

Abstract Book

22nd Annual Alzheimer Day

Thursday, May 12, 2016



Cognitive Neurology and
Alzheimer's Disease Center

Welcome



Dear Friends and Colleagues,

It is my great pleasure to welcome you to the 2016 Annual Alzheimer Day.

This year's event is particularly significant.

You will be glad to know that we just emerged from peer review with flying colors and that we will remain funded by the National Institute on Aging for another 5 years. With this renewal, we will be maintaining the coveted designation of an NIH-funded Alzheimer's Disease Center for 25 years, a quarter of a century!

None of this would have been possible without the dedication of our clinicians, investigators, advisory board members, patients, and families. As in past years, our collective mission is to be at the forefront of research on Alzheimer's disease and related conditions and to make patients and families the beneficiaries of resulting advances.

Today's program has something for everyone. The keynote address by Professor Yaffe will focus on promising prospects for preventing Alzheimer's disease and promoting successful aging. The afternoon program will highlight our work on personalized psychosocial interventions. In between these two sessions, we will have poster presentations that showcase the achievements of clinicians and scientists affiliated with our center.

Welcome and enjoy the day.



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

Schedule of Events

The 22nd Annual Alzheimer Day

Thursday, May 12, 2016

11:30 AM

Welcoming Remarks

M.-Marsel Mesulam, MD, Director, CNADC, and Ruth Dunbar Davee Professor of Neuroscience, Feinberg School of Medicine

Presentation of Marie and Carl Duncan Prize in Memory Research

John Disterhoft, PhD, Associate Director, Ernest J. and Hattie H. Magerstadt Memorial Research Professor of Physiology, Feinberg School of Medicine

12:00 PM

The Mendelson Lecture

“Lifestyle Strategies for Prevention of Dementia”

Kristine Yaffe, MD, Professor of Psychiatry, Neurology, and Epidemiology; Roy and Marie Scola Endowed Chair in Psychiatry; and Vice Chair of Research at the University of California, San Francisco

1:00 PM

Lunch and Scientific Poster Viewing

2:30 PM

“Individualizing Care: The Care Pathway Model”

Sandra Weintraub, PhD and Darby Morhardt, PhD, LCSW
A family shares their story.

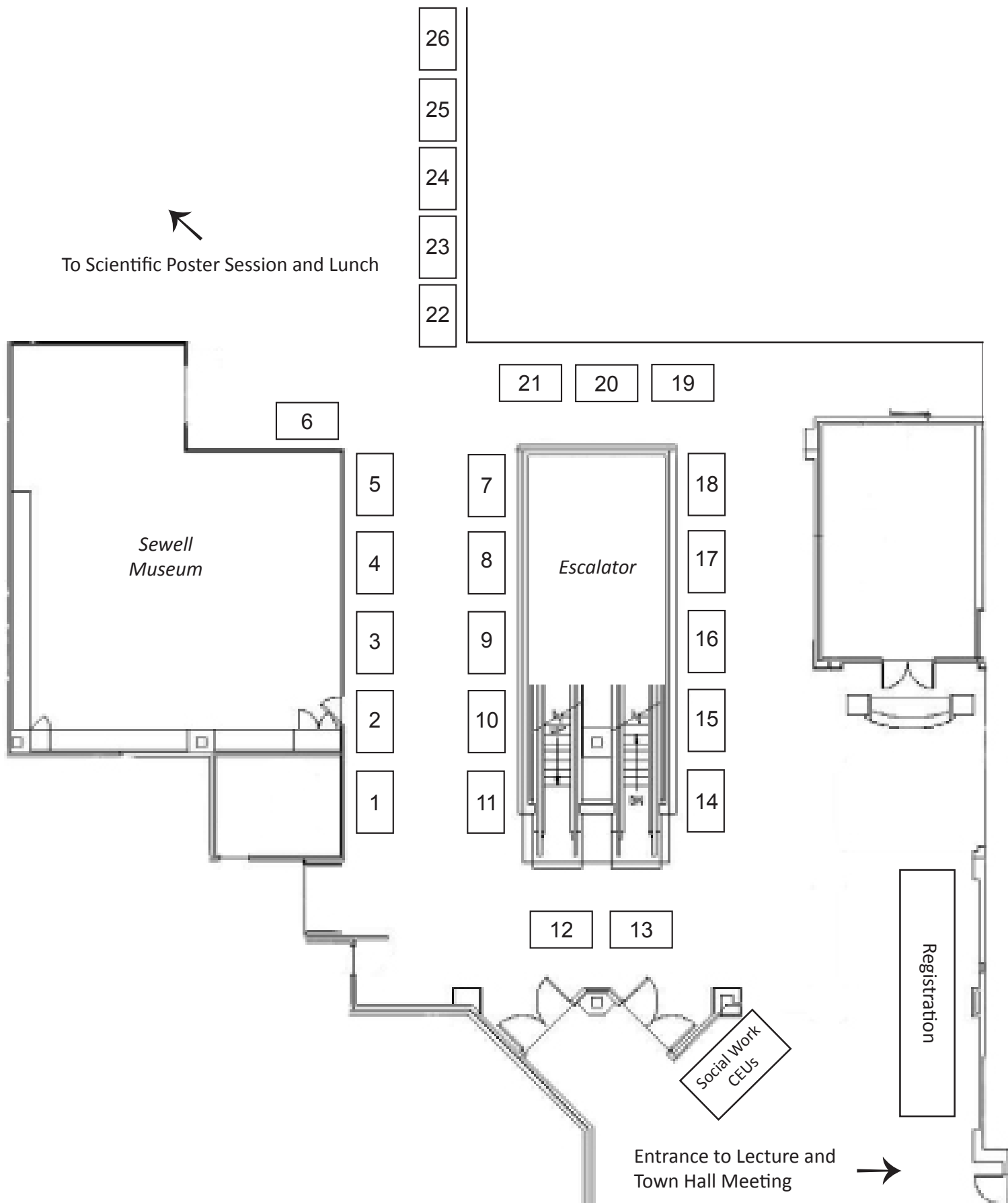
Panel Discussion with Northwestern clinicians

Moderated by Lauren Dowden, MSW, LSW

4:00 PM

Adjourn

Map of Vendor Fair



List of Vendor Tables by Number

The numbers for each vendor correspond to the **Map of Vendor Fair** on Page 3.

1	Peck Ritchey, LLC
2	Belmont Village
3	Regency Rehab Center
4	Home Instead Senior Care
5	Alzheimer's Association - Greater Illinois Chapter
6	Freedom Home Care
7	The Clare
8	CJE SeniorLife
9	Chicagoland Methodist Senior Services
10	Arden Courts
11	Warren Barr
12	Northwestern Cognitive Neurology and Alzheimer's Disease Center (CNADC)
13	Northwestern CNADC Research
14	St. Paul's House
15	SeniorBridge
16	Terra Vista
17	All Trust Home Care
18	Elderwerks
19	BrightStar
20	JourneyCare
21	Silverado Senior Living
22	Northwestern Geriatric Medicine
23	Northwestern Health Learning Center
24	Loyola University Museum of Art
25	Skyline Village
26	SOAR - Streeterville Organization of Active Residents



Voices of Belmont Village

"The staff was able to see through Dad's dementia to recognize and appreciate his real personality."

When the symptoms of dementia affect a loved one, it can be confusing and heartbreaking.

Created in partnership with leading universities, Belmont Village memory programs help residents and family members focus on what is there — not what is lost. Through uniquely personalized care and research-based exercises and activities, our specially trained staff

provides the structure and support you both need.

He'll always be your dad.

BELMONT *Village*

SENIOR LIVING

OAK PARK

Distinctive Residential Settings | Chef-Prepared Dining and Bistro
Premier Health and Wellness Programs | Award-Winning Memory Care
Professionally Supervised Therapy and Rehabilitation Services

**Belmont Village proudly salutes the extraordinary work of
Northwestern University's Cognitive Neurology and Alzheimer's Disease Center.**

The Community Built for Life.®

708-848-7200 • belmontvillage.com

Winner of the George Mason University Healthcare Award for the Circle of Friends® memory program for Mild Cognitive Impairment.



© 2016 Belmont Village, L.P. | SC License 52076

Alzheimer's Planning Attorneys

Estate Planning – Guardianship – Litigation

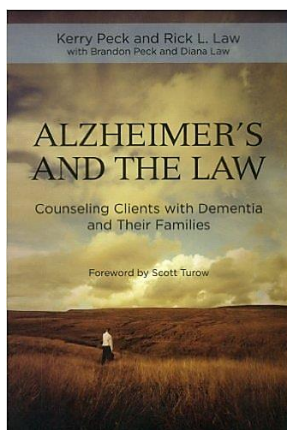


Do you have a family member recently diagnosed with Alzheimer's disease?

Peck Ritchey's Alzheimer's Planning Attorneys will assist you in meeting your family's needs to protect quality of life and financial security for the entire family.

Do you have a family member in the later stages of Alzheimer's disease without advanced planning in place?

After an individual is no longer deemed capable of making decisions for themselves, it can become complicated for them and family members to make medical and financial decisions legally. Having an attorney experienced in Alzheimer's disease planning will help your family gain control over this difficult situation as well as safeguard their wellbeing.



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".

Peck Ritchey's attorneys possess unique expertise to provide guidance and implement legal solutions to protect your family.

Chicago
Northbrook
Oak Brook
Orland Park

Call Today!
312-201-0900
847-509-1099

Email
info@peckritchey.com

PECK RITCHEY, LLC
ATTORNEYS AT LAW

Over 100 years combined experience

www.PeckRitchey.com

Chicago's premier choice for post-acute care



WB
WARREN BARR
GOLD COAST

66 West Oak Street | Chicago, Illinois 60610 | 312.705.5100 | warrenbarr.com

THE GOLD STANDARD IN TRANSITIONAL CARE

WB
WARREN BARR
LINCOLNSHIRE

150 Jamestown Lane
Lincolnshire, Illinois 60069
224.543.7100

WB
WARREN BARR
NORTH SHORE

2773 Skokie Valley Road
Highland Park, Illinois 60035
847.266.9266

WB
WARREN BARR
SOUTH LOOP

1725 South Wabash Avenue
Chicago, Illinois 60616
312.922.2777

Thank You

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

*We greatly appreciate the support of our **Gold Sponsors**:*



PECK RITCHEY, LLC

ATTORNEYS AT LAW

CHICAGO | NORTHBROOK | ORLAND PARK

312.201.0900

www.PECKRITCHEY.com



Thank You

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

Silver Sponsor



Bronze Sponsors

All Trust Home Care
Alzheimer's Association - Greater Illinois Chapter
BrightStar
Chicagoland Methodist Senior Services
CJE SeniorLife
The Clare
Elderwerks
Freedom Home Care
Home Instead Senior Care
JourneyCare
Regency Rehab Center
St. Paul's House
SeniorBridge
Terra Vista

The 22nd Annual Alzheimer Day Planning Team

Lauren Dowden
Anya Drew
Kristine Zachrich
Darby Morhardt, Director of Education

Thank you to all volunteers who have made this day a success!

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

Morning Session

M.-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 is past president of the Organization for Human Brain Mapping and past vice president of the American Neurological Association. 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, is Associate Director of the Northwestern University Alzheimer's Disease Center and is Executive Director of the Northwestern University Behavioral Phenotyping Core.

“Lifestyle Strategies for Prevention of Dementia”



Kristine Yaffe, MD

Dr. Kristine Yaffe attended Yale University for her undergraduate degree, received her medical degree at the University of Pennsylvania, and completed residencies in Neurology and Psychiatry at the University of California, San Francisco. She is a Professor of Psychiatry, Neurology and Epidemiology, the Roy and Marie Scola Endowed Chair and Vice Chair of Research in Psychiatry at UCSF. She is also the Chief of NeuroPsychiatry and Director of the Memory Evaluation Clinic at the San Francisco Veterans Affairs Medical Center. In both her research, clinical work, and mentoring, she has directed her efforts towards improving the care of patients

with cognitive disorders and other geriatric neuropsychiatric conditions.

Dr. Yaffe serves on the Council of the German Center for Neurodegenerative Diseases and Alzheimer's Association Medical & Scientific Advisory Council. As the current principal investigator of 7 NIH grants as well as several other DOD and foundation grants, Dr. Yaffe's research focuses on the epidemiology of cognitive aging. In addition to publishing over 400 peer-reviewed articles (H-index=106) in numerous prestigious journals including the Lancet, BMJ, JAMA, and NEJM, Dr. Yaffe also edited a book published by Oxford Press, "Chronic Medical Disease and Cognitive Aging: Toward a Healthy Body and Brain." She was recognized as one of Thomas Reuters World's Most Influential Scientific Minds in 2014, and she has been honored by the American Association for Geriatric Psychiatry with the Distinguished Scientist Award as well as by the American College of Psychiatrists with the Award for Research in Geriatric Psychiatry.

Afternoon Session

“Individualizing Care: The Care Pathway Model”

Lauren Dowden, MSW, LSW

Lauren Dowden is a social worker at the Cognitive Neurology and Alzheimer’s Disease Center, Northwestern University Feinberg School of Medicine, where she works closely with individuals and families, who are living with a dementia diagnosis or changes in cognition. She holds a Masters in Social Work from Loyola University Chicago specializing in mental health with a gerontology sub-specialization and a BA in Theater Arts from Pennsylvania State University. She is also an alumna of The Second City (Las Vegas) and is an adjunct faculty member and director at the Second City Training Center in Chicago. She teaches medical improvisation for medical students at Northwestern University Feinberg School of Medicine and was an instructor at the 2014 & 2015 Woltman Medical Improv Workshop for medical interdisciplinary teams at Indiana University. Ms. Dowden has developed improvisation curriculum for populations with Parkinson’s disease, anxiety disorders, substance abuse disorders and emotional trauma and is a facilitator for the CNADC and Lookingglass Theatre’s Memory Ensemble - an improvisational workshop for individuals with dementia. As an intern at the CNADC, she was instrumental in helping facilitate the first Northwestern CNADC storytelling workshop, Don’t Look Away: Using Storytelling to Give Voice, Find Connections, and Change Perceptions, which she continues to develop and research.

Jane Godfrey

Jane Godfrey is a resident of Chicago via Dowagiac, MI, Pine Mountain, GA, New Orleans, LA, and most recently, Nevada City, CA. She has a degree in Horticulture from Michigan State University and after 10 years making a career in native plant restoration, is just days away from receiving her Master’s in Speech Language Pathology to begin a new career path. Jane lives Chicago with her husband, Will, their spoiled dog, Oena, and two cats. When she’s not learning about speech, language, and cognition, Jane teaches group fitness classes for Chicago Athletic Clubs and is an avid distance runner.

Judy O’Brien

Judy was born and raised in Dowagiac, Michigan, a small town in Southwest Michigan. She graduated from Michigan State University with a degree in Education and returned to Dowagiac to begin her teaching career. Judy retired from classroom teaching in Dowagiac after 30 years. She continued her career as an adjunct professor in the College of Education at MSU where she taught new educators and was part of team that developed a mentoring system for newly graduated teachers. Judy retired to her country home in Dowagiac in 2008. Judy proudly raised two daughters, Rhiannon and Jane and the three girls have enjoyed many amazing travels together including a week in Ireland and, most recently, numerous adventures in Chicago on Northwestern’s downtown campus. Judy loves gardening, feeding the birds and spending as much time as possible with her two grandchildren. She also enjoys many great adventures with all of her amazing friends, aka ‘Judy’s Buddies.’

Afternoon Session

“Individualizing Care: The Care Pathway Model”

Rhiannon Mulligan

Rhiannon Mulligan was born and raised in Dowagiac, Michigan. She graduated from Michigan State University with a degree in Zoology. After teaching environmental education on a tall ship in Long Island Sound she returned to Michigan and began her career in the education department at John Ball Zoo in Grand Rapids and is now the Education Program Manager. Rhiannon married her high school sweetheart, Brian, in 2004. They live in Rockford, Michigan with their two children, Alanna, 10 and Teague, 8. They enjoy gardening and raising chickens and pigs on their small hobby farm with their collie, Sadie.

Darby Morhardt, PhD, LCSW

Darby Morhardt, PhD, LCSW is Associate Professor and Director of Education for the Cognitive Neurology and Alzheimer’s Disease Center, Northwestern University Feinberg School of Medicine. Dr. Morhardt holds a PhD in social work from Loyola University Chicago. She also completed postgraduate work in family therapy at University of Illinois at Chicago. Dr. Morhardt has over 30 years of clinical experience with cognitively impaired individuals and their families. Her research interests include the experience of families living with Alzheimer’s disease and related dementias such as frontotemporal dementia and primary progressive aphasia, the process of tailoring of care to needs and symptoms; in addition to the development and evaluation of quality of life programs, support groups and other therapeutic interventions. Dr. Morhardt partners with underrepresented communities to raise awareness, identify service and education needs, and promote research participation with the goal of improving health outcomes for persons with dementia and their families.

Sandra Weintraub, PhD, ABCN/ABPP

Sandra Weintraub, PhD, is Professor of Psychiatry and Behavioral Sciences, Neurology and Psychology at Northwestern University Feinberg School of Medicine and has been the Director of the Clinical Core of the Cognitive Neurology and Alzheimer’s Disease Center (CNADC), funded since 1996 by the National Institute on Aging (NIA). She was one of the two Scientific Honorees recognized at the Rita Hayworth Gala of the Alzheimer’s Association in 1997. She served on the Alzheimer’s Disease Clinical Task Force, a special advisory committee to the NIA, to create a method for standardizing the information collected by all 30 centers funded by the NIA across the US. She was a member of three special work groups to redefine the 2011 criteria for the clinical diagnosis of dementia of the Alzheimer type, behavioral variant frontotemporal dementia, and primary progressive aphasia. Dr. Weintraub received her bachelor’s degree from McGill University and PhD from Boston University and was on the faculty at Harvard Medical School before coming to Northwestern. She is board certified in Clinical Neuropsychology by the American Board of Professional Psychology. She directs the outpatient clinical neuropsychology service at the Neurobehavior and Memory Clinic of Northwestern Medicine, a multidisciplinary clinic dedicated to state-of-the-art diagnostic, treatment and research resources for patients with dementia and their caregivers. Dr. Weintraub has authored over 200 articles and book chapters on the neuropsychology of dementia and aging, aphasia and attention.

Afternoon Session

“Individualizing Care: The Care Pathway Model”

Borna Bonakdarpour, MD

Dr. Bonakdarpour received his medical degree from Tehran University of Medical Sciences. His doctoral research on aphasia therapy received international attention and brought him to Northwestern University for his research fellowship in aphasia rehabilitation and neuroimaging of language. Following that he finished his residency in neurology at The University of Arizona and Rosenstone cognitive neurology clinician/investigator fellowship at the CNADC. He is board certified in neurology and behavioral neurology and was recently received a 5 year career development award by the NIH to study pathophysiology of primary progressive aphasia using functional and structural neuroimaging. He is also an active member of the CNADC clinical trials team and primary investigator of the Connect trial for Alzheimer disease.

Aside from research/scientific lectures he has been giving invited lectures for patients and family members, medical and physician assistant students, neurology residents and fellows, primary care physicians and medical specialists caring for patients with cognitive impairments and dementias. Dr. Bonakdarpour has authored more than 40 publications, including original scientific papers, reviews, and book chapters.

Sheila Nicholes

Sheila was born and raised in Chicago. Her alma mater is Chicago State and Cappella Universities. Her focus and degrees in psychology directed her career into family counseling, juvenile delinquency counseling, academic advising and college recruitment. She retired from the Illinois Institute of Technology College of Architecture as Director of Graduate Admission for Architecture. She was a member of the 1996 Olympics planning committee for the Mayors Office of Atlanta Georgia and also one of the special events coordinator for the Olympics. She was a volunteer facilitator for Jobs for Youth Chicago, also an active member on the South Shore Cultural Center Advisory Council and member of Hyde Park Kenwood Community Conference. Sheila and Luthers' blended family consists of 7 children, 13 grandchildren and 12 great grandchildren

Luther Nicholes

Luther was born and raised in Chicago and currently lives in Hyde Park with his wife Sheila, of 23 years. As an Alum of Marshall High School he was inducted into the Marshall High School Hall of Fame for Lettering and Football. He was also volunteer football coach for 20 years for the Chicago public school system. Luther worked as an Investigator Supervisor for the Department of Public Aid Bureau of Investigation in Chicago, Rockford and Springfield for 42 years until retirement in 2009. He also served as President of the United Council on Welfare Fraud. He received the Dorothy L. Forney Memorial Award in recognition for his outstanding contribution toward the elimination of welfare fraud. Also an appreciation award from the United Council on Welfare Fraud for his many years of outstanding service as a member of the board of directors representing region 5. Luther is a member of Northwestern Memory Ensemble and Early Stage Support group, and currently enrolled in the research program here at the Cognitive Neurology Alzheimer's Disease Center. He also mentored a NU medical student through the Buddy Program.

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

- 2015** | **Dina Simkin, PhD**
Calbindin-D_{28K} Restores the Intrinsic Excitability Properties of Aged CA1 Pyramidal Neurons to Young-Like State
- 2014** | **Daniel M. Curlik II**
Ameliorating Age-Related Cognitive Impairments by Reducing Expression of L-Type Calcium Channels in Area CA1 of the Hippocampus
- 2013** | **Diana Schwab Himmelstein**
Characterization of the Oligomeric Form of Tau
- 2012** | **Tharinda Rajapaksha**
The Alzheimer's β -Secretase Enzyme BACE1 is Required for Accurate Olfactory Sensory Neuron Axon Guidance and Normal Glomerulus Formation in the Olfactory Bulb
- 2011** | **Carmen Westerberg**
Electrically Enhancing Memory Consolidation During Sleep: A Novel Method for Reducing Age-Related Memory Decline
- 2010** | **Nicolas Kanaan**
Phosphorylation in the N-Terminal Region of Tau Can Regulate Tau-Mediated Inhibition of Anterograde Fast Axonal Transport in the Squid Axoplasm
- 2009** | **Katherine Sadleir**
The Role of EIF2- α Phosphorylation in A β ₄₂ Induced BACE1 Elevation
- 2008** | **Carmen Westerberg**
Relationships Between Poor Sleep and Poor Memory in Mild Cognitive Impairment



Innovators in Memory Care

Arden Courts' mission for 20 years has been to provide a home-like, safe and supportive setting that nurtures the individuality of those living with memory impairments and provides their families peace-of-mind.

Arden Courts:

- Arden Courts is 100% dedicated to memory care.
- Arden Courts is the first national company to use the Namaste Care Program.
- Through experience and research, our umbrella of programming has been carefully developed to maximize our residents' capabilities and independence.
- Arden Courts is a part of the HCR ManorCare family and continuum of care which includes skilled nursing, rehabilitation, IV therapy and hospice care.
- For the past seven years, the number one reason families have chosen Arden Courts is due to its good reputation for care.*

* 2008-2014 survey data ("excellent" and "good" responses) from annual My InnerView customer satisfaction results.

