

NORTHWESTERN UNIVERSITY FEINBERG SCHOOL OF MEDICINE

# Mesulam Center NEWS

A Publication of the Mesulam Center for Cognitive Neurology and Alzheimer's Disease

FALL 2020



## MESULAM CENTER FOR COGNITIVE NEUROLOGY AND ALZHEIMER'S DISEASE

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

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

On the cover: Research study assistant Fatima Eldes presented her research, "Rates of Cortical Atrophy in Adults Aged 80+ with Superior Memory Compared to Cognitively Average Middle-Age Adults" at the Organization for Human Brain Mapping virtual conference in summer 2020.



**DEAR FRIENDS AND COLLEAGUES:** Greetings and welcome to our 2020 Newsletter!

Would you believe that more than six months have elapsed since the beginning of the COVID-19 emergency? I am sure I do not need to remind you that the pandemic is still here. In addition, we are in the midst of a societal upheaval in reaction to racial injustice, and we are in the year of an unusually polarizing presidential election. Faced with these momentous events, it may appear insensitive to dwell on the achievements of our center. Nonetheless, I will follow the traditional purpose of these introductory remarks to offer you a brief status report.

Let me start by thanking the faculty, administration, staff, fellows, and students of our center for exemplary resilience and creativity. Despite emergency restrictions, patient care has remained uninterrupted thanks to telehealth; teaching has continued through video; reports of scientific discoveries have been written (from home) and published in top journals; proposals for major projects have been submitted and awarded; and lectures have been given locally, nationally, and internationally through webinars. Just a few weeks ago, the NIH-funded Alzheimer's Disease Research Center that I established in 1996 and led for more than 20 years submitted its fifth consecutive five-year renewal application, this time under the leadership of Robert Vassar and Sandra Weintraub. And within the same month, a proposal was submitted, under the leadership of Emily Rogalski and Changiz Geula, to establish an international consortium on SuperAging, an unusual form of aging that represents the polar opposite of Alzheimer's disease and that may offer clues for preventing age-related memory decline.

As you know, the annual AD-Day is the signature event of our center. The 26th annual AD-Day was scheduled for May 14. As COVID-19 forced us to cancel the event, we faced the painful option of interrupting a tradition that we had maintained for a quarter of a century. Darby Morhardt and her colleagues averted this mishap by organizing a virtual AD-Day on September 24. The event exceeded all expectations and attracted an online attendance of nearly 400, with Sandra Weintraub giving the keynote address as the Mendelson Lecturer.

In response to the national crisis of healthcare disparities, I am glad to report that a Diversity, Equity, and Inclusion Committee has been established to craft an action plan, specific to our center. As part of this initiative, we have intensified the research recruitment of participants from underrepresented minorities so they can benefit from all related developments. Increased diversity in the center workforce remains a top priority. With respect to COVID-19, we have initiated a renormalization process guided by a committee of faculty and staff and implemented by our center administrator, Thongsy Singvongsa. At the current phase of renormalization, our headquarters on Tarry 8 is gradually being repopulated so we can reestablish the spatial contiguity and multidisciplinary teamwork that is the hallmark of our center. Furthermore, many of our patients are now being seen in person at our Neurobehavior Clinic on Arkes 9, while others continue to be served through telehealth. We are also on the verge of resuming in-person, patient-based research, especially in the area of clinical trials, where the goal is the discovery of new drugs to combat Alzheimer's disease and frontotemporal dementias. Basic science research was the least effected by the lockdown and is functioning at a level that is close to the pre-pandemic level.

I am obviously not suggesting that business is proceeding as usual; far from it. However, as you will see in the pages of this newsletter, our center has not been missing too many beats in pursuing its mission of patient care, scientific discovery, and teaching.

Stay well and stay safe and do not hesitate to contact me or any other center member with comments or questions.

A handwritten signature in black ink, appearing to read "M. Marsel Mesulam".

