathology**  
   Garam Kim, Aras Rezvanian, Tamar Gefen, Sandra Weintraub, Emily Rogalski, M.-Marsel Mesulam, Changiz Geula
POSTER SESSION

CLINICOPATHOLOGIC STUDIES, CONT.

10 Asymmetry in Primary Progressive Aphasia, Probable Alzheimer Disease and Frontotemporal Dementia
Missia Kohler, Qinwen Mao, Christina Appin, Emily Rogalski, Tamar Gefen, Sandra Weintraub, Alfred Rademaker, Marsel Mesulam, Eileen Bigio

11 GRN Mutations Cause Unique CA1 Pathology
Qinwen Mao, Missia Kohler, Tamar Gefen, Jayson Wilson, Zachary Parton, Haibin Xia, Rosa Rademakers, Emily Rogalski, Sandra Weintraub, Marsel Mesulam, Eileen H. Bigio

12 Shrinking Cortex and Tau Burden in the Aphasic Variant of Alzheimer Disease
Adam Martersteck, Jaiashre Sridhar, Allison Rainford, M.-Marsel Mesulam, Emily Rogalski

13 Quantification and Distribution of Neuropathologic Changes in PART
JM Walker, TE Richardson, K Farrell, JF Crary, E Lee, EH Bigio, C Foong, P Shang, CL White

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14 Neuroimaging at the Northwestern Alzheimer’s Disease Center
Jaiashre Sridhar, Allison Rainford, Christina Sauer, Benjamin Rader, Beth Makowski Woidan, Stacey Juthapan, Niki Sabet, Rhiana Schafer, Marie Saxon, Anisha Basu, Amanda Cook, Adam Martersteck, Dan Ohm, Kristine Lipowski, Borna Bonakdarpour, Marco Catani, Lucio D’Anna, Derin Cobia, Sandra Weintraub, M Marsel Mesulam, Emily Rogalski

NEUROSCIENCE

15 On-Line Sentence Processing in Primary Progressive Aphasia
Elena Barbieri, Matthew Walenski, Kaitlyn A Litcofsky, Brianne Chiappetta, Chien-Ju Hsu, Marek-Marsel Mesulam, Cynthia K. Thompson

16 Non-Dominant Hemisphere Network Alterations in Primary Progressive Aphasia: Evidence for Potential Neuroplasticity Using Resting State Functional Connectivity
Anisha Basu, Emily Rogalski, Jaiashre Sridhar, M.-Marsel Mesulam, Borna Bonakdarpour

17 Amyloid Beta Oligomers (AβO) Drive Morphological Shift in Microglia in Animal Models for Alzheimer’s Disease
ZM Brahmbhatt, MA Bicca, KL Viola, WL Klein

18 Defining Proteome-Wide Subcellular Redistribution in ALS Disease Models
EL Daley, JA Ortega, M Marks, EA Hall, TF Gendron, CJ Donnelly, U Pandey, JN Savas, E Kiskinis
| 19 | Measurement of the Kinetic Behavior of Newly Generated BACE1-Cleaved APP in the Human Central Nervous System in Alzheimer's Disease: Initial Proof-of-Concept |
| Justyna A. Dobrowolska Zakaria, Randall J. Bateman, Bruce W. Patterson, Robert J. Vassar |
| 20 | Imaging Amyloid β Oligomers by Molecular MRI: Diagnosing Early-Stage Alzheimer's Disease |
| Abhay Gupta, Adrian Bebenek, Kirsten L. Viola, Erika N. Cline, Vikas Nandwana, E. Alex Waters, Chad R. Haney, Vinayak P. Dravid, William L. Klein |
| 21 | Primary Progressive Aphasia Research Program at Northwestern University's CNADC |
| Stacey Juthapan, Benjamin Rader, Christina Sauer, Rhiana Schafer, Marie Saxon, Allison Rainford, Jaiashre Sridhar, Elizabeth Rogers, JungMoon Hyun, Matthew Nelson, Darby Morhardt, Cynthia Thompson, Sandra Weintraub, Emily Rogalski, M.-Marsel Mesulam |
| 22 | The Effects of Learning and Aging on Functional Characteristics of Layer V Pyramidal Neurons of the Lateral Entorhinal Cortex |
| KB Kelly, C Lin, MM Oh, JF Disterhoft |
| 23 | SuperAging Study: Correlates of Active Engagement in Life in the Elderly |
| Beth Makowski-Woidan, Niki Sabetfakhri, Emmaleigh Loyer, Maureen Connelly, Marie Saxon, Tamar Gefen, Amanda Cook-Maher, Stephanie Kielb, Jaiashre Sridhar, Allison Rainford, Garam Kim, Alfred Rademaker, Dan McAdams, Gina Logan, Sandra Weintraub, Changiz Geula, M-Marsel Mesulam, Emily Rogalski |
| 24 | Latent Word-Comprehension Impairments in Agrammatic and Logopenic Primary Progressive Aphasia Patients Revealed through Eye Movement Analyses |
| Matthew Nelson, Stacey Juthapan, Maureen Connelly, Emily Rogalski, Sandra Weintraub, Robert Hurley, M-Marsel Mesulam |
| 25 | LRRK2 Phosphorylation of Auxilin Mediates Synaptic Defects in Dopaminergic Neurons from Patients with Parkinson's Disease |
| Maria Nguyen, Dimitri Krainc |
| 26 | Targeted Stimulation Improves Associative Memory and Hippocampal-Cortical Network Function in Older Adults |
| Aneesha S. Nilakantan, John A. Walker, Sandra Weintraub, Stephen VanHaerents, Donna J. Bridge, M-Marsel Mesulam, Joel L. Voss |
| 27 | Prominent Microglial Activation in Cortical White Matter is Selectively Associated with Cortical Atrophy in Primary Progressive Aphasia |
| Daniel T. Ohm, Garam Kim, Tamar Gefen, Alfred Rademaker, Sandra Weintraub, Eileen Bigio, M-Marsel Mesulam, Emily Rogalski, Changiz Geula |
28 Alteration or Inputs from the Subthalamic Nucleus to the Distinct External Globus Pallidus Neuron Classes in Parkinson’s Disease
Arin Pamukcu, Qiaoling Cui, Harry Xenias, Brianna Berceau, Alexandra Granados, Savio Chan

29 Gene Expression Reveals Molecular Insight for Selective Vulnerability in Alzheimer’s Disease
Jessica Park, Esra Ozaltin, Hande Ozdinler

30 Plasminogen Activator Inhibitor-1 Antagonist TM5A15 Reduce Neuropathology and Memory Deficits in APP/PS1 Mice
Guadalupe Rodriguez, Sky Dominguez, Toshio Miyata, Douglas E. Vaughan, Hongxin Dong

31 Disappearance of TDP-43 Inclusions Following Prolonged Transgene Expression is Associated with Cortical Atrophy in a Conditional Transgenic Mouse Model of FTLD
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32 AD Diagnostic Molecular Imaging Probes That Target Amyloid β Oligomers Have Therapeutic Benefits
Kirsten L. Viola, Maira A. Bicca, Erika N. Cline, Adrian Bebenek, Ting-Tung Chang, Chad R. Haney, Abhay Gupta, Zach Brahmbhatt, Jake Vitrofsky, Alex L. Qin, Clarissa Valdez, Henry Weiss, Mecca Islam, Anderson Peck, Brittany Merrifield, Michael Dykstra, William Klein

33 Type 3 Diabetes and High Cholesterol as Two Diet Induced Models of Alzheimer’s Disease
Craig Weiss, Kirsten Viola, William Klein, John Disterhoft

34 Differential Regional Buildup of Distinct Aβ Oligomer Species in the 5xFAD Mouse Model of Alzheimer’s Disease
Anthea Weng, Erika Cline, Josette Kamel, Savio Chan, William Klein

35 Remembering with High Fidelity: Evidence Implicating Sleep and Sleep Spindles
Sarah J. Witkowski, Jessica D. Creery, Leonardo E. Dionisio, Ken A. Paller

PHARMACOLOGY

36 Transient Receptor Potential Ankyrin1 (TRPA1) as a Target for Alzheimer’s Disease

37 Memory Improvement through Nicotine Dosing (MIND)
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M.-Marsel Mesulam, Sandra Weintraub, Ian Grant, Borna Bonakdarpour, Kristine Lipowski, Jordan Robson

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39 Autophagic Regulation of Lifespan and Healthspan in Alzheimer’s Disease Mice
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40 Delayed or Absence of Primary Progressive Aphasia Diagnosis among Racial and Ethnic Minority Communities
Borna Bonakdarpour, Jana Wingo, Mallory Ward, Darby Morhardt

41 Innovative Strategies to Meet the Needs of Persons Living with Dementia: Development and Lessons Learned
Fawn Cothran, Mary Zonsius, Darby Morhardt, Erin Emery-Tiburcio, Robyn Golden

42 Dyadic Storytelling: A Supplemental Education Tool to Facilitate Understanding of the Lived Experience of Dementia
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43 My Mentor and Me
Anna Hershner, Marcia Spira, Darby Morhardt

44 Northwestern Alzheimer’s Disease Center Outreach and Recruitment Core (OR Core) 2017-18
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45 The SEED Program: Evaluation of an 8-Week Psychoeducation and Support Program for Persons Living with Early Dementia and Their Families
Therese Nelson, Joshua Kaplan-Lyman, Lauren Dowden, Darby Morhardt

46 Northwestern’s Buddy Program Increases Medical Student Knowledge, Empathy, and Attitudes Towards People with Dementia
Annika Nilsen, Anil Wadhwanii, Neil Lim, Berkley Davis, Sandra M. Sanguino, Alfred Rademaker, Darby Morhardt
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47 Chicago Memory Café
Adria Ososkie, Marcia Spira, Lauren Dowden, Therese Nelson, Joe Fisher, Erica Bohac, Sherrie All, Darby Morhardt

48 Communication Enhancement Training: A Novel Dyad Conversation Strategy Intervention in Dementia
Angela Roberts

49 Communication Bridge: A Person-Centered Internet-Based Intervention for Individuals with Primary Progressive Aphasia
Marie Saxon, Elizabeth Rogers, Angela Roberts, Kathryn Borio, M.-Marsel Mesulam, Aimee Mooney, Becky Khayum, Emily Rogalski

50 REACH to Faith 2.0: Building the Dementia Friendly Woodson Library
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51 Northwestern Alzheimer’s Disease Center (NADC) Clinical and Data Management and Biostatistics Cores
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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 long after irreversible synapse loss and neurodegeneration, thus it is important to better understand early mechanisms of AD pathology. Molecularly, AD is characterized by misfolding and aggregation of proteins, especially amyloid beta (Aβ). Aβ accumulation occurs well before any other dysfunction takes place and this accumulation is thought to trigger downstream toxic events. However, how accumulating Aβ confers toxicity to cells remains poorly understood. One hypothesis is that Aβ impairs normal protein degradation causing certain proteins to stick around the cell longer, possibly disrupting healthy cellular functions. My project aims to identify proteins that persist in the cell due to Aβ accumulation.

To investigate protein degradation dynamics, I utilize metabolic labeling via Stable Isotope Labeling in Cell Culture or in Mammals (SILAC and SILAM), followed by quantitative mass spectrometry (MS). In both methods proteins are labeled with heavy isotopes, then “chased” with light isotopes. 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. For the SILAM paradigm, I 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, I can determine which proteins are abnormally persisting in the brain.

In my preliminary experiments, I found many synaptic proteins persisted in the cortex and hippocampus following Aβ accumulation. Furthermore, these synaptic proteins were unchanged in the cerebellum, a brain region where Aβ does not accumulate until very late in the disease. More specifically, these persisting proteins were enriched for proteins involved with synaptic vesicle release and recycling. The synapse is a specialized cell junction that mediates communication between neurons. Synaptic transmission is a critical aspect of learning and memory, and synaptic dysfunction correlates very tightly with the cognitive deficits of AD, suggesting synapses are a critical component to disease. Synaptic vesicle machinery tightly controls synaptic transmission, thus synaptic vesicle protein dysfunction may be a driving force for AD pathology. These preliminary results suggest that Aβ accumulation may cause impairments to synaptic vesicle protein degradation, which may trigger further dysfunction.

Proteomic investigations into protein degradation dynamics in response to Aβ accumulation has never been investigated, especially in APP knock-in mice. These experiments may reveal novel protein pathways that are critical to Alzheimer’s pathology, and thus may serve as new therapeutic targets to help prevent or delay AD progression.
POSTER 2

ROLE OF UNC5C, AN ALZHEIMER’S RISK GENE IN LATE-ONSET ALZHEIMER’S DISEASE IN A NOVEL MOUSE MODEL
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Purpose: Alzheimer’s disease (AD) is characterized by amyloid plaques, neurofibrillary tangles, and synaptic and neuronal loss. The mechanism of neuron death in AD, however, remains unexplored. 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). This 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 T85M that were crossed with 5XFAD amyloid mouse model. Brain sections obtained from Unc5c<sup>KI/KI</sup>;5XFAD mice and littermate controls were imaged by immunofluorescence confocal microscopy for neurons (NeuN), Aβ deposits (Thiazine Red, Aβ<sub>42</sub>, Aβ<sub>total</sub>), apoptosis (TUNEL), astrocytes (GFAP), and microglia (Iba1). We also employed unbiased proteomics. 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 Aβ<sub>42</sub>, 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, proteomics analysis of KI and wildtype (WT) mice brains showed upregulation of apoptotic proteins and down-regulation of neuronal proteins. Moreover, when neurons were counted in NeuN-stained brain sections of Unc5c<sup>KI/KI</sup>;5XFAD mice, we observed that ~40% of neurons were lost in cortical layer 5 of Unc5c<sup>KI/KI</sup>;5XFAD compared to UNC5C<sup>+/+</sup>;5XFAD mice. Neuron loss in Unc5c<sup>KI/KI</sup>;5XFAD mice correlated strongly with the presence of Aβ deposits in layer 5. Primary KI neurons showed an increased cell death in the presence of cytotoxic stressors.