For additional information about our services or to schedule a tour, call 847.795.9000 or email Northbrook@arden-courts.com

Experience makes a difference.

Arden Courts of Northbrook
3240 Milwaukee Avenue
Northbrook, IL 60062
847.795.9000

Arden Courts 
Memory Care Community

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:

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

Research Areas

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

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.

320 East Superior Street
Searle 11th Floor
Chicago, IL 60611
Phone: 312-908-9339
Fax: 312-908-8789
CNADC-Admin@northwestern.edu
<http://www.brain.northwestern.edu>

Neurobehavior and Memory Clinic

Care for Patients and Families

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

Services Include

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

A Dedicated Clinical Team

Behavioral Neurologists

M.-Marsel Mesulam, MD, Director
Borna Bonakdarpour, MD
Jay Gottfried, MD, PhD
Shoaib Memom, MD

Neuropsychiatrists

Deborah Reed, MD
Fred Ovsiew, MD

Neuropsychologists

Nancy Kennedy, PhD, ABPP-CN
Jana Wingo, PhD
Sandra Weintraub, PhD, ABPP-CN

Social Workers

Darby Morhardt, PhD, LCSW
Lauren Dowden, MSW, LSW

Clinic Manager

Megan Atchu, MA

Psychometrist

Nicole Wright, BA, CSP

Patient Access Representatives

Cheryl Brown
Anthony Nowaske

Call for an appointment: 312-695-9627

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

The Cognitive Neurology and Alzheimer's Disease Center

Executive Committee Members

Administrative Core

M.-Marsel Mesulam, MD

Director, Cognitive Neurology and Alzheimer's Disease Center

Ruth Dunbar Davee Professor in Neuroscience and Neurology

John Disterhoft, PhD

Associate Director

Ernest J. and Hattie H. Magerstadt Memorial Research Professor of Physiology

Kevin Connolly

Administrator

Clinical Core

Sandra Weintraub, PhD

Professor

Departments of Psychiatry, Neurology, and Psychology

Data Management & Statistics Core

Alfred Rademaker, PhD

Professor

Department of Preventive Medicine

Outreach, Recruitment and Education Core

Darby Morhardt, PhD, LCSW

Research Associate Professor

Cognitive Neurology and Alzheimer's Disease Center

Neuroimaging Core

Emily Rogalski, PhD

Research Associate Professor

Cognitive Neurology and Alzheimer's Disease Center

Neuropathology Core

Eileen Bigio, MD

Professor

Department of Pathology

Advisory Board

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

Executive Committee of the Advisory Board

Terry Chapman, Co-Chair (2016-2018)

Craig C. Grannon, Co-Chair (2016-2018)

David Moscow, Past Chair (2014-2016)

Current Members

Jason Boschan

Terry Chapman

Susan Chapman

Carole Feiger

Joyce Gallagher

Bill Goldberg

Ivan Himmel

Melissa Kahn

David Mendelson

Life Members

Robert Mendelson

Linda Mendelson

John Van Cleave

Kay Van Cleave

Donna Elrod

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 Kevin Connolly 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

- Access to latest findings and research
- I find it interesting and am hoping it will shed some light on Alzheimer's
- To help find a cure
- To learn more about dementia and its progression
- Looking for the opportunity to find answers to eliminate or prevent the symptoms of this disease
- To contribute to the science and knowledge of brain changes with aging
- I feel we should always try to help others
- I hope that what I have to offer in life and death will help people in the future
- As a former teacher, mom wants to help others learn from her disease



“To assist in the development of greater understanding of the disease and potentially find a cure”

- Opportunity to assist in much needed research
- Some fear of losing memory
- Concerned about the heredity factor with our children and grandchildren
- I have symptoms of memory problems
- Dementia is such a dreadful disease that I am happy to contribute to diminishing its scope
- Because I feel as if I'm part of something bigger and that we've stepped into a world that “gets” what we are experiencing
- So that my husband can get all the help that is currently available at this time
- We care about the issue

“Because so many are afflicted and I'm hopeful I can help”



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

Core Center Research Study

Goals

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

Participants May Receive

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



Initial Research Visit Include

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

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

Annual Return Visits Include

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

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

Research Coordinators: Bitu Rad and Laura Martindale
(312) 926-1851

www.brain.northwestern.edu

-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

What is involved?

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

Why?

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

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

Where?

**Northwestern University CNADC
320 E. Superior Street, Searle Building, Chicago, IL**

**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

Language in Primary Progressive Aphasia Research Study

Funded by the National Institute of Deafness and Other Communication Disorder
and the National Institute on Aging

INFORMATION ABOUT THE STUDY

The study lasts three days total, about seven hours each day including breaks and lunch. On days one and two, 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 two days, you will have a magnetic resonance imaging (MRI) scan and participate in an event-related potentials (ERP) task. On the third 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 and another that includes ERP testing.

Over 100 people with PPA and 60 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 must be:

- 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 three 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.



FOR MORE INFORMATION, PLEASE CONTACT:

Benjamin Rader, benjamin.rader@northwestern.edu, (312) 908-9681
Northwestern University CNADC
320 E Superior Street, Searle 11-579
Chicago, IL 60611

Clinical Trials: A4 Study



If you are a healthy older adult with normal thinking and memory abilities, **now is the time** to join the fight to prevent memory loss associated with Alzheimer's disease.



NOW IS THE TIME

What is the A4 Study?

The A4 Study (also known as the Anti-Amyloid Treatment in Asymptomatic Alzheimer's study) is a landmark clinical trial to prevent the memory loss associated with Alzheimer's disease (AD). The A4 study is for individuals ages 65 to 85 who may be at risk for AD-related memory loss but who have no outward signs of the disease.

The A4 study is investigating a new treatment that may reduce the impact of a protein known as "amyloid" or "beta amyloid" which forms plaques in the brain. Scientists believe that the accumulation of amyloid in the brain may play a key role in the eventual development of AD-related memory loss.

The investigational treatment used in A4 targets the excess amyloid in the brain with the aim of slowing possible AD-related damage in the brain and delaying symptoms of memory loss.

Learn more about the A4 study:

Cognitive Neurology and Alzheimer's Disease Center (CNADC) at Northwestern University
PI Sandra Weintraub, PhD | STU00087736
1-855-NU-STUDY (312-503-6227)
Email: nustudy@northwestern.edu
<http://tinyurl.com/CNADC-trials>



Phone: 844-A4STUDY (247-8839)
Email: brainlink@ucsd.org

A4study.org

Join the fight to prevent memory loss associated with Alzheimer's disease.

What is involved in the A4 study?

The study lasts approximately three years and participants will be required to visit the clinical research site once a month. Participants will have their health monitored throughout the study using assessments such as:

- Memory and thinking tests
- ECGs
- PET scan
- MRI scans
- Blood and urine tests

You may be eligible to participate in the A4 study if you:

- Are 65 to 85 years old
- Have normal thinking and memory abilities
- Have an A4 study partner who has at least weekly contact with you and can answer questions once a year
- Are willing and able to receive intravenous infusions (IV) of the investigational treatment or placebo (monthly infusions).

A4 participants must be willing and able to participate in all required procedures for the duration of the A4 study.

Clinical Trials: SNIFF Study



SNIFF – the Study of Nasal Insulin to Fight Forgetfulness

A Multi-Center, Double-Blind, Placebo-Controlled Phase II/III Study to Evaluate the Impact of Nasal Inhaled Insulin in Participants with Mild Memory Impairment and early Alzheimer's Disease

What is the SNIFF study?

The purpose of the SNIFF study is to find out whether insulin, when administered as a nasal spray, improves memory in adults with a mild memory impairment or Alzheimer's disease (AD). The rationale behind the study is growing evidence that insulin carries out multiple functions in the brain and that poor regulation of insulin may contribute to the development of AD. Insulin resistance, reduced cerebrospinal fluid insulin levels, and reduced brain insulin signals have been found in AD patients, suggesting that a therapy aimed at correcting these deficiencies may be beneficial.

In this study participants will be given a nasal spray device either with insulin or placebo. Participants will be randomly assigned to the treatment or the placebo group for 12 months, followed by six months in which all participants will receive insulin. During the first 12 months neither study participants nor study staff will know who is receiving active treatment and who is receiving placebo.

We are looking for 240-300 adults diagnosed with amnesic mild cognitive impairment (aMCI) or early AD who would like to participate in this study. The study will take place at about 30 research clinics nationwide.

Are you eligible to participate?

Researchers are looking for people who meet the following criteria:

- Age 55-85
- Have a diagnosis of aMCI or probable mild AD
- Fluent in English or Spanish
- Have a partner available to attend most clinic appointments and someone available to assist with drug preparation and administration twice a day
- Stable medical condition for three months prior to screening visit
- Stable medications for four weeks prior to screening and baseline visits
- Do NOT take drugs for diabetes (type I or II)
- Willing and able to undergo clinic assessments (for example – blood and urine lab tests, MRI, lumbar puncture, ECG, neuropsychological tests)

For more information contact:

Kristine Lipowski, MA, CCRC
Research Project Manager
Phone: (312) 503-2486
Email: k-lipowski@northwestern.edu
Northwestern University IRB STU00085066
Principal Investigator: Marsel Mesulam, MD

This study is being conducted by the University of Southern California, Alzheimer's Therapeutic Research Institute (USC ATRI) and Wake Forest School of Medicine through a grant from the National Institute on Aging (NIA), one of the National Institutes of Health (NIH).

Clinical Trials: CONNECT Study



Connect

*A Multi-Center, Double-Blind,
Placebo-Controlled Phase IIa Study
to Evaluate an Investigational Medicine
to Treat Mild-Stage Alzheimer's Disease*

What is the CONNECT Study?

The CONNECT study will test whether an oral, experimental drug, AZD0530 (saracatinib), will slow progression in mild-stage Alzheimer's disease (AD). Although the cause of AD is unknown, several lines of evidence suggest that a peptide known as beta-amyloid plays a central role. Convergent evidence in recent years has yielded a refinement of the "amyloid hypothesis", suggesting that neurotoxicity of beta-amyloid oligomers leads to Alzheimer's disease. The protein Fyn kinase, a member of the Src family kinases, may play a fundamental role in the pathway by which beta-amyloid oligomers damage neurons. AZD0530 is a selective inhibitor of Src family kinases that was previously developed as a cancer therapy but may hold greater promise as a treatment for AD.



CONNECT researchers will use PET imaging to evaluate whether the drug is effective in slowing decline in brain metabolism and will also determine whether it is safe and well tolerated in patients with AD. Screening will occur over six weeks followed by a



52-week treatment period. The study requires a minimum of four visits during the screening and 13 to 14 visits during the course of the treatment.

Researchers are looking for people who:

- Are 55-85 years of age
- Have a diagnosis of mild Alzheimer's disease
- Are willing to undergo a variety of clinic assessments
- Have a study partner willing to attend clinic visits and have at least 10 hours/week of contact with study participant.

For more information on the CONNECT study please contact:

Kristine Lipowski, MA, CCRC
Research Project Manager
Phone: (312) 503-2486
Email: k-lipowski@northwestern.edu
Northwestern University IRB STU00200256
Principal Investigator: Borna Bonakdarpour, MD

This study is being conducted by the University of Southern California, Alzheimer's Therapeutic Research Institute (USC ATRI) and Yale University through a grant from the National Center for Advancing Translational Sciences (NCATS), one of the National Institutes of Health.

Quality of Life Programs & Research Opportunities

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.

ilLUMAnations

Designed as a program for people with memory loss and their care partners, the primary goal of ilLUMAnations 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.

*The Cognitive Neurology and Alzheimer's Disease Center would like to thank
the **Glen and Wendy Miller Family Foundation**
for their generous support of our Quality of Life programs.*

SEED: Support & Education for Early Dementia Program

The SEED 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 Session 2016

When: Mondays from 10:00am-12:00pm

Where: Northwestern University, Chicago, IL

September 12th

Welcome & Introductions

September 19th

The Basics of Dementia with a Behavioral Neuropsychologist

September 26th

Coping with Changes: Practical and Functional Interventions Utilizing Speech and Occupational Therapy

October 3rd

Coping with Changes: Maintaining Your Relationships and Disclosing the Diagnosis with Others

October 10th

Coping with Changes: Supportive Community Resources and Interventions

October 17th

Pharmacological Interventions & Current Research Update

October 24th

Legal and Financial Considerations for the Future with an Elder Law Attorney

October 31st

Life After SEED: Creative & Supportive Interventions and Q&A with Families Living with a Diagnosis
(Schedule is subject to change)

Interview Required to Participate

There is a \$150 charge per person for the program (scholarships are available)

Please contact facilitators with any questions:

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

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

Poster Session

Poster	Author(s)	Abstract Title
1	Elena Barbieri , Jennifer E. Mack, Sarah D. Chandler, M.-Marsel Mesulam, Cynthia K. Thompson	Grammatical Production Deficits in PPA: Relating Narrative and Structured Task Performance
2	Borna Bonakdarpour , Allan Wang, Marsel Mesulam, Robert Hurley	Distinct Pathophysiologic Pathways Underlying Variants of Primary Progressive Aphasia: A Resting State Functional Magnetic Resonance Imaging Study
3	Borna Bonakdarpour , Allan Wang, Emily Rogalski, Robert Hurley, Marsel Mesulam	Neural Network Underlying Abnormal Syntax Processing in Primary Progressive Aphasia: Evidence from Resting State Functional Magnetic Resonance Imaging
4	Letizia Borges , Borna Bonakdarpour	Memantine-Induced Chorea and Dystonia
5	Erika Cline , Arighno Das, Izolda Popova, Saad Mohammad, Owen Skinner, Kirsten Viola, Madeline Rollins, Lynn Zieske, Philip Compton, Neil Kelleher, Robert Vassar, William Klein	Improving the Tool Kit for Characterization of A β Oligomers in Alzheimer's Disease Pathogenesis
6	Kevin Connolly , Anthony Nowaske, Cheryl Brown, Nicole Wright, Megan Rising	Improving Patient Satisfaction and Likelihood to Recommend
7	Amanda Cook , Stephanie Kielb, Emmaleigh Loyer, Sandra Weintraub, M. Marsel Mesulam, Dan McAdams, Regina Logan, Emily Rogalski	Psychological Well-Being in Cognitive SuperAgers and Non-Demented Elderly
8	Amanda Cook , Emmaleigh Loyer, Sandra Weintraub, Hans Breiter, M. Marsel Mesulam, Emily Rogalski, James Reilly	A Modified-Sternberg Paradigm Measures Load and Delay Components of Working Memory in SuperAgers
9	Justyna A. Dobrowolska-Zakaria , Robert J. Vassar	β - and α -Secretase Processing of Amyloid Precursor Protein in Human Central Nervous System: Implications for Alzheimer's Disease
10	Lauren Dowden , Mary Rastetter, Darby Morhardt	Preserving Relationships: Using Dyadic Storytelling as a Strengths-Based Approach
11	Anya Drew , Lauren Dowden, Darby Morhardt	Dementia and Hospitalization: The Experience of Two Families
12	M Esmaeili , Z Charmchi, B Heydari	Effect of Norharmaline on Memory Retention of Streptozotocin-Induced Alzheimer's Rats Model on Passive Avoidance and Morris Water Maze Test
13	Kelsey Gradwohl , James W. Antony, Jessica D. Creery, Ken A. Paller	A Novel Technique to Boost Memory During Sleep

Poster Session

Poster	Author(s)	Abstract Title
14	Veronika Hanko , Kathryn I. Alpert, Kristen N. Warren, Julie A. Schneider, Konstantinos Arfanakis, David A. Bennett, Lei Wang	Ante-Mortem Structural MRI Markers for Post-Mortem Pathology for TDP-43 and AD in the Hippocampus
15	Ellie Hong , Arin Pamukcu, Savio Chan	Alterations in Excitability of CA1 Neurons from Pre-Plaque to Plaque-Burdened Ages in 5xFAD Mice
16	Monica Janeczek , Mehrnoosh Samimi-Gharai, Sandra Weintraub, Emily Rogalski, Eileen Bigio, M.-Marsel Mesulam, Changiz Geula	Acetylcholinesterase-Positive Cortical Pyramidal Neurons: Emergence in Adult Human Life and Down-Regulation in Cognitively Average Elderly and Elderly with Superior Memory Capacity
17	Devi Krishna Priya Karunakaran , Jasvinder K. Atwal, Robert J. Vassar	Molecular Mechanisms of the Alzheimer's Risk Gene Unc5c in Neuronal Death
18	Stephanie Kielb , Emily Rogalski, Sandra Weintraub, Alfred Rademaker	Objective Cognitive and Functional Loss and Dementia Risk in Subjective Cognitive Decline
19	Garam Kim , Shahrooz Vahedi, Sandra Weintraub, Eileen Bigio, Marsel Mesulam, Changiz Geula	Asymmetric Distribution of Activated Microglia in a Left-Handed Patient with Primary Progressive Aphasia, TDP-43 Pathology and Right Hemisphere Language Dominance
20	Lokesh Kukreja , Garam Kim, Katherine Sadleir, Lei Wang, Hongxin Dong, John Csernansky, M-Marsel Mesulam, Robert Vassar, Changiz Geula	Time-Dependent Formation and Disappearance of TDP-43 Inclusions in a Conditional Transgenic Mouse Model of FTL
21	Okkes Kuybu , M-Marsel Mesulam, Emily Rogalski, Robert Hurley	Verbal and Non-Verbal Auditory Processing Impairments in Primary Progressive Aphasia: An Event-Related Potential Investigation
22	Carmen Lin , M Matthew Oh, John Disterhoft	Functional Changes of the Principal Neurons of the Lateral Entorhinal Cortex in Learning and Aging
23	M.-Marsel Mesulam , Sandra Weintraub, Borna Bonakdarpour, Kristine Lipowski, Jordan Robson	Cognitive Neurology & Alzheimer's Disease Center (CNADC) Clinical Trials 2016
24	Borna Bonakdarpour , Kristine Lipowski, Jordan Robson	Connect Trial for Alzheimer's Disease
25	Kristine Lipowski , Okkes Kuybu, Carly Oboudiyat, Raj C. Shah, Neelum T. Aggarwal, Sandra Weintraub	Efficiency of Telephone Prescreening for the A4 Trial

Poster Session

Poster	Author(s)	Abstract Title
26	Emmaleigh Loyer , Marie Saxon, Maureen Connelly, Tamar Gefen, Amanda Cook, Stephanie Kielb, Jaiashre Sridhar, Lokesh Kukreja, Payam Abbassian, Daniel Ohm, Sandra Weintraub, Changiz Geula, M-Marsel Mesulam, Emily Rogalski	SuperAging Study: Correlates of Active Engagement in Life in the Elderly
27	Qinwen Mao , Kimmo Hatanpaa, Yanqing Li, Jayson Wilson, Sandra Weintraub, Haibin Xia, Charles White, Marsel Mesulam, Eileen Bigio	Distribution of Granulins in FTLD-TDP and Normal Brains
28	O. Hecmarie Meléndez-Fernández , Eric Y. Kao, Sandra Weintraub, Eileen Bigio, M-Marsel Mesulam, Changiz Geula	Comparative Distribution of Early and Late Appearing Tau Epitopes in Tauopathies
29	Robyn Golden , Erin Emery-Tiburcio, Michelle Newman, Raj C. Shah, Carol Farran, Fawn Cothran, Rebecca Johnson, Darby Morhardt	Collaborative Action Team training for Community Health-Older adult Network (CATCH-ON)
30	Pamela Ambrose , Natasha Ritsma, Marlea Edinger, Barbara Weeks, Leonard Caramela, Chris Benoodt, Mary Reynolds, Anya Drew, Lauren Dowden, Darby Morhardt	ilLUMAnations: A Museum Based Art Program for Persons with Cognitive Impairment and Their Families
31	Ji Myong Kim , Yoon Tae Chong, Inchul Choi, Darby Morhardt	KARE - Korean American Alzheimer's Research and Education
32	Darby Morhardt , Kristine Zachrich, Lauren Dowden, Anya Drew	Northwestern Alzheimer's Disease Center Outreach, Recruitment and Education Core (ORE Core) 2015-16
33	Melvin Thompson , Etta McGregor-Jones, Joan Owens, Catherine Chandler, Jaunita Carr, Audrey Coleman, Dorothy Jenkins, Virginia Julion, Shawnya Owens, Cynthia Brown, Jiles Taylor George, Barbara Little, Fawn Cothran, Jakita Baldwin, Darby Morhardt	REACH to Faith: Research and Education for African American Caregiver Health
34	Aneesha Nilakantan , Donna Bridge, Elise Gagnon, Jane Wang, Joel Voss	Improved Precision of Successful Recollection 24 Hours After Targeted Stimulation of Posterior Hippocampal Cortical Network
35	Yasushi Nishihira , Qinwen Mao, Sandra Weintraub, Nailah Siddique, Teepu Siddique, M-Marsel Mesulam, Eileen H Bigio	Pathology of ALS with Dementia
36	Carly Oboudiyat	Leukodystrophy with Axonal Spheroids Presenting as Primary Progressive Aphasia

Poster Session

Poster	Author(s)	Abstract Title
37	Daniel Ohm , Garam Kim, Adam Martersteck, Sandra Weintraub, Eileen H. Bigio, M.-Marsel Mesulam, Emily Rogalski, Changiz Geula	Histopathologic Markers Are Related to <i>In Vivo</i> Cortical Atrophy in Primary Progressive Aphasia with Alzheimer Pathology
38	Ming-Hsuan Ou-Yang , Tharinda W. Rajapaksha, Katherine R. Sadleir, Robert J. Vassar	Conditional BACE1 Knockout Mouse as a New Model for Studying Tissue Specific and Temporal BACE1 Inactivation
39	PA Papalambros , G Santostasi, RG Malkani, S Weintraub, KA Paller, PC Zee	Acoustic Stimulation Increases Slow-Wave Activity and Improves Declarative Memory in Older Adults
40	Zach Parton , Changiz Geula, Eileen Bigio	Regressive Gallyas Staining of Paraffin Embedded Human Brain Tissue
41	Hadley Pfalzgraf , Jessica D. Creery, Ken A. Paller	Can Memory Be Improved with Oscillating Sounds That Promote Beneficial Brain Oscillations During Learning?
42	Michael Priest , Yevgenia Kozorovitskiy	Characterization of Neurons Expressing the Neuroprotective Peptide Urocortin
43	Benjamin Rader , Marie Saxon, Emmaleigh Loyer, Allison Rainford, Jaiashre Sridhar, Robert Hurley, Ken Paller, Cynthia Thompson, Sandra Weintraub, M.-Marsel Mesulam, Emily Rogalski	Primary Progressive Aphasia Research Programs at Northwestern University's CNADC
44	Aras Rezvanian , Lokesh Kukreja, Eric Y Kao, Ling Guo, Sandra Weintraub, Eileen Bigio, M.-Marsel Mesulam, Joseph El Khoury, Changiz Geula	Characterization of High Passage Adult Human Microglia Cultures
45	Ashlee E. Rubino , Sana Afreen, Adriana Ferreira	Internalized Tau ₄₅₋₂₃₀ Aggregates Can Spread Tau Pathology and Neuronal Degeneration in Alzheimer's Disease and Related Disorders
46	Katherine R. Sadleir , Patty C. Kandalepas, Virginie Buggia-Prevot, Daniel A. Nicholson, Gopal Thinakaran, Robert Vassar	Presynaptic Dystrophic Neurites Surrounding Amyloid Plaques Are Sites of Microtubule Disruption, BACE1 Elevation, and Increased A β Generation in Alzheimer's Disease
47	Marie Saxon , Rebecca Khayum, Kathryn Borio, Hannah McKenna, Marya Corden, M.-Marsel Mesulam, Emily Rogalski	The Communication Bridge Research Program - Using Internet-Based Speech Therapy to Improve Quality of Life and Access to Care