#### **M. Marsel Mesulam, MD**

Mesulam Center for Cognitive Neurology and Alzheimer's Disease director and Ruth Dunbar Davee Professor of Neuroscience

# SuperAger Resilience: Taking Control of Their Future



**S**ome of us are lucky enough to find one calling in life. Liz Lautner can count approximately nine passions that she has had in her 88 years on Earth. She has been a professional dog trainer, a private and commercial pilot, a videographer, a photographer, a newsletter manager, a greeting card

maker, a refrigerator magnet creator, a wife, and a mother. "Every time I started to do something, I did it well," she said. "People call me talented, and yes, I guess I am, but when I do something, I go at it with a lot of focus."

Her focus is one of the reasons Lautner qualified for the SuperAgers study at the Mesulam Center. A SuperAger is someone age 80 or older who tests at an episodic memory capacity of someone 20 or 30 years their junior. "They have to be testing at a 50- or 60-year-old episodic memory capacity," said Beth Makowski-Woidan, senior research study

**"This year, I have really got something planned. I am expecting to take a first or a best of show award."**

LIZ LAUTNER

coordinator. "It's very impressive." Each SuperAger visits the Mesulam Center every two years for cognitive testing, along with MRI and PET scans, which are then used to track neurological changes and trends.

## Increasing possibilities as senior citizens age

For Lautner, joining the group brought a new level of activity to her historically busy life. "This program has confirmed to me that I am a much stronger person and a much more intelligent person than I ever thought I was," she said.

That is one advantage of the program, investigators say. "It offers an opportunity to highlight how expectations can be different in aging," said Emily Rogalski, PhD, professor of Psychiatry and Behavioral Sciences and the principal investigator on the SuperAgers study. If you expect that your memory and intelligence will decline as you get older, it can make you feel defeated. However, that model does not fit everyone, and the SuperAger study looks for patterns to



SuperAger Liz Lautner creates prize-winning art on eggshells and rocks.

better understand cognitive aging. "If there isn't that expectation for memory loss, then there is new opportunity for decreasing stigma and increasing the possibilities in aging," Rogalski said.

## Taking control of her future

For Lautner, the program offers a way for her to take control of her future, as she has done all her life. When her husband passed away, she was left as a single mom of two little boys. With a high school education and a household to run, Lautner entered the workforce. Years later, tragedy would strike her life again. Her youngest son was killed in an accident at 16. Her eldest son, David, went on to graduate from college and become a pilot. "We actually got our private pilot licenses on the same day, his seventeenth birthday," she said.

Today, Liz lives in an independent senior living community in her home state of Texas. Even during the pandemic, she volunteered as a cashier in her building's dining room for the complex's nurses, other staff, and residents. When she isn't volunteering, she often paints on more than just canvases. Her artistry on eggshells and rocks has won her second and third place in a state-wide senior citizen arts competition called Arts Inspire. "This year, I have really got something planned," she said. "I am expecting to take a first or a best of show award."

*For more information about the SuperAgers program, please contact Beth Makowski-Woidan at [beth.makowski-woidan@northwestern.edu](mailto:beth.makowski-woidan@northwestern.edu).*

## LATEST FUNDING: R01 GRANT

Over the summer, an R01 grant from the National Institutes of Health (NIH) focused on studying SuperAgers was renewed for another five years. The goal of the SuperAger study is to identify aging factors of individuals who continue to better their lives through intellectual, volunteer, or professional work. The study, titled **"Cognitive SuperAging: A model to explore resilience and resistance to aging and Alzheimer's disease,"** was very successful in its first five years of being funded by the NIH. The next five years will focus on clarifying those initial insights and extending those observations.

# Collaborating and Leading on the Local, National, and International Stage

Even with the groundbreaking research taking place at the Mesulam Center, faculty and clinicians take time to lead and advocate for aging populations at every level. That helps ensure that their research and work makes its way directly to people who need it the most.