Significance: 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.
BACE1 is the β-secretase enzyme that initiates production of the toxic Aβ peptide that accumulates in Alzheimer’s disease brain. As such, BACE1 is a prime therapeutic target and several BACE1 inhibitor drugs are currently being tested in clinical trials. However, the safety of BACE1 inhibition is unclear. Germline BACE1 knockout mice have multiple neurological phenotypes, although these could arise from BACE1 deficiency during development. To address this question, we report that tamoxifen-inducible conditional BACE1 knockout mice in which the Bace1 gene is ablated in the adult largely lack the phenotypes observed in germline BACE1 knockout mice. However, one BACE1-null phenotype, that of reduced length and disorganization of the hippocampal mossy fiber infrapyramidal bundle, an axonal pathway maintained by adult neurogenesis of dentate gyrus granule cells, is induced after BACE1 gene deletion in the adult brain. This defect of axonal organization correlated with reduced BACE1 cleavage of the neural cell adhesion molecule CHL1, which has previously been associated with an axon guidance mechanism. Although our results indicate that BACE1 inhibition in the adult may avoid phenotypes associated with BACE1 deficiency during development, they also suggest that BACE1 inhibitor drugs for Alzheimer’s disease may disrupt the organization of an axonal pathway in the hippocampus, an important structure for learning and memory.
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 have used conditional expression of the mutant G protein-coupled receptor, hM4Di, which is exclusively activated by exogenous otherwise inert ligand CNO. I produced double transgenic mice, Ascl1-CreERT2; R26<sup>LSL-hM4Di</sup>, 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 the CNO-induced hyperpolarization of the membrane potential. Furthermore, CNO substantially decreased the number of evoked action potentials in hM4Di-expressing neurons. These data suggest that the hM4Di/CNO-based method can effectively decrease the excitability of newborn hippocampal neurons in adult mice. Next, I tested the behavioral effects of this selective inhibition. Adult Ascl1-Cre<sup>ERT2</sup>; R26<sup>LSL-hM4Di</sup> mice received fluoxetine (to increase neurogenesis) or saline together with CNO or buffer supplementation for 3 weeks. By this way, newborn neurons were silenced during the entire period of antidepressant treatment. At the end of the 3rd week, behavioral assessment showed that fluoxetine treatment alone improved the depression-like behavior. However, CNO supplementation together with fluoxetine treatment blocked the ameliorative effects of the antidepressant. Moreover, CNO supplementation in the absence of hM4Di did not alter behavioral phenotypes. My next goal is to determine whether increased neurogenesis, resulting from the inhibition of BMP signaling, is causal to long-term enhancement of hippocampus-dependent cognitive/affective function in aged mice by using hM4Di/CNO-based method. Even though it is still early to know whether DREADDs will translate well to the human brain, primate studies show similar patterns of neuronal activity modulation and behavioral effects of DREADDs as seen in rodents. Additionally, AAV vectors, which are routinely used to express DREADDs in preclinical experiments, are commonly used and well tolerated in human gene therapy clinical trials, including in neural tissue in Alzheimer’s and Parkinson’s Diseases. In summary, DREADDs could offer relatively non-invasive, selective and reversible modulation of neuronal populations and pathways to regulate cognitive/affective function in aging population.
SLEEP TALKING AND PRIMARY PROGRESSIVE APHASIA: REPORT OF A CASE OF PRIMARY PROGRESSIVE APHASIA WITH OVERLAPPING DEMENTIA WITH LEWY BODIES
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Background
Although sleep talking in adults is fairly common, with current prevalence of 17.7%, the presence of parasomnias in older adults may be related to an underlying neurodegenerative processes such as Dementia with Lewy Bodies, Alzheimer Disease or Frontotemporal dementia. In fact, sleep talking has been found to be useful in the clinical discrimination of Dementia of Lewy Bodies from other types of dementia. Still, little is known about the mechanisms underlying sleep talking for patients presenting with language deficits such as primary progressive aphasia. Here we present a case of PPA who, also had concurrent sleep talking.

Presentation of Case
A 74-year-old left handed man presented with progressive language impairment over the past four years, per neuropsychological testing. Specifically, he had difficulty with word finding, reading, writing and calculations suggesting logopenic primary progressive aphasia (PPA-L) and Gerstmann syndrome. MRI demonstrated mild atrophy in the left perisylvian and middle temporal pole, suggesting left hemispheric language dominance. The patient’s family reported difficulty sleeping, without dream enactment, which progressed to limb movements and dream enactment and hypersomnia. Although he was unable to effectively communicate towards the end of his life, his partner reported sleep-talking. Although he originally presented with symptoms consistent with a PPA-L syndrome, a combination of sleep disturbance, reduced sense of smell, past history of constipation and later drop in orthostatic pressure, led to a diagnosis of Dementia with Lewy Bodies concurrent with PPA. Later he was found to have both Alzheimer and Lewy body disease pathology on autopsy.

Discussion
This case demonstrates preserved language abilities that appear during sleep but are somehow inaccessible during wakefulness. Despite language deficits during the day, the individual presented here was able to produce partial sentences while asleep. This case study provides an example of language use during sleep which has not been often reported in the literature. Previous studies have found an increase in sleep talking in different forms of dementia (e.g. multiple systems atrophy and Dementia of Lewy Bodies), but to our knowledge no study has outlined sleep talking concurrent with PPA and how it would manifest itself. It may be important for physicians to gather information from bed partners about sleep talking or other sleep-related behaviors, even for individuals with language deficits, as this may be helpful to have a better understanding of the underlying cause. Additionally, educating family members about sleep-talking in such individuals may be helpful in understanding that language abilities may be inaccessible rather than completely eliminated. This case report demonstrates the importance of working towards a better understanding of parasomnias in different dementia populations.
CHALLENGES IN DIAGNOSIS OF PRIMARY PROGRESSIVE APHASIA: REPORT OF TWO CASES
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Introduction
Primary progressive aphasia (PPA) is a neurodegenerative disease that impairs language initially and progresses to involve other cognitive domains. Despite a consensus paper (Gorno-Tempini et al., 2011), clinical diagnosis of PPA can still be challenging in clinical settings. We present two cases of PPA that were initially diagnosed as mild cognitive impairment (MCI).

Case series
Case 1 was a 68-year-old right handed, bilingual business owner who complained of a 3-year history of forgetting names of places and details of conversations. His wife reported significant anxiety and somewhat depressed mood. Family history was significant for dementia in his 66-year-old sister. Cognitive testing suggested mild anomia (interpretation was limited due to English being his second language), verbal working memory weakness, and relatively spared executive function. FDG-PET-CT of the brain and brain MRI were read as unremarkable. He was diagnosed to have cognitive changes due to mood disorder and sleep apnea. One year later, he complained of worsening verbal memory. Cognitive exam revealed worsening of word finding in both languages, and PET showed new asymmetric (L>R) temporal hypometabolism. CSF analysis suggested a non-Alzheimer underlying pathology. The diagnosis was changed to anomic PPA.

Case 2 was a 68-year-old man who presented after an episode of apparent confusion while giving a lecture. Cognitive exam suggested mildly impaired verbal short-term memory. MRI showed very mild, bilateral temporoparietal lobe atrophy. He was diagnosed with MCI of Alzheimer type. Two years later, he continued to be functional at work and it was noted that he had more trouble with word finding. Cognitive exam showed anomia with verbal memory weakness secondary to impaired verbal retrieval. PET showed asymmetrical (L>R) temporoparietal hypometabolism, and MRI showed asymmetrical (L>R) perisylvian atrophy. CSF analysis showed amyloid and tau elevations consistent with Alzheimer disease. The diagnosis was changed to logopenic PPA.

Conclusions
In both cases, PPA was distinguished from initial diagnosis based on the lack of significant functional impairment and progressive impairment mostly in the language domain. Follow-up PET and MRI helped support the clinical diagnosis, as they showed asymmetric (L>R) temporoparietal hypometabolism.

Diagnosis remains challenging for both Alzheimer and non-Alzheimer cases of PPA. In patients with aphasia, poor performance on tests of verbal and working memory may actually be due to language impairment. In addition, bilingualism and other concomitant medical diagnoses may complicate the clinical picture, as with the first case. Finally, these cases presented similarly, yet only one had Alzheimer pathology, emphasizing that symptoms often do not follow pathology.
VON ECONOMO NEURONS IN THE HUMAN ANTERIOR CINGULATE CORTEX: AGE-RELATED CHANGES AND VULNERABILITY TO ALZHEIMER’S DISEASE

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Throughout the human aging lifespan, post-mitotic neurons acquire an unusually high burden of wear and tear; it is likely why age is considered the strongest risk factor for Alzheimer's Disease (AD). The AD stage is preceded by a prodromal amnestic mild cognitive impairment stage (aMCI) where Alzheimer pathology is less abundant and cognitive impairment is less pronounced. In “normal”, healthy individuals, age-related cognitive decline is considered to be part of typical aging, leading to the inference that neurodegenerative disease is both ubiquitous and somewhat typical. What remain unclear are the intrinsic vulnerabilities of specific neuronal subpopulations that potentially contribute to neurodegeneration.

In a previous investigation, von Economo neurons, a highly specialized spindle-shaped cell unique to the anterior cingulate in primate hominoids, and implicated in higher-order cognition, was found in abundance in a group of extraordinary individuals called “SuperAgers” (persons over age 80 with memory scores equal-to-or-above individuals 30 years younger) compared to normal controls and aMCI individuals. Also pertinent, a prior study showed early VEN loss in behavioral variant Frontotemporal Dementia (Seeley, 2010). In the current study, we sought to determine whether VENs were preferentially reduced across the lifespan and in AD.

Post-mortem brain specimens stained with Nissl were analyzed using modified stereological methods (StereoInvestigator, MBF) from the following cohorts (N = 5, per group): SuperAgers, normal older controls (age 65+ years), normal younger controls (age 20-60), individuals pre-morbidly diagnosed with amnestic Mild Cognitive Impairment (aMCI), and individuals with severe post-mortem AD pathology. VEN density and total neuronal counts were analyzed in anterior cingulate regions (Brodmann area 24).

Stereological results revealed greatest mean density of VENs in SuperAgers compared to other groups. Old controls and young controls showed no difference in VEN count; aMCI showed less VENs that control groups, and AD showed lowest counts compared to all groups. These patterns were consistent when accounting for total neuronal density. Interestingly, total neuronal counts in cingulate cortex were highest in young controls, and lowest in AD specimens.