Poster Session

Poster	Author(s)	Abstract Title
48	Anne Seltzer , Vanessa Ramirez-Zohfeld, Lee A. Lindquist, Darby Morhardt	Successfully Aging in Place: Planning Rather Than Reacting to Life's Crises
49	Jaiashre Sridhar , Allison Rainford, Mark Plantz, Benjamin Rader, Emmaleigh Loyer, Marie Saxon, Maureen Connelly, Adam Martersteck, Allan Wang, Kristine Lipowski, Carly Oboudiyat, Robert Hurley, Borna Bonakdarpour, Marco Catani, Derin Cobia, Sandra Weintraub, M-Marsel Mesulam, Emily Rogalski	Neuroimaging at the Northwestern Alzheimer's Disease Center
50	Clarissa Valdez	Progranulin and Cathepsin D- A Potential Mechanism for Neurodegeneration
51	Allan Wang , Marsel Mesulam, Borna Bonakarpour	Decreased Baseline Brain Activity in Early-Stage Primary Progressive Aphasia Using Resting-State Functional Magnetic Resonance Imaging
52	Mallory Ward , Laura Martindale, Bitu Rad, Alfred Rademaker, Borna Bonakdarpour, Carly Oboudiyat, Mustafa Seckin, Okkes Kuybu, Lauren Dowden, Mary Rastetter, Darby Morhardt, Emily Rogalski, M-Marsel Mesulam, Sandra Weintraub	Northwestern Alzheimer's Disease Center (NADC) Clinical and Data Management and Biostatistics Cores
53	Xiao-Wen Yu , Daniel M. Curlik II, M. Matthew Oh, Jerry C. P. Yin, John F. Disterhoft	CREB Overexpression in Dorsal CA1 Ameliorates Memory Deficits in Aged Rats
54	W. Zhang , B. van Alphen, F. Xu, M. Zhang, R. Allada	Neuroprotective Effects of Sleep on β -Amyloid Induced Loss of Circadian Rhythms in <i>Drosophila</i>

Grammatical Production Deficits in PPA: Relating Narrative and Structured Task Performance

Elena Barbieri, Jennifer E. Mack, Sarah D. Chandler, M.-Marsel Mesulam, & Cynthia K. Thompson
Northwestern University, Department of Communication Sciences and Disorders, Evanston, IL
elena.barbieri@northwestern.edu

Introduction. Grammatical production impairments in primary progressive aphasia (PPA) have been investigated using structured language tasks and analysis of narrative language samples (for review see Thompson & Mack, 2014; Wilson et al., 2012). However, little research has examined the relationship between them in PPA. Whereas structured tasks often assess production accuracy at different levels of syntactic complexity (e.g., Thompson et al., 2013), narrative measures typically assess overall lexical and grammatical usage (e.g., % grammatical sentences; noun-to-verb ratio), with lesser emphasis on complexity. The present study investigated the relationship between narrative measures of grammatical production and performance on structured language tests in the domains of syntax, verb morphology, and verb-argument structure (VAS).

Materials and methods. Data from 101 individuals with PPA were included. Participants completed a test battery including the Northwestern Assessment of Verbs and Sentences (NAVS, Thompson, 2011), the Northwestern Assessment of Verb Inflection (NAVI, Lee & Thompson, experimental version) and the Northwestern Anagram Test (NAT, Thompson, Weintraub, & Mesulam, 2012). Grammatical production deficits were quantified as follows: for syntax, accuracy of non-canonical sentence production on the NAVS Sentence Production Priming Test (SPPT) and the NAT; for morphology, the accuracy on finite verbs on the NAVI; for VAS, the accuracy of sentences produced with 2- and 3-argument verbs on the NAVS Argument Structure Production Test (ASPT).

Cinderella narrative samples were analyzed using the Northwestern Narrative Language Analysis system (e.g., Thompson et al., 2012). For syntax, complexity was measured by the ratio of syntactically complex to simple sentences produced, whereas accuracy was indexed by computing the proportion of words with a locally grammatical lexical category. Morphological accuracy was measured by the proportion of correctly inflected verbs. VAS complexity was measured by the mean number of arguments produced per verb (i.e., the verb-lemma complexity index), whereas accuracy was assessed by the proportion of verbs with correct argument structure.

Within each grammatical domain, multiple regression was used to determine if narrative measures were predictive of structured task performance.

Results. For syntax, measures of narrative complexity and accuracy significantly predicted performance on both the NAVS SPPT and NAT. Performance on the NAVI was predicted by the proportion of correctly inflected verbs produced in narratives. VAS production on the NAVS ASPT was predicted by the measure of narrative accuracy, but not complexity. Scores obtained on structured tasks were all highly correlated, with the exception of NAVI and NAVS ASPT.

Discussion. The results indicate significant relationships between measures of grammatical production ability from structured tasks and narratives in PPA. Measures of narrative accuracy predicted structured task performance across all domains, suggesting that the two methods may yield similar results in quantifying grammatical impairments. However, measures of narrative complexity predicted structured task performance only in the syntactic domain, suggesting that the complexity of verb phrases produced in narratives may not reflect impairments in VAS as measured by structured tasks. The study emphasizes the importance of quantifying grammatical impairments in PPA using both standard tests and analysis of spontaneous speech.

Distinct Pathophysiologic Pathways Underlying Variants of Primary Progressive Aphasia: A Resting State Functional Magnetic Resonance Imaging Study

Borna Bonakdarpour, Allan Wang, Marsel Mesulam, Robert Hurley

Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL

bbk@northwestern.edu

Objective: Primary progressive aphasia (PPA) is known to have three different variants: agrammatic, logopenic, and semantic. Previous studies have revealed association between specific areas of brain cortical thinning (atrophy) and aspects of language impairment in these three variants. However, there has been a paucity of studies that investigated changes in the language network physiology as measured by functional MRI (fMRI). The objective of the current study was to investigate changes in RSFC of the language network in PPA using our three-node (inferior frontal gyrus [IFG], middle temporal gyrus [MTG], and anterior temporal lobe [ATL] nodes) resting state fMRI model. Due to similarities of agrammatic and logopenic variants we combined them as a non-semantic group (PPA-NS). We anticipated decreased RSFC along the dorsal language stream in PPA-NS and decreased RSFC along the ventral stream in the semantic PPA (PPA-S) group.

Methods: Thirty three cognitively healthy individuals and 43 persons with PPA (18F/25M, age= 65.0 + 6.3), recruited through Northwestern PPA program, had resting state fMRI scans and were included in this study (28 PPA-NS, and 15 PPA-S). Western Aphasia Battery Aphasia Quotient was 76.52 (± 17.9)/100. Nodes of the language network were defined as spherical regions with a radius of 10 mm located in the left IFG, MTG, and ATL. RSFC between these nodes were measured in the PPA and the control groups. RSFC within IFG-MTG and MTG-ATL node pairs were compared across the PPA and control groups via *t*-tests.

Results: The PPA-NS group showed significant ($p=0.037$) decline in RSFC between the left IFG-MTG nodes ($r=0.23$) when compared to controls ($r=0.35$). In contrast, RSFC of the left MTG-ATL ($r=0.20$) did not significantly differ ($p=0.32$) from controls ($r=0.26$). In the PPA-S group, there was significant decline ($p=0.00002$) in RSFC between the left MTG-ATL nodes ($r=0.02$) as compared to the control group ($r=0.26$). In contrast, RSFC of the left IFG-MTG nodes ($r=0.22$) did not significantly differ ($p=0.11$) from controls.

Conclusions: The pattern of neural network breakdown underlying aphasia in PPA-NS and PPA-S were different and specific. In line with structural imaging studies, specific decrease in IFG-MTG connectivity in the PPA-NS group suggests a breakdown in the dorsal language stream associated with phonological and syntax processing. In contrast, decreased MTG-ATL connectivity in PPA-S group suggests a breakdown in the ventral language stream related to lexical/semantic processing. These results show that RSFC is sensitive to pathophysiologic changes in PPA. Our next step is to determine the degree by which physiologic changes contribute to symptoms as compared to the effect of cortical atrophy. Findings will have implications for planning of neuromodulatory interventions and also for measuring efficacy of therapeutic interventions.

Neural Network Underlying Abnormal Syntax Processing in Primary Progressive Aphasia: Evidence from Resting State Functional Magnetic Resonance Imaging

Borna Bonakdarpour, Allan Wang, Emily Rogalski, Robert Hurley, Marsel Mesulam
Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL
bbk@northwestern.edu

Background: Once attributed to Broca's area, there has been growing evidence that processing of syntax (grammar) relies on a network of regions located at the dorsal aspect of left sylvian fissure (dorsal language stream). In persons with primary progressive aphasia (PPA) brain cortical thinning within these regions is associated with difficulty in producing grammatical sentences (agrammatism). This however, has not been well investigated at physiologic large scale network level. In this study, we investigated the relationship between connectivity of dorsal language stream regions and sentence processing abilities in PPA using task-free fMRI. We hypothesized that processing of syntax would correlate with resting state functional connectivity (RSFC) within dorsal language network but not with the control non-language related networks.

Methods: Participants included 48 persons with PPA (Age= 64.92 ± 6.54 ; 23F/25M), who were recruited through Northwestern PPA program and had resting state functional MRI (fMRI) scans. Western Aphasia Battery Aphasia Quotient was 77.51 ± 17.20 (/100) and they scored 14.65 ± 6.64 (/30) on a combined test of grammatical processing (Northwestern Assessment of Verbs and Sentences, [NAVS]; and Northwestern Anagram Test, [NAT]). Using Pearson test, we investigated correlation between NAT-NAVS score and strength of RSFC between two 10 mm spherical nodes: the supramarginal gyrus (SM), and the inferior frontal gyrus pars opercularis (PO). We also investigated correlation between NAT-NAVS score and strength of RSFC in two non-language networks: (1) Network connecting right hemisphere counterparts of the PO and SM (contralateral) nodes; and (2) network connecting left PO/SM nodes and a ventral sensorimotor node.

Results: The RSFC between the left hemisphere PO and SM was found to correlate significantly with NAT-NAVS scores ($r= 0.409$, $p=0.0088$). This was in contrast to the contralateral RSFC between right hemisphere PO and SM, which did not correlate with NAT-NAVS scores ($r=-0.127$, $p=0.433$). Similarly none of the sensorimotor connections ($r= -0.09$, $p=0.580$ for OP, and $r=0.027$, $p=0.868$ for SM) correlated with NAT-NAVS results.

Conclusions: In persons with PPA, scores of syntax processing correlated with a left lateralized parieto-frontal network but not with its contralateral right hemisphere counterpart or with sensorimotor connections, confirming specificity of our finding. Historically processing of grammar was attributed to Broca's area (mostly PO). However, by providing physiologic evidence, our finding adds to a growing literature that supports involvement of a network (containing both PO and SM) in syntax processing. By providing targets for intervention, this study may be useful for guiding therapeutic neuromodulation of the language network (e.g. repetitive transcranial magnetic stimulation).

Poster 4

Memantine-Induced Chorea and Dystonia

Letizia Borges, Borna Bonakdarpour

Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL

legb16@gmail.com

INTRODUCTION: Memantine is rarely associated with myoclonus. Here, we present a case of a person with Dementia of the Alzheimer Type (DAT) who developed chorea and dystonia after memantine was switched from immediate release (IR) to extended release (XR) form. Chorea and dystonia have not been reported as a side effect of memantine. The case report proposes discuss possible underlying mechanisms for chorea and dystonia.

METHODS: Case Report

RESULTS: A 76-year-old woman who was diagnosed with DAT was started on memantine IR with no complications. Subsequently, when memantine IR was switched to XR, she developed chorea and dystonia. She was found to have been taking doubled dose of memantine XR due to a mistake in administration. Chorea and dystonia improved after memantine XR was discontinued.

DISCUSSION: Memantine is an uncompetitive N-methyl-D-aspartate receptor antagonist, however, it also has an indirect dopaminergic action at high concentrations. Chorea and dystonia in our patient was likely related to this dopaminergic effect. This case emphasizes the need to ensure proper administration of memantine XR when switching from IR to XR. With increasing use of memantine XR and switch from IR to XR, it is important that neurologists are aware of this potential error. It might be essential that a health care provider would actively monitor correct administration during this switch. Additionally, this report provides evidence that additional studies are necessary to understand dopaminergic effect of memantine.

Improving the Tool Kit for Characterization of A β Oligomers in Alzheimer's Disease Pathogenesis

Erika Cline, Arighno Das, Izolda Popova, Saad Mohammad, Owen Skinner, Kirsten Viola, Madeline Rollins, Lynn Zieske, Philip Compton, Neil Kelleher, Robert Vassar, William Klein
Northwestern University, Department of Neurobiology, Evanston, IL
erika.cline@northwestern.edu

Amyloid beta oligomers (A β Os) accumulate early in Alzheimer's disease (AD) and experimentally cause memory dysfunction and the major cellular pathologies associated with AD (e.g., tau abnormalities, synapse loss, oxidative damage, etc.). However, the structures of the A β O species most germane to AD pathogenesis are ill-defined. This uncertainty regarding the pathophysiologically relevant A β O structures has impeded therapeutic advances (e.g., high-profile failures of A β immunotherapies in clinical trials) and, consequently, diminished the perceived therapeutic value of A β . My long-term research goal is to elucidate the structural characteristics of A β Os that contribute to their role in the pathogenesis of AD. As a first step towards this goal, I have been working to develop improved methods for A β O stabilization, structural characterization, and quantification. This poster will present: (1) The development of an intramolecular cross-linking protocol, which locks A β in an oligomeric conformation. This technology has the potential to facilitate high-resolution structural characterization of A β Os and enable improvement of AD animal models induced by injection of stable A β Os. (2) An ultrasensitive immunoassay for A β O quantification that has enabled correlation of A β O levels in brain extracts of AD mouse models with A β O distribution in brain tissue, age, and cognition. This assay has the requisite sensitivity for A β O quantification in human brain extracts and CSF. (3) A human scFv antibody fragment specific for a small sub-population of synapse-binding A β Os. The specificity of this scFv, and others in our A β O-specific scFv library, makes them promising tools for characterization of individual A β O conformations, as well as AD therapeutics and diagnostics. Each of these new tools hold the promise to advance our knowledge of AD-relevant species of A β Os, with respect to their biochemical and biophysical nature and emergence in AD pathology. In light of the past failures of disease-modifying therapies, this knowledge will facilitate the development of more effective AD therapeutics, as well as diagnostics for early detection.

Poster 6

Improving Patient Satisfaction and Likelihood to Recommend

Kevin Connolly¹, Anthony Nowaske², Cheryl Brown², Nicole Wright², Megan Rising, M.A.²

¹*Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL*

²*Northwestern Medical Group, Neurobehavior and Memory Clinic, Chicago, IL*

matchu1@nm.org

OBJECTIVES

As part of the effort to achieve a "Patients First" mission at the Northwestern Medical Group (NMG), it is important to assess patients' perceptions of their care and understand what matters most to them. At NMG, this is achieved through Press Ganey patient satisfaction surveys. The Neurobehavior and Memory clinic of the Cognitive Neurology and Alzheimer's Disease Center (CNADC) decided to focus on the Likelihood to Recommend (LTR) metric as it is the closest measure of patient loyalty available to us in our patient satisfaction data. One of the primary referral sources for new patients come via word of mouth referrals, and the LTR score is a significant indicator of whether or not we have a favorable reputation.

METHODS

Several interventions were executed to improve patient satisfaction. Managing patient expectations was achieved by providing the patient with a comment card during the check-in process asking if there was anything the clinic staff could assist them with for the visit. The comment card followed the patient as they moved through their appointment to ensure that all parties involved in their care had a chance to view the comments. The practice manager then rounded with the patient at the end of their appointment to ensure all questions had been answered. Daily huddles were implemented to allow the clinic staff to assemble and look ahead on the schedule to anticipate the needs of patients coming in that day. A focus on professionalism and how it impacts patient scores paved the way for Environment of Care rounds, an effort that engages clinic and department leadership to assess the physical space and ensure that any concerns related to the patient and staff work areas are addressed. To keep clinic faculty and staff engaged in the LTR initiative, the practice manager compiles patient satisfaction and referral data and distributes them on a monthly basis in the form of an email bulletin. In this forum, positive recognition is used to motivate staff and providers. In addition to electronic bulletins, scores are reviewed in person at monthly clinical rounds with clinic staff in attendance.

RESULTS

At the close of the first quarter of the fiscal year (November), data from Press Ganey surveys found the CNADC with an overall LTR baseline score of 72%, representing 11.2 percentage points below target and ranking in the 13th percentile nationally. By the third quarter (March), we have exceeded the target and dramatically increased our scores to the 86th percentile with a LTR of 85.7%, marking an improvement of 13.7 percentage points from baseline. From January through March, the CNADC was the only NMG clinic to achieve 100% LTR each month.

CONCLUSION

These promising results suggest that the interventions implemented by clinic and department leadership, clinic staff, and providers were an overwhelming success in improving our patient satisfaction.

Psychological Well-Being in Cognitive SuperAgers and Non-Demented Elderly

Amanda Cook, Stephanie Kielb, Emmaleigh Loyer, Sandra Weintraub, M. Marsel Mesulam, Dan McAdams, Regina Logan, & Emily Rogalski
Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL
AmandaCook2017@u.northwestern.edu

Background: The Northwestern SuperAging Program seeks to identify factors that enable individuals over age 80 to perform at least as well as individuals 20-30 years their junior on tests of episodic memory. While psychological well-being reportedly declines after age 80, greater levels of psychological well-being positively correlate with cognitive performance and may thus contribute to successful cognitive aging in SuperAgers. The present study investigates whether psychological well-being and satisfaction with life can distinguish cognitive SuperAgers from same-age, cognitively average-for-age peers and from middle-age adults who share the SuperAgers' level of cognitive functioning.

Method: 30 SuperAgers (80-96 years-old), 11 cognitively average-for-age elderly (81-96 years-old), and 37 middle-age adults (54-59 years-old) with similar education levels completed the Satisfaction with Life Scale (SWLS) and Psychological Well-Being (PWB)-42 questionnaire. One-way ANOVAs with Bonferroni correction were used to compare the groups' responses on the SWLS and PWB subscales: Autonomy, Environmental Mastery, Personal Growth, Positive Relations, Purpose in Life, and Self-Acceptance.

Results: Both SuperAgers and cognitively average-for-age elderly adults endorsed greater Satisfaction with Life, Environmental Mastery, and Self-Acceptance compared to middle-age adults (p 's < 0.05). SuperAgers also endorsed greater levels of Positive Relations with others compared to cognitively average-for-age elderly (p < 0.05). Groups did not differ on other measures.

Conclusion: Results suggest that psychological well-being does not decline in cognitively average and above average elderly adults and may perhaps contribute to the maintenance of cognitive abilities in advanced age. Further, positive relationships with others differentiate cognitively-average elderly adults from SuperAgers and may thus be an important factor for exceptional cognitive aging.

A Modified-Sternberg Paradigm Measures Load and Delay Components of Working Memory in SuperAgers

Amanda Cook, Emmaleigh Loyer, Sandra Weintraub, Hans Breiter, M. Marsel Mesulam, Emily Rogalski, & James Reilly

Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL

AmandaCook2017@u.northwestern.edu

Objective: The Northwestern University SuperAging Program studies individuals over age 80 (SuperAgers) who perform at least as well as middle-age adults on tests of episodic memory in order to identify neurobiologic factors that contribute to successful cognitive aging. Previous research suggests that decline in working memory underlies age-related impairment in episodic memory, possibly due to reduced ability to hold information in working memory. Traditional working memory tasks do not differentiate components of working memory such as the amount of information held (load) and the duration over which it is held (delay). The present pilot study aimed to validate the use of a novel modified-Sternberg task that allows for the differentiation and quantification of working memory components in SuperAgers.

Method: Four SuperAgers (ages 83-86) and 6 cognitively average Middle-age Controls (ages 57-63) completed a novel computer-based modified Sternberg task that consisted of 4 blocks of 32 trials over which arrays of 1-7 boxes (load) were briefly presented. After a variable delay (1-10 seconds), a probe box appeared and subjects indicated whether the probe was in the same or different location as any box in the preceding array. Response accuracy (hit and false alarm rates), d-prime (sensitivity to detect a correct target among noise), and beta (decision threshold to report a signal) were calculated at each load, as was response time for correct response trials (correct hit or rejection). Repeated Measures General Linear Models were used to compare the groups on each measure.

Results: SuperAgers did not differ from Middle-age Controls with regard to response accuracy, d-prime, or beta (p 's > 0.05). As expected, both groups demonstrated an increase in false alarm rate and beta with increasing load (p 's < 0.001) as well as a decrease in d-prime (p < 0.001) and trend towards a decrease in hit rate (p = 0.14) with increasing load. Both groups demonstrated increased response time with increasing load (p < 0.001) yet SuperAgers were significantly slower overall (p < 0.01).

Conclusions: Preliminary results from a novel working memory task suggest that SuperAgers perform as accurately as younger adults on tests of working memory. While performance accuracy was similar between the groups, SuperAgers took longer to make their response, consistent with literature that documents age-related decline in processing speed. Slower response time may reflect a compensatory mechanism that supports the maintenance of cognitive abilities with increasing age. Overall, task demands appear appropriate for continued use in SuperAgers as a means of investigating components of working memory.

β - and α -Secretase Processing of Amyloid Precursor Protein in Human Central Nervous System: Implications for Alzheimer's Disease

Justyna A. Dobrowolska-Zakaria, PhD, and Robert J. Vassar, PhD

Northwestern University, Department of Cell and Molecular Biology, Chicago, IL

justyna.dobrowolska@northwestern.edu

The amyloid hypothesis proposes that increased production or decreased clearance of amyloid-beta ($A\beta$) leads to higher order amyloid structures, such as oligomers and plaques that initiate a cascade of events, culminating in neuronal death which manifests as Alzheimer's disease (AD). $A\beta$ is generated from the sequential cleavage of Amyloid Precursor Protein (APP) by β - and γ -secretase. APP, a transmembrane protein, may be processed in one of at least two pathways, and is initially cleaved by either α -secretase or β -secretase. α -secretase cleavage, which occurs more frequently under physiological conditions, precludes the formation of $A\beta$ and produces non-toxic soluble APP- α (sAPP α). Alternatively, in the β -secretase pathway APP is first cleaved by β -secretase releasing soluble APP- β (sAPP β), and is subsequently cleaved by γ -secretase producing $A\beta$ [1]. Some studies found β -secretase protein and sAPP β are increased in CSF and post-mortem AD brain [2-4]. My previous data demonstrate an increase in the CSF sAPP β to sAPP α ratio in AD subjects versus cognitively normal age-matched controls, indicating a shift toward β -secretase processing of APP under pathophysiological conditions [5]. Further, there is a high positive correlation between sAPP β and $A\beta$ concentrations in human CSF. Additionally, a recent stable isotope labeling kinetics (SILK) study suggests that about 50% of AD patients may overproduce $A\beta$ [6]. Taken together, these findings propose increased β -secretase activity may cause increased $A\beta$ in at least a subpopulation of AD patients. However, this has not been previously directly assessed.