"It's very important for us to take whatever we learn from a diverse range of research to the care of the person," said Sandra Weintraub, PhD, professor of Psychiatry and Behavioral Sciences. "We are able to directly translate what we know into ways we can help them."

## Local

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- Borna Bonakdarpour, MD, assistant professor of Neurology, is co-director of the Northwestern Virtual Orchestra, which supported health care professionals during the COVID-19 pandemic. Bonakdarpour also helped found the Northwestern Civitas Music Cafe with the Chicago Symphony Orchestra to design musical performances for people with mild dementia.
- The Chicago Department on Aging appointed Darby Morhardt, PhD, research professor at the Mesulam Center, for her third year to the Age Friendly Chicago Commission. Increasing accessibility to older adults in urban environments connects Chicago to the World Health Organization's Global Network of Age-Friendly Cities.
- Emily Rogalski, PhD, professor of Psychiatry and Behavioral Sciences at the center, was appointed president of Feinberg's Medical Faculty Council (MFC). The MFC acts as a liaison between the Feinberg faculty and medical school administration to help foster collaboration.

## State

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- In March 2020, Bonakdarpour received the Advocacy Award from the American Music Therapy Association, Illinois Chapter. The award is given to professionals who have shown long-term effort in developing and growing the field of music therapy.
- Both Marsel Mesulam, MD, center director, and Morhardt were appointed to the Alzheimer's Disease Advisory Committee (ADAC). The ADAC acts as an Alzheimer's task force for the Illinois Department of Public Health.

- Morhardt, a founding member of the Illinois Cognitive Resources Network (ICRN), has extended her expertise on educational programming in communities to become a Dementia Friendly Illinois Network Leader for the ICRN.

## National

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- Maggie Flanagan, MD, assistant professor of Pathology in the Division of Neuropathology, is an active member of the Alzheimer's Association Young Champions initiative. The program incorporates a diverse group of emerging leaders who are passionate about changing the face of Alzheimer's disease and dementia by increasing education about the diseases across generations.
- The American Academy of Neurology recently selected Sandra Weintraub, PhD, professor of Psychiatry and Behavioral Sciences at the center, as a 2019 fellow for her work both as a clinician and a researcher.

"It's very important for us to take whatever we learn from a diverse range of research to the care of the person."

SANDRA WEINTRAUB, PHD  
PROFESSOR OF PSYCHIATRY AND BEHAVIORAL SCIENCES

## International

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- Bob Vassar, PhD, scientific director of behavioral neurology in the Department of Neurology, was recently selected as a member of the Scientific Advisory Board for the Institute on Aging and Brain Disorders at the University of Science and Technology of China. The institute's mission involves accelerating the transfer of basic science discoveries into the clinic through multidisciplinary programming.
- As a founding member of the International Society for Frontotemporal Dementias, Weintraub has been able to help the society's mission to better understand the nervous system and other illnesses that play a role in these dementias.
- Rogalski was invited to speak at an international conference hosted by the University of Southern California titled "New Horizons in Human Brain Imaging: Neuroimaging across the Lifespan." The February 2020 meeting examined cutting-edge brain imaging technology and its role in cataloguing dementia disorders.

# Training Global Leaders

The Mesulam Center has earned an international reputation that attracts some of the brightest dementia researchers in the field to come learn about cutting-edge techniques and care programs they can draw upon in their own work across continents.



Dr. Mesulam and Gülüstü Salur. Gulustu's daughter Nazlı, middle, was born in Chicago and is studying molecular biology, genetics, and psychology.



## **Gülüstü Salur, MD**

65+ Elder Rights Association Turkey,  
Istanbul, Turkey

After completing a three-and-a-half year fellowship at the Mesulam Center from 1998 to 2002, Gülüstü Salur returned home to Turkey, where she now chairs the 65+ Elder

Rights Association. Founded six years ago, the association helps develop social policies that benefit the elderly population. Salur is also one of the founders of the Alzheimer's Association of Turkey and has been an adjunct faculty member at various institutions in Istanbul, including in Boğazici University's Department of Psychology.