VENs in human anterior cingulate cortex are vulnerable to AD pathology, and appear to be preserved in both young and old individuals who show well-preserved cognition antemortem. Further research will clarify the biochemical signature of VENs and its association with pathogenesis.
Aggregation and propagation of misfolded proteins in the form of abnormal inclusions is a common feature of numerous neurodegenerative diseases. A hallmark of frontotemporal lobar degeneration (FTLD) is the abnormal aggregation of inclusions containing hyper-phosphorylated tau (FTLD-tau) or the 43-kDa transactive response element DNA-binding protein (TDP-43) (FTLD-TDP). While pathologic spread has been suggested to act through axonal pathways and prion-like mechanisms, the evidence has been limited to qualitative and semi-quantitative observations at the regional level. Using unbiased stereological techniques, this study aims to quantitatively investigate trans-synaptic propagation of abnormal TDP-43 precipitates in the well-established neural circuitry of the hippocampus, which encompasses a highly ordered chain of intrinsic single synaptic connections that link cytoarchitectonically distinct zones. Whole-hemisphere sections from brains of three participants with clinical diagnoses of primary progressive aphasia—a neurodegenerative disorder in which language is the most salient deficit—and post-mortem diagnoses of FTLD-TDP, were immunohistochemically stained using an antibody to phosphorylated TDP-43 (pS409/410-2). All participants were right-handed and had asymmetric atrophy (Left>Right). TDP-43-positive mature (darkly stained, fibrillar) and pre-inclusions (diffuse nuclear and/or cytoplasmic staining prior to becoming a mature inclusion) were quantified in the granular cell layer of the dentate gyrus (DG) and the pyramidal cell layers of Cornu Ammonis (CA)3, CA2, and CA1. Across all regions, the highest density of mature TDP-43 inclusions were found in the granule neurons of DG, followed by significantly fewer inclusions in the pyramidal neurons of CA3 (one synaptic relay away), and still fewer inclusions in CA1 and CA2 (p<0.05) pyramidal neurons (two synapses away). TDP-43 pre-inclusions, on the other hand, showed highest densities in either DG or CA3, followed by lower densities in CA1 and CA2. The relationship between patterns of pre- and mature inclusions support the idea that pre-inclusions are present in greater abundance prior to the formation of mature TDP inclusions, before developing through progressive stages into dark mature aggregates. Our quantitative results of mature inclusion densities suggest a direct evidence for trans-synaptic propagation of intracellular inclusions of TDP-43.
Recent reports indicate that a subpopulation of cognitively normal elderly meet pathologic criteria for diagnosis of Alzheimer’s disease (AD) at post-mortem examination, characterized by high densities of neurofibrillary tangles (NFTs) and amyloid plaques (APs). In a previous semi-quantitative investigation of a cohort of eight 90+ participants (95-100 years) with relatively superior memory performance, we reported the full range of Alzheimer pathology; despite similarly superior memory performance, some brains displayed very sparse NFT/pre-NFTs and diffuse APs, while others showed extensive distributions of NFTs and cored/neuritic plaques. The purpose of the current study was to quantitatively investigate NFT and AP burden in the hippocampus and prefrontal cortex (Brodmann area 9) of these brains. Antibodies to paired helical filaments (PHF-1) and amyloid-β peptide (6E10) were used to visualize pre-NFTs/NFTs and APs, respectively. Pre-NFTs/NFTs were quantified numerically and AP burden was assessed using ImageJ software to calculate the percent area occupied by plaques. In the hippocampus, the density of NFTs was lowest in the brain designated as Braak stage I (BS I) of tangle deposition, and highest in a case with BS VI, showing a very consistent correlation between Braak staging and NFT density (p<0.005; r=0.9674). NFT burden in BA9 showed the same trend, such that a higher NFT density in the hippocampus accurately predicted a greater density of NFTs in BA9 (p=0.0049; r=0.9248). There was no correlation between AP densities in the hippocampus and BA9 (p>0.05; r=0.3159). The relationship between pre-NFTs/NFTs and APs remained close in both the hippocampus (p=0.0043; r=0.7762) and BA9 (p=0.0013; r=0.2439). Qualitative examination of HLA-DR-positive microglial activation, a marker of inflammation, showed a general increase in deposition with progressive Braak staging, suggesting that microglia closely correlate with pathologic burden. These results indicate that a range of AD pathology, including densities and distributions consistent with pathologic diagnosis of AD, can be present in the oldest old with similar above-average memory capacity. It appears that brains of some elderly are protected from processes that lead to NFT/AP formation, while others are resistant to the deleterious effects of NFT/APs.
Primary progressive aphasia (PPA) is a clinical syndrome characterized by progressive language impairment that is caused by an underlying neurodegenerative disease that can be of any pathologic type. Previous studies have demonstrated that PPA has greater atrophy, neuronal loss and gliosis, and molecular pathology in the language-dominant, usually left, hemisphere. This is independent of the underlying molecular pathology. The purpose of this study is to confirm the leftward asymmetry in PPA and to assess the distribution of atrophy, neuronal loss and gliosis and molecular pathology in probable Alzheimer disease (PRAD) and frontotemporal dementia (FTD).

The cases chosen were clinically diagnosed with PPA (n=16), FTD (n=16), and PRAD (n=16), and consecutively accessioned between 2014 and 2017. The degree of gross atrophy, neuronal loss and gliosis, superficial microvacuolation and the molecular pathology were scored using a semi-quantitative method with statistical analysis of the data performed. In cases with PPA, gross atrophy, neuronal loss and gliosis, and the molecular pathology all showed a statistically significant difference between hemispheres with the left showing greater involvement. For PRAD and FTD, there was no statistical difference between hemispheres. In conclusion, the leftward asymmetry in PPA is a unique, reproducible feature that is specific to this clinical syndrome and is not seen in PRAD and FTD.
Heterozygous loss-of-function mutations in the progranulin gene (GRN) cause FTLD-TDP, a common form of autosomal dominant neuropathology leading to dementia. Progranulin (PGRN) is a highly conserved, secreted glycoprotein, and may function in the central nervous system as a growth factor and key modulator of microglial function. Hence, it has been suggested that altered microglial function caused by PGRN deficiency is tied to the pathogenesis of FTLD-TDP. Our previous studies showed that microglial PGRN had regional hippocampal changes, with relatively low expression in the CA1 region. We next aimed to evaluate the relationship of low CA1 microglial PGRN expression in FTLD with GRN mutation with other CA1 pathologies, such as neuronal loss and gliosis, TDP-43 pathology, and density of IBA-1 positive microglia. We found that the low density of PGRN-positive microglia correlated with very low levels of neuronal loss and gliosis (13/14 cases), frequent TDP-43 neurites (13/14 cases), and frequent IBA-1 positive rod-like microglia (10/14 cases). In FTLD-TDP without GRN mutations, the CA1 region showed a higher density of PGRN positive microglia than in cases with GRN mutations, moderate to severe hippocampal sclerosis (12/17), sparse TDP-43 neurites (16/17), and a lower density of IBA-1 positive rod-like microglia. In Alzheimer's disease with and without hippocampal sclerosis, the CA1 region also showed a higher density of PGRN positive microglia, none to sparse TDP-43 neurites, and minimal rod-like IBA-1 positive microglia. We conclude that PGRN haploinsufficiency results not only in a low density of PGRN positive microglia in CA1 but also leads to high density of TDP-43 neurites and rod-like microglia, and minimal neuronal loss in this region.
**POSTER 12**

**SHRINKING CORTEX AND TAU BURDEN IN THE APHASIC VARIANT OF ALZHEIMER DISEASE**

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**Background:** Primary progressive aphasia (PPA) is a clinical dementia syndrome often characterized by asymmetric atrophy of the language-dominant (usually left) hemisphere. Common neuropathologies reported for PPA include Alzheimer’s disease (AD) or a form of frontotemporal lobar degeneration. In line with post-mortem studies of neurofibrillary tangles, early cross-sectional studies examining flortaucipir tau PET (\(^{18}\)F-AV-1451) in AD have reported a close relationship with atrophy.

**Objective:** Determine if elevated flortaucipir PET signal correlated with baseline and the longitudinal change in cortical atrophy in an atypical form of AD.

**Methods:** Seven participants with PPA and suspected underlying Alzheimer’s disease pathology (PPA-AD\(^{\text{bio+}}\); \(^{18}\)F-florbetapir whole-cerebellar SUVR > 1.17) underwent flortaucipir PET imaging and structural MR imaging. Furthermore, four underwent longitudinal MRI (mean 2.04 years apart). Freesurfer (FS) v6.0.0 was used to reconstruct the T\(_1\)-weighted MRI scan, calculate atrophy (grey volume), and for Müller-Gärtner modified partial volume correction (PVC). Thirty-five normal controls were used to calculate atrophy z-scores. The annualized symmetrized percent change in atrophy, baseline atrophy z-score, and tau PET load was measured in 68 regions from the left and right hemisphere Desikan-Killiany atlas in subject native space.

**Results:** Baseline atrophy and PVC flortaucipir in the 68 regions for seven PPA-AD\(^{\text{bio+}}\) was strongly correlated, \(r(474) = -0.450, p < 0.0001\). The annualized percent change in cortical volume showed a similar negative correlation with baseline PVC tau PET signal in four PPA-AD\(^{\text{bio+}}\) participants, \(r(270) = -0.471, p < 0.0001\). Correlations repeated using non-PVC tau PET data remained highly significant (\(r = -0.430\) for cross-sectional atrophy and \(r = -0.468\) for longitudinal, both \(p < 0.0001\)).

**Conclusions:** A preliminary study of tau PET and longitudinal atrophy in an atypical form of AD supports the close relationship found in previous cross-sectional studies. A more extensive evaluation with a larger sample will be required to determine the robustness of these early results. Tau PET imaging shows promise for clinical trials and research designed to target or investigate hyperphosphorylated tau, a hallmark of Alzheimer disease.
Primary age-related tauopathy (PART) is a neuropathologic entity characterized by neurofibrillary degeneration that is primarily restricted to Braak stage I-IV neurofibrillary degeneration, absent or sparse neocortical neuritic plaques (by CERAD criteria), and Thal amyloid phase 0-2. Previously, many PART cases with significant cognitive impairment were categorized as tangle-predominant senile dementia or tangle-only dementia. In symptomatic patients, clinical features generally consist of a milder, mostly amnestic type impairment and longer lifespan than Alzheimer disease (AD) patients. The objective of the PART Working Group project is to test the hypothesis that PART cases have distinct clinical, neuropathologic and genetic characteristics that distinguish them from AD and other neurodegenerative disorders. The rationale is that distinguishing these disorders will provide insight into the mechanisms of tau and amyloid deposition and degradation, and will allow clinicians to formulate more specific and accurate diagnoses, which will eventually guide more specific prognostication and therapeutic intervention.

We assessed the regional distribution of abnormal tau burden in a series of 50 subjects with PART. One preliminary finding is a predilection of the hippocampal CA2 segment for tau pathology at low to intermediate Braak stages. 78% (39/50) of the PART cases analyzed with Braak stage III or IV harbor CA2 tau pathology that is greater than or equal to the CA1 tau pathology. This is in contrast to AD cases, which generally demonstrate sparing of CA2, especially in early to intermediate stages. The CA2 neurofibrillary tangles present in PART demonstrate both 3R- and 4R-tau immunoreactivity similar to AD tangles, but in contrast to the CA2 neurofibrillary degeneration observed in restricted 4R tauopathies. This selective vulnerability of CA2 for 3R/4R tau-immunoreactive neurofibrillary degeneration appears to be a unique and early histopathologic feature of PART.
The Neuroimaging Core at the Cognitive Neurology and Alzheimer’s Disease Center (CNADC) was created 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 FTLD spectrum of disorders. The Neuroimaging Core contains data from scans that provide optimal quantitative information on brain structure (MPRAGE), white matter properties (FLAIR), axonal pathways (DTI), resting state hemodynamic fluctuations for establishing functional connectivity (rsfMRI), amyloid (Amyvid – PET) or tau (18F AV 1451 – PET) binding and glucose (18F FDG – PET) uptake. Neuroimaging data are available 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 our Center.
ON-LINE SENTENCE PROCESSING IN PRIMARY PROGRESSIVE APHASIA
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Introduction
Evidence from off-line tasks indicate that, among Primary Progressive Aphasia (PPA) subtypes, agrammatic (PPA-G) show difficulty on grammatical measures, whereas patients with logopenic PPA (PPA-L) generally do not. Only a few prior studies have investigated on-line processing of grammatical information in PPA, with inconsistent results. Two used a visual word detection paradigm and reported opposite findings in PPA-G, showing either intact but delayed [5] or completely impaired [6] processing of morpho-syntactic violations. However, a recent eye-tracking study found that both PPA-G and PPA-L participants were able to use verb meaning to predict and integrate direct objects, with only PPA-G participants showing inability to generate object arguments on-line [7]. This study investigated the electrophysiological (ERP) correlates of on-line semantic and syntactic processing in patients with PPA-G and PPA-L by focusing on two ERP components: the N400, usually elicited by semantic violations and reflecting mechanisms of semantic integration [8], and the P600, elicited by sentences requiring syntactic re-analysis or repair (e.g. following a morpho-syntactic violation [9]). Although to date, no studies have investigated on-line sentence processing patterns in PPA using ERP, based on previous studies with people with stroke-induced aphasia [10, 11], we expected both PPA-G and PPA-L to show a normal-like N400 to semantic violations, but to exhibit dissociated patterns to syntactic violations. Specifically, syntactic violations were expected to show impaired processing in PPA-G, but a normal-like P600 was predicted for PPA-L.

Methods
Two groups of healthy participants (younger: 18-33 years (n=19); older: 35-78 years (n=16)) and a group of 19 PPA patients (age 52-76 years; PPA-G (n=10), PPA-L (n=9)) performed an auditory sentence acceptability judgment task while EEG was recorded from 32 scalp electrodes.

The study included three conditions: (a) a semantic condition, with verb-object incongruencies (e.g. *Owen was mentoring [vs. carving] pumpkins at the party), (b) a verb argument structure (VAS) condition, with violations created by deleting obligatory direct objects of the verb (e.g. *Jason was trimming [vs. shaving] in the bathroom), and (c) a morpho-syntactic condition with violation of subject-verb agreement (e.g. The actor [vs. The actors] were singing in the theater).

Mean amplitude in pre-selected time windows was extracted for each participant in each condition, and entered as the dependent variable in a mixed-effect regression model. Participant was entered as random factor, and sentence type (correct, violation) and electrode region (anterior right and left, midline, posterior right and left) were entered as fixed effects. Separate regression models were run for each participant group.

Results
Semantic violations elicited a significant N400 in the 400-800 msec time window following onset of the direct object for all participant groups (Figure 1). However, whereas both healthy participant groups exhibited a significant P600 in the 470-870 msec window from preposition onset in the VAS condition (younger: p<.001; older: p=.011), both patient groups showed abnormal ERP signatures, with the PPA-L group exhibiting a delayed, but significant P600 (470-870 msec: ns; 870-1170 msec: p=.004), and the PPA-G group showing no P600 in either time window (Figure 2). Finally, morpho-syntactic violations elicited a significant P600 in the 550-950 msec window following the
onset of the auxiliary in both healthy participant groups (p<.001 for both) as well as in the PPA-L group (p<.001), while no significant P600 was found in the PPA-G group (Figure 3).