Using my previously developed highly sensitive SILK/immunoprecipitation/liquid chromatography-mass spectrometry methods [7] I am quantifying sAPP β and sAPP α kinetics in cerebrospinal fluid from 100 human subjects (AD) and cognitively normal age-matched controls, in order to determine β - and α -secretase activity in the human CNS. We hypothesize that approximately half of AD patients overproduce $A\beta$ due to increased β -secretase activity, while the other half have decreased $A\beta$ clearance. By directly measuring production rates of sAPP β and sAPP α , we will determine if, and by how much, β -secretase activity is increased in AD subjects, and this would allow for characterization of AD sub-populations most likely to benefit from β -secretase inhibitor treatment. These results will elucidate human CNS APP physiology and pathophysiology in AD. Further, outcomes of this study may prove useful for measuring pharmacodynamic effects of candidate therapeutics, such as β -secretase inhibitors. β -secretase is currently a high priority target for AD, and results of altered β -secretase activity in AD are critical for understanding AD pathophysiology and the development of disease modifying therapeutics.

References [1] G. Thinakaran, E. H. Koo, J Biol Chem 283, 29615 (Oct 31, 2008). [2] H. Fukumoto et al., Am J Pathol 164, 719 (Feb, 2004). [3] H. Zetterberg et al., Arch Neurol 65, 1102 (Aug, 2008). [4] A. Gabelle et al., Brain Res 1357, 175 (Oct 21, 2010). [5] J.A. Dobrowolska et al., PLoS One 9: e89998 (March 2014) [6] K. G. Mawuenyega et al., Science 330: 1774 (Dec 2010) [7] J. A. Dobrowolska et al., J Neurosci 34: 8336 (June 2014)

Preserving Relationships: Using Dyadic Storytelling as a Strengths-Based Approach

Lauren Dowden, Mary Rastetter, Darby Morhardt

Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL

lauren.dowden1@northwestern.edu

INTRODUCTION: Dementia affects both the person with the diagnosis (PWD) and their family. As the disease progresses, the family often takes on many caregiving duties and the relationship can devolve into “patient and caregiver”. Dyadic approaches have produced positive outcomes such as identifying and building the couple’s strengths, improved communication between caregiver and the PWD, and improvements in caregiver well-being (Scherrer, Ingersoll-Dayton & Spencer, 2013). The CNADC developed a storytelling pilot workshop with two persons with dementia and their spouses to help them co-create a story that they shared at the 2014 Alzheimer’s Day. Participants noted anecdotal therapeutic benefits from co-creating a story as it invited them to talk about moments in their life that they may not have done otherwise, reminisce about their shared history, and connect with other families in a group setting.

METHODS: In 2015, the CNADC received a Northwestern University Alumnae Grant to study this dyadic storytelling intervention. The project objective was to explore the impact of the dyadic storytelling workshop utilizing qualitative and quantitative measures examining: a) interpersonal communication, b) preservation of relationship, c) coping with cognition, behavior and mood changes, and d) social isolation/social engagement. Another 8-week storytelling workshop was offered, building upon the pilot program and developing a curriculum. The two family dyads living with dementia – one married couple and one parent/child dyad - met for 8 weeks for 1.5 hours, and through in-class writing exercises, homework assignments, and “witness” feedback, the families co-created their shared story that they presented in the final session. Looking at the storytelling process from a strengths-based narrative perspective, the dyads were invited to build on their strength and resilience as a “couple” as they reminisced about their relationship through the lens of a shared history. In addition to the workshop results, previous storytelling workshop couples have presented their stories to over 1000 medical and healing professionals, students, scientists and community members. Evaluation outcomes have been recorded.

RESULTS: Preliminary findings from the 2015 workshop demonstrate benefits for families as they navigated the progressive changes of the disease, built on historical strengths and resilience in their relationship, and addressed role changes. The strengths of the couples were further fortified by the team of “witnesses” who offered feedback and moments of connection validating their experience. Lastly, sharing stories with others appears to deepen the understanding of the lived experience of families with dementia from both the perspective of the listener and the storytellers themselves.

CONCLUSION: The symptoms of dementia including Alzheimer’s disease can be stigmatizing for both the person with dementia and their loved ones. The dyadic storytelling process invites the pair as a unit to be the focus of support, building upon the strengths of their relationship, and offering families an opportunity to connect and learn from others living with a diagnosis in a safe environment.

Dementia and Hospitalization: The Experience of Two Families

Anya Drew, MSW; Lauren Dowden, MSW, LSW; Darby Morhardt, PhD, LCSW
Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL
adrew1@luc.edu

Significance: Individuals with Alzheimer's or related dementias are twice as likely to be hospitalized and 26% of these hospitalizations are due to a fall and resulting trauma (Alzheimer's Association, 2016). Research on dementia and hospitalization has shown there is a lack of knowledgeable healthcare staff regarding dementia and dementia care. The experience of hospitalization for individuals with dementia often results in unsatisfactory care and poor health outcomes (Jirik & Morhardt, 2015). Descriptions of support group members' emotionally distressing experiences in a hospital setting prompted the first author to probe this issue further.

Methods: A semi-structured in-person interview was conducted with a purposive sample of two families: one spouse and one adult child caregiver using open-ended questions. The interview lasted approximately one hour. Field notes were taken during the interview and immediately following. Questions included: 1) Can you tell me about a time when your loved one was taken to the emergency room or hospital?; 2) After the experience, was there anything you wish had occurred differently?; 3) Do you have any advice for a caregiver who might find themselves in a similar situation?; and 4) Do you have any advice for hospital staff who might find themselves in a similar situation? Field notes were read and discussed among authors to highlight emerging themes.

Results: There were several themes between the two families. In both case studies, the individual with the diagnosis experienced a distressing fall while in the presence of a caregiver that involved head trauma. Both individuals were taken to an emergency room where the hospital staff introduced an intravenous apparatus; that is, an IV or catheter. Both individuals consistently attempted to pull out the apparatus and were restrained. In both instances the caregiver, upon learning of the patient's attempts to remove the IV or catheter, had to repeatedly explain the patient's dementia diagnosis to multiple hospital staff. While both caregivers felt as though their loved one ultimately received good care, they expressed frustration regarding the lack of communication of the patient's dementia diagnosis among the clinicians. Both caregivers expressed feelings of distress due to their loved one's vulnerability in this situation, namely, their inability to advocate and speak on their own behalf. The caregivers believed their presence was vital to their family member getting appropriate attention and care within the hospital setting.

Conclusion: Overall, in these two case examples of a person with dementia requiring hospitalization, reminders to hospital staff about the patient's dementia diagnosis and limitations were needed and caregivers stated their need to consistently advocate for their loved one regarding their dementia diagnosis. It was necessary for a family member or family friend to inform medical staff of the person's diagnosis to help explain behavior and advocate for the patient with dementia. It is possible to assume that the patient's care could have been compromised if the caregiver had not been present. Further research is needed to establish best practice models for caring for persons with dementia in the hospital setting.

Alzheimer's Disease Facts and Figures (2016). Alzheimer's Association, Alzheimer's & Dementia, 12(4).

Jirik, S & Morhardt, D. (2015). Dementia and Hospitalization: An Overview of the Problem and Movement Toward Dementia-Friendly Care. The 21st Annual Alzheimer Day Conference Abstracts, Cognitive Neurology and Alzheimer's Disease Center, Northwestern University Feinberg School of Medicine.

Effect of Norharmane on Memory Retention of Streptozotocin-Induced Alzheimer's Rats Model on Passive Avoidance and Morris Water Maze Test

M Esmaeili, Z Charmchi, B Heydari

Northwestern University, Department of Neurology, Les Turner ALS Research Lab, Chicago, IL

Qazvin University of Medical Science, Department of Medicine, Qazvin, Iran.

zeinabcharmchi@gmail.com

Alzheimer's disease (AD) is the most common neurodegenerative disease worldwide. Present available pharmacological treatments can only slow down the progression of symptoms but cannot treat the disease. It is well established that benzodiazepines and related agonists at the benzodiazepine site of GABA receptor present anxiolytic and amnesic properties, whereas β -carboline alkaloids exert anxiogenic and learning-enhancing actions. The goal of the present study was to investigate the therapeutic efficacy of Norharmane (NH) as a Benzodiazepine receptor inverse agonist on learning and memory of the streptozotocin (STZ) rat model of AD. 40 male Wistar rats (200–300 gr), were divided into: control, STZ+ vehicle and STZ+ NH groups. For induction of AD, STZ (3 mg/kg, i.c.v, 10 μ l each) was administered bilaterally into lateral ventricles. Two weeks later rats in the vehicle and NH groups received ethanol (0.2 ml) or NH (1, 2, and 4 mg/kg, i.p.) for 10 days before training. Learning and memory performance of the rats were evaluated in the Morris water maze (MWM) and shuttle -box separately starting 24 h after the last (11th day) injection of NH or vehicle. An i.c.v. injection of 3mg/kg STZ significantly increased escape latency, distance and number of crossed quadrants in comparison with the control group ($P < 0.01$). Pretreatment with low doses of NH (1, 2 mg/kg) protected learning and memory against impairment induced by STZ whereas pretreatment with high doses of NH (4 mg/kg) led to further impairment of learning and memory in the STZ rat model of sporadic AD. In the MWM test there was no significant difference between the control and STZ+ NH (2 mg/kg) group, whereas the difference between the control and the other STZ-induced AD groups in the majority of training days was significant. Also, the percentage of time spent and distance swimming in the target quadrant in the probe test in the STZ+ NH (2 mg/kg) group rats similar to control groups rats were significantly higher than those in the other STZ-induced AD groups. In the Passive Avoidance test, the step-through latency (STL) in the STZ+ NH (2 mg/kg) group rats similar to the control group was significantly higher than those in the other STZ-induced AD groups ($P < 0.001$). Our data suggested that administration of NH in low doses (1, 2 mg/kg), improves learning and memory retrieval in the STZ rat model of AD, whereas in high doses (4 mg/kg), it further worsen the learning and memory. According to these findings, NH as an inverse agonist of benzodiazepine receptors in low doses may be effective in the treatment of Alzheimer's disease by its ability to influence the GABAergic system.

A Novel Technique to Boost Memory During Sleep

Kelsey Gradwohl, James W. Antony, Jessica D. Creery, and Ken A. Paller

Northwestern University, Department of Psychology, Evanston, IL

KelseyGradwohl2012@u.northwestern.edu

The ability to retain and recall information is essential for day-to-day function. Memory abilities of this sort may depend critically on a consolidation process that transpires regularly during sleep and that has been linked with certain aspects of sleep physiology such as slow waves and sleep spindles (burst of oscillatory neuroelectric activity at .5-4 Hz and 11-15 Hz, respectively). Many of the relevant neurophysiological details remain to be worked out. The present study aimed to test the hypothesis that sleep spindles play a causal role in memory consolidation. We systematically manipulated the occurrence of sleep spindles during slow-wave sleep via oscillating stimulation, while simultaneously promoting memory processing using learning-associated sounds (i.e., targeted memory reactivation). Oscillating environmental sounds were presented at a low intensity so as to avoid arousal from sleep. Prior to sleep, participants memorized 54 sound-picture pairs, each consisting of a picture of a famous person or landmark and an unrelated sound. Next, participants learned the distinct location of each picture on a computer screen. In this way, participants memorized 54 sound-picture-location associations (e.g., “meow” + Obama’s face + an upper left location). Following learning, participants took a 90-min nap during which 17 of the sounds were played in their original form, 17 were played in an altered form shown to induce sleep spindles (13.5-Hz amplitude-modulated sounds), and 17 were not played. EEG recordings were made during both the learning and the nap phases. Subsequent testing of location recall revealed that memory was most accurate when sounds were played during sleep with the 13.5-Hz oscillation. These results thus provide initial evidence that sleep spindles represent a neurophysiological process that can be promoted noninvasively via auditory stimulation and that can operate to improve memory storage during sleep. In the future this technique may be utilized when devising methods for memory enhancement in those with certain memory deficits.

Acknowledgement: Partially supported by a Research Grant from the University Research Grants Committee at Northwestern University, and by the Army Research Office under Cooperative Agreement Number W911NF-16-2-0021. The views and conclusions are those of the authors and should not be interpreted as representing the official policies, either expressed or implied, of the Army Research Office or the U.S. Government.

Ante-Mortem Structural MRI Markers for Post-Mortem Pathology for TDP-43 and AD in the Hippocampus

Veronika Hanko¹, Kathryn I. Alpert¹, Kristen N. Warren², Julie A. Schneider³, Konstantinos Arfanakis^{3,4}, David A. Bennett³, Lei Wang^{1,5}

¹*Department of Psychiatry & Behavioral Sciences, Neuroimaging and Applied Computational Anatomy Laboratory, Northwestern University Feinberg School of Medicine, Chicago, IL*

²*Interdepartmental Neuroscience Program, Northwestern University, Chicago, IL*

³*Rush Alzheimer's Disease Center, Rush University Medical Center, Chicago, IL*

⁴*Department of Biomedical Engineering, Illinois Institute of Technology, Chicago, IL*

⁵*Department of Radiology, Northwestern University Feinberg School of Medicine, Chicago, IL*

veronika.hanko@northwestern.edu

Background: Despite advances in the development of biomarkers for early detection of AD dementia, accurate antemortem diagnosis remains a challenge since a variety of neuropathologic disease states can coexist and contribute to the AD dementia syndrome. Several studies have utilized structural MRI to classify dementia based on patterns of atrophy, but few have confirmed their results with neuropathologic indices. Here we report a neuroimaging study correlating ante-mortem hippocampal deformity with regional AD and TDP-43 pathology burden.

Methods: Ante-mortem T1-weighted MPRAGE images were collected from 42 subjects from the Rush Alzheimer's Disease Center's Memory and Aging Project and Religious Orders Study (1,2). After each subject's death, autopsy was performed and neuropathologic burden was quantified for PHFtau tangles, β -amyloid, and TDP-43 by immunohistochemistry. We generated the hippocampal surface and corresponding subfields (whole hippocampus, CA1, CA2-4+GD, subiculum) in all subjects using FS-LDDMM (3) with atlas selection. Hippocampal shape measures for overall hippocampus and each subfield were obtained using principal component analysis. Multiple linear regression models on the shape measures was used to correlate shape of overall hippocampus and each subfield with pathology measures while accounting for covariates. To localize these relationships on specific hippocampal surface locations, vertex-wise multivariate multiple regression models were constructed.

Results: Significant relationships existed between higher global PHFtau tangle burden and inward surface deformity in CA1 and CA2-4+GD, between higher β -amyloid load and inward subiculum deformity (trend), with differing patterns along the hippocampal surface. No significant relationship between surface shape and TDP-43 pathology was observed.

Conclusion: PHFtau tangles and β -amyloid AD pathology burdens were related to specific regional hippocampal surface deformity, with differing patterns on the surface. We did not find associations between TDP-43 inclusions and surface deformity. These findings provide support that specific patterns of hippocampal atrophy may be biomarkers for specific AD pathologies. These results need to be further validated in larger samples.

Practical Implications: Structural MRI may provide a non-invasive way to identify which underlying neuropathologic disease states are at play in individuals with early stage dementia.

1. Bennett DA, Schneider JA, Buchman AS, Barnes LL, Boyle PA, Wilson RS. Overview and findings from the Rush Memory and Aging Project. *Curr. Alzheimer Res.*, 9(2012): 646-663.

2. Bennett DA, Scheider JA, Arvanitakis Z, Wilson RS. Overview and findings from the religious orders study. *Curr. Alzheimer Res.*, 9(2012): 628-645.

3. Khan AR, Wang L, & Beg MF. FreeSurfer-initiated fully-automated subcortical brain segmentation in MRI using Large Deformation Diffeomorphic Metric Mapping. *NeuroImage*, 41(3), 735-46.

Alterations in Excitability of CA1 Neurons from Pre-Plaque to Plaque-Burdened Ages in 5xFAD Mice

Ellie Hong, Arin Pamukcu, Savio Chan

Northwestern University, Interdepartmental Neuroscience Program, Chicago, IL

ellie.hong@northwestern.edu

Altered glutamate signaling has been proposed to underlie neuronal dysfunction seen in Alzheimer's disease (AD). In particular, aberrant glutamate homeostasis can lead to excessive glutamate receptor activation and cause phenomenon seen in AD such as circuit hyperactivity, exacerbated beta-amyloid deposition, and neuronal loss. As cognitive deficits in AD correlate most closely with synaptic loss in the hippocampus, properties of the Schaffer collateral-CA1 synapse have been widely studied. In contrast, the intrinsic properties of hippocampal CA1 neurons have been underexamined. Using whole cell patch-clamp recordings from CA1 pyramidal neurons in wildtype and 5xFAD mice on a C57BL/6 background, we determined differences in excitability at time points that span pre-plaque to plaque-burdened ages (3, 6, 9 mo). We found a progression from low excitability at 3 mo to high excitability at 9 mo in the wildtype mice. In 5xFAD mice, however, CA1 neurons at all time points exhibited high excitability. Changes in the progression of CA1 excitability between wildtype and 5xFAD mice can offer a deeper understanding of the course of neuronal dysfunction in AD.

Acetylcholinesterase-Positive Cortical Pyramidal Neurons: Emergence in Adult Human Life and Down-Regulation in Cognitively Average Elderly and Elderly with Superior Memory Capacity

Monica Janeczek, Mehrnoosh Samimi-Gharai, Sandra Weintraub, Emily Rogalski, Eileen Bigio, M.-Marsel Mesulam and Changiz Geula

Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL

c-geula@northwestern.edu

We have described an extensive network of cortical pyramidal neurons in the human brain that display an acetylcholinesterase (AChE)-rich pattern by adulthood, but not during childhood. The emergence of these neurons in young adulthood, a time associated with intellectual maturation, and their greater prominence in humans than in other species, led us to hypothesize that this neuronal system may be involved in the development and maintenance of higher cognitive processing in man. In the present set of experiments, we investigated the number and staining intensity of AChE-positive cortical pyramidal neurons in children/teens (0-19 years, n=4), normal young adults (20-64 years, n=8), cognitively average elderly (65-95 years, n=15), and cognitively superior elderly (SuperAgers) defined as individuals above 80 years with performance on tests of memory equal to or better than 50-65 year-olds (n=4). A sensitive histochemical procedure was used to visualize AChE-positive cortical pyramidal neurons. Density of these neurons was determined in the supplementary motor cortex (Brodmann area 6), prefrontal cortex (area 9), middle temporal gyrus (area 21), inferior parietal lobule (area 39-40) and the anterior cingulate cortex (area 24) using modified stereologic techniques in three representative sections through each cortical area. Staining intensity of AChE reaction product was determined using optical density measures. The numerical density and staining intensity of AChE-positive pyramidal neurons in young adult brains was higher when compared with brains of children/teens (34.5% and 32.6% respectively). In young adult and normal elderly, area 6 had the highest density and staining intensity of AChE-positive pyramidal neurons. A consistent decrease in the density of these neurons was observed in the normal aged (5.1-20.8%; $p>0.05$) and a further decrease in SuperAgers (19.8-66.7%; statistically significant in areas 6, 9 and 40; $p<0.01-0.05$). The staining intensity of AChE reaction product displayed a similar decrease in the normal aged (9.15-28.6%; statistically significant in areas 6, 40 and 24; $p<0.01-0.05$) and a further decline in the SuperAged (10.0-41.1%; statistically significant in areas 9 and 21; $p<0.01-0.05$). These findings suggest significant plasticity of cortical pyramidal neurons during the aging process. Decreased cortical AChE, and the potential resultant increased availability of acetylcholine, a neurotransmitter involved in the cognitive processing of memory and attention, may help maintain cognitive function in normal elderly and contribute to enhanced cognitive performance in SuperAgers.

Sources of Support: National Institute on Aging (AG045571) and The Davee Foundation. Part of the tissue used in these experiments was obtained from the Brain Bank of the National Institute on Aging Northwestern University Alzheimer's Disease Center (AG013854).

Molecular Mechanisms of the Alzheimer's Risk Gene Unc5c in Neuronal Death

Devi Krishna Priya Karunakaran, Jasvinder K. Atwal, Robert J. Vassar

¹Northwestern University, Department of Cell and Molecular Biology, Chicago, IL

²Genentech, Department of Neuroscience, South San Francisco, CA

devi.karunakaran@northwestern.edu

Significance: The mechanism of neuronal death in AD is unknown. 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, and identify novel therapeutic targets for reducing neuron loss in AD and potentially other neurodegenerative diseases.

Purpose: 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, Unc5c T835M could accelerate neuronal death via enhanced activation of the Unc5c death domain.

Hypothesis: Unc5c T835M mutation will exacerbate neuronal death in the 5XFAD brain via increased sensitivity to A β -induced neurotoxicity and Unc5c death domain activation.

Methodology: We will employ the mouse knock in (KI) model of Unc5c T85M that we will cross with our 5XFAD mouse model of amyloid pathology and robust neuron loss. We will investigate mechanisms of cell death in 5XFAD; Unc5c T835M KI mice by behavioral, biochemical, and cellular approaches, and RNA deep sequencing (RNAseq). We will translate our murine findings to human AD by validating the activation of Unc5c-related cell death molecules in AD brain samples.

Conclusions: Immunohistochemistry (IHC) using the neuronal marker NeuN was performed on brain sections from 2-month old WT and KI homozygous animals, showing no overt histological differences between the genotypes. Also, TUNEL staining was performed to assess the neuronal cell death, showing no difference between the WT and KI. Overall, our preliminary 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, suggesting that the stress in the form of 5X FAD transgene might exacerbate neuronal cell death in these KI animals.

Objective Cognitive and Functional Loss and Dementia Risk in Subjective Cognitive Decline

Stephanie Kielb, Emily Rogalski, Sandra Weintraub, Alfred Rademaker

Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL

StephanieKielb2012@u.northwestern.edu

Objective

Subjective cognitive decline (SCD) is common in cognitively normal for age individuals but is not well understood. We analyzed SCD in relation to [1] longitudinal cognitive scores, [2] functional activities of daily living, and [3] incidence of mild cognitive impairment (MCI) and dementia in a large, longitudinal dataset from the National Alzheimer's Coordinating Center.