Understanding the diverse nature of dementia was just one of the many lessons Salur learned during her inspiring years in Chicago. Center director Marsel Mesulam's emphasis on both broad understanding and in-depth analysis of dementia inspired Salur to open up her own Cognitive Neurology Dementia and Movement Disorders Clinic when she returned to Istanbul in 2002. "Exposure to all aspects of research, clinical work, and education at Mesulam Center enabled me to address the whole spectrum of cognitive, psychological, physical, social, and societal problems brought on by dementia syndromes."

Working with dementia and movement disorder patients for almost 25 years has put Salur in front of individuals who struggle on a daily basis. "However, my years at the Mesulam Center equipped me with an understanding of our limits, but also working despite and against those limits," Salur said.



## **Mustafa Seckin, MD**

Acibadem University, Istanbul, Turkey

Neurologist Mustafa Seckin joined the Mesulam Center as a postdoctoral research fellow in 2013. While here, Seckin developed a sophisticated method to find comprehension deficits in patients with primary progressive aphasia (PPA), a form of dementia that primarily affects language, by measuring eye movements. After his fellowship, Seckin went to Istanbul and founded a clinical and research program on aging and dementia at Acibadem Taksim Hospital.

Beyond PPA research, Seckin conducted neurological examinations of SuperAgers at the center with Emily Rogalski, PhD, principal investigator on the study. "Working with Dr. Rogalski and Dr. Robert Hurley improved my skills in designing and conducting a scientific experiment," he said. After publishing scientific papers during his fellowship, he received prestigious awards from international institutions, including the World Federation of Neurology, the European Commission Marie Curie Actions 7th Framework Programme, and the Center for Advanced Studies at LMU-Munich. "Besides the research training, the knowledge I gained about project management at the Mesulam Center helped me become an independent researcher," he said.

As a member of the Turkish Society of Neurology Dementia and Behavioral Neurology Working Group, the World Federation of Neurology Aphasia Dementia and Cognitive Disorders Research Group, and the German Consortium for Frontotemporal Lobar Degeneration, Seckin has been able to take the lessons learned at the Mesulam Center around the world.

# NEW FACULTY SPOTLIGHT

## Maggie Flanagan, MD

ASSISTANT PROFESSOR OF PATHOLOGY  
IN THE DIVISION OF NEUROPATHOLOGY



Maggie Flanagan joined the Mesulam Center in November 2019 and became the Neuropathology Core leader in March 2020. The Neuropathology Core assists basic science researchers with investigations that apply to human brain tissue. Flanagan

pursued her medical degree at Trinity College in Dublin after completing her bachelor's degree in cytotechnology at the University of North Dakota. Her research focuses on investigating the protein TDP-43's role in neuroinflammatory regulation in the development of amnesic dementia syndromes, as well as in the development of non-amnesic dementia syndromes, such as primary progressive aphasia. Flanagan's research also emphasizes the importance of studying those with cognitive resilience, such as SuperAgers.

With 20 neurological publications already under her belt, her recent investigations include being a co-principal investigator on the grant titled "Retinal Changes in Alzheimer's Disease (AD) Correlated with Cerebral Amyloid Staging. A Promising Early Biomarker in AD." In addition, she was also a co-author on the research paper, "Limbic-predominant age-related TDP-43 encephalopathy (LATE)" (April 2019), describing a unique pathology that causes dementia.

Flanagan's latest peer-reviewed publication was accepted by the *Journal of Neuropathology and Experimental Neurology* (September 2020). This clinical neuropathology-focused publication described an extraordinarily rare case of "Epstein Barr Virus Positive Diffuse Large B-Cell Lymphoma in the CNS associated with Hemophagocytic Lymphohistiocytosis."