**Discussion**

Results from semantic violations indicate that semantic processing (indexed by the N400) was mostly preserved in both PPA-G and PPA-L groups. These results are in line with previous studies reporting a significant – albeit reduced in amplitude - N400 in these patient groups in a picture-word matching task (as opposed to non-significant N400 effect in patients with semantic PPA (PPA-S)) [12]), and intact ability to integrate the direct object with verb meaning in an eye-tracking paradigm [7].

While both VAS and morpho-syntactic violations triggered processes of re-analysis and repair (indexed by the P600) in healthy participants, patients with PPA-G showed no evidence of such processes, consistent with our predictions and with off-line studies showing impaired processing of VAS and morpho-syntactic information [2].

Patients with PPA-L showed, as expected, normal re-analysis/repair processes to morpho-syntactic violations. However, re-analysis processes following VAS violations were significantly delayed. This finding suggests that on-line processing of lexically bound (VAS) syntactic violations may be partially impaired in patients with PPA-L, possibly secondary to difficulties in accessing the lexical representations of verbs.

The study provides neurophysiological evidence that supports the differentiation between the clinical profiles of agrammatic and logopenic PPA, and therefore contributes to the differential diagnosis of PPA subtypes.
Non-Dominant Hemisphere Network Alterations in Primary Progressive Aphasia: Evidence for Potential Neuroplasticity Using Resting State Functional Connectivity

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Background
In right handed individuals with primary progressive aphasia (PPA), cortical thinning (atrophy) mostly affects the dominant (left) hemisphere. However, with progression of the disease, the rate of atrophy is slower in the non-dominant (right) hemisphere (Rogalski et al., 2013). Therefore the right hemisphere may have a potential for physiologic compensatory changes to cope with the left hemisphere pathology. Two studies support this notion by demonstrating increased right hemisphere activation in PPA using task based functional magnetic resonance imaging (fMRI; Sonty et al, 2003; Van den Bulken et al., 2004). However, compensatory changes in the logopenic variant PPA (PPA-L) have not been well studied. In this study, we aimed to investigate changes in the right hemispheric network connectivity in PPA-L using resting state fMRI (rsfMRI).

Methods
We analyzed rsfMRI scans of 20 PPA-L patients and 33 healthy controls. Two nodes of the language network (posterior middle temporal gyrus [MTG] and anterior temporal lobe [ATL], that serve as hubs involved in naming, were identified based on what was repeatedly reported in the literature. Using REST-PLUS software, whole brain connectivity of these nodes and their right hemisphere equivalents was evaluated. Two sample t-tests were used to compare the patient and control groups looking for clusters with increased connectivity with the MTG and ATL seeds on both sides in PPA-L. Correlation between these clusters and Boston Naming Test (BNT) scores was then evaluated. Cortical thickness in PPA-L was measured using FreeSurfer and was compared to a group of 35 controls at an FDR<0.05 threshold.

Results
PPA-L patients had a pattern of atrophy which was significantly worse in the left superior temporal, temporoparietal junction, and posterior frontal regions. Cortical atrophy was relatively less in the right hemisphere, sparing right ATL. When compared to the control group, PPA-L individuals had increased connectivity between the right and left ATL regions. In the PPA-L group, the strength of connectivity within the ATL regions showed positive correlation to Boston Naming Test (BNT) scores ($r = 0.402$, $p = 0.039$). The other three seeds showed decreased connectivity on the left side but no increased pattern on the right side that was of significance.

Discussion
Commonly in PPA the right hemisphere displays less atrophy than the left hemisphere, even later in the course of the disease. Increased right hemispheric functional connectivity in PPA patients could be an indication of compensation for degenerating left hemisphere neural structures. In the absence of significant atrophy in the right ATL region, increased connectivity between this region and the left ATL was associated with better naming, suggesting a shift in network connectivity to adjust to disease related changes. This finding has clinical significance, as neuromodulation of right hemispheric and inter-hemispheric connectivity could provide a way to enhance network compensations in PPA.
AMYLOID BETA OLIGOMERS (AβO) DRIVE MORPHOLOGICAL SHIFT IN MICROGLIA IN ANIMAL MODELS FOR ALZHEIMER’S DISEASE

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Neurodegeneration and cognitive impairment in Alzheimer’s disease (AD) are believed to be driven by the accumulation of the Aβ peptide and phosphorylated tau protein. Recent research suggests that in addition to Aβ peptide and phosphorylated tau deposition, neuroinflammation plays a pivotal role in Alzheimer’s disease dementia. Microglia are the resident macrophages of the brain’s immune system that are responsible for antigen presentation and inflammatory signaling. In the presence of soluble, neurotoxic forms of Aβ, known as Aβ oligomers (AβO), microglia have been hypothesized to be activated and differentiated into a more proinflammatory phenotype that drives deleterious AD neuroinflammation. As we lack clear models for microglial activation in response to AβOs, we determined to investigate the 5XFAD mouse model as well as AβO-injected simian and rat models. Here, we confirm that microglia are functionally activated using Iba1 antibody immunofluorescent staining of activated microglia in the models. However, our results show that the relationship between microglia and Aβ oligomers is more complex than the literature predicts, as Aβ oligomers induce morphological changes in microglia. Our analysis of various brain regions exhibits that these morphological changes are regionally specific, but all stimulate an increase in morphologies associated with deadly proinflammatory behavior at later ages in AD brain. Further understanding of the relationship between microglial morphology and phenotype can lead to future AD therapeutic techniques and targets.
A G\textsubscript{4}C\textsubscript{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.
MEASUREMENT OF THE KINETIC BEHAVIOR OF NEWLY GENERATED BACE1-CLEAVED APP IN THE HUMAN CENTRAL NERVOUS SYSTEM IN ALZHEIMER’S DISEASE: INITIAL PROOF-OF-CONCEPT

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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 proof-of-concept study, newly generated sAPPβ and sAPPα were measured in six elderly human subjects who had undergone [U-13C6]leucine labeling and hourly CSF collection over 36 hours. Two of the subjects had brain amyloidosis (Amyloid+), and the remaining four 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=0.018) which was significantly higher than the Amyloid- group (m=0.012; p=0.02); 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 proof-of-concept study to include a larger sample size. 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.
IMAGING AMYLOID B OLIGOMERS BY MOLECULAR MRI: DIAGNOSING EARLY-STAGE ALZHEIMER’S DISEASE.
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Alzheimer’s disease is a neurodegenerative disorder characterized by deterioration of memory, visuospatial ability, and executive function. Neurodegeneration associated with Alzheimer’s disease is progressive and irreversible, and it is believed that long-term prognosis of patients would be significantly improved with an early diagnosis. Various diagnostic approaches have been developed, including those that target amyloid plaques, yet plaques exhibit a weak correlation with disease progression. Amyloid-β oligomers are regarded as the putative initiators of disease pathogenesis, triggering tau pathology and instigating the neuronal damage that underlies dementia. Here, we report the development of a sensitive molecular magnetic resonance imaging (MRI) contrast probe that is specific for Aβ oligomers. The probe’s robust imaging signal is attributed to the coupling of an oligomer-specific targeting antibody to mixed metal magnetic nanostructures that yield enhanced contrast in MRI. The specificity of the probe was verified through a series of experiments that established the probe’s AβO targeting properties in comparison to its parent antibody. Immunohistological analysis demonstrates that the probe is stable and detects Aβ oligomers on hippocampal cells and brain tissue. Intranasal administration of the probe to an Alzheimer’s disease mouse model revealed a pronounced, disease-dependent MRI signal in the hippocampus. The molecular MRI contrast probe shows potential as a freestanding diagnostic that targets Aβ oligomers to identify Alzheimer’s disease at its earliest stages when therapeutics are most potent. Early diagnosis allows patients to access available treatments, build a care team, and enroll in clinical trials, benefitting both the patient and their loved ones.
PRIMARY PROGRESSIVE APHASIA RESEARCH PROGRAM AT NORTHWESTERN UNIVERSITY’S CNADC

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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 a cure, the Cognitive Neurology and Alzheimer’s Disease Center (CNADC) seeks to advance PPA research through a collaborative program aimed at studying, educating, and improving treatment for patients with PPA.

Over the past decade, more than 200 participants from 35 US states, Canada, Singapore, and Spain have enrolled in PPA studies at the CNADC. Participants visit Chicago every 1-2 years to complete neuropsychological assessments that precisely measure language, memory, and thinking abilities and experimental studies of language processing using eye tracking technology. Participants also undergo multiple brain imaging examinations with MRI and PET scanners in the state-of-the-art Center for Translational Imaging. Researchers combine cognitive testing with these advanced neuroimaging techniques to better understand the underlying mechanisms of language decline in the PPA brain.

Some participants choose to take part in the CNADC’s speech/language therapy and educational research programs. These life-enrichment interventions use innovative technology to improve access to care. In addition to several multi-day visits throughout the disease course, most CNADC PPA research participants agree to take part in our brain donation program to allow for further scientific investigation. 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 Institute of Health, Illinois Department of Public Health, Run4Papa campaign, and generous personal donations, have provided the opportunity for the CNADC to research novel diagnostic and therapeutic initiatives in PPA. In order to leverage these resources, the CNADC has maintained a centralized website to facilitate international collaboration in PPA research. Currently, there are over 270 registered researchers representing 170 institutions across 34 different countries. By engaging in these partnerships, as well as employing a multidisciplinary approach for both patients and their families, Northwestern University’s CNADC remains one of the top referral centers in the world for PPA.
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.
Many individuals have come to expect that as they grow older, their memory and other cognitive abilities will begin to deteriorate. Though such decline is common, the SuperAging Project at the Northwestern University Cognitive Neurology and Alzheimer’s Disease Center (CNADC) 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. Some participants have undergone a guided “Life Story” interview detailing their life experiences, which allows researchers to evaluate the correlation between psychological well-being and superior cognitive aging. All participants are invited to take part in a brain donation program, providing researchers the opportunity to further investigate the biological mechanisms behind SuperAging.

Previous neuroimaging results have shown that SuperAgers have thicker brains compared to their cognitively average, same-age peers and do not demonstrate cortical atrophy compared to middle-age adults. Over a period of 18-months, the rate of cortical brain atrophy was approximately two times faster in Elderly Controls compared to SuperAgers. Over this same 18-month period, SuperAgers tend to maintain outstanding cognitive performance on tests of episodic memory. Most recently, SuperAgers endorsed greater levels of positive social relationships than their cognitively average-for-age peers; suggesting that perceived high-quality social relationships may be an important factor in cognitive SuperAging.

Since its inception, the SuperAging Project has used a multidisciplinary approach to study successful cognitive aging. 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.
LATENT WORD-COMPREHENSION IMPAIRMENTS IN AGRAMMATIC AND LOGOPENIC PRIMARY PROGRESSIVE APHASIA PATIENTS REVEALED THROUGH EYE MOVEMENT ANALYSES
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The classic description of language in the brain paints the left posterior temporal lobe as the seat of word comprehension because of the impairments resulting from strokes to this area (i.e. Wernicke’s aphasia). In contrast, among Primary Progressive Aphasia (PPA) patients, degradation in the left anterior temporal lobe (ATL) but not the posterior temporal lobe leads to severe disruption of word comprehension. One possible explanation of this discrepancy is that both ATL and the posterior temporal lobe are necessary for word comprehension, but the degradation that occurs to the latter in PPA is not sufficiently severe to cause severe impairments. If this is correct, then we would still expect subtle word comprehension deficits to exist in PPA patients with degradation in this area. We tested this in a sample of PPA patients and age-matched control subjects performing a word-to-picture matching task while we recorded their eye movements. Subjects were given a noun cue followed by an array of pictures and were asked to touch the drawing that matched the noun cue. We use PPA subtype as a proxy for the locus of neural degeneration. Logopenic (PPA-L), agrammatic (PPA-G) and semantic (PPA-S) subtypes are associated with degradation in the posterior temporal, frontal, and ATL regions, respectively, of the left hemisphere. Preliminary results show that relative to control subjects, PPA-L and PPA-G patients show consistent modest increases in viewing times of foils, while PPA-S patients show very large increases. PPA-L and PPA-G patients further show increases in semantic blurring - defined as the proportion of time spent viewing semantically related versus unrelated foils - particularly on retrieval error trials in which they could not name the target item in an offline naming test. PPA-S patients show a similar increase, however they show the strongest semantic blurring on correct trials. This surprising finding might reflect a fundamental difference in word-comprehension impairments between the groups. Altogether these results support a view that the left ATL is key for word comprehension, but the left posterior temporal cortex serves an ancillary function. The subtle word comprehension deficits observed here for PPA-L and PPA-G patients have implications for their care and treatment.
LRRK2 PHOSPHORYLATION OF AUXILIN MEDIATES SYNAPTIC DEFECTS IN DOPAMINERGIC NEURONS FROM PATIENTS WITH PARKINSON’S DISEASE