Participants and Methods

The sample included participants who were over age 65, designated as having "normal cognition" (CDR=0, MMSE>26), with at least two annual neuropsychological evaluations (mean=4.5) and no more than "mild" baseline depression (GDS<8/15). SCD was based on the single question, "Does the subject report a decline in memory relative to previously attained abilities?" at baseline (no=763, yes=3152). T-tests and Chi-square analyses were used to compare groups on average rates of change (best linear unbiased predictors) on 8 neuropsychological tests, total baseline Functional Assessment Questionnaire scores, and incidence rates of MCI and dementia over a five-year period.

Results

Compared to the group without SCD, the group with SCD had greater decline in processing speed (Coding, Trails A), naming (Boston Naming Test), and executive attention (Trails B), reduced episodic memory practice effects (Logical Memory Immediate and Delayed Recall) (all $p < 0.005$), more restrictions in independent living abilities at baseline ($p < 0.001$), and higher five-year incidence of both MCI (17% v 12%) and dementia (6% v 4%, both $p < 0.05$).

Conclusions

Results support the hypothesis that SCD may be a harbinger of cognitive decline and dementia. In a sizable sample of cognitively normal older adults, those with SCD showed subtle weaknesses in longitudinal cognitive performance and independent living abilities and were more likely to develop MCI and dementia. Reduced psychomotor speed and a lack of episodic memory practice effects may be objective cognitive markers related to SCD.

Asymmetric Distribution of Activated Microglia in a Left-Handed Patient with Primary Progressive Aphasia, TDP-43 Pathology and Right Hemisphere Language Dominance

Garam Kim, Shahrooz Vahedi, Sandra Weintraub, Eileen Bigio, Marsel Mesulam, & Changiz Geula
Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL
gkim@northwestern.edu

Primary progressive aphasia (PPA) is a neurodegenerative clinical dementia syndrome characterized by language deficits as the most salient clinical feature and atrophy in the perisylvian language network in the dominant hemisphere (usually the left). The asymmetric nature of the language network and focal atrophy render PPA an excellent model for investigation of the relationships between the regional distribution of pathologic markers, cortical atrophy and clinical phenotype. The subject in this study was a left-handed patient with PPA in whom the language network was lateralized to the right hemisphere as indicated by functional MRI before death. In a preliminary stereological analysis we had observed significantly high densities of TDP-43 inclusions in the superior temporal gyrus (STG) and the inferior temporal gyrus (ITG), with asymmetry favoring the right hemisphere, matching the patterns of atrophy as seen by structural MRI. The next highest density of TDP-43 inclusions was observed in other language-related cortical areas such as inferior frontal gyrus (IFG), inferior parietal lobule (IPL) and middle frontal gyrus (MFG, area 9), but without hemispheric asymmetry. The lowest density of TDP-43 inclusions was detected in the memory related area entorhinal cortex (ERC). In this study, an antibody to HLA-DR was used to obtain measures of activated microglia bilaterally, and to determine concordance with TDP-43 inclusion density and cortical atrophy. Unbiased stereological techniques were used to quantify activated microglia in IFG, MFG, IPL, STG, ITG, and ERC. Activated microglia were found in relatively high density in all cortical areas, with slightly lower density in ERC. Significantly, microglial density displayed substantial asymmetry favoring the right hemisphere in all cortical areas. However, this asymmetry was greatest in STG and ITG, matching the asymmetry in TDP-43 inclusions. These findings suggest that microglial activation does not share a linear relationship with the density of TDP-43 inclusions. However, the two pathological markers share a pattern of greatest asymmetric distribution in the same cortical areas and display concordance with the PPA clinical phenotype and patterns of atrophy.

Time-Dependent Formation and Disappearance of TDP-43 Inclusions in a Conditional Transgenic Mouse Model of FTLD

Lokesh Kukreja¹, Garam Kim¹, Katherine Sadleir², Lei Wang³, Hongxin Dong³, John Csernansky³, M-Marsel Mesulam¹, Robert Vassar², Changiz Geula¹

¹ *Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL*

² *Northwestern University, Department of Cell and Molecular Biology, Chicago, IL*

³ *Northwestern University, Department of Psychiatry and Behavioral Sciences, Chicago, IL*

lokesh.kukreja@northwestern.edu

Dementias caused by Frontotemporal lobar degeneration (FTLD) constitute the third most prevalent dementia, after those caused by Alzheimer's disease and Lewy bodies, and are among the most prevalent dementias of early-onset. The vast majority of these cases contain abnormal precipitates of a phosphorylated and mislocalized form of the Tar DNA/RNA-binding protein-43 (TDP-43). Moreover, overexpressing wild-type or mutant human TDP-43 gene in transgenic animals results in the formation of inclusions and neuronal loss, which have led to the conclusion that TDP-43 pathology leads to FTLD. To directly investigate the temporal sequence of the appearance of TDP-43 inclusions and its relationship to pathology, we employed a conditional transgenic mouse line in which expression of wild-type human TDP-43 is under the control of tetracycline operator sequences. In this study, transgene expression was switched off from birth until weaning age by doxycycline treatment in the mouse diet in order to avoid previously reported complex phenotypes of early neuronal development. In accordance with previous findings, the induction of human TDP-43 recapitulated features of FTLD-TDP, including the formation of phospho-TDP-43 neuronal cytoplasmic inclusions and progressive neurodegeneration. Our immunohistochemical analyses using an antibody that recognizes TDP-43 phosphorylated at Ser-403/404 revealed that inclusions appear as early as 5 days following TDP43 transgene expression. Mice which express the transgene for 10 days show a moderate density of inclusions. The inclusions appear to peak by 14 to 19 days post-transgene expression and decline rapidly thereafter. At these early days of TDP-43 transgene expression, the inclusions are present across frontal, parietal, and temporal cortical areas, and the hippocampus. While inclusions were absent at 8 weeks and 24 weeks of TDP-43 transgene expression, qualitative analysis showed severe neuronal loss in the dentate gyrus. However, the dentate gyrus contained among the lowest densities of inclusions. Thus, the density of TDP-43 inclusions does not directly correlate with neuronal loss in this animal model. It is likely that intracytoplasmic accumulation of TDP-43 oligomers plays a more direct role in neuronal loss and perhaps explains neurodegeneration in the absence of inclusions. Our findings suggest that this TDP-43 mouse model might provide critical information towards understanding how TDP-43 aggregation is linked to neurodegeneration and behavioral deficits in FTLD.

Verbal and Non-Verbal Auditory Processing Impairments in Primary Progressive Aphasia: An Event-Related Potential Investigation

Okkes Kuybu, M-Marsel Mesulam, Emily Rogalski, Robert Hurley

Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL

hurley@northwestern.edu

Primary progressive aphasia (PPA) is a disorder of declining language caused by neurodegenerative disease. As an aphasic syndrome, auditory word processing is impaired in PPA, but previous behavioral results (Goll JC, 2010) showed that processing of object sounds (e.g. a dog's barking) can also be abnormal in PPA, suggesting that auditory agnosia often accompanies aphasia in PPA. In this study we investigated the processing of complex non-verbal and verbal sounds in 12 patients with PPA and 13 healthy age-matched controls, at both the behavioral and electrophysiological levels. Participants completed a test in which they first heard a sound, which was either verbal (the name of the object, e.g. "dog) or non-verbal (the sound the object makes, e.g. "barking"), followed by a picture, and then judged whether the sound and picture matched. Behavioral results showed that PPA patients were slower and less accurate at this task, in both the verbal and non-verbal conditions. Electrophysiological activity was also examined during the task via the event-related potential (ERP) technique, in which electrical activity on the scalp is measured in response to stimuli. The PPA patients generated lower amplitude N400 ERPs than controls in both conditions, providing further electrophysiological evidence that both verbal and non-verbal auditory processing is impaired in PPA. This suggests that patients with PPA often have a secondary auditory agnosia in addition to aphasia. Future studies can help determine whether auditory agnosia in PPA has an apperceptive (sensory) or associative (conceptual) basis.

Functional Changes of the Principal Neurons of the Lateral Entorhinal Cortex in Learning and Aging

Carmen Lin, M Matthew Oh, John Disterhoft

Northwestern University, Department of Physiology, Chicago, IL

CarmenLin2018@u.northwestern.edu

Aging is often associated with learning and memory impairments. Yet, some aged individuals remain free of any impairment. Numerous studies have sought to understand the neurobiological mechanisms that underlie the aging-related impairments and what separates those with impairments (aged impaired--AI) from those without (aged unimpaired--AU). The majority of these studies, however, have focused mainly on the hippocampus, an important neural substrate for learning and memory. The entorhinal cortex (EC) is another important neural substrate for learning and memory, as it serves as the relay station for information flow between cortical regions and the hippocampus. The EC is not only an important site for learning and memory, but is also highly susceptible to aging-related changes. For example, Alzheimer's disease, a neurodegenerative disorder whose major risk factor is increasing age, initially manifests itself within the EC. Understanding the mechanism within the neurons of the EC that support learning (e.g. in Y and AU animals) and how these mechanisms can go awry in AI animals will therefore provide a medium by which potential therapeutics for alleviating aging-related learning deficits may be developed. Whole cell current clamp recordings were performed on fan cells in the lateral entorhinal cortex of young adult (3-6 month old) and aged (27-31 month old) male F1 F344xBN rats. Fan cells are responsible for the perforant path projections, which project to the dentate gyrus and make up the first leg of the trisynaptic circuit in the hippocampus. Measures of intrinsic excitability include the postburst afterhyperpolarization (AHP) and accommodation. Preliminary data suggests that fan cells from aged animals are less excitable relative to their young counterparts. This is in line with previous studies that show that pyramidal neurons in the CA1 hippocampal neurons from aged animals are less excitable than neurons from young adult animals. A decrease in CA1 neuronal excitability in certain aged animals has been shown to underlie the learning deficits observed. These data therefore suggest that a decrease in excitability within the EC may also underlie aging-related learning deficits.

Cognitive Neurology & Alzheimer's Disease Center (CNADC) Clinical Trials 2016

M.-Marsel Mesulam MD, Sandra Weintraub PhD, Borna Bonakdarpour MD, Kristine Lipowski MA, CCRC, Jordan Robson
Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL
k-lipowski@northwestern.edu

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 Disease Collaborative Studies (ADCS) group, 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 CNADC 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 study that will run in parallel to A4. Participants will be followed for 3 years and will receive another PET scan at the end of the study. **3) CONNECT**: This is a Phase IIa study that 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. Screening will occur over six weeks followed by a 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 amnesic 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. All participants will receive insulin for the remaining 6 months of the study. **5) Alzheimer's Disease Neuroimaging Initiative – 2 (ADNI2)**: This study is designed to identify biomarkers that may be useful in the diagnosis of early AD, by examining annual MRIs, PET scans, lumbar punctures, blood tests and cognitive assessments in AD, early Mild Cognitive Impairment (eMCI), late Mild Cognitive Impairment (lMCI), healthy control subjects, and control subjects with significant memory concerns (SMC).

Connect Trial for Alzheimer's Disease

Borna Bonakdarpour, MD, Kristine Lipowski, MA, CCRC, Jordan Robson

Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL

k-lipowski@northwestern.edu

This is a Phase IIa proof of concept study that will evaluate whether an investigational medicine called AZD0530 (Saracatinib) will slow progression in early- to mild-stages of Alzheimer's disease (AD). Saracatinib inhibits FYN kinase and decreases formation of toxic phosphorylated tau protein in nerve cells threatened by Alzheimer's pathology. Based on animal studies Previously, Saracatinib has been shown to be effective in delaying neuropathologic consequences of Alzheimer's disease. A Phase I trial of 187 individuals concluded that the drug was generally safe and well tolerated. One hundred and fifty-two participants will be randomly assigned to receive either an active dose of AZD0530 or a dose of a placebo. Screening will occur over six weeks followed by a 52-week treatment period. The study requires a minimum of four visits during the screening and 13 to 14 visits during the course of the treatment. Participants will be monitored by the study team closely for the duration of the study. Stabilization of the disease will be evaluated through measurement of metabolic brain activity using fluorodeoxyglucose positron emission tomography (FDG-PET). Memory and cognitive measures (ADAS-Cog, ADCS-ADLs, and CDR) also will be evaluated during regular visits to power a subsequent Phase III trial. Since inclusion criteria is based on biomarker diagnosis of Alzheimer's disease using Amyloid PET scan, individuals with atypical forms of Alzheimer's disease are eligible for this trial also. Therefore, participation by individuals with primary progressive aphasia (PPA), posterior cortical atrophy (PCA), or frontal variant of Alzheimer's disease is encouraged. We continue to screen and enroll additional participants for the Connect Trial. Since many participants referred by Northwestern Neurobehavior and Memory Clinic do have biomarker information, screening failure for this trial has been very low.

Efficiency of Telephone Prescreening for the A4 Trial

Kristine Lipowski¹, Okkes Kuybu¹, Carly Oboudiyat¹, Raj C. Shah², Neelum T. Aggarwal², Sandra Weintraub¹

¹*Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL*

²*Rush Alzheimer's Disease Center, Chicago, IL*

k-lipowski@northwestern.edu

Background: The screening process for clinical trials is the essential first step to ensure fidelity of the results of the trial. This process, however, is time-consuming and expensive. The Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease Trial (A4 Trial) is a landmark effort to prevent the cognitive decline associated with amyloid accumulation in the brain, a risk for dementia of the Alzheimer type. This trial has stringent inclusion/exclusion criteria, which can result in many screen fails during the 5 in-person screening visits conducted for this study.

Methods: Two Chicago study sites, one at Northwestern University and one at Rush University, developed a pre-screening telephone questionnaire to identify those who might fail in-person study screening. The questionnaire focused on potential participants who had contacted our centers after learning of the A4 trial via a variety of sources. They were contacted over the phone prior to an on-site visit and were asked 34 questions covering inclusion/exclusion criteria for the trial.

Results: From August 2014 through August 2015, 81 telephone pre-screens were conducted at Northwestern and 30 at Rush. Of the 81 Northwestern individuals screened, 25 were male (31%) and 56 (61%) were female. The average age of the sample was 71.5 years (71 years for males, 72 for females). The majority of our sample, 73 individuals, was Caucasian (90%), 4 were Hispanic (5%), and 4 were African-American (5%). The screening resulted in the exclusion of 26 participants (32%). Telephone screen fails were subdivided by reason for failure, which included logistical problems (i.e. unwillingness to undergo infusions, no study partner), the presence of exclusionary medical conditions, and inability to undergo study procedures, for example, MRI ineligible due to metal. Half of those excluded by the phone screen were excluded by a single criterion, while the other half were excluded for multiple reasons. We calculated that the exclusion of 26 participants who may have otherwise been scheduled for an on site visit resulted in savings of approximately 104 hours of staff time, and at least \$19,500 dollars for screen study costs. Data from Rush will be analyzed in the similar manner to highlight similarities and differences in findings and will also be presented.

Conclusions: A relatively brief telephone screening questionnaire was useful in eliminating 32% of potential participants for the A4 clinical trial who would have failed the first in-person screening visit. This method can save staff time, reduce costs and prevent unnecessary visits of participants likely to fail screening at a later time.

SuperAging Study: Correlates of Active Engagement in Life in the Elderly

Emmaleigh Loyer, Marie Saxon, Maureen Connelly, Tamar Gefen, Amanda Cook, Stephanie Kielb, Jaishre Sridhar, Lokesh Kukreja, Payam Abbassian, Daniel Ohm, Sandra Weintraub, Changiz Geula, M-Marsel Mesulam, Emily Rogalski

Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL

emmaleigh.loyer@northwestern.edu

Many individuals have come to expect that as they grow older, their memory and other cognitive abilities will begin to deteriorate. Though such decline may be common, the SuperAging study at the 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 SuperAging Project, which began nine years ago, has identified a group of individuals over the age of 80 with exceptional memory ability that more closely resembles 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.

Participants visit our center every 2 years for a comprehensive cognitive evaluation, structural and functional MRI scans, and a 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.

Over 1,000 individuals have contacted the CNADC to join the study. However, fewer than 110 people have met the stringent criteria to participate. 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 within the average range for their age and education on non-memory cognitive domains according to published normative values.

Previous neuroimaging results have shown that SuperAgers exhibit a thicker cortex in a region of the anterior cingulate compared to cognitively average age-matched controls and healthy 50-60 year olds. Study findings also reveal that SuperAgers tend to maintain outstanding cognitive performance on tests of episodic memory over an 18-month period. Additionally, SuperAgers have a lower frequency of the E4 allele of the apolipoprotein gene, which is a risk factor for Alzheimer's Disease.

Since its inception, the SuperAging Project has used a multidisciplinary approach when studying 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 the factors that promote resistance to age-related changes in the brain and allow individuals to maintain high memory capacity in old age.

Distribution of Granulins in FTLD-TDP and Normal Brains

Qinwen Mao, Kimmo Hatanpaa, Yanqing Li, Jayson Wilson, Sandra Weintraub, Haibin Xia, Charles White, Marsel Mesulam, Eileen Bigio

Northwestern University, Department of Pathology, Chicago, IL

q-mao@northwestern.edu

Frontotemporal lobar degeneration (FTLD) is the second most common dementia in patients younger than 65 years. Heterozygous loss-of-function mutations in *GRN*, the progranulin gene, are a common genetic cause of the disorder. Progranulin is a highly conserved, secreted glycoprotein and may function in the central nervous system as a growth factor, or an anti-inflammatory agent. The holoprotein can be cleaved by proteolytic enzymes into individual granulin peptides, whose functions in peripheral tissues seem to oppose those of progranulin. It has been predicted that granulins may play important roles in the pathogenesis of neurodegenerative diseases. However, there is little data regarding the distribution and function of granulins in the brain because of the lack of good anti-granulin antibodies. Even if an antibody to an individual granulin were available, the utility of this antibody for immunohistochemistry would be limited, because it may recognize both full-length PGRN and the specific granulin fragment. Recently, we have produced highly sensitive and specific monoclonal antibodies to each of the granulins A, B, C, D, E, F, and G. With the availability of a full panel of anti-granulin antibodies, it becomes possible to reveal the specific distribution of each single granulin by comparative evaluation of the results of the panel of immunostains. We show that some of the granulins have different cellular distribution patterns from others in the normal cortex, and that the patterns are altered in diseased cortex. For example, granulin D reveals membranous immunopositivity in neocortical neurons in normal brains, and shows decreased staining intensity in the diseased brains. In addition, when compared with other hippocampal regions, CA1 section shows less intense PGRN/granulin immunostains. Interestingly, this area is also vulnerable to hippocampal sclerosis with TDP-43 abnormality. These data suggest that differential distribution of granulin fragments in various brain regions may influence the pathogenesis of FTLD.

Comparative Distribution of Early and Late Appearing Tau Epitopes in Tauopathies

O. Hecmarie Meléndez-Fernández, Eric Y. Kao, Sandra Weintraub, Eileen Bigio, M-Marsel Mesulam and Changiz Geula
Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL
hecmarie@u.northwestern.edu

Tauopathy occurs in a range of diseases, and is characterized by hyperphosphorylation of the tau protein. The aggregation of this protein contributes to the distinct pathology of each. Throughout the course of tangle formation, different phosphorylation and truncation patterns can be distinguished with the use of antibodies aimed at the tau epitope variants. In the current study we aimed to determine and compare the presence of early versus late tau epitopes across the following tauopathies: Alzheimer's disease, (AD, hippocampus [Hpc]) progressive supranuclear palsy (PSP, pons), corticobasal degeneration (CBD; Hpc) and Pick's disease (PiD; superior frontal gyrus). To this end we used the novel antibody tau oligomeric complex 1 (TOC1) as a marker for early epitopes of tau, and MN423, as a marker for late epitopes. TOC1 identifies oligomeric forms of tau, and has a similar staining pattern as AT8, the widely used antibody against early epitopes of P-tau, primarily employed for diagnostic purposes. We used AT8-stained sections to select tissue with tau aggregate load. Our findings suggest that TOC1 is robustly present in all tauopathies analyzed. We observed neurites and intracellular inclusions across all cases. Additionally, we found inclusions and astrocytic plaques in AD, globose tangles in PSP, and Pick bodies in PiD. With MN423 we observed neurites and small inclusions in AD and PiD, and few astrocytic plaques in AD. Meanwhile, we detected sparsely distributed neurites and occasional intracellular staining in PSP and CBD. These findings are consistent with previous studies which showed that PSP and CBD pathology although similar between the two, is distinct from that of AD. Furthermore, this evidence lends support to the findings that PSP and CBD share the H1 tau haplotype. Distinguishing the specific epitopes found in each tauopathy can contribute to better understanding the progression of pathology and the tailoring of imaging techniques designed to identify specific and distinct tauopathy presentations.

Collaborative Action Team training for Community Health-Older adult Network (CATCH-ON)

Robyn Golden¹, Erin Emery-Tiburcio², Michelle Newman¹, Raj C. Shah^{3,4}, Carol Farran⁵, Fawn Cothran⁵, Rebecca Johnson⁶, Darby Morhardt⁷

¹Rush Health and Aging, ²Department of Behavioral Sciences, ³Department of Family Medicine, ⁴Rush Alzheimer's Disease Center, ⁵Rush College of Nursing – ^{1,2,3,4,5}Rush University Medical Center, ⁶Buehler Center on Aging, Health & Society, ⁷Cognitive Neurology and Alzheimer's Disease Center – ^{6,7}Northwestern University Feinberg School of Medicine

Robyn_L_Golden@rush.edu

Significance: The geriatric population in Illinois is growing faster than the nation. Minority older adults increased by nearly 40% since 2000, 8% live in poverty, and 17% live in rural areas. The ratio of rural physicians is 30% lower than in urban communities despite the higher percent of older adults in rural areas. Even in urban areas, finding geriatric providers is challenging. Illinois has made progress addressing the needs of older adults, especially individuals with Alzheimer's Disease and Related Dementias (ADRD), but gaps remain. In Illinois, the rate of older adults with multiple chronic conditions (MCC) is 15.5% higher than the national average. MCC are associated with health decline, decreased quality of life, increased emergency room visits, hospital stays, and post-operative complications. It is critical for the wellbeing of older adults in Illinois, and the nation, to enhance the geriatric workforce capable of managing MCC, including ADRD. In July 2015, the Health Resources Service Administration (HRSA) awarded a grant to a collaboration of 34 statewide partners in Illinois led by Rush University Medical Center to establish a Geriatric Workforce Enhancement Program (GWEP). This collaboration is entitled Collaborative Action Team training for Community Health-Older adult Network (CATCH-ON).

Methods: CATCH-ON has two primary aims: (1) Educate older adults, families, caregivers, direct care workers, health professions providers, students, residents, fellows, and faculty about person-centered, culturally competent management of MCC among diverse older adults, especially those with cognitive decline, and ADRD); and (2) Transform existing primary care systems to meet the needs of older adults with MCC/ADRD by implementing evidence-based programs that utilize provider, patient and community resources. Weekly and quarterly meetings among all collaborators have been effective in building and maintaining partnerships and achieving goals.