The Mesulam Center has exceeded Flanagan's expectations both personally and professionally. "It's almost like it's too good to be true," Flanagan said. "All of the research here is aligned with my own personal research interests. I love all of the collaborations I'm already starting to get involved in, and everybody in the center has been so welcoming and wonderful to work with."

Flanagan's commitment to Alzheimer's and dementia research is personal. Her father was diagnosed with Alzheimer's disease while she was in medical school. She was planning to become a cytopathologist, but after her father's diagnosis, she said, "I found neuropathology and Alzheimer's disease and became so interested in the brain."

## Maureen Daly, PhD

HEALTH SYSTEM CLINICIAN OF PSYCHIATRY  
AND BEHAVIORAL SCIENCES



Maureen Daly joined the Mesulam Center as a clinical neuropsychologist in January 2020. Prior to becoming a health system clinician in Psychiatry and Behavioral Sciences at the Feinberg School of Medicine, she completed her master's and doctoral

degrees in psychology and clinical neuropsychology, respectively, at the Graduate Center of the City University of New York. Daly also holds a bachelor's degree in psychology from the University of Wisconsin-Madison. She completed her internship in clinical neuropsychology at Massachusetts General Hospital and fellowship in clinical neuropsychology at Massachusetts General Hospital/Brigham & Women's Hospital in Boston.

Daly's research interests throughout undergraduate and graduate school were in psychosis proneness and schizophrenia. Specifically, she studied indicators of vulnerability for schizophrenia.

Daly eventually decided to pursue dementia care full time because of its intersectional nature. "I like understanding neurodevelopmental aspects of brain functioning and cognition, and how various factors across the lifespan can impact brain behavior relationships," she said.

Daly was drawn to the Mesulam Center after having read the research of center director Marsel Mesulam and center faculty member Sandra Weintraub. Daly remembered, "When I was an undergrad, I realized I wanted to do neuropsychology. Dr. Weintraub is one of the seminal leaders in our field. Since I trained on the east coast, in New York and then Boston, a lot of the people who trained me were mentees or colleagues of Mesulam and Weintraub."

Daly was also attracted to the center's emphasis on interdisciplinary training. "I really wanted to be in a multidisciplinary setting. Having people from different training backgrounds, different perspectives, and different areas of expertise is really how we can best understand normal aging and neurodegenerative processes," she said.

# Caring from a Distance During the COVID-19 Pandemic

## PROGRAMS SHIFT ONLINE TO SERVE CENTER PARTICIPANTS

**F**or the last 26 years, the Mesulam Center has provided individualized care for people with dementia. In 2020, the center remained committed to providing care from a distance to participants and families during the COVID-19 pandemic.

With social distancing guidelines in place throughout most of the year, the ability to adapt has never been more important. Each core team faced unique challenges to administering care and conducting research, but research groups, clinical rounds, and faculty meetings have continued to run alongside dozens of other programs at the Mesulam Center during the pandemic.

"It's been an opportunity for incredible teamwork," said Marsel Mesulam, MD, center director. "Everyone has stuck together, and we have patched up the pieces mostly through videoconferencing. We have remained very regimented and very scheduled."