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Recently identified Parkinson’s disease (PD) genes involved in synaptic vesicle endocytosis, such as DNAJC6 (auxilin), have further implicated synaptic dysfunction in PD pathogenesis. However, how synaptic dysfuction contributes to the vulnerability of human dopaminergic neurons has not been previously explored. Here, we demonstrate that the commonly mutated, PD-linked leucine-rich repeat kinase 2 (LRRK2) mediates the phosphorylation of auxilin in its clathrin-binding domain at Ser627. Kinase activity-dependent LRRK2 phosphorylation of auxilin led to differential clathrin binding resulting in disrupted synaptic vesicle endocytosis and decreased synaptic vesicle density in LRRK2 patient-derived dopaminergic neurons. Moreover, impaired synaptic vesicle endocytosis contributed to the accumulation of oxidized dopamine that in turn mediated pathogenic effects such as decreased glucocerebrosidase activity and increased α-synuclein in mutant LRRK2 neurons. Importantly, these pathogenic phenotypes were partially attenuated by restoring auxilin function in mutant LRRK2 dopaminergic neurons. Together, this work suggests that mutant LRRK2 disrupts synaptic vesicle endocytosis leading to altered dopamine metabolism and dopamine-mediated toxic effects in patient-derived dopaminergic neurons. The work from this project expands the range of proteins for therapeutic intervention to those located at the synapse, potentially leading to the development of targeted treatments for patients with Parkinson’s disease.
Healthy aging is associated with episodic memory decline, consistently correlated with altered hippocampal-cortical connectivity at rest and abnormal hippocampal activity during memory formation. Here, we used noninvasive repetitive transcranial magnetic stimulation (rTMS) to test the causal role of hippocampal-cortical network connectivity in age-related memory decline. To probe this network, participant-specific stimulation targets in parietal cortex were determined based on high resting-state functional connectivity with the hippocampus. Fifteen older adults (age range: 60-80 years) completed five consecutive days of targeted full intensity stimulation and five consecutive days of low intensity sham stimulation over two separate weeks in counter-balanced order. Participants completed an associative memory task, which involved cued recall of object-scene and object-locations, before and 24-hours after each week of stimulation. Targeted stimulation selectively improved associative recollection, but not item recognition. Notably, these recollection improvements were concurrent with increased activity among the targeted hippocampal-cortical network during memory formation. These findings suggest that changes in hippocampal memory network function are causally related to episodic memory impairment in aging, and demonstrate that noninvasive stimulation can be used to alter memory-related network function in older adults. Interestingly, increased hippocampal activity after full intensity stimulation predicted better recollection one-week later. The long-lasting effect of targeted stimulation motivate future clinical interventions and suggest new approaches for studying the network basis of memory impairments in older adults.
Aims: Primary progressive aphasia (PPA) is a clinical syndrome characterized by selective language impairments associated with focal cortical atrophy favoring the language dominant hemisphere. PPA is associated with Alzheimer’s disease (AD), frontotemporal lobar degeneration (FTLD), and significant accumulations of activated microglia. Activated microglia can initiate an inflammatory cascade that may contribute to neurodegeneration, but their quantitative distribution in cortical white matter and their relationship with cortical atrophy are unknown. We investigated white matter activated microglia and their association with grey matter atrophy in 10 PPA cases with AD or FTLD-TDP pathology.

Methods: Activated microglia were quantified with optical density measures of HLA-DR immunoreactivity in two regions with peak cortical atrophy, and one non-atrophied region within the language dominant hemisphere of each PPA case. Non-atrophied contralateral homologues of the language dominant regions were examined for hemispheric asymmetry.

Results: Qualitatively, greater densities of activated microglia were observed in cortical white matter when compared to grey matter. Quantitative analyses revealed significantly greater densities of activated microglia in the white matter of atrophied regions compared to non-atrophied regions in the language dominant hemisphere (p<0.05). Atrophied regions of the language dominant hemisphere also showed significantly more activated microglia compared to contralateral homologues (p<0.05).

Conclusions: White matter activated microglia accumulate more in atrophied regions in the language dominant hemisphere of PPA. While microglial activation may constitute a response to neurodegenerative processes in white matter, the resultant inflammatory processes may also exacerbate disease progression and contribute to cortical atrophy.
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ALTERATION OR INPUTS FROM THE SUBTHALAMIC NUCLEUS TO THE DISTINCT EXTERNAL GLOBUS PALLIDUS NEURON CLASSES IN PARKINSON’S DISEASE

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Basal ganglia are a highly interconnected group of nuclei involved in motor control. The external globus pallidus (GPe) critically influences processing of motor information through its GABAergic projections to all basal ganglia nuclei. GPe contains two principal GABAergic projection neurons. Parvalbumin (PV)-expressing (PV) GPe neurons and Npas1-expressing (Npas1) GPe neurons have distinct electrophysiological properties, projections targets, and responsiveness in a mouse model of PD, arguing for distinct roles in movement. STN provides the principal glutamatergic input to the GPe and pathological activity in the STN-GPe loop is one of the hallmarks of Parkinson’s Disease (PD). However the cellular specificity of the STN input to PV+ GPe neurons and Npas1+ GPe neurons and how this connectivity changes in PD is not known. We have investigated the STN input to the two GPe neuron classes in health and how the STN-GPe subcircuits are differentially altered in a 6-Hydroxydopamine (6-OHDA) mouse model of PD.
There are millions of neurons in the cerebral cortex and yet in neurodegenerative diseases, a select set of neuron population display initial vulnerability and undergo progressive degeneration, while other neurons and cells retain health and function. The underlying factors that contribute to this selective and early vulnerability is not fully understood. For example, in Alzheimer’s disease (AD), the hippocampal neurons degenerate, and more interestingly not all neurons in the hippocampus are equally affected. Even within discrete regions of the brain, there is refined and complex neurodegeneration. We believe that selective gene expression is directly linked to selective vulnerability.

Since not all neurons express the same genes, we hypothesize that the genes they select to express not only help them gain their identity and function, but also makes them vulnerable to degeneration in case of mutations, dysfunctions and perturbations. Therefore, identification of genes that are selectively expressed in distinct regions of the hippocampus would reveal the canonical pathways that are active, the protein-protein interaction networks that are mostly specific to that region, as well as modulators and genetic regulators of the region.

The set of genes that are expressed in distinct regions of the hippocampus, such as Subiculum, CA1, CA2, CA3, CA4, Dentate Gyrus, was determined by using gene expression profiles determined by in situ hybridization assays in publically available Allen Brain Atlas database. The Allen Brain Atlas data portal contains coronal images of in-situ hybridization expression of genes. These gene profile data were then analyzed using the large-data Ingenuity Pathway Analysis (IPA), which revealed crucial genes, canonical pathways, and networks active in distinct hippocampal regions. Our data suggests the presence of a molecular signature that determines differences between these links and different neuron populations. It is now time to investigate whether our findings which originate from detailed investigation of mouse hippocampal neurons, are recapitulated in human patients with AD. Our findings will for the first time link gene expression to neuronal vulnerability and will shed light onto the cellular mechanisms that are selectively disrupted in distinct regions of the hippocampus. This information is important to reveal novel targets for therapeutic interventions in the future and to identify potential biomarkers that would inform about the extent and the location of degeneration in AD patients and patients in which hippocampus is affected.
PLASMINOGEN ACTIVATOR INHIBITOR-1 ANTAGONIST TM5A15 REDUCE NEUROPATHOLOGY AND MEMORY DEFICITS IN APP/PS1 MICE

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The pathological hallmark of Alzheimer's disease is the aggregation of amyloid beta peptides in the brain which then form into plaques, causing a varying degree of cognitive deficits. Amyloid beta peptides are metabolized through biosynthesis and degradation and it is a crucial equilibrium that is needed in order to prevent brain pathologies. Plasmin, a serine protease, plays an important role in the degradation of Aβ. Several previous studies have shown that there is an increase level of plasminogen activator inhibitors present in the plasma of AD mice models as well as in AD patients. However, whether reversing the increased plasminogen activator inhibitor could prevent neuropathogenesis of AD has not been well investigated. In this study, we test whether a novel plasminogen activator inhibitor-1 (PAI-1) antagonist, TM5A15, can ameliorate cognitive deficits and decrease the Aβ plaques deposition in APP/PS1 mice, an animal model of Alzheimer's disease. We administered 3 month old APP/PS1 mice with TM5A15 for up 6 months via chow diet. Mice underwent behavior testing of locomotor activity, novel object recognition, Morris water maze, and spontaneous alternation after 3 months of treatment and 6 months of treatment to assess the mice learning and memory performance. Blood serum was collected from all samples and mice were then sacrificed to collect brain tissue for biochemical and immunohistochemistry analysis. Behavioral tests showed there was no significant affect after 3 months treatment with TM5A15, when APP/PS1 mice were 6 months, however, after 6 months of treatment, the APP/PS1 mice displayed significant improvement in spontaneous alteration (p<0.01), novel object recognition (p<0.01), and Morris water maze (p<0.05) when they were 9 months of age. Biochemical results indicated a decrease of amyloid plaque deposition in the whole brain for APP/PS1 treated animal samples compared to those APP/PS1 mice that did not receive treatment. These data suggests that increased PAI-1 activity contributes to Aβ aggregation in APP/PS1 mice and TM5A15 could prevent the formation of Aβ plaques during aging.
Dementia due to Frontotemporal lobar degeneration (FTLD) constitutes the third most prevalent dementia after those caused by Alzheimer’s Disease and Lewy bodies. A primary pathological marker of FTLD is abnormal precipitation of phosphorylated and mislocalized Tar DNA/RNA-binding protein-43 (TDP-43). Wild-type and mutant TDP overexpression in transgenic animals leads to the formation of inclusions and degeneration. To investigate the temporal sequence of inclusion formation and degeneration in transgenic animals, we employed a conditional transgenic model under the control of the tetracycline operator sequences. Mice were kept on a diet of doxycycline allowing them to mature while keeping the TDP-43 transgene inactive. In line with previous studies, activation of the TDP-43 transgene recapitulated key features of FTLD, including the formation of phospho-TDP-43 neuronal cytoplasmic inclusions. Brains of TDP transgenic mice were cut into 40-µm sections and immunohistochemically processed using an antibody against TDP-43 phosphorylated at Ser-403/404. The number of TDP-43-positive inclusions were quantified in the frontal, temporal and parietal cortex in 10 animals each at the following periods of transgene expression: 5, 10, 14, and 19 days, and 8 and 24 weeks. The area (mm²) of all investigated cortical regions was measured using Image J as an indicator of neurodegeneration. Inclusions appeared as early as 5 days after TDP-43 expression, followed by a gradual increase in the number of inclusions until 14 to 19 days of post-weaning expression, when peak inclusion densities were detected. While the 14-day group of mice showed among the highest number of inclusions, cortical measurements revealed no observable atrophy. At 8 and 24 weeks of transgene expression, inclusions were rarely encountered, but the brains showed the most severe degeneration / atrophy. In particular, the piriform cortex contained a high density of inclusions after 14 days of transgene expression with no significant atrophy, while it displayed significant atrophy but only sparse inclusions after 8 and 24 weeks of transgene expression. These observations suggest that, after prolonged transgene expression, TDP-43 inclusions disappear as neurons are lost. They also indicate that the direction of correlation between inclusions and neurodegeneration would be expected to change during the course of disease in FTLD. Our TDP-43 mouse model may be a valuable tool in examining the appearance and disappearance of TDP-43 inclusions and their association with neuronal degeneration.
One of the greatest improvements in the diagnosis of Alzheimer’s disease (AD) has been the inclusion of positron emission tomography (PET) imaging using probes that target amyloid fibrils. However, these fibrils are not closely linked to the development of the disease. It is now thought that early stage biomarkers that instigate memory loss comprise of Aβ oligomers (AβOs). AβOs accumulate early in AD and experimentally cause memory dysfunction and the major cellular pathologies associated with AD (e.g., tau abnormalities, synapse loss, oxidative damage, etc.). AβOs are widely regarded as the aggregated form of Aβ responsible for AD onset. An important resource currently unavailable to clinicians and researchers is a probe that can image buildup of AβOs in vivo. Available probes exclusively quantify ThioS-positive amyloid plaques and are not useful for imaging AβOs. Because AβOs are regarded as the first toxin to appear in disease progression, they provide an excellent target for diagnostic imaging. Our long-term goal is to develop a diagnostic for early prodromal detection of AD and for evaluating the disease-modifying efficacy of INDs. With an AβO probe it would be possible to correlate AβO buildup with emergence of cognitive dysfunction, providing a significant new means to investigate the AβO hypothesis and to assess the experimental efficacy of investigational new drugs (INDs). Using positron emission tomography (PET), immunocytochemistry, immunohistochemistry, and the behavioral assay ‘Open-field novel object recognition’ (NOR) to assay hippocampal-based and cortical-based memory, we provide compelling evidence that we can not only detect AβOs early in disease development, but can also improve memory. Evidence presented here shows that an antibody-based AβO PET probe strikingly distinguishes transgenic AD mice from wild-type littermates. AD-dependent PET signals were obtained with 5-7 month old mice, shortly after the age when memory dysfunction first occurs. Moreover, a single inoculation showed profound impact on memory. Animals receiving the antibody-based PET tracer showed normal memory 1 month after injection while animals receiving non-specific IgG tracer continued to show impaired memory 1 month after injection. Even more surprising was that this improvement persisted as much as 4 months after injection. Taken together, these data suggest that not only can antibody-based PET tracers be used to diagnose AD at very early stages, but that these tracers may have therapeutic benefits as well.
TYPE 3 DIABETES AND HIGH CHOLESTEROL AS TWO DIET INDUCED MODELS OF ALZHEIMER’S DISEASE
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Objective: The purpose of this study is to develop a non-transgenic animal model of sporadic Alzheimer’s Disease (AD).