Results to Date: Critical innovations to achieve the above aims have included progress toward development of interactive, universally accessible online modules regarding MCC/ADRD for all learners, regional and state-wide Learning Communities, geriatric case-based curriculum materials to be infused into existing graduate and undergraduate health programs, and Health Ambassadors for community health, in addition to the development of the collaboratively developed CATCH-ON Community Health primary care model and multi-site Readiness Assessment process. CATCH-ON Community Health aims to transform existing primary care systems to meet the needs of older adults, including those with ADRD, by integrating evidence-based programs that utilize provider, patient and community resources with current service delivery. Plan, Do, Study, Act rapid cycles are being utilized within the RE-AIM framework to develop and improve products and processes.

Conclusion:

CATCH-ON is positioned to bring significant change the geriatric workforce in the state of Illinois, upper Midwest region, and nation by demonstrating how multiple partners can work effectively and efficiently to identify training needs, adapt and deliver education which is fit for purpose and, in the process, build a new care delivery model based on shared experience.

ilLUMAnations: A Museum Based Art Program for Persons with Cognitive Impairment and Their Families

Pamela Ambrose¹, Natasha Ritsma¹, Marlea Edinger¹, Barbara Weeks¹, Leonard Caramela¹, Chris Benoodt¹, Mary Reynolds¹, Anya Drew², Lauren Dowden², Darby Morhardt²

¹Loyola University Museum of Art (LUMA), Chicago, IL

²Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL

d-morhardt@northwestern.edu

Background: Over the past 30 years, research has advanced our understanding of Alzheimer's disease; however, there are no truly effective medical treatments that can prevent or cure it. Research has demonstrated the positive impact of non-pharmacological interventions, particularly engagement with the arts, on persons with cognitive impairment.

Methods: ilLUMAnations is modeled on New York City's Meet Me at MoMA program and was launched in 2013 by the Northwestern CNADC and Loyola University Museum of Art (LUMA). Program aim is to explore impact on the person with dementia and their care partner. ilLUMAnations held 5 sessions per year for the first 3 years and 9 in this last year 2015-16 for a total of 24 sessions. During each 90-minute session, specially trained docents guided small groups of persons with dementia (PWD) and their care partners around museum exhibitions, exploring the art in a manner that encouraged meaningful interaction and open expression. This past year, dance and music programs were introduced. Sessions are held during the museum's off hours and time was allotted for socialization following each session. PWD and care partner dyads were recruited from the Northwestern CNADC's Neurobehavior and Memory Clinic. During 2013-16, 24 PWD enrolled into the ilLUMAnations program (18 male, 6 female) along with 24 care partners. Age range of PWD is 62-80, all in the mild to moderate stages. Data collection included observational field notes during the exhibit discussion, focus groups and informal discussion over refreshments following each session. This qualitative data was shared and discussed among both Northwestern and Loyola project staff and emerging themes were identified.

Results: Thematic analysis of qualitative data demonstrated participants in the ilLUMAnations program experienced the following benefits through their participation: 1) cognitive stimulation; 2) social engagement; 3) confidence; 4) comfort and a sense of belonging; and 5) inspiration and motivation. Care partners revealed a sense of surprise at the level of discussion with the person with dementia around the art resulting in an increased feeling of normalcy and intimacy. Documentation by the docents revealed their initial assumptions regarding persons with dementia were challenged. They also discussed how they modified their role as docent to accommodate persons with cognitive impairment and how their view of the art changed as a result of this experience.

Conclusion: ilLUMAnations is an art-based program for PWD and families that provides multiple benefits. It enhances remaining strengths and quality of life for the cognitively impaired, helps to preserve relationships between PWD and their care partners, and has the potential to challenge larger societal assumptions (stigma) about living with dementia.

KARE - Korean American Alzheimer's Research and Education

Ji Myong Kim¹, Yoon Tae Chong¹, Inchul Choi¹, Darby Morhardt²

¹*Korean American Community Services*

²*Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL*
d-morhardt@northwestern.edu and jkim01@kacschicago.org

Background: Korean American Community Services (KACS) and the Northwestern CNADC were the recipients of two community based participatory research (CBPR) seed grants from Northwestern University's Alliance for Research in Chicagoland Communities (ARCC), Center for Community Health, Institute for Public Health and Medicine in 2011 and in 2012. Results revealed Korean American caregivers and older adults have a range of attitudes toward dementia and a deeply rooted misunderstanding and ill-informed beliefs regarding the cause. They expressed the need for a variety of educational and support services and programs to help them. Furthermore, focus group and follow-up discussions identified the need for Alzheimer's Disease and dementia programming within KACS senior housing residences due to stigmatization and marginalization of the cognitively impaired living in these settings.

Methods: The Retirement Research Foundation awarded a direct service funding grant to KACS and the Northwestern CNADC in January 2016 to respond to the needs of the Korean American community regarding dementia. Project objectives are: 1) to conduct six 75-minute brain health workshops to six Chicagoland Korean American senior communities in the 2016 calendar year; 2) create a bilingual (Korean and English) brain health informational booklet that incorporates basic information on brain health and the key concerns of the senior community on Alzheimer's disease and brain health, and 3) tailor senior housing brain health workshops with special attention on communication skills toward persons with cognitive impairment in their communities. Program evaluation includes pre/post knowledge tests and focus groups to explore concerns and attitudes around brain health, dementia, and communication with persons who exhibit changes in cognitive function.

Expected Outcomes: The expected outcomes include an increase in knowledge and attitudes regarding brain health, Alzheimer's disease/dementia and helpful communication strategies within the Chicago area Korean American community leading to the reduction of stigma toward people with cognitive impairment.

Conclusion: There is a wide range of needs for Korean American seniors living with AD and dementia and their families. Korean American Alzheimer's Research and Education (KARE) project hopes to eventually become a comprehensive resource for the Korean American community on Alzheimer's disease, dementia, and overall brain health.

Northwestern Alzheimer's Disease Center Outreach, Recruitment and Education Core (ORE Core) 2015-16

Darby Morhardt (Director), Kristine Zachrich, Lauren Dowden, Anya Drew

Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL

d-morhardt@northwestern.edu

INTRODUCTION: ORE Core specific aims are: 1) Provide outreach and educational programs for the recruitment of underrepresented groups to the Northwestern ADC; 2) Optimize the recruitment of subjects 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: ORE Core social workers assess patient and family coping, determine needed resources, provide education and counseling and tailor recommendations to needs and symptoms, as part of our clinical services and to enhance our recruitment and retention mission of the ADC. ORE Core offers innovative Quality of Life Enrichment research programs and support groups. A new program was introduced this year, Support and Education for Early Dementia (SEED) offering two successful 8-week sessions for newly diagnosed individuals and their families. An African American teaching artist has been trained to conduct the Memory Ensemble (an improvisational theatre experience and collaboration of the Northwestern CNADC and Lookingglass Theatre). A replication of the Memory Ensemble will take place Summer 2016 at Oak Street Health Blue Island Clinic, made possible through a Civic Practice Lab project grant to Lookingglass Theatre, the mission of which is to bring theatre to the community.

ORE Core continues to collaborate with the African American community via partnerships with the Endealeo Institute and 6 faith-based organizations in, REACH to Faith: Research and Education for African American Caregiver Health (see separate abstract). We offered the play *Forget Me Not* in collaboration with USAgainstAlzheimer's and Rush Alzheimer's Disease Center at the DuSable Museum of African American Art increasing disease awareness and research participation. We continue to partner with the Atlas Regional Senior Center for research recruitment and retention. A new Retirement Research Foundation grant with Korean American Community Services expands the work of KARE: Korean American Alzheimer Research and Education (see separate abstract). ORE Core is a founding member of LA CARE (Latina/o Alzheimer's Coalition for Advocacy, Research and Education), which continues to build its capacity to conduct research and raise disease awareness. ORE Core leader is on the advisory panel for HRSA (Health Resources & Services Administration) Dementia Curriculum for Healthcare Professionals; in addition to the state-wide collaboration for the HRSA Geriatrics Workforce Enhancement Program with Rush and Southern IL Universities (see separate abstract).

The ORE Core continues to be responsive to collaborative efforts articulated by the National Alzheimer's Project Act (NAPA), via the state-wide initiative, Illinois Cognitive Resources Network (ICRN). As a leader in the ICRN and to address the goal to make Illinois a "dementia capable" state, the ORE Core helped develop and is working on the dissemination of training materials for the larger Illinois aging and disability network in addition to working toward the enhancement of the ICRN website: ilbrainhealth.org.

ORE Core is pivotal to dementia-related education of trainees and fellows. The CME-accredited AD seminar series is a successful educational program for Northwestern researchers and clinicians. The Storytelling Program (see separate abstract) received a Northwestern Alumnae Award this year and has supplemented the education of the lived experience of dementia for multidisciplinary audiences; namely, medical, physician assistant and social work students in addition to the general community.

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

REACH to Faith: Research and Education for African American Caregiver Health

Melvin Thompson¹, Etta McGregor-Jones⁷, Joan Owens², Catherine Chandler², Jaunita Carr², Audrey Coleman³, Dorothy Jenkins⁴, Virginia Julion⁵, Shawnya Owens⁵, Cynthia Brown⁶, Jiles Taylor George⁷, Barbara Little⁷, Fawn Cothran⁸, Jakita Baldwin⁹, Darby Morhardt⁹

¹The Endealeo Institute, ²Beth Eden Baptist Church, ³Faith Community of St. Sabina, ⁴Fernwood United Methodist Church, ⁵Oakdale Covenant Church, ⁶Third Baptist Church of Chicago, ⁷Trinity United Church of Christ, ⁸Rush University College of Nursing, ⁹Northwestern University, Chicago, IL
d-morhardt@northwestern.edu

Introduction: African Americans (AA) are two times more likely to be diagnosed with Alzheimer's disease or related dementias (ADRD) than White Americans (Alzheimer's Association, 2010); however, disproportionately receive less dementia care and education. Despite the proliferation of caregiver intervention research, few interventions have been geared specifically toward the needs of AA caregivers. A distinctive characteristic of the AA community is the prominent role of religion and religious organizations; however, few researchers have involved faith communities in caregiver intervention research.

Methods: Beginning 2013, non-profit faith-based corporation, The Endealeo Institute, engaged 6 faith-based organizations (FBOs) and Northwestern University (CNADC) to establish a partnership to better understand the needs of the AA community around the issues of ADRD and caregiving. In addition to holding monthly meetings to build our partnership and research capacity, we held a caregiver conference for AA families, in addition, to conducting two focus groups for family caregivers exploring what they know about ADRD, what services are needed and an opportunity to describe their lived experience. Faculty from Rush College of Nursing has also joined the collaboration.

Results: African Americans from Chicago's south side neighborhoods are underserved in terms of knowledge, education, medical and support services around ADRD. Existing services do not meet the physical and mental health needs for persons with dementia and caregiving families and there are numerous barriers to reaching out for and obtaining care. These barriers include lack of knowledge regarding dementia, lack of awareness regarding the diagnostic and support resources available to persons experiencing cognitive impairment, a sense of stigma and shame around the diagnosis and symptoms, and a longstanding mistrust of the medical community. AA caregiving families frequently identified prayer and faith as the way they cope with caring for a family member with dementia. Grant proposals are being pursued to build upon this work.

Conclusion: A successful community/academic partnership has been established among Northwestern, Endealeo Institute, 6 Chicago faith based communities and Rush College of Nursing for the purposes of exploring and better understanding the needs and experience of African Americans caring for persons with Alzheimer's disease with the goal of ultimately developing helpful interventions.

Improved Precision of Successful Recollection 24 Hours After Targeted Stimulation of Posterior Hippocampal Cortical Network

Aneesha Nilakantan, Donna Bridge, Elise Gagnon, Jane Wang, Joel Voss

Northwestern University, Interdepartmental Neuroscience Program, Chicago, IL

aneeshan@u.northwestern.edu

Normal aging is associated with episodic memory decline consistently related to the degradation of hippocampal-cortical connectivity. The posterior hippocampal-cortical network, including the medial temporal lobe, posterior cingulate, lateral parietal cortex, and retrosplenial cortex is thought to support spatial context associations and episodic memory. We have previously shown that multiple-day repetitive transcranial magnetic stimulation (rTMS) increases functional connectivity among these network regions and improves associative memory. We aimed to extend these findings and examine the neural correlates of associative spatial retrieval following multiple-day rTMS to understand how this network specifically supports spatial memory. To probe this network, subject-specific stimulation targets in parietal cortex were determined based on strong intrinsic resting-state functional connectivity with the hippocampus. Twelve young adults completed five consecutive days of targeted hippocampal-cortical network stimulation (STIM) and five consecutive days of vertex (SHAM) stimulation over two separate weeks in counter-balanced order. 24-hours before and 24-hours after each week of stimulation, participants completed an associative memory task which involved recall of 96 object-locations. Successfully recollected object locations were more precisely recalled (i.e., placed closer to the studied location) following network-targeted stimulation, relative to sham. Event related correlates of the recollection precision improvement included reduced late-positive amplitude and 6-11Hz power at parietal and central electrodes, relative to pre-stimulation. Targeting the posterior hippocampal-cortical network with multiple-day rTMS therefore improves recollection precision and modulates neural correlates of memory retrieval for at least 24 hours after stimulation. These results provide evidence for a causal role of posterior hippocampal-cortical networks in precision tuning of associative memory. Findings suggest new possibilities for studying the network basis of memory impairments in older adults and could motivate future clinical interventions.

Pathology of ALS with Dementia

Yasushi Nishihira¹, Qinwen Mao¹, Sandra Weintraub², Nailah Siddique³, Teepu Siddique³, M-Marsel Mesulam², Eileen H Bigio^{1,2}

¹*Northwestern University, Department of Pathology, Chicago, IL*

²*Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL*

³*Northwestern University, Department of Neurology, Chicago, IL*

nishihira.yasushi@northwestern.edu

OBJECTIVE: This study examines autopsy cases of clinical ALS with or without dementia in order to determine the prevalence of FTLD-TDP in a large ALS cohort. We also compare the distribution of FTLD-TDP sub-types in the ALS cases and in FTLD-TDP presenting with dementia. Lastly, we aimed to determine the pathologic basis of dementia in those cases of clinical ALS with dementia having no FTLD-TDP pathology.

METHODS: Two hundred fifty cases of ALS with (n=37) or without (n=161) dementia, and dementia without clinical ALS and with pathologic FTLD-TDP (n=52) were examined clinicopathologically. TDP-43 immunostains were performed on all cases.

RESULTS: Seventeen cases with clinical ALS without dementia (11%) had pathologic FTLD-TDP and 30 cases (81%) with clinical ALS with dementia had FTLD-TDP pathology. Twelve cases (23%) with clinical dementia without clinical ALS and with FTLD-TDP pathology also had ALS pathology. Interestingly, seven cases (19%) of ALS with dementia had no FTLD-TDP pathology. Most brains from patients with clinical ALS with FTLD-TDP pathology had FTLD-TDP type B, and in clinical dementia without clinical ALS and with FTLD-TDP pathology FTLD-TDP type A predominated. In the seven cases of clinical ALS with dementia but without FTLD-TDP pathology, there was one case of Alzheimer disease pathology with hippocampal sclerosis and medial temporal TDP-43 pathology, one case with a thalamic microinfarct, and two cases with neuronal loss and gliosis in the thalamus and unique ubiquitin and p62 positive cytoplasmic inclusions in the thalamus and other brain regions. The other three cases had no pathologic changes to correlate with dementia.

CONCLUSUION: The findings suggest that not all brains from patients with clinical ALS with dementia have FTLD-TDP. Interestingly, pathologic evaluation of two cases of clinical ALS with dementia but no FTLD-TDP pathology revealed unique ubiquitin and p62 positive pathology.

Leukodystrophy with Axonal Spheroids Presenting as Primary Progressive Aphasia

Carly Oboudiyat

Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL

carly.oboudiyat@northwestern.edu

Background: Primary Progressive Aphasia is a focal dementia affecting primarily language for at least the first two years of disease. There are several well-described underlying pathologies of Primary Progressive Aphasia, primarily frontotemporal lobar degeneration with TDP-43 or tau inclusions, and Alzheimer's pathology with atypical anatomical distributions of plaques and tangles. Leukodystrophies have not been previously reported in association with this syndrome.

Methods: A case report of a patient with Adult-Onset Leukodystrophy with Axonal Spheroids and Pigmented Glia presenting as Primary Progressive Aphasia, with a description of the cognitive, imaging, genetic, and autopsy findings.

Results: The patient had a clinical phenotype of primary progressive aphasia, logopenic subtype. The initial MRI showed left parietal white matter lesions, and cortical atrophy. Follow-up imaging studies revealed extensive progression of the white matter signal abnormalities. An autopsy confirmed Adult-Onset Leukoencephalopathy with Neuroaxonal Spheroids and Pigmented Glia. Even in the advanced disease state, the left hemisphere remained the primary site of pathology. Genetic testing for known mutations of hereditary leukodystrophy with axonal spheroids was negative.

Conclusion: This case describes a new pathologic correlate of Primary Progressive Aphasia, and further shows that the common denominator of diseases causing this syndrome is the asymmetric predilection for the language-dominant hemisphere rather than the cellular nature of the pathology. The patient-specific factors that determine the selective vulnerability of the language-dominant hemisphere in Primary Progressive Aphasia remain to be identified.

Histopathologic Markers are Related to *In Vivo* Cortical Atrophy in Primary Progressive Aphasia with Alzheimer Pathology

Daniel Ohm, Garam Kim, Adam Martersteck, Sandra Weintraub, Eileen H. Bigio, M.-Marsel Mesulam, Emily Rogalski, and Changiz Geula

Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL

DanielOhm2012@u.northwestern.edu

The neurobiological substrates of cortical atrophy are not well understood in neurodegenerative diseases that cause dementia. We quantified the regional specificity of Alzheimer disease (AD) pathology (i.e., amyloid- β plaques [APs] and neurofibrillary tangles [NFTs]) and cortical atrophy measures in two patients with primary progressive aphasia (PPA) and AD pathology (PPA-AD) that had structural magnetic resonance imaging (sMRI) within 18 months of death. PPA is a clinical dementia syndrome associated with autopsy-confirmed AD pathology in approximately 40% of cases, as well as a signature pattern of asymmetric atrophy concentrated in the left perisylvian language network. The neuroanatomical selectivity of PPA allows for unique within-subject comparisons between compromised and relatively spared regions (e.g., left versus right hemispheres; language versus memory regions). This study compared two control regions of interest (ROIs) (memory-related entorhinal cortex and primary visual cortex) to five language ROIs: 1) inferior frontal gyrus, 2) anterior superior temporal gyrus, 3) posterior superior temporal gyrus, 4) anterior inferior parietal lobule, and 5) posterior inferior parietal lobule. The cortical volume of each ROI was quantified from the PPA-AD subjects' sMRI using FreeSurfer software and compared to a group of 22 age-matched cognitively healthy adults in order to quantify volume loss. ROIs delineated by the neuroimaging analysis served as boundaries for unbiased stereology performed on whole-hemisphere sections to quantify NFT and AP densities. Both PPA-AD subjects displayed a leftward asymmetry of cortical atrophy, with the most prominent volume loss in the posterior language ROIs, especially the anterior and posterior inferior parietal lobules. Negligible volume loss was found bilaterally in control ROIs in comparison to the language ROIs. NFT densities exceeded AP densities in all ROIs except primary visual cortex for both PPA-AD subjects. The largest densities of NFTs were found within the language ROIs, while AP densities were evenly distributed across both language and control ROIs. These preliminary measures suggest that NFT deposits parallel cortical atrophy in their neuroanatomical distribution. The findings further highlight the regional selectivity of neurodegenerative markers within the perisylvian language network in PPA-AD.

Conditional BACE1 Knockout Mouse as a New Model for Studying Tissue Specific and Temporal BACE1 Inactivation

Ming-Hsuan Ou-Yang, Tharinda W. Rajapaksha, Katherine R. Sadleir and Robert J. Vassar

Northwestern University, Department of Cell and Molecular Biology, Chicago, IL

ming-hsuan.ou-yang@northwestern.edu

BACE1, known as the β secretase, is the enzyme that initiates the production of amyloid β deposited in the brain of Alzheimer's disease patients (AD). Subsequently, BACE1 has become a prime drug target for AD to lower or inhibit the generation of amyloid β . BACE1 knockout mice, however, have complicated cognitive and neurochemical phenotypes due to insufficient cleavage over a broad range of BACE1 substrates. The goal of this study is to better understand BACE1 physiology roles in the brain and whether it is dispensable in the adult in order to provide insights to the ongoing and future clinical trials on BACE1 inhibitors.

We have generated conditional BACE1 mouse line in which the exon 2 of the BACE1 gene is flanked by loxP sites (BACE1^{fl/fl} mice) and BACE1 gene deletion occurs upon the expression of Cre recombinase. In this study, we crossed BACE1^{fl/fl} mice to two cre-driver mouse lines: CamKII-cre that leads to BACE1 deletion in the forebrain excitatory neurons and to CreER^{T2} which is a tamoxifen-induced model enabling temporal studies on the effects of BACE1 knockout at different stages. Cohorts at different time points were subjected to a battery of behavior tests for anxiety, general activity, motor coordination and learning/memory. Brains were collected at the conclusion of behavior tests for biochemistry and histology analyses.

In BACE1^{fl/fl}/CamKII-cre mice where Cre expression is turned on at early postnatal stage, we found significant rescues in high lethality and underweight phenotype compared to conventional BACE1 knockout mice. There was no difference in motor function, learning and memory between young BACE1^{fl/fl}/CamKII-cre and control BACE1^{fl/fl} littermates. However, in aged BACE1^{fl/fl}/CamKII-cre mice, we have observed similar phenotypes reported in conventional BACE knockout mice including seizures, hyperactivity and worse performance in water maze. Current findings indicate that excitatory neurons are the important cell type that modulates the above phenotypes and despite that BACE1^{fl/fl}/CamKII-cre mice appear to be overall normal at young age, the phenotypes in aged mice suggest that the phenotypes are developed over time or are aging dependent which is expected to be answered in our tamoxifen-inducible BACE1^{fl/fl}/CreER^{T2} mouse model.

While BACE1 inhibitors are advancing as drug candidates for AD, there remains a remarkable gap in the knowledge of BACE1 physiological function. The findings of this study are expected to provide information to fill in for this gap and which may be used to predict mechanism-based side effects of ongoing trials.