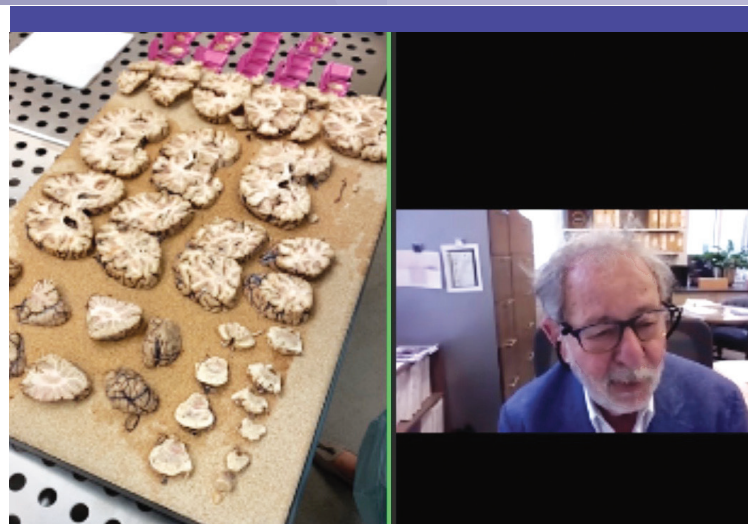
### Building a virtual community

"COVID-19 has brought a lot of challenges," said Emily Rogalski, PhD, professor of Psychiatry and Behavioral Sciences at the Mesulam Center. "One thing I hope remains is the easing of barriers on telehealth delivery of care." Communication Bridge, one such telehealth clinical trial, provides speech-language therapy for individuals living with primary progressive aphasia (PPA), a dementia syndrome characterized by difficulties with language. (Read more on page 11.)

"My hope is that this will pave a path so that telemedicine will be more accessible," said Rogalski, who is the principal investigator on the project. "Our Communication Bridge data was one of many components that was going to help pave the way for the benefits of a telemedicine path, but COVID-19 might have actually accelerated that path and made the implementation trials that we had in mind more feasible." In addition to the ongoing clinical trial, the center clinicians used videoconferencing to continue to meet with participants and conduct testing.

### Safely completing brain autopsies

Brain autopsies have also been able to continue under the guidance of Maggie Flanagan, MD, assistant professor of Pathology. Since March 21, members of the clinical core team ensured the successful brain donations from 25 research participants.



With lab capacity limited, the team hosted virtual brain cuttings to allow Dr. Mesulam and others to provide insight.

Flanagan has kept safety precautions up to Centers for Disease Control and Prevention and World Health Organization standards, which often changed on a daily basis. To keep up operations, other centers have contracted some autopsies out to third-party entities.

The Mesulam Center has been able to perform all donations in-house. Brain autopsy protocol had to be adapted numerous times to ensure safety when performing cases. "It has been very challenging," Flanagan said. "We also had to implement rapid COVID testing prior to the autopsies to know which safety precautions to take and determine which tissue banking protocol should be used for each individual case."

COVID-19 has also brought inspiration and understanding to the Mesulam Center. "I am continuously impressed by the Neuropathology Core team's hard work and dedication," Flanagan said. "This entire situation has made me appreciate my team even more than I already did, since it truly has been a team effort."

### Staying together while apart

To bridge the gap of isolation for participants, the Mesulam Center shifted the Miller Family Quality of Life Programs online. The team hosted virtual versions of Art in the Moment, Memory Ensemble, the Buddy Program, and SEED (Support and Education for Early Dementia) for participants and their care partners to take part in from the comfort of their own homes. In partnership with Borna Bonakdarpour, MD, the center hosted Northwestern Civitas Music Café, which included virtual performances from the musicians in the Chicago Symphony Orchestra.

Virtual monthly support groups helped to ease feelings of isolation for many individuals and their care partners. In particular, center social workers hosted nine caregiver forums during the pandemic that brought caregivers into conversation with each other and with experts in the field. The overwhelming response from these meetings spotlighted how important it was to see other people dealing with similar difficulties.

One caregiver said their favorite part was "listening to others and learning from their experiences. We are all going through this with loved ones, and while we are all handling it differently, we really need support and to know it is okay to feel challenged."

# A Heterogenous, Holistic Approach to Dementia Care

## CENTER WORKS TO EDUCATE, ENRICH EACH INDIVIDUAL ACCORDING TO THEIR NEEDS

**A**t the Mesulam Center, we believe that each person is unique in their own way, especially when it comes to care. In fact, taking a heterogenous approach to dementia care is a pillar of the center.