Background: Most cases of AD are sporadic in nature, i.e. not associated with any known genetic mutations. In contrast, most animal models of AD use transgenic mice that express one or more of the relatively rare human sequences for amyloid that are associated with AD. The rabbit amino acid sequence for amyloid is nearly identical to that of the human sequence, and rabbit lipid metabolism is more similar to human lipid metabolism than is mouse and human lipid metabolism. These similarities between human and rabbit suggest that the rabbit is a good species to examine two risk factors for AD, i.e. high cholesterol and diabetes which may induce a state of neuronal insulin resistance, or Type 3 diabetes (de la Monte & Wands, 2008). Therefore, we have been using the aging, non-transgenic rabbit as a preclinical model system to study cognitive impairment and AD-like pathology.

Methods: We used aging female rabbits to compare the effects of a diet enriched with either 2% cholesterol or 10% sucrose against a diet of standard rabbit chow. Cognitive impairment was assessed with the novel object and novel location recognition tests (NOR/NLR) to test cortical and hippocampal function respectively. A discrimination index was calculated based on the time investigating novel or familiar objects or locations, i.e. (Novel – Familiar) / (Novel + Familiar). Scores range between 0 and 1.0 with 1.0 representing exclusive investigation of the novel object or place, and 0 representing random (equal) exploration of the novel object or place. Pathology was assessed by staining brain sections containing hippocampus and frontal cortex with NU4, an antibody specific for amyloid oligomers. Diabetes was assessed by results from an iv glucose tolerance test.

Results: Cognition was tested after approximately 20 weeks of the designated diet. High cholesterol diet impaired both object location and object recognition tests (mean scores of 0.06 and 0.10, respectively) relative to rabbits on standard diet (mean score of 0.70). High sucrose diet impaired object recognition (0.19 vs 0.44 control diet), but not the object location test (0.72 vs 0.70). Blood glucose levels (BGL) and insulin levels revealed a large spike in insulin release for rabbits on sucrose diet, and those rabbits exhibited BGL that returned to baseline more quickly than the BGL of the other two groups. Analysis of immunoreactivity to amyloid oligomers with the NU4 antibody revealed a 20 and 35 fold increase respectively in hippocampus and frontal cortex relative to sections from control rabbits.

Conclusion: Diets that promote high cholesterol or diabetes can impair neuronal metabolism, increase AD-like pathology, and decrease cognitive functions. Given that the amino acid sequence for rabbit and human amyloid is nearly identical, and that the two species have similar lipid metabolism, the rabbit is likely to be a good model system to understand mechanisms related to the onset and progression of AD.

Scientific Relevance: New animal model systems are necessary to understand the genesis and progression of AD, and to develop successful therapeutics. We propose that similarities between rabbit and human amyloid and lipid metabolism make the rabbit a strong candidate for a model system that avoids issues related to transgenic mice, and given the suitability of rabbits for magnetic resonance imaging, the potential for translational noninvasive imaging of AD-like pathology is high.
DIFFERENTIAL REGIONAL BUILDUP OF DISTINCT $\alpha\beta$ Oligomer Species
IN THE 5xFAD MOUSE MODEL OF ALZHEIMER’S DISEASE
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Purpose. Alzheimer’s disease (AD) is a progressive, neurodegenerative disease and is the sixth leading cause of death in the U.S. Amyloid beta oligomers ($\alpha\beta$Os) have been found to contribute to AD pathogenesis and have been shown to cause pathologies linked to AD such as synaptic loss. Extracellular and membrane-associated $\alpha\beta$O species have been found in the AD brain and evidence indicates that these $\alpha\beta$Os vary in abundance during AD progression. However, it is not known which $\alpha\beta$O type is most prevalent throughout AD pathogenesis. My long-term research goal is to characterize the abundances of different $\alpha\beta$O types that are present in the AD brain. In this project, I have been mapping the buildup of different $\alpha\beta$Os in the 5xFAD mouse model as the mice age through multiple antibodies and immunoassays.

Methodology. The 5xFAD mouse model has been shown to exhibit many pathologies characteristic of AD, including $\alpha\beta$O buildup. I have been utilizing the 5xFAD mouse model at selected time points (3, 6, 9 months) to measure the abundances of water-soluble and membrane-associated $\alpha\beta$Os present during AD progression. I am also testing three brain regions: hippocampus and cortex, which are associated with AD and the cerebellum, which is not. Antibodies (NU2, NUsc1) with $\alpha\beta$O specificity have been used in dot immunoblots and ELISA assays to measure the amounts of water-soluble $\alpha\beta$Os, membrane-associated $\alpha\beta$Os and insoluble $\alpha\beta$ present. Our antibody NUsc1 is of interest due to its specificity for a toxic subpopulation of $\alpha\beta$Os.

Findings. As expected, we have found that the amount of $\alpha\beta$Os in the 5xFAD mouse brain increases as the mice age. Preliminary data also indicates that the abundance of water-soluble $\alpha\beta$Os, membrane-bound $\alpha\beta$Os, and insoluble $\alpha\beta$ varies with brain regions. Water-soluble and membrane-associated $\alpha\beta$Os are more abundant in the hippocampus and the cortex in comparison to the cerebellum. Water-soluble $\alpha\beta$Os increased in abundance in the hippocampus and the cortex over time, with the majority of water-soluble $\alpha\beta$Os accumulating in the hippocampus. Membrane-associated $\alpha\beta$Os remained constant in the hippocampus, while also showing sudden accumulation in the cortex at 9 months. This may be indicative of water-soluble and membrane-associated $\alpha\beta$O regional specificity. We have also found a NUsc1-reactive $\alpha\beta$O subpopulation present in the hippocampus of 3- and 6-month 5xFAD mice.

Practical Implications. This data can lead us to understand if water-soluble and membrane-associated $\alpha\beta$Os are abundant during each stage of AD and in each brain region. This data can also be used to diagnose AD stages if a $\alpha\beta$O species progression trend is identified. Additionally, the antibody NUsc1 has shown specificity for a toxic $\alpha\beta$O population, which could potentially lead to its use as a diagnostic and/or therapeutic tool.
REMEMBERING WITH HIGH FIDELITY: EVIDENCE IMPLICATING SLEEP AND SLEEP SPINDLES
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Current theories of sleep postulate that memories can be strengthened through replay. This replay is thought to be engaged spontaneously during sleep, and has tentatively been associated with fast sleep spindles in EEG recordings (brief increases in oscillatory activity at 13.5-15 Hz). In this study, we investigated EEG sleep physiology and memory using a difficult object-recognition test and a spatial-recall test. Participants first learned the locations of 64 objects on a grid. Each object was presented with a related sound. After a pre-nap test of this spatial knowledge, participants took a 90-minute nap, and 32 object sounds were presented softly during slow-wave sleep. Upon waking, participants were given a surprise recognition test with 96 objects, including 32 old (seen before), 32 similar (same category as one seen before), and 32 new objects. Participants attempted to identify each object as old, similar, or new, and then took a post-nap spatial recall test. A recognition specificity score was calculated as the sum of correctly recognized old and similar objects from the object-recognition task. Fast spindle density during sleep (spindles per minute) correlated with the specificity score, but not with spatial recall accuracy. Cues during sleep produced a relative improvement for top-half learners in spatial recall, as observed in previous studies of targeted memory reactivation (TMR). Recognition specificity was not influenced by TMR. Overall, these results provide further evidence that fast spindles play a role in memory consolidation during sleep, particularly for memory precision with respect to remembering which specific objects were seen before. This study supports prior research that sleep not only protects memory, but specifically can aid memory consolidation.
INTRODUCTION: TRPA1 is a member of the transient receptor potential (TRP) superfamily well known to be expressed in the spinal horn and other tissues, and recognized to mediate a diversity of pain and inflammatory states. Alzheimer’s disease (AD) is a degenerative disease characterized by accumulation of both tau and Aβ peptides, and for having the disease course affected by progressive oxidative stress and brain inflammation. Products of inflammation, notably reactive oxygen species (ROS) and Ca^{2+} are augmented during AD initiation and progression. Intriguingly, these are endogenous molecules known to be able to activate TRPA1.

PURPOSE: However, the possible role of TRPA1 in AD pathogenesis is still unknown and we aimed to investigate it.

METHODS: We used different approaches (primary cell culture treated with AβOs, AβOs-injected mice, 5xFAD AD mouse model and AD human brains; including respective controls to each) and also two distinct preparations AβOs_{40} and AβOs_{42}. Besides behavioral assessments, a variety of molecular and biochemical techniques, namely the evaluation of ROS formation, mitochondrial membrane potential determination, immunocytochemistry, immunofluorescence in brain slices, western blotting, co-immunoprecipitation, electron microscopy and others.

FINDINGS AND DISCUSSION: Here we report TRPA1 is largely expressed in neurons and microglia in the brain. TRPA1 is relevant to AβOs binding and AβOs-induced oxidative stress/death in neuronal cells. We demonstrated the correlation between the up-regulation and spreading of both AβOs and TRPA1, in all the approaches used. Herein, we are also reporting TRPA1 augmented expression in the microglia and its possible role in the inflammation process. Of note, TRPA1 selective antagonist (HC030031) oral treatment improved memory deficits in the different mouse models of approach. Besides, reduced Aβ burden in plaques and oligomers with consequent improvement on AβOs-induced synaptic loss.

CONCLUSION AND PRATICAL IMPLICATIONS: These actions identify a role for TRPA1 in regulating AD pathogenesis; thus, we propose TRPA1 as an appealing target for future AD therapy.
This is a Phase II multi-center, placebo-controlled study that will evaluate whether long-term use of transdermal nicotine patches enhances attentional functioning and memory in patients with mild cognitive impairment (MCI). In previous studies, nicotinic stimulation has shown positive cognitive effects in diseases in which attention and/or memory is impaired (i.e. Alzheimer’s disease, ADHD, and Tourette’s syndrome). A Phase I trial of 67 individuals concluded that the drug was safe and well tolerated. Three hundred participants with MCI (150 in the placebo arm and 150 in the active treatment arm) will be randomly assigned to receive patches with either an active dose of nicotine or a dose of placebo for 24 months. Screening will occur over 4 weeks followed by a 24 month treatment period, in addition to a 3-week tapering off period. The study requires a minimum of 2 visits during the screening and baseline period, and up to 12 visits during the course of treatment. Participants will be monitored by the study team closely for the duration of the study. Memory, functional, and cognitive measures (CPT, CGIC, CDR, and paragraph recall) also will be evaluated during regular visits to power a subsequent Phase III trial. Enrollment for this trial is open and we continue to screen and enroll additional participants for the MIND trial. Participants do not need to have a diagnosis of MCI in order to be considered eligible for this trial. Since this study does not require MR imaging or collection of cerebrospinal fluid (both are sub-studies that willing participants can agree to participate in), interest in this trial has been high and the screen fail rate across sites has been fairly low.
The treatment of Alzheimer’s disease (AD) is a central aim for the Cognitive Neurology and Alzheimer’s Disease Center (CNADC). In response to promising new treatments and efforts to design biomarkers for AD and other forms of dementia, the CNADC has joined forces with the Alzheimer’s Therapeutic Research Institute (ATRI), a consortium supported by the National Institutes of Aging and industry, 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 CNADC. Recruitment of eligible individuals from the Clinical Core of the CNADC, advertising in the Chicago area community, and aging registries throughout Northwestern Medical Group are aided by the Outreach, Recruitment, and Education (ORE) Core. This cross-core collaboration emphasizes the inclusion of participants from all minority groups and otherwise underserved communities.