Acoustic Stimulation Increases Slow-Wave Activity and Improves Declarative Memory in Older Adults

PA Papalambros, G Santostasi, RG Malkani, S Weintraub, KA Paller, PC Zee

Northwestern University, Interdepartmental Neuroscience Program, Chicago, IL

npapalambros@u.northwestern.edu

Age-related decrease in the amount of slow-wave sleep has been postulated to play a role in impaired cognitive function. Acoustic stimulation during sleep has been shown to increase slow-wave activity (SWA) and improve memory retention in young adults, but has not been examined in older adults. The aim of this study is to examine the ability of acoustic stimulation to increase SWA and improve declarative memory in older adults. Thirteen healthy and cognitively intact adults (age 75.2 60-84, 3 men) completed one night of acoustic stimulation and one night of sham stimulation in counterbalanced order. During sleep, an adaptive phase-locked loop (PLL) algorithm was used to lock on to endogenous slow-waves recorded from the midline frontopolar electroencephalogram in real time. Bursts of 1/f noise were delivered when the PLL system predicted the positive upstate of the slow-wave. Tones occurred in blocks of 5 pulses ("ON blocks") followed by a refractory period of equal length ("OFF blocks"). Participants completed an 88-word pair recall with feedback, before and after sleep, to assess declarative memory. Power spectral analysis was used to identify power in delta frequency band (0.5 Hz-4 Hz). Performance was measured as percent change in word recall from evening to morning. Non-parametric t-tests were used to evaluate differences between stimulation and sham conditions. We found a significant increase in delta power in the ON blocks relative to OFF blocks during the stimulation night compared to the sham night (16% v. -2.3%, $p=0.002$). Delta power during ON blocks of the stimulation night was 8% higher compared to ON blocks of the sham night ($p=0.002$). Overall delta power across the entire night was not significantly different. Participants recalled significantly more words following a night of acoustic stimulation compared to a night of sham stimulation (27.2% v. 4.5%, $p=0.008$). Acoustic stimulation delivered during sleep increases slow-wave activity and improves declarative memory performance in older adults. Acoustic stimulation could prove to be a non-pharmacological approach to enhancing memory in older clinical populations experiencing memory decline.

Regressive Gallyas Staining of Paraffin Embedded Human Brain Tissue

Zach Parton, Changiz Geula, Eileen Bigio

Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL

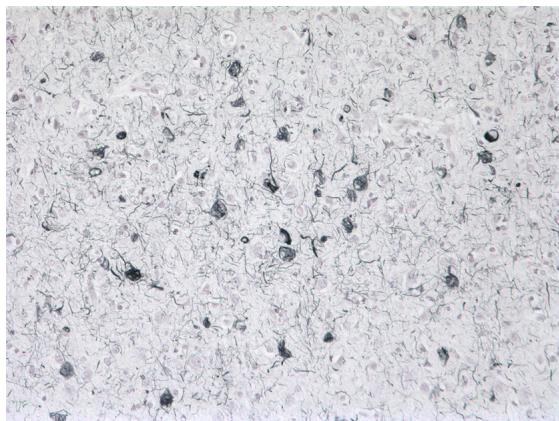
zachary.parton@northwestern.edu

The goal of this endeavor was to find a means of combining Gallyas' argyrophillic stain with the convenience of paraffin embedded blocks which would result in staining with a high signal-noise ratio and require few additional steps. A version of the stain on paraffin-cut sections was tested, and is described below. The addition of a differentiation step results in the stain becoming "regressive," where finer details are visible against a clearer background. The final preparations are soundly compatible with counter-staining.

Mounted sections are de-parrafinized and rehydrated, pre-treated with potassium permanganate and oxalic acid, immersed in an alkali silver nitrate solution, treated with acetic acid, and developed with a common developer solution. Following another acetic acid treatment and distilled water-wash, the slides are differentiated with a low concentration of potassium ferricyanide in distilled water for 20 minutes on a shaker. This method allows re-intensification in developer after differentiation. The slides are finally immersed in gold-chloride and all developmental reactions stopped with sodium thiosulfate. Counterstaining may be performed as desired. With prepared slides, the entirety of the procedure can be completed in approximately four hours; counterstaining adds additional time.

By reducing background and noise producing inhomogeneities, this protocol describes a means to increase the utility of diagnostic staining for tauopathies that can be carried out anywhere Gallyas protocols are currently implemented. At the cost of an additional step and hazardous waste handling, a much more consistent and revelatory procedure is implemented in a timely fashion.

There is also good reason to believe that this method could be used as a robust pre-staining procedure for immunohistochemical investigations of tauopathies. Future experiments will investigate the extent of compatibility with IHC, compatibility with modern whole-mount clearing techniques, ability to reuse reagents as a cost-saving measure, and the possibility of using H_2O_2 as a differentiation agent.



Can Memory Be Improved with Oscillating Sounds That Promote Beneficial Brain Oscillations During Learning?

Hadley Pfalzgraf, Jessica D. Creery, and Ken A. Paller

Northwestern University, Cognitive Neuroscience Program, Evanston, IL

HadleyPfalzgraf2018@u.northwestern.edu

Rhythms observed in electrophysiological recordings from the brain are thought to reflect important neural processing relevant for cognitive function. For example, oscillations at theta and beta frequencies (3-7 Hz and 13-30 Hz, respectively) have often been observed during memory processing. Various speculations about beta and theta rhythms have been made in relation to memory functions, but a clear picture linking these rhythms to neural mechanisms of memory storage has yet to emerge. In particular, it is unknown if beta and theta oscillations are merely a byproduct of information processing or if they reflect causal stages in the process of memory encoding. If these oscillations are causal in memory processing, inducing them at the proper moment during memory formation should beneficially influence subsequent memory performance. In the current study, we attempt to examine the importance of brain activity at theta and beta frequencies by pairing sounds at corresponding frequencies with to-be-remembered objects shown to participants in a spatial memory task. Participants learned the screen locations of 60 objects while each object was paired with one of three different types of pink noise (20 objects each). Noise modulated at 6 Hz was intended to induce theta oscillations, noise modulated at 15 Hz was intended to induce beta oscillations, and constant noise was included as a control condition. Each object was paired with the same sound throughout the study. After a 10-min break, participants attempted to recall the location of each object. The distance between the recalled location and the correct location (recall error) was compared across conditions. Spatial memory was found to be superior for objects learned in conjunction with beta-modulated sound, implicating beta brain rhythms in memory formation. Future analyses of EEG oscillations may provide additional substantiation of this link between beta activity and memory processing. This approach of facilitating learning using auditory entrainment at beta frequencies may thus yield a noninvasive strategy for memory improvement and also a useful tool for investigating neural mechanisms of memory storage.

Characterization of Neurons Expressing the Neuroprotective Peptide Urocortin

Michael Priest and Yevgenia Kozorovitskiy

Northwestern University, Department of Neurobiology, Evanston, IL

michael.priest@northwestern.edu

Urocortin is a neuropeptide within the corticotropin-releasing factor family of peptides that has been implicated in anxiety, feeding, and alcohol consumption. The major site of urocortin-containing neurons in the brain is in the Edinger-Westphal nucleus, a brain region that has been shown to undergo cell loss in Alzheimer's disease and to develop Lewy bodies in Parkinson's disease and dementia with Lewy bodies. Additionally, urocortin has been suggested to be neuroprotective against both hippocampal and dopaminergic cell loss, suggesting a possible therapeutic role in both Alzheimer's disease and Parkinson's disease. In spite of these numerous putative roles in both health and disease, the study of urocortin in mouse models has remained hampered by a lack of available genetic tools. To overcome this problem, we have used immunofluorescence and confocal laser scanning microscopy to discover a previously created transgenic mouse line that also provides genetic control over the primary population of urocortin-containing neurons in the brain. Additional studies will combine viral injections with patch clamp electrophysiology, two-photon calcium imaging, and optogenetic stimulation to determine the functional connections of this population of neurons. Optogenetic can also be used to define the role of urocortin release in behavior with new levels of spatiotemporal specificity. Given the broad range of effects of urocortin on crucial systems including stress, eating, and neurological disorders, characterizing the circuitry of this population should help guide future development of therapeutics.

Primary Progressive Aphasia Research Programs at Northwestern University's CNADC

Benjamin Rader, Marie Saxon, Emmaleigh Loyer, Allison Rainford, Jaiashre Sridhar, Robert Hurley, Ken Paller, Cynthia Thompson, Sandra Weintraub, M.-Marsel Mesulam, Emily Rogalski
Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL
benjamin.rader@northwestern.edu

Primary progressive aphasia (PPA) is a neurodegenerative dementia syndrome characterized by a progressive loss of language function. PPA is relatively rare and has a low prevalence in clinical practice. The Cognitive Neurology and Alzheimer's Disease Center (CNADC) seeks to learn and understand more about PPA through several ongoing studies.

The Language in Primary Progressive Aphasia program has enrolled over 140 participants from close to 35 states and Canada over the last nine years. This program is funded by the National Institute on Deafness and Other Communication Disorders. Participants visit our center every two years for three days. At each of these visits, participants complete neuropsychological testing, language-processing studies, electrophysiological experiments, and magnetic resonance imaging (MRI) scans. Investigators develop and administer a range of language tasks that target various aspects of our participants' language comprehension and production. Most participants agree to take part in our brain donation program, which provides an invaluable opportunity to study the relationship between neuropathology and disease subtype.

Determinants of Neurodegenerative Decline in Primary Progressive Aphasia, led by Dr. Emily Rogalski, is in its fifth year of operation and has enrolled over 45 participants. This research program is funded by the National Institute of Neurological Disorders and Stroke. Participants complete four visits that occur at six month intervals and involve neuropsychological testing, functional and structural MRI scans, and an amyloid positron emission tomography (PET) scan using Florbetapir-F18. The results from this study will be important for defining objective biomarkers of disease type and progression, which will inform therapeutic treatment strategies.

The Communication Bridge Speech Therapy Study is an Internet-based speech-language therapy (SLT) study. This study is funded by the Run4Papa campaign, the Association for Frontotemporal Degeneration Pilot Grant and an Alzheimer's Association grant. This study currently has enrolled over 40 participants from 21 states, Canada and Singapore. The goals of this study are to identify the most effective SLT methods for PPA patients and to improve access to care for PPA patients by providing web-based video SLT.

Tau Imaging in Atypical Dementias is a new neuroimaging initiative being launched by the CNADC. This research is looking to map deposits of the abnormal tau protein in patients with PPA using a novel PET tracer. These scans will contribute important knowledge about disease mechanisms and may eventually address diagnostic limitations of other PET imaging modalities. Funding from the Run4Papa campaign has helped make this new study possible.

IMPPACT, the International PPA Connection, is a web resource maintained by the CNADC. It supports international, collaborative research between institutions and serves as a centralized location for PPA resources. The site currently has 245 registered researchers that represent 156 institutions across 32 different countries.

The Northwestern CNADC remains one of the top referral centers in the world for PPA by employing a multidisciplinary approach (research, education, treatment) for both patients and their families.

Characterization of High Passage Adult Human Microglia Cultures

Aras Rezvanian, Lokesh Kukreja, Eric Y Kao, Ling Guo, Sandra Weintraub, Eileen Bigio, M-Marsel Mesulam, Joseph El Khoury and Changiz Geula

Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL

aras.rezvanian@northwestern.edu

A great deal of what has been learned regarding microglia biology is based on in vitro studies, the overwhelming majority of which have used cells isolated from the rodent brain. However, the greater anatomic and functional complexity of the human brain, and species differences in microglia response, make imperative the use of human microglia to ascertain that the results obtained in rodents are applicable to man. Investigation of microglial function in the adult brain, in which many inflammatory and anti-inflammatory microglial responses occur, requires isolation of microglia from adult human brains. Microglia cultured from embryonic human brains show substantial proliferative capacity. However, microglia cultured from adult brains have low levels of proliferation. Therefore, while methods for isolation of microglia from adult postmortem human brains exist, they provide limited quantities of microglia isolated and cultured from each case. A new technique we have developed allows culturing microglia from postmortem adult human brains to high passage. To date, we have successfully cultured human microglia to passage 20. We characterized cultured microglia at various passages using immunoreactivity for the specific microglia marker cluster of differentiation (CD68) and the specific astrocyte marker glial fibrillary acidic protein (GFAP). Both immunohistochemical staining and Western blot analysis revealed the presence CD68 but not GFAP immunoreactivity in cultured cells, indicative of purity of the microglia cultures. In contrast, cortical brain tissue homogenates contained both CD68 and GFAP immunoreactivity using the same antibodies. No differences in CD68 immunoreactivity was observed when cultures of relatively early passage (P3-6) were compared with cultures of late passage (P10-16). Microscopic analysis indicated that nearly 100% of cultured cells endocytosed acetyl low density lipoprotein (Ac-LDL), a ligand for scavenger receptor activity and a marker of microglia. No differences were observed in Ac-LDL uptake by microglia at various passages. These results were confirmed by a preliminary fluorescent activated cell sorting analysis. Finally, microglia cultures of various passages produced substantial reactive oxygen species (ROS) in response to fibrillar amyloid- β (A β) peptide. Of great interest, microglia cultured from normal and Alzheimer disease cortex showed no differences in immunoreactivity for CD68, Ac-LDL uptake or ROS production in response to A β . In conclusion, this new technique results in postmortem adult human microglia that proliferate and survive to high passage in culture with maintained phenotype.

Internalized Tau₄₅₋₂₃₀ Aggregates Can Spread Tau Pathology and Neuronal Degeneration in Alzheimer's Disease and Related Disorders

Ashlee E. Rubino, Sana Afreen, and Adriana Ferreira

Northwestern University, Department of Cell and Molecular Biology, Chicago, IL

a-ferreira@northwestern.edu

We have previously shown that beta-amyloid-induced calpain activation leads to tau cleavage and the generation of the tau₄₅₋₂₃₀ fragment in Alzheimer's disease (AD) and related disorders. In addition, the expression of this fragment in otherwise healthy hippocampal neurons induces neurodegeneration followed by cell death. More recently, we generated and characterized transgenic mice that express tau₄₅₋₂₃₀ in pyramidal hippocampal neurons. The analysis of their phenotype showed enhanced neuronal death, synapse loss, and behavioral defects when compared to wild type controls. To get insights into the mechanisms underlying the neurotoxic effects of tau₄₅₋₂₃₀, we have assessed its ability to aggregate in the context of these diseases. For these studies, brain samples obtained from AD and other tauopathy subjects were homogenized and Western blot analyses were performed under non-denaturing conditions. Homogenates of brain samples obtained from age-matched subjects were used as controls. Our results showed the presence of tau₄₅₋₂₃₀ aggregates of ~68 and 168 kDa molecular weight, respectively, in all AD and other tauopathy brain samples analyzed. These aggregates differ in their susceptibility to sarkosyl. Thus, while most of the 168 kDa aggregates were sarkosyl-insoluble, only half of the 68 kDa ones remained after incubation with this detergent. We determined next to what extent tau₄₅₋₂₃₀ aggregates are neurotoxic. For these experiments, recombinant tau₄₅₋₂₃₀ was aggregated in the presence of arachidonic acid. Oligomeric tau₄₅₋₂₃₀ was purified and added directly to the culture medium of hippocampal neurons. Seven days in culture hippocampal neurons were incubated in the presence or absence of these aggregates for 24 hrs and their morphology and viability were assessed. Our results showed that tau₄₅₋₂₃₀ aggregates were incorporated into neurons and induced degeneration and cell death. Together, these studies provide insights into the mechanisms responsible for the transmission of tau pathology and its deleterious effects on neuronal viability in the context of Alzheimer's disease. In addition, they identified new targets for therapeutic intervention in this devastating disease.

Presynaptic Dystrophic Neurites Surrounding Amyloid Plaques Are Sites of Microtubule Disruption, BACE1 Elevation, and Increased A β Generation in Alzheimer's Disease

Katherine R. Sadleir, PhD¹, Patty C. Kandalepas, PhD¹, Virginie Buggia-Prevot, PhD², Daniel A. Nicholson, PhD³, Gopal Thinakaran, PhD², and Robert Vassar, PhD¹

¹*Northwestern University, Department of Cell and Molecular Biology, Chicago, IL*

²*The University of Chicago, Departments of Neurobiology, Neurology, and Pathology, Chicago, IL*

³*Rush University, Department of Neurological Sciences, Chicago, IL*

krdoherty@northwestern.edu

Alzheimer's disease (AD) is characterized by amyloid plaques composed of the β -amyloid (A β) peptide surrounded by swollen presynaptic dystrophic neurites consisting of dysfunctional axons and terminals that accumulate the β -site amyloid precursor protein (APP) cleaving enzyme (BACE1) required for A β generation. The cellular and molecular mechanisms that govern presynaptic dystrophic neurite formation are unclear, and elucidating these processes may lead to novel AD therapeutic strategies. Previous studies suggest A β may disrupt microtubules, which we hypothesize have a critical role in the development of presynaptic dystrophies. To investigate this further, here we have assessed the effects of A β , particularly neurotoxic A β 42, on microtubules during the formation of presynaptic dystrophic neurites *in vitro* and *in vivo*. Live-cell imaging of primary neurons revealed that exposure to A β 42 oligomers caused varicose and beaded neurites with extensive microtubule disruption, and inhibited anterograde and retrograde trafficking. In brain sections from AD patients and the 5XFAD transgenic mouse model of amyloid pathology, dystrophic neurite halos with BACE1 elevation around amyloid plaques exhibited aberrant tubulin accumulations or voids. At the ultrastructural level, peri-plaque dystrophies were strikingly devoid of microtubules and replete with multi-lamellar vesicles resembling autophagic intermediates. Proteins of the microtubule motors kinesin and dynein and other neuronal proteins were aberrantly localized in peri-plaque dystrophies. Inactive pro-cathepsin D also accumulated in peri-plaque dystrophies, indicating reduced lysosomal function. Most importantly, BACE1 accumulation in peri-plaque dystrophies caused increased BACE1 cleavage of APP and A β generation. Our study supports the hypothesis that A β induces microtubule disruption in presynaptic dystrophic neurites that surround plaques, thus impairing axonal transport and leading to accumulation of BACE1 and exacerbation of amyloid pathology in AD. This suggests that the use of brain-penetrant microtubule stabilizers could be of use in treating or preventing the cognitive decline in AD by preventing dystrophic neurite formation around plaques that lead to increased A β generation.

The Communication Bridge Research Program - Using Internet-Based Speech Therapy to Improve Quality of Life and Access to Care

Marie Saxon, Rebecca Khayum, Kathryn Borio, Hannah McKenna, Marya Corden, M-Marsel Mesulam, Emily Rogalski

Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL
marie.saxon@northwestern.edu

Language impairment (aphasia) is the defining feature of primary progressive aphasia (PPA) and a common symptom of other clinical dementia syndromes. Although there are no effective pharmacologic treatments for aphasic dementias, limited research suggests that speech therapy may be helpful for maintaining communication abilities and independence for activities of daily living. Unfortunately, many speech-language pathologists do not receive formal training on how to differentiate treatment strategies for patients with PPA versus those with stroke-induced aphasia, resulting in limited access to appropriate intervention for this population.

The Communication Bridge study circumvents both geographic limitations and poor access to care by delivering speech-language therapy through a user-friendly, personalized, Internet-based web-application. Designed in collaboration with the Center for Behavioral Intervention Technologies (CBITs), the web-application provides participants with a platform for connecting to web-based speech-language therapy (SLT) sessions, home exercises, and instructional speech therapy strategy videos. Rather than focusing on rote learning of generic words, as found in prior therapy studies, the speech-language therapy in this study focuses on providing individualized care, optimizing generalizability, and maximizing impact on quality of life.

To enroll in the study, participants must have mild to moderate aphasia symptoms due to dementia. Over the course of a year, participants receive an initial evaluation, eight speech-language therapy sessions, and three post-treatment evaluations at 2-, 6-, and 12-months after enrollment to determine the duration of therapy benefit. In addition to the speech-language therapy administered through the web-application, participants undergo neuropsychological testing and complete surveys to determine the effectiveness of SLT on functional communication ability, quality of life measurements, and interpersonal communication.

Since the study's inception, over 40 participants and their communication partners (care-partner or person who knows the patient well) have enrolled in the study across 21 different states and Canada. As one of the largest speech therapy studies for patients with aphasic dementia, the study continues to garner interest and receive positive participant feedback. Moving forward, the study seeks to demonstrate the feasibility of web-based SLT, which may be used to modify existing insurance coverage for SLT, and guide speech and language pathologists on effective strategies for providing therapy in neurodegenerative cases.

Successfully Aging in Place: Planning Rather Than Reacting to Life's Crises

Anne Seltzer, LSW; Vanessa Ramirez-Zohfeld, MPH; Lee A. Lindquist MD, MPH, MBA; Darby Morhardt, PhD, LCSW

Northwestern Memorial Hospital, Division of General Internal Medicine and Geriatrics, Chicago, IL
aseltzer@nm.org

Purpose: Seniors regularly plan for their end of life but very few people consider their support and health needs that they will encounter during their 70's, 80's, and 90's - the "4th Quarter" of life. During this time period, remaining in one's own home is often a high priority for seniors; however, as their functional and cognitive needs increase, seniors are likely to need more support to safely remain in their homes. We developed and tested the www.PlanYourLifespan.org (PYL) tool to assist seniors in making informed choices about issues in their health trajectory that may influence their ability to remain safely in their own homes. PYL is a web-based planning tool that enables seniors to explore issues related to hospitalizations, falls, memory loss, and connect to community-based resources in order to better plan for their future health.

Methods: We conducted a multi-site, two-arm randomized controlled trial of the PYL tool as compared to an attention control arm, in rural and urban settings in Chicago, IL; Fort Wayne, IN; and Houston, TX. Participants were English-speaking individuals 65 years and older who currently live independently in the community. After consent, participants were randomly assigned to one of the two interventions using equal (1:1) allocation and random permuted block design. Participants completed an in-person survey, followed by exposure to the intervention or attention control websites. Participants then completed a one-month and three-month telephone survey. Our primary endpoint was a planning behavior score (range 5-25; higher score signifies more planning behavior).

Findings: Among 385 participants randomized, the mean age was 71.9 (SD=5.6), 79.5% were female; 64.4% identified as White and 24.2% as African American. After controlling for baseline behavior score, participants in the PYL arm had a one-month behavior score that was significantly higher than those in the attention control arm (1.25 points, CI 0.37-2.12, $p = 0.0054$).

Conclusion/Practical Implications: PlanYourLifespan.org demonstrated efficacy in helping seniors plan for their health and support needs that typically follow health crises. This free, nationally available tool may help seniors and caregivers better understand, plan, and communicate their options and preferences for their future support needs in the event of health crises (hospitalization, falls, Alzheimer's disease).

Neuroimaging at the Northwestern Alzheimer's Disease Center

Jaiashre Sridhar, Allison Rainford, Mark Plantz, Benjamin Rader, Emmaleigh Loyer, Marie Saxon, Maureen Connelly, Adam Martersteck, Allan Wang, Kristine Lipowski, Carly Oboudiyat, Robert Hurley, Borna Bonakdarpour, Marco Catani, Derin Cobia, Sandra Weintraub, M-Marsel Mesulam, Emily Rogalski

Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL

jaiashre.sridhar@northwestern.edu

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 from 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 (MP--RAGE), white matter properties (FLAIR), axonal pathways (DTI), resting state hemodynamic fluctuations for establishing functional connectivity (rsfMRI), and amyloid (Amyvid – PET) or tau (¹⁸F--AV--1451 – PET) binding. 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.