Heterogeneous care means treating, developing, and understanding a disease as a one-of-a-kind experience for each individual. In fact, heterogeneity refers to many aspects of our approach to research and care. Heterogeneity means that a single brain disease (e.g., Alzheimer's) can cause different symptoms early in the course of illness — not only memory loss, but also visuospatial changes or even personality changes. It also refers to the fact that a single symptom (e.g., memory loss) can also be caused by other diseases, such as Lewy Body Disease or frontotemporal diseases.

"Our center was really a pioneer in the term 'heterogeneity' because we recognized very early on that when you've seen one dementia, you've seen one dementia, especially in the early stages," said Sandra Weintraub, PhD, professor of Psychiatry and Behavioral Sciences and Neurology, who helped launch the center.

### Tailoring enrichment with Care Pathway Program

From the very beginning, the Mesulam Center has taken steps to ensure that every person's care is tailored to their strengths and weaknesses.

The Care Pathway Program allows for personalized enrichment of each individual's life based on an assessment of a person's strengths and weaknesses. After the assessment, the individual then has the option to select from an assortment of interventions specifically designed to improve both their and their family's quality of life. These interventions include Miller Family Quality of Life Programs, which can involve participating in programming at the art museum, partnering with a first-year medical student in a yearlong Buddy Program, or engaging in improvisational theatre sessions. (Read more about the Miller Family Quality of Life Programs on page 8.)

This collaborative nature aimed at finding the best personalized care plan for each person was even reflected in the physical architecture of the center, which was renovated in December 2018. "When we first moved into the center, the idea was that everyone was going to be together so that we would each learn from one another about the many layers of information necessary to diagnose, treat, and study people with dementia," Weintraub said.

When the architects were first outlining the space, they said, "Well, the social workers do not need to be there, the social workers can be in the other building," Weintraub remembered. "We said, 'Absolutely not!'"

The social worker has to sit next to the brain bank because that's how we communicate with one another. We really need to know what each collaborator is doing." Weintraub emphasized that being physically together benefits the nature of the work so that faculty and staff can work more effectively with research participants and patients.

Heterogenous care includes symptom management and more, according to Darby Morhardt, PhD, LCSW, research professor at the Mesulam Center. "Heterogeneity is more than clinical profiles. It also includes age of onset of the disease, family functioning, family history," Morhardt explained. "People all come with various histories that are unlike each other, and that all impacts how a patient and family cope and live with this disease."

### Understanding how each disease may present itself

Because each person's manifestation of dementia truly is different, "we need to educate families on the different symptoms that they are seeing, so they can respond in the most helpful way rather than having a more generic understanding of dementia," Morhardt said.

There are many different kinds of dementia, and symptoms for each variant often show up differently. "How does that affect how you're going to go home with this diagnosis?" Weintraub said. "We really don't have any effective pharmacological treatments right now. What we can help patients and families with is understanding their symptoms and how to best deal with them."

At the Mesulam Center, heterogeneity is more than just a word: it is a way to change lives. With this multidisciplinary approach, achieved by blending together neuropsychologists, neurologists, social workers, and basic scientists, we gain a better understanding of the disease.

## THE FOUR NEUROCOGNITIVE PROFILES OF DEMENTIA

MEMORY

BEHAVIORAL

LANGUAGE

SPATIAL  
PERCEPTION



# Creating a Buddy Community Across the Country



Medical student Brandon McNichol speaks at the Buddy Program Match Day, October 2019.

## PROGRAM PAIRS STUDENTS WITH THOSE LIVING WITH A NEURODEGENERATIVE DISEASE

It all started 24 years ago, when a Northwestern physician was diagnosed with dementia and could no longer practice medicine. It was a sad turn of events, but not a hopeless one. Marsel Mesulam, MD, director of the Mesulam Center, recognized that this physician still had strengths and capabilities, including the ability to mentor a young medical student.

After discussing the realization with Darby Morhardt, PhD, research professor at the Mesulam Center, he paired the retired physician with a first-year Feinberg School of Medicine student. From there, the Buddy Program was born.