Current trials are as follows: 1) Anti-Amyloid Treatment in Asymptomatic Alzheimer’s Disease (A4): A4 is a secondary prevention trial aimed at treating amyloid-positive but otherwise healthy individuals (aged 65-85) at risk for developing Alzheimer’s disease (AD). Individuals with normal cognitive test scores will be screened with PET amyloid imaging. Those with positive amyloid PET scans will be enrolled into the study and will be treated for 3 years with an anti-amyloid drug 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 amyloid-negative participants. Therefore, participants who do not show evidence of elevated amyloid will be enrolled in this 3-year study that will run in parallel to A4. 3) CONNECT: This Phase IIa study will evaluate an investigational medicine called AZD0530 (saracatinib) to treat early AD. In this study, 152 participants will be randomly assigned to receive either an active dose of AZD0530 or a dose of a placebo for the 52-week treatment period. 4) Study of Nasal Insulin to Fight Forgetfulness (SNIFF): This study is designed to determine whether insulin administered as a nasal spray improves memory in patients diagnosed with amnestic Mild Cognitive Impairment (aMCI) or Alzheimer’s disease (AD). Previous studies have shown that insulin is responsible for multiple functions in the brain, and poor regulation of insulin may contribute to the development of AD. All participants will be randomly assigned to receive insulin or placebo for 12 months. 5) Alzheimer’s Disease Neuroimaging Initiative – 3 (ADNI3): This cohort study is designed to identify biomarkers that may be useful in the diagnosis of early AD, by examining annual cognitive assessments, blood and cerebrospinal fluid samples, MRI and PET scans. ADNI3 will enroll 400 participants and will follow them for up to 5 years. 6) Memory Improvement through Nicotine Dosing (MIND): The purpose of the study is to see if use of a daily transdermal nicotine patch is able to produce a significant cognitive, clinical and functional improvement in participants with Mild Cognitive Impairment (MCI). Neuronal nicotinic receptors have long been known to play a critical role in memory function in preclinical studies, with nicotine improving attention, learning, and memory function. The study will enroll 300 participants for 2 years.
Alzheimer’s disease (AD) is the most common neurodegenerative disorder leading to cognitive decline in aged populations. High failure rates of strategies targeting the disease-specific peptide amyloid β (Aβ) suggest that reducing Aβ production or aggregation alone may not be sufficient to prevent AD progression. Autophagy is an essential lysosomal degradation pathway, induced by stress such as fasting and exercise. Although autophagy defect is observed in AD patients and autophagy gene deletion exacerbates cognitive impairment in AD animals, the role and mechanism of autophagy in AD progression is complex and poorly understood. Paradoxically, autophagy has been reported to promote Aβ production and secretion, evidence by reduced, rather than elevated, brain Aβ plaque levels in autophagy-gene knockout mice, which supports the idea that removal of amyloid plaques alone may not be an effective strategy against AD. Thus, the neuroprotective role of autophagy is likely mediated by mechanisms in addition to direct turnover of disease-specific aggregate-prone proteins (amyloid). Recently, we discovered a mutation in an essential autophagy gene Beclin1 (Beclin1^{F121A}) that causes hyperactive autophagy in vivo. We found that AD mice expressing this high-autophagy mutation have longer lifespan and better cognitive function than their counterparts with normal levels of autophagy. In addition, normal Beclin1^{F121A} mice (with no AD-causing mutations) have an extended lifespan and improved healthspan, including enhanced insulin sensitivity, delayed cardiac aging, and reduced age-associated malignancy during aging. Our data suggest that autophagy may prevent AD by systemically improving healthspan during aging, and systemic (and not only central) restoration of autophagy prolongs healthspan and delays AD progression. Our ongoing research will demonstrate the mechanistic link between autophagy-mediated longevity and AD protection in mice.
Background
Prior research suggests that the diagnosis of dementia and its underlying cause is delayed in ethnic and racial minority communities. In addition, regardless of ethnic background, time to diagnosis is known to be delayed for non-Alzheimer type dementias and atypical presentations of Alzheimer disease. Primary progressive aphasia (PPA) is a language based dementia which is caused by Alzheimer disease in about 45% of cases and by frontotemporal lobar degeneration in about 55% of cases. The status of timely PPA diagnosis in ethnic and racial minority communities has not been well investigated, but it is known that these groups are underrepresented in clinical and research settings. Here we present 4 cases where a diagnosis of PPA was never made or was made incorrectly before final diagnosis was reached.

Presentation of Cases
Cases 1 and 2 were African American (a man and a woman respectively). Their disease started with worsening language function. Symptoms became worse over time to include non-language cognitive domains. They were both diagnosed as having a stroke. Final diagnosis was reached after 3 years post-onset (non-fluent agrammatic PPA) in Case 1 and after 7 years in Case 2 (semantic PPA). The first case was due to Alzheimer disease based on spinal fluid exam and the second case was most likely due to a frontotemporal degeneration.

Cases 3 and 4, were Latino, both spoke only Spanish with the beginning symptoms being word finding difficulty. Case 3 was diagnosed with Alzheimer dementia 5 years into the disease and 10 years post-onset she was found to have a corticobasal syndrome with severe right sided spasticity suggesting a more focal disease. Case 4, progressed to difficult word comprehension and was later diagnosed with advanced semantic PPA, 8 years post onset.

Discussion
In these 4 cases, the average time to diagnosis was 8 years from symptom onset. A recent query from National Alzheimer Coordinating Center (NACC) looking at Frontotemporal lobar degeneration cases (including PPA) shows that African Americans and Latinos constitute 6% of this research cohort, while they are 30% of the US population. Therefore, we believe that PPA is not diagnosed, misdiagnosed, or diagnosed much later, in minority communities.

Northwestern Alzheimer disease center is working to raise awareness regarding all dementias in racial and ethnic minority communities through community based lectures and community engaged research and by engaging primary care physicians. As more communities and primary care physicians are becoming familiar with the disease, we expect to have a better coverage of minorities.
INNOVATIVE STRATEGIES TO MEET THE NEEDS OF PERSONS LIVING WITH DEMENTIA: DEVELOPMENT AND LESSONS LEARNED
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Purpose: Currently, over 5 million Americans have a diagnosis of Alzheimer’s disease and Related Dementias (ADRD) and these numbers are expected to triple by 2050. As the older adult population and persons living with dementia continues to increase, the need for specialized healthcare providers is of national significance. Yet, the number of providers prepared in geriatric care lags behind. 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. Through regular meetings, the ADRD team provides input on content for the development of interactive educational materials and resources to help current and future health professionals build vital skills to address the health needs of older adults living with dementia.

Findings: Three comprehensive, interactive online modules related to ADRD were developed. Online modules focus on the basics of evaluating memory concerns and other symptoms of cognitive impairment, person-centered dementia care, and treatment of behavioral changes. The online modules have been completed by professionals and older adults with positive feedback. An in-person workshop aligned with the Dementia Friendly America initiative for professionals and consumers was offered during Fall 2017 with positive feedback from attendees across settings/roles. The workshop focused on how attendees can use existing knowledge and learn new information at the training to teach their colleagues and staff who work with people living with dementia. All educational materials are free and continuing education is available. Materials continue to be disseminated and refined for different audiences.

Conclusion: CATCH-ON ADRD provides accessible, interactive resources and materials to facilitate geriatric and ADRD education. Through these educational efforts, the health professions workforce is equipped with essential competencies to lead practice change in the care of those living with ADRD. The educational materials have practical implications for patients, caregivers, community based organizations, public health policy makers, and other stakeholders as they provide needed geriatric and dementia education to enhance the primary care workforce.
INTRODUCTION: Alzheimer’s disease and other types of dementia affects both the patient and their partner individually and relationally. Non-pharmacological interventions that focus on the quality of life and well-being of both the person with dementia (PWD) and their care partners have been increasingly given greater attention. In 2014, the Northwestern CNADC developed a dyadic storytelling program for persons with a dementia diagnosis [PWD] and their care partner. Initial research findings using qualitative measures indicate that it, 1) invited couples to safely embrace and adjust to the unambiguous losses and 2) strengthened relational connectivity for the couple, with the other storytellers in the group and with family using the story as a legacy. An observed unintended consequence was the impact the story had on the audience and their understanding of the lived experience navigating Alzheimer’s and other dementia through the lens of the PWD and their care partner via their shared story. Anecdotally it was noted that audience members valued hearing the real life account as it helped them better understand the dyad’s relational resilience and losses that can often accompany such diagnoses. Since the original storytelling presentation in May 2014, storytellers have been invited to share their story at universities, health care and medical settings, community outreach programs, businesses, conferences and places of worship.

METHODS: Over the successive five storytelling workshops, a cadre of seven storytelling couples have continued to share their story in-person to over 1600 people in the Chicagoland area. Qualitative (audience reflections) and quantitative (a Likert scale measuring presenter clarity and knowledge of subject matter) data has been collected from 340 student audiences. 35 high school sophomores, juniors and seniors in a healthcare interest group and 110 first-year undergraduate students interested in neurosciences wrote brief reflections about their experience watching the stories. A Likert scale questionnaire was given to 195 social work, medical and physician assistant students evaluating their experience hearing the stories. The reflections and questionnaires were designed to capture whether the dyadic story contributed to their understanding of the disease and its impact on PWD’s and care partners navigating such diagnoses. Program staff gathered the data and calculated the mean score of the quantitative measure and qualitative reflections were reviewed by program staff and faculty for emerging themes.

RESULTS: These reflections and questionnaires recorded the stories’ impact from an educational viewpoint. The Likert scores reflected that 94.4% of the students noted that the storytellers’ presentations were conducive to their understanding of the lived experience of dementia, 96.4% felt that the storytellers were clearly understood, 97.6% shared that the dyad was able to answer questions clearly and concisely and 96.4% considered the storytellers knowledgeable on the subject. 96% of the students stated they would ask the presenters to return. The student’s written reflections noted that the stories: 1) challenged stereotypes they may have had regarding dementia and aging, 2) guided their understanding of how individuals and families are impacted by these types of diagnoses, and 3) helped them focus on the person behind the clinical diagnosis.

CONCLUSION: Dyadic storytelling may be another tool for medical and healthcare students and practitioners as well as policy makers and researchers to aid their understanding of the complex challenges that PWD and their care partners face as they navigate a neurodegenerative diagnosis.
INTRODUCTION: Persons diagnosed with dementia (PWD) may feel a loss of value and purpose when the limitations imposed by the disease decrease or force disconnection from activities around which personal identity was organized. Professional and social roles that provided connection to work and social communities may be significantly diminished and eventually lost. This may result in frustration, social isolation and consequent symptoms of depression and anxiety.

My Mentor and Me replicates the aims and intentions of the Buddy Program, a program pairing first year medical students with persons with early stage dementia, created by Dr. Darby Morhardt at the Northwestern University Cognitive Neurology and Alzheimer’s Disease Center.

METHODS: Recruitment of the mentor involved contact with several memory support centers to engage potential community partners. Social work students were recruited through the graduate school course, Social Work with Older Adults. One student was selected and given a pre-test of knowledge and attitudes toward dementia and then matched with a person with early-stage dementia selected based on program inclusion criteria. The student and Dr. Spira made a visit to the home of the person with dementia where the student had the opportunity to meet her mentor, while Dr. Spira interviewed the mentor’s spouse. During the home visit the student gathered information about her mentor and facilitated conversation about interests and preferred activities. The mentor and student agreed to meet on a specific date and begin their regular activity schedule (4 hours a month for the academic year). The student provided activity logs and reflections of her experience after each activity. Between sessions the student met with Professor Spira for debriefing and supervision.

RESULTS: The student and her mentor met 12 times over a 6-month period. Activities ranged from an architectural tour in Chicago, an art museum in Evanston, and lunch. Student journal reflections and debriefing sessions with Dr. Spira revealed that the student a) gained knowledge regarding the person’s subjective experience living with cognitive changes, b) was sensitized to the nuances of communication with a person with dementia, c) understood the importance of building a reliable and consistent relationship to sustain social connection and self-esteem, and d) developed an increased appreciation of the complexity of living with cognitive impairment.

CONCLUSION: Loyola University is the first School of Social Work to replicate the Buddy Program. Results indicate that My Mentor and Me has the potential for students to increase their knowledge and sensitivity to people with cognitive impairment. Future research will evaluate the impact of the program on PWD as well as the student.
INTRODUCTION: OR Core specific aims are to: 1) Provide outreach and educational programs for the recruitment of underrepresented groups to the Northwestern ADC; 2) Optimize the recruitment of participants into the Clinical Core and their retention through novel non-pharmacological interventions; and 3) Initiate and coordinate public education programs in conjunction with city, state and national entities.

METHODS/RESULTS: The OR Core continues to approach the mission of outreach, recruitment and retention through the establishment of collaborative local community partnerships, particularly with underrepresented groups (URGs), recognition and support for the psychosocial needs of research participants and families, and the design and evaluation of innovative programs that support patients’ and families’ strength and resilience. Community education and training is aligned with city, state and national goals and objectives.

As part of its activities during the past year, the OR core organized a total of 179 local outreach/educational activities that reached 4,154 community members. These events always culminate into the largest event hosted by our ADC and organized by the OR Core - the annual Alzheimer’s Day (AD-Day). Last year there were 412 attendees, of which nearly half were persons living with dementia, caregivers and community members. The AD-Day is a day-long program that includes the Director’s statement on the ‘State of the ADC,’ a keynote address by a national leader in AD research, a poster session showcasing clinical and basic research by Northwestern ADC members, and an afternoon session emphasizing psychosocial and life enrichment themes. The OR core also publishes the annual Northwestern ADC Newsletter. Last year, we mailed 8,329 newsletters to community members. The OR Core is also responsible for the Northwestern ADC Website that had 99,896 visitors last year.

OR Core's specially trained social workers attend to the psychosocial needs of research participants and their families at enrollment and are available for ongoing follow-up in the Clinic. The 8-week Support and Education for Early Dementia (SEED) program is offered to newly diagnosed patients and families twice a year.

The OR Core of the Northwestern ADC has pioneered the development of psychosocial interventions. These programs include: 1) The Memory Ensemble, an improvisational theatre project, 2) iLUMAnations, an art-based project to stimulate creative dialogue, 3) The Buddy Program (see separate abstract), 4) Don’t Look Away: Using Storytelling to Give Voice, Find Connections and Change Perceptions (see separate abstract), and 5) a new collaborative initiative, the Chicago Memory Café (see separate abstract).

CONCLUSION: The OR 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.
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: A neurocognitive diagnosis such as Alzheimer’s disease brings new questions and concerns, as well as the need to develop new coping mechanisms. While Alzheimer’s disease and related disorders progressively affect a person’s cognitive functions, diagnosed persons in the early stages retain many strengths and abilities. The early stage thus presents a unique window where persons with a diagnosis and their care partners can participate in education, discussion, and care planning. Previous research has demonstrated that early-stage support and education are of benefit to both persons with diagnoses and their families. Benefits have been seen in improved quality of life, more motivated care planning, improved psychological well-being, and stronger social connections.