Progranulin and Cathepsin D- A Potential Mechanism for Neurodegeneration

Clarissa Valdez

Northwestern University, Department of Neurology, Chicago, IL

ClarissaValdez2018@u.northwestern.edu

Frontotemporal Dementia (FTD) encompasses a group of neurodegenerative disorders characterized by cognitive and behavioral impairments as a result of progressive degeneration of frontal and temporal lobes. A mutation in the gene encoding progranulin (PGRN) accounts for up to 25 percent of familial FTD and results in decreased PGRN expression. PGRN is normally expressed in neurons and microglia within the CNS but the function of PGRN and why its decrease leads to disease is still unknown. PGRN was originally identified as a growth factor and has since been implicated in a wide array of biological functions including inflammation, early embryogenesis, wound repair and neurite outgrowth. Previous literature however, demonstrates that there is strong genetic evidence suggesting that PGRN is involved in lysosomal function. Recently, it was shown that a complete loss of PGRN, due a homozygous PGRN mutation, leads to neuronal ceroid lipofuscinosis (NCL), a group of neurodegenerative lysosomal storage disorders. However, there is no direct evidence that PGRN is involved in lysosomal function. Our research has demonstrated that a decreased level of PGRN impairs the ability of the lysosome to break down proteins. Furthermore, we have identified a potential mechanism by which decreased PGRN levels cause lysosomal dysfunction. We have shown that the expression of a specific lysosomal hydrolase, cathepsin D, is particularly affected by expression of PGRN. We also demonstrated that PGRN interacts with cathepsin D and can increase its activity *in vitro*. Taken together, these experiments suggest that PGRN, or individual granulins, may as an activator of cathepsin D. This PGRN-cathepsin D interaction may provide a potential mechanism by which PGRN haploinsufficiency leads to lysosomal dysfunction. This project has the potential to identify a mechanism that leads to the neurodegeneration observed in FTD patients with a PGRN mutation and contribute to our understanding of the pathogenesis that leads to neurodegeneration. Furthermore, validation of PGRN-cathepsin D interaction as a mechanism of neurodegeneration would identify a potential therapeutic target to combat FTD.

Decreased Baseline Brain Activity in Early-Stage Primary Progressive Aphasia Using Resting-State Functional Magnetic Resonance Imaging

Allan Wang, Marsel Mesulam, Borna Bonakarpour

Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL

allanwang2017@u.northwestern.edu

Objective: Primary Progressive Aphasia (PPA) is a neurodegenerative disease characterized by progressive language decline. PPA has three variants based on the profile of language impairment: agrammatic, logopenic, or semantic. Our previous research using resting-state fMRI (rs-fMRI) to study language network changes in a group of individuals with the agrammatic variant of PPA (PPA-G) revealed a decrease in the resting state functional connectivity (RSFC) between the left inferior frontal gyrus (IFG) and the left middle temporal gyrus (MTG). However, the physiologic mechanism underlying this decoupling of RSFC is still unclear. In this study, we used the fractional Amplitude of Low Frequency Fluctuations (fALFF), a measure of baseline brain activity, to investigate specifically which regions of the brain exhibited abnormal physiology in our previously studied PPA-G group. We hypothesized that the fALFF would be decreased in the frontal region of the language network.

Methods: The PPA group included 10 individuals with early stage PPA-G who showed no significant cortical atrophy at the single-subject level and had available rs-fMRI scans. Thirty-three healthy subjects were used as a control group. fALFF values for each subject were calculated on a voxel-wise basis. A two-sample *t*-test was conducted to identify regions of the brain that demonstrated significantly lower fALFF in the PPA group than in controls.

Results: The two-sample *t*-test comparing the PPA and control groups showed clusters of significantly decreased fALFF in the left IFG (both pars triangularis and opercularis), bilateral caudate nuclei (more in the left hemisphere), and bilateral thalami (more in the left hemisphere) ($p < 0.01$).

Conclusions: In this study of a group of individuals with early stage PPA-G, we identified cortical and subcortical regions of the language network that exhibited abnormal baseline brain activity using fALFF analysis. Signal amplitude was decreased in the left IFG but not the left MTG, indicating that the disrupted IFG-MTG connectivity observed in the previous study was most likely due to underlying abnormal physiology in the IFG. This is in line with previous pathologic studies of PPA-G that showed greater accumulation of underlying pathology within the left IFG. These results also reveal leftlateralized physiological changes in the caudate and the thalamus, two subcortical regions known to be implicated in speech and language control. Our next step is to extract individual fALFF values to identify how these physiological changes affect speech and language function at the group and individual levels. Identifying specific regions of abnormal physiology in PPA may potentially produce future targets for neuromodulatory treatments, such as transcranial magnetic stimulation.

Northwestern Alzheimer's Disease Center (NADC) Clinical and Data Management and Biostatistics Cores

Mallory Ward BA, Laura Martindale BA, Bitra Rad BA, Alfred Rademaker PhD, Borna Bonakdarpour MD, Carly Oboudiyat MD, Mustafa Seckin MD, Okkes Kuybu MD, Lauren Dowden MSW, Mary Rastetter MSW, Darby Morhardt PhD, Emily Rogalski PhD, M-Marsel Mesulam MD, Sandra Weintraub PhD

Northwestern University, Cognitive Neurology and Alzheimer's Disease Center, Chicago, IL
mallory.ward@northwestern.edu

INTRODUCTION: The Northwestern Alzheimer's Disease Center (NADC) is entering its 21st 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 1996-2016 the Clinical Core has enrolled more than 1,993 participants, and the current active cohort is 521 (Figure x). In the past year, the Clinical Core supported over 15 different investigators and 22 studies being conducted in the areas of cognitive neuroscience, clinical trials, neuroimaging and neuropsychology (Table x). A total of 50 publications 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.

CREB Overexpression in Dorsal CA1 Ameliorates Memory Deficits in Aged Rats

Xiao-Wen Yu¹, Daniel M. Curlik II¹, M. Matthew Oh¹, Jerry C. P. Yin², John F. Disterhoft¹

¹*Northwestern University, Department of Physiology, Chicago, IL*

²*University of Wisconsin-Madison, Department of Genetics, Madison, WI*

xiaowenyu2016@u.northwestern.edu

Humans and animals often display learning and memory impairments as they age, however the underlying mechanisms of these impairments are poorly understood. Identifying the molecular pathways that mediate these impairments will allow us to design therapeutics to prevent or ameliorate these deficits. Increasing activity of the transcription factor cAMP response element-binding protein (CREB) in young adult rodents has been shown to facilitate their behavioral performance and increase intrinsic cellular excitability – both are impaired in normal aged animals. To test if increasing CREB activity would ameliorate age-related cognitive deficits, we overexpressed CREB in CA1 of dorsal hippocampus using an adeno-associated viral vector. Young and aged rats both received CREB or control virus, then underwent Morris water maze training. CREB overexpression in aged animals ameliorated the deficits in long-term memory seen in control animals, while surprisingly; young animals were unaffected by CREB overexpression. Concurrently, cells overexpressing CREB in aged animals were found to have a reduced post-burst afterhyperpolarization i.e., increased excitability. These results indicate that dysfunction in CREB signaling may mediate age-related cognitive deficits.

This work was supported by NIH R37 AG008796 and T32 AG020506, and the Glenn/AFAR Scholarship for Research in the Biology of Aging.

Neuroprotective Effects of Sleep on β -Amyloid Induced Loss of Circadian Rhythms in *Drosophila*

W. Zhang¹, B. van Alphen², F. Xu², M. Zhang², R. Allada²

¹Northwestern University, Master of Biotechnology Program, Evanston, IL

²Northwestern University, Department of Neurobiology, Evanston, IL

weichaozhang2016@u.northwestern.edu

Alzheimer's disease is associated with accumulation of pathogenic β -amyloid peptides in the brain. Growing evidence has demonstrated disease link between sleep and Alzheimer's disease, where impaired sleep is a prodromal symptom of the disease. Recent mouse and fly studies suggest that sleep plays a crucial role in clearing β -amyloid from the brain. In this study, we are trying to understand how Alzheimer's disease impacts sleep and circadian rhythms and how sleep and circadian rhythms modulate Alzheimer's disease. Pan-neuronal expression of toxic β -amyloid peptides (arctic A β 42) using ELAV-Gal4 and *daughterless*-GS-Gal4 drivers in *Drosophila melanogaster* reduces their lifespan. Accumulation of β -amyloid peptides in the brain leads to reduced and fragmented sleep and loss of circadian rhythm. In addition, sleep deprivation increases β -amyloid levels in the Calyx of the *Drosophila* mushroom body and accelerates the loss of circadian rhythm, suggesting that loss of sleep speeds up Alzheimer's progression. Moreover, β -amyloid expressing flies subjected to constant light show exacerbated sleep phenotypes. We also use our *Drosophila* Alzheimer's model to conduct genetic screens to identify genes that either suppress or enhance these sleep and circadian phenotypes. These identified gene candidates could reveal the molecular mechanism that connects sleep and/or circadian rhythms and neurodegenerative diseases, and to provide potential drug targets for novel therapies.

DUCTION & CASEY P.C.

ATTORNEYS AT LAW



Janna Dutton



Kathryn C. Casey

ATTORNEYS

Janna Dutton | Attorney

Kathryn Casey | Attorney

Helen Mesoloras | Attorney

Michaela Franco | Attorney

Melissa LaPointe | Attorney

Chicago 312.899.0950
Suburbs 847.261.4708

contact@duttonelderlaw.com
www.duttonelderlaw.com

Appointments are available in Arlington Heights, Chicago, Skokie, and Westchester, Illinois, or via video conferencing or telephone.

Both Janna Dutton and Kathryn Casey are **Certified Elder Law Attorneys (CELA)**. The Certified Elder Law Attorney is the only American Bar Association approved designation for elder law.

PRACTICE AREAS

- ◆ Estate Planning (Wills, Powers of Attorney, Trusts)
 - ◆ Special Needs Planning
 - ◆ Long-Term Care Planning
 - ◆ Probate and Trust Administration
 - ◆ Guardianship
 - ◆ Will and Trust Litigation
 - ◆ Litigation for Vulnerable Adults Against Abuse, Neglect, and Financial Exploitation
 - ◆ Elder Law
 - ◆ Medicaid Planning and Applications
 - ◆ Senior Housing Contracts, Admissions and Discharges
 - ◆ Mental Health Law
 - ◆ Care Navigation and Advocacy
- Full-time clinical social worker and certified care manager on staff.**

The Supreme Court of Illinois does not recognize certifications of specialties in the practice of law and the CELA designation is not a requirement to practice law in Illinois.



Enhancing the Quality of Life of Older Adults Through Life Enrichment, Supportive Resources, Healthcare, Research and Education.

A comprehensive network of care for older adults and their families, including:

- ♦ Assisted Living and Memory Care at Weinberg Community for Senior Living in Deerfield
- ♦ Short-term Rehabilitation, Alzheimer's Special Care Unit and Long-term residential care at Lieberman Center for Health and Rehabilitation in Skokie
- ♦ Art in the Moment Tablet App, designed for people with cognitive disabilities
- ♦ Adult Day Services in Evanston, Deerfield and Downtown Chicago and the award-winning Culture Bus™
- ♦ Your Eldercare Consultants, our team of geriatric care managers
- ♦ Holocaust Community Services
- ♦ Counseling and Support Groups

cje SeniorLife
Jewish values for positive aging



CJE SeniorLife™ is a partner with the Jewish United Fund in serving our community.

873.4.2016

For more information about CJE SeniorLife, call 773.508.1000 or visit www.cje.net.



EXPERIENCE A HIGHER STANDARD OF HOME CARE

- › Alzheimer's and Dementia Care
- › Hourly & Live-in Care
- › Bathing & Personal Care
- › Housekeeping & Meal Prep
- › Medication Reminders
- › 24/7 Live Support
- › Guaranteed Compatibility®
- › RN Oversight
- › No Minimums


BrightStar Care®
A HIGHER STANDARD OF HOME CARE



Call for your complimentary in-home assessment!

BrightStar Care Locations Serving Chicagoland
866 618 STAR (7827)
www.brightstarcare.com

All Chicagoland BrightStar Care agencies are accredited by The Joint Commission and independently owned & operated.

***“Mom’s getting more confused.
She forgot to eat again.”
“What if she wanders off?
That would be horrible.”
“We need to keep her safe at home.
We need more help.”***

If you’re struggling to care for a loved one with dementia or other challenges with aging, we can help.

homeinsteadchicago.com

773.784.4024 or 773.463.3500

**Home
Instead**
SENIOR CARE®
To us, it's personal.®

**Don't just hope for a cure.
Help us find one.**

Everyone can help advance Alzheimer's disease research.

Designed for:

- * Individuals with Alzheimer's
- * Caregivers seeking trials for themselves and for the person they care for
- * Healthy volunteers who would like to help advance research
- * Physicians in search of trials for their patients
- 130+ studies
- 500 trial sites nationwide
- Pharmacological (drug) and non-pharmacological (non-drug) studies



alzheimer's  association®
trialmatch®

POWERED BY  EmergingMed

alz.org/trialmatch | 800.272.3900



Expanding horizons in palliative,
supportive & end-of-life care

Consider the moments that make up a lifetime. Some are big—a graduation, a wedding, retirement—and easy to remember. Some are smaller—a personal goal achieved, a day in the park with your child, a sunset with a special someone—but no less important. Others are life changing, like a serious illness or the loss of a loved one...these are the moments when you need someone by your side, a partner in care to help you live your life on your own terms. These moments are made for JourneyCare...we are with you and your loved ones every step of the way.

We are here for you 24-hours a day, 7 days a week. Anyone can call to inquire about services. We will work with you, your family and your doctors

Referrals: 224-770-2489

Other inquiries: 847-467-7423

journeycare.org

Honoring the legacies of
Horizon Hospice & Palliative Care, Midwest Palliative & Hospice CareCenter and JourneyCare

The state-of-the-art Memory Support neighborhood at St. Pauls House offers a comfortable, home-like environment for those experiencing Alzheimer's disease and other forms of memory loss. This completely individualized program explores the tapestry of each resident's life—his or her unique experiences, preferences and rhythms of life—to create a personalized care plan that enhances well-being and a sense of security.


ST. PAULS HOUSE
A COMMUNITY AS UNIQUE AS YOU.

MyTapestry

he was married 62 years to his childhood sweetheart ...
is a night-owl ...
raised four boys ...
likes his coffee strong and black ...
refinished antiques ...
likes his eggs over-easy ...
and his steak well-done ...
made yearly trips to visit family in Ireland ...
knows a few magic tricks ...
liked playing chess in the park ...
likes breakfast at 11 and lunch at 3 ...
can still dance a jig ...
has met three U. S. presidents ...
and so much more ...
enjoys old movies ...
is still a Cubs fan ...
owned a rare book store ...
walked three miles every day ...

every life is a tapestry

Call (773) 478-4222 today to schedule a personal tour.

3800 N. California Avenue | Chicago, Illinois 60618 | Phone: (773) 478-4222 | StPaulsHouse.org

Empowering vibrant, grace-filled living across all generations.

Lutheran Life Communities welcomes people of all faiths, beliefs and traditions.



Changing the View on Alzheimer's Care FOR ASSISTED LIVING...

**Terra Vista is a new assisted living community
100% dedicated to Alzheimer's and other dementias**

Our one-of-a-kind memory care community includes...



**SPECIALIZED
MEMORY CARE**



**GUARANTEED
ALL-INCLUSIVE RATE**



**INNOVATIVE
TECHNOLOGIES**



**BARRIER-FREE
ENVIRONMENT**



**COMPASSIONATE
CAREGIVER SUPPORT**

Terra Vista
of Oakbrook Terrace
Changing the View on Alzheimer's Care
An assisted living community 100% dedicated
to Alzheimer's and other dementias.

For more information,
call **630-534-0886**
or visit **TerraVista.org**.



1635 S ARDMORE AVE, OAKBROOK TERRACE, IL 60181 | 630-534-0886 | TERRAVISTA.ORG

SeniorBridge®

Professional home care you can trust

SeniorBridge in-home care specializes in caring for people who have medical, functional and behavioral challenges including expertise with dementia and Alzheimer's care.

SeniorBridge services include:

- Assessment of medical, psychosocial and environmental factors
- Customized care plans to meet specific life management goals
- Medication management
- Socialization and cognitive stimulation
- Family respite and support
- Coordination with healthcare providers and social services
- Hourly and live-in caregivers offering assistance with personal care, companionship, meal preparation and errands



Contact us for a free and immediate consultation

Call (312) 329-9060
www.SeniorBridge.com

Humana

At Home™

SeniorBridge is a private pay offering of Humana At Home.



CHAP accreditation certifies that
SeniorBridge meets the highest
recognized standards in healthcare.

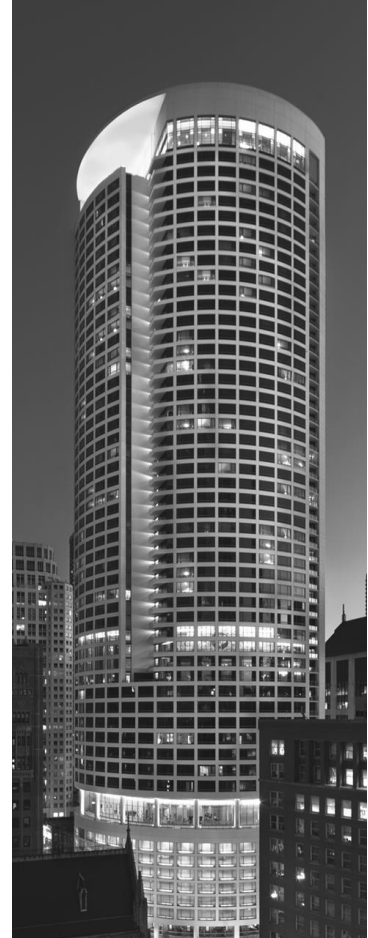
The
TERRACES
at THE CLARE



Memory Support at The Terraces at The Clare has been structured, staffed and designed to help individuals and their families cope with the challenges that come with memory loss. Our mission is to constantly strive to enhance the lives of residents and give their families the reassurance they are being given the best support possible in a first class environment

The Terraces' progressive approach to Memory Support is focused on creating positive interactions with each and every resident. Our specially trained professionals take the time to learn each resident's story – grandchildren, career, hobbies, travels – resulting in a nurturing relationship that goes far beyond simply providing care

*If your family chooses The Terraces,
you can feel confident knowing your loved one will be comfortable, safe and cared for in a
very personal way.*



55 E. PEARSON STREET • CHICAGO, IL 60611 • p 312.442.2156 • f 312.784.8069 • www.TheClare.com



ALL TRUST HOME CARE

Place ALL TRUST in us

***Providing compassionate, professionally trained
Caregivers specializing in Memory Care***

Our Extensive Hiring and Screening Process Includes

**Professionally Trained Caregivers
Nationwide Background Checks
Drug Testing/DMV Records
Skill Assessments/Reference Checks
Plus Several Additional Screening Tools**

**Dan Kuhn, LCSW, Vice President of
Education provides Advanced
Dementia Training to our Caregivers**

Services We Can Provide

**Medication Reminders
Safety and Supervision
Assist with Bathing and Dressing
Driving to Appointments
Meal Preparation
Laundry/Housekeeping Assistance
Live In or Hourly Caregivers
Licensed/Insured/Bonded
Available 24 Hours**

Hinsdale 630-920-9999 • www.alltrushomecare.com • Deerfield 847-947-8511

Licensed by the Illinois Department of Public Health



Freedom Home Care

Extraordinary Health
& Wellness
Right at Your Doorstep



Introducing our exclusive Freedom Client Wellness Tracking System (FreedomCWTS).

- live tracking of clients vital signs
- notification alerts when health changes occur
- online access to family portal
- prevents readmissions

Health & Wellness Services:

- Case Management
- Medication Management & Reminders
- Diabetic Care & Supervision
- On-going & Chronic Illness Supervision
- Accompanying Clients to Appointments
- Basic Wound Care & Dressing Changes
- Post-Hospital Care & Day Surgery
- Companion Care
- Respite Care
- Bedside Care in Hospitals & Nursing Homes
- Alzheimer's / Dementia Care

Companion Home Services:

- Client Transportation
- Running Errands & Shopping
- Light Housekeeping & Personal Laundry
- Meal Preparation Following Special Dietary Needs
- Personal Care Services Including Grooming, Bathing & Dressing Assistance
- Morning Wake-up & Evening Tuck-in
- Concierge Services Available Upon Request
- Hospital Recommended

1 Hour to 24/7 Coverage

"I have been working with seniors for over 20 years as a Gerontologist and Geriatric Care Manager... I truly love working with seniors and their families. My clients come from different hospital systems and the North Shore community at large. When guiding seniors and their families who need private duty home care, I feel a sense of security and comfort when Freedom Home Care works with me and my clients. They strive to provide exceptional quality care to seniors in need!"

Julie Fohrman, MA
Gerontologist in Highland Park, IL

Caregivers • Companions • Nurses • CNAs

847-433-5788

www.freedomhomecare.net

Serving the North Shore, Chicago, and the Western Suburbs Since 1997

Chicago's Trusted Memory Care Resource

Caring for Older Adults on Chicago's North Side Since 1898

At Chicagoland Methodist Senior Services, we understand that it requires a variety of programs and a dedicated, specialized staff to support those suffering from memory loss.

We offer memory care in two communities: an assisted living community at Hartwell Place, designed specifically for those with memory care needs, and a more advanced program at Wesley Place for those whose health necessitates round the clock nursing supervision and an increased level of security.

Both communities are state-designated special care programs exclusively for memory care — reinforcing the resident's remaining abilities, interests and preferences.

We're proud to be a resource for families, and we are happy to listen to your questions and explain your options.

Call 773-506-6950 today to schedule a tour.

773-506-6950 • cmsschicago.org



**CHICAGOLAND METHODIST
SENIOR SERVICES**

The First Lutheran Senior Services Midwest On Chicago's North Side



GENERATIONS AT REGENCY

Rehabilitation & Skilled Nursing



With all the luxuries of home, your loved one will enjoy great comfort and care at Generations at Regency. With a vast amount of accommodations and services available, the residents at Generations at Regency experience a living quality unlike other healthcare facilities.

Our services include:

- 24-Hour Skilled and Intermediate Nursing Care
- State Certified Alzheimer's & Dementia Unit
- Occupational, Physical and Speech Therapy
- Cardiac Rehabilitation Program
- Orthopedic Rehabilitation Program
- Diabetes Management Program
- IV and Respiratory Services
- On-Site Dialysis Unit
- Hospice & Palliative Care
- Recreational Therapy
- Long and Short-Term Stays
- Gourmet Meals & Award Winning Dining
- Free Wi-Fi Internet



**Call today for
more info
847-647-7444**

Our family caring for your family for generations to come.

6631 N. Milwaukee Ave., Niles, IL 60714
Phone: 847-647-7444 Fax: 847-647-6403

www.GenerationsRegency.com



www.Elderwerks.com

**When you're looking for help, information and resources
call Elderwerks for Complimentary Assistance**

Elderwerks is a free senior housing and care information and referral service. Your personal Consultant will help guide you to the best option for your loved one. Not all memory care facilities are created equal or meet everyone's needs. Call today to discuss your situation.

855-462-0100

Notes