METHODS: The Support and Education for Early Stage Dementia (SEED) program was developed by the Northwestern Cognitive Neurology and Alzheimer’s Disease Center (CNADC). After an initial recruitment screening, participants are invited to eight weekly 2.5 hour sessions, where they have opportunities to socialize, learn, and connect with others. Educational presentations from experts in the field give particular emphasis to topics that help participants cope with changes, such as: the basics of dementia, supportive community resources and interventions, maintaining relationships and disclosing the diagnosis to others, research trends and opportunities, practical and functional interventions utilizing speech and occupational therapy, legal and financial considerations for the future, and creative and supportive interventions after SEED.

At each session, participants participate in a facilitated support group in which they have the opportunity to discuss the educational portion of the day, talk about their or their partner’s diagnosis and its impact on functioning and quality of life, and give and receive support. At the end of each session, participants complete a session evaluation. During the final session, participants take part in a focus group where they can speak about their experience and provide feedback on ways to improve the workshop. This information will be transcribed and coded for emerging themes.

RESULTS: The Northwestern CNADC has held five eight-week SEED programs since September 2015 demonstrating the program’s feasibility. Participant evaluations and focus group data reveal the benefit of the program to participants’ learning and connection to others with similar experiences.

CONCLUSION: SEED seeks to take advantage of the window of learning available early in the cognitive disease process to help participants adapt to life changes associated with dementia. While early-stage programs have demonstrated effectiveness, there is still a perceived dearth of programs and psychosocial services for persons with early-stage dementia. Further research is needed to discover how the programs like SEED benefit persons with diagnoses and their care partners.
NORTHWESTERN’S BUDDY PROGRAM INCREASES MEDICAL STUDENT KNOWLEDGE, EMPATHY, AND ATTITUDES TOWARDS PEOPLE WITH DEMENTIA

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Background: Age is the greatest risk factor for dementia and 50% of people over the age of 85 are estimated to have Alzheimer’s Disease (AD). Approximately 13.3% of the current US population is aged 65 and older—a number which is projected to double by 2060. Therefore, it increasingly important that medical students are equipped with appropriate knowledge, skills, and attitudes to meet the medical needs of this aging population, including exposure to and understanding of dementia. The Buddy Program is an experiential learning program that pairs first-year medical students at Northwestern University Feinberg School of Medicine with persons with dementia (mostly due to AD) in the greater Chicago community for a year of activities and relationship-building. The main goal of this program is to educate students about AD and similar conditions by a) enhancing their dementia knowledge, b) introducing them to the wide spectrum of capabilities of patients with cognitive impairment, c) providing opportunities to observe how patients adapt throughout the progression of disease, and d) familiarizing them with the day-to-day care and support of patients with AD and their families.

Although the Buddy Program has been operating for 20 years, the program’s impact on medical students has not yet been quantitatively analyzed.

Objective: The purpose of this study is to elucidate the Buddy Program’s impact on first-year medical students and 1) their understanding of dementia, 2) their level of empathy for those with dementia, and 3) their attitudes towards, and stigma associated with these patients.

Methods: Pre- and post-test data from 202 first-year medical students who participated in the Buddy Program over the past 20 years were collected and analyzed for responses to the following: 1) NU BP Dementia Knowledge Test (n=149 pre-intervention, n=129 post-intervention), measuring familiarity with dementia, 2) Boston PAIRS test (n=66 pre-intervention, n=65 post-intervention) and Jefferson Empathy Scale (n=44 pre-intervention, n=40 post-intervention), measuring empathy, 3) Young Adults Attitudes Scale (n=44 pre-intervention, n=37 post-intervention) and Dementia Attitudes Scale (n=44 pre-intervention, n=38 post-intervention), measuring attitudes towards those with dementia, and 4) Stigma in AD Scale (n=16 pre-intervention, n=18 post-intervention), measuring stigma associated with AD. Statistical comparisons were conducted via paired t-test.

Results: There were significant increases in medical students’ knowledge of dementia (6.5% increase in NU BP Dementia Knowledge test, p<0.0001), empathy towards those with dementia (8.1% increase in Boston PAIRS test, p<0.0001 and 12.2% increase in Jefferson Empathy Scale, p<0.0001), and positive attitudes towards those with dementia (2.5% increase in Young Adults Attitudes Scale, p=0.066 and 13.5% increase in Dementia Attitudes Scale, p<0.0001). There was also a statistically significant decrease in stigma towards those with AD (12.5% decrease in the Stigma in AD Scale, p=0.023).

Conclusion: This study demonstrates that experiential learning programs such as the Buddy Program can significantly improve knowledge and attitudes towards those with dementia while also reducing stigma. These encouraging results suggest that this program may serve as an excellent model for improving knowledge of other similarly stigmatized conditions while enhancing students’ understanding of what it means to live with chronic disease.
INTRODUCTION: Persons living with dementia (PLWD) and their care partners often experience social disengagement and disconnection as they navigate the disease progression. Isolation can cause multiple challenges for the PLWD and their care partners including depression, a decline in health, and worsening of symptoms. This can cause further isolation as well as strain on the PLWD and care partner’s relationship. Increasing social connection can assist with maintaining mental, emotional and physical health. PLWD and their care partners often find that meeting with others who share a similar experience can increase their social connection and decrease isolation.

The concept for the Memory Café began in Holland as a grassroots movement in 1997 and spread quickly through Canada, Europe, Australia, and the United States. Each café is unique, designed to serve the specific community in which it is held. The cafés provide support and social connection to individuals at any stage of the disease process. Participants are encouraged to gather together in a non-medical setting diminishing the focus on the diagnosis. Information and resources are often available; however, the aim of a Memory Café is to provide a supportive community setting for PLWD and their care partners to enjoy time together while socializing with others who may be experiencing similar challenges.

Feedback from a care partner focus group at the Northwestern Cognitive Neurology and Alzheimer’s Disease Center (CNADC) revealed the need for more programming for individuals with dementia and their care partners. The development of a Memory Café was identified as a way to help meet this need.

METHODS: Northwestern University CNADC reached out to Renewal Care, the Chicago Center for Cognitive Wellness, and Loyola University of Chicago (LUC) and in addition, held a Town Hall meeting for PLWD and their care partners to collaborate in the creation of the CMC. Program objectives were to: 1) create a monthly social gathering for individuals living with dementia and their care partners that would include creative and meaningful programming during a two-hour gathering; and 2) provide an independent study learning opportunity for a LUC graduate social work student interested in working with this population. PLWD and their care partners worked with academic and agency partners on the overall development of the CMC and remain integral to ongoing CMC planning and execution. Sponsorships for programming and refreshments are sought in order to make the CMC free to participants.

RESULTS: The CMC has met monthly since January 2018 with an average attendance of 45 per cafe. Structured programming has included ice breaker exercises to encourage social engagement, chair yoga, scrapbooking and dance. Program evaluations reveal CMC participants enjoy meeting others, sharing similar experiences, trying something new, and spending time together. LUC graduate social work student has demonstrated learning through increased knowledge of cognitive impairment and an appreciation of the importance of social connection in a supportive community of others who share the same challenges.
CONCLUSION: The Chicago Memory Cafe demonstrates a feasible method for meeting identified needs for social connection and engagement for persons living with dementia and their families and an opportunity to contribute to social work education. The active involvement of persons living with dementia and their care partners in the project’s development is an important element in this process.
COMMUNICATION ENHANCEMENT TRAINING: A NOVEL DYAD CONVERSATION STRATEGY INTERVENTION IN DEMENTIA

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Background: Dementia Alzheimer’s type (DAT) negatively impacts the effectiveness and quality of conversations for the person with dementia (PwD) and their family communication partners (FCP). The need for dyad-centered therapies that include both the PwD and their FCP is a critical gap in dementia care (Savundranayagam & Orange, 2011). Yet, few studies have evaluated communication interventions delivered within a dyad model.

Method: A multiple baseline, randomized, single case pilot study was implemented to evaluate a novel dyad-based intervention for reducing conversation breakdowns, improving communication quality of life, and reducing care partner burden in four dyads living with DAT (mild-moderate severity). The 8-week, once weekly, intervention targets: 1) dyad-centered strategies for reducing barriers to meaningful conversations; 2) development and mastery of dyad-centered conversation strategies; and 3) dementia education. Active learning approaches with on- and off-line clinician feedback are used to enhance dyad problem solving. In-home recordings (pre-, during, and post intervention) are used to evaluate strategy generalization to the home environment. Conversation analysis methods are used to measure changes in conversation breakdowns and repair strategies. Standardized measures of perceptions of conversation difficulty, communication quality of life, and care partner burden are also collected.

Results: Data collection is ongoing. In preliminary data from 4/5 dyads, a 21.23% increase in conversation turns initiated by the PwD and a similar 23% increase in turns initiated by the FCP was observed. The number of unresolved conversation breakdowns reduced by an average of 17.9% across dyads. The proportion of overlapping talk reduced by more than 40% across dyads. On the Perception of Conversation Index-Dementia Alzheimer’s Type and on the Montgomery Burden Interview FCPs reported modest reductions in the severity of conversation difficulties, improvements in strategy effectiveness, and reductions in objective burden post treatment.

Conclusions: Preliminary results are positive. Strengths, limitations, and potential barriers for broader implementation in Alzheimer’s dementia will be presented. The framework for the intervention design and the pilot results will be discussed in the context of Kitwood’s theories of personhood (1992) and the Communication Enhancement Model (Ryan et al., 1995).
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 that 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 goal of the Communication Bridge Pilot study was to determine if Internet-based SLT to individuals with PPA and other forms of progressive aphasia was feasible, and if so, what the best SLT methods for this population were.

Results for the first 34 participants in our pilot study were published and showed that functional gains and increased confidence in communication were documented after 8 weeks of SLT and were maintained for the following 4 months. Overall, in our initial study, we enrolled 57 individuals with PPA and other forms of progressive aphasia and their communication partners from 26 states, Singapore, Canada, and Spain, suggesting web-based therapy is feasible and improves access to care.

The next phase of this research study, which delivers web-based SLT and support from a custom web application, is a randomized controlled trial. We will recruit 90 individuals with mild PPA and their communication partners over the next few years to participate in the study. Participants will be in the study for approximately one year and take part in 15 SLT sessions, 5 SLP Evaluations, and exercises to support communication with the support of a custom web-application.
POSTER 50

REACH TO FAITH 2.0: BUILDING THE DEMENTIA FRIENDLY WOODSON LIBRARY

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Introduction: The African American population represents roughly 39% of the local Chicago population aged 65 and older. African Americans are two to three times more likely to be diagnosed with dementia than white Americans and disproportionately receive less dementia care and education. Simultaneously communities have identified caregiver determination to care for a loved one as a potential barrier to seeking early support. Taken together these factors provide a clear rationale for increasing dementia education and awareness among African American populations. During the past year, the Endeleo Institute spearheaded a community-led, $10 million restoration of the Carter G. Woodson Regional Library which re-opened February 2018. This project brings together city agencies, area research and academic institutions and community members to transform the Woodson Library into the city’s first dementia friendly* library and a ‘go to’ safe space for dementia education and resources.

Partners: This project is a community engagement partnership between Endeleo Institute, the nonprofit arm of Trinity United Church of Christ on Chicago’s Far South Side, and Northwestern with seed funding from Northwestern’s Alliance for Research in Chicagoland Communities at the Center for Community Health. A multi-sector advisory board is guiding the Woodson library to implement dementia-friendly programs, practices and interventions. The project is a continuation of a successful faith-based community academic partnership (REACH to Faith 1.0).

Purpose of Study: To build a collaborative partnership of multi-sector community-based stakeholders with a vision to create a “dementia friendly” community. Our mission is to work together to share knowledge and expertise about dementia care and education and to design, develop and implement a dementia care and education program for the region’s first Dementia Friendly Library.

Method: An ongoing iterative process evaluation of Advisory Board meetings includes review of recorded discussions through meeting transcriptions and identification of shared resources. The wider community will be engaged in a Town Hall discussion about the disease trajectory and its impact on family relationships. Participants will be invited to vote for priority programs, activities and resources which the community deems best to deliver dementia knowledge and understanding about caring for persons with dementia in the African American community. An evaluation of the day will be completed.

Conclusion: Short term goals delivered to date include: 1) Provision of a trusted source of resources about dementia care and support, 2) Collaboratively agreeing and presenting a program of activity, and 3) Self-assessment by REACH to FAITH members of the dementia friendliness of faith sector. Goals in progress include: 1) Increasing awareness of the importance of seeking support early among AA caregivers and loved ones living in Washington Heights, and 2) Understanding participant experience of the Dementia Friendly library space.

A longer-term goal is to enable all sectors of Washington Heights to become “dementia-friendly” and to evaluate the impact of participation on older adult and caregiver health outcomes.

*Dementia Friendly Illinois was formed in 2017 and efforts to build dementia friendly communities through various sectors of society have been implemented since then.
INTRODUCTION: The Northwestern Alzheimer’s Disease Center (NADC) is entering its 23rd 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 and Neuropathology cores to recruit and enroll subjects, facilitate brain donations, support investigations of dementia and aging, and educate the public on effectively coping with these illnesses.

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 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 1996-2018 the Clinical Core has enrolled more than 2,109 participants, and the current active cohort is 517. In the past year, the Clinical Core supported over 15 different investigators and 25 studies being conducted in the areas of cognitive neuroscience, clinical trials, neuroimaging and neuropsychology. A total of 27 original publications, 28 published/online abstracts, and 4 book chapters have been supported over the past year and new funding has been generated with the use of Clinical Core resources.

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