Through the program, students spend a minimum of four hours a month with their buddy and learn to step into the shoes of someone living with a neurodegenerative disease. At Northwestern, the Buddy Program is also open to pre- and post-doctoral students conducting lab research who may not have the chance to meet a person for which their research may one day benefit.

Now, the process of matching persons living with dementia with medical students has been replicated in 15 universities nationwide. Boston University was the first school to replicate the program in 2006. By 2008, Morhardt had written a manual to send to institutions to implement the program. Institutions like New York University, Dartmouth College, and University of California San Francisco soon replicated the matching process.

Though it started with medical students, Buddy Programs now include nursing students, social work students, undergraduates, and even public health mentees at other institutions. "Facilitators tailor it to their center and their unique environment," said Morhardt, who

developed and runs Northwestern's Buddy Program. "It's really a simple, elegant concept. It allows the student to get to know someone living with a chronic illness outside of the clinical setting and to see the person is more than their disease."

### Giving young students a sense of purpose

In St. Louis, Washington University's Knight Alzheimer's Disease Research Center (ADRC) created their version of the Buddy Program called Dementia Understanding Opportunity (DUO).

"When we began DUO in 2012, we adopted a lot of the outcome measures that Darby so graciously shared with us," said Andrea Denny, co-leader of the DUO program and head of the outreach, recruitment, and engagement CORE at Knight ADRC. "I think people who get a diagnosis want an opportunity to feel like they are contributing to the future," Denny explained. "Research is one way to do it, but volunteering their time to improve medical practice and to help medical students become better doctors in their careers gives them a real sense of purpose and pleasure."

### Finding a common interest

For students, getting an in-person look at a disease they are learning about is invaluable. "You hear a lot on the news about Alzheimer's and other related cognitive diseases, but when you actually spend time with someone who is diagnosed, they are just like any other normal person," said Brandon McNichol, one of 13 Feinberg students who participated in this year's program. "The diagnosis does not define who you are. It doesn't erase your whole history. It doesn't erase the possibility of making a future. It was really fun to be a part of this program and realize that."

McNichol found that he and his buddy Bruce were both interested in music. McNichol is a classical music fan, while Bruce, a former administrator at the University of Chicago, is a jazz enthusiast. "A lot of the time we spent together involved going to concerts and open mics," McNichol said. "After one of my exams, some of my friends actually went to a concert with Bruce. It's a way to forget about school for a little bit and enjoy something else."

Recognizing the importance of humanizing a disease did not escape McNichol during his year in the Buddy Program. "More medical students should have earlier exposure to see if neurology is something they would be interested in," he said. "We need to have not only the scientific background but also the interpersonal skills to relate to patients and get to know them past their diagnosis."

*Funding for the Buddy Program and other quality of life programs is thanks to the generous support of the Glen and Wendy Miller Family Foundation.*

# One Family's Gift Makes an Impact



Buddy Program participants met via Zoom to share their experiences of staying connected to their mentors during the pandemic.

## MILLER FAMILY QUALITY OF LIFE PROGRAMS HELP THOSE WITH DEMENTIA LIVE A FULL AND HAPPY LIFE

**R**ecognizing the dignity of the whole person is important at the Mesulam Center. For decades, this focus has transcended research breakthroughs. Yet it was one family, the Miller family, who supported the institutional development of programs designed specifically to help individuals with a diagnosis of dementia continue to live a full and happy life.

Thanks to a \$1.25 million commitment made by the Glen and Wendy Miller Alzheimer's Family Support Program at the Feinberg School of Medicine, the center has developed several activities that support the strengths of people with dementia. These programs include the Buddy Program, Art in the Moment, The Memory Ensemble, and Support and Education for Early Dementia (SEED), all of which have given patients and caregivers a place to learn, have fun, and grow together.

### Encouraging mentorship, experiencing art

The Buddy Program, the first initiative supported by the Miller Family, encourages mentorship between first-year medical students and individuals living with the early stages of Alzheimer's disease and related dementias. Art in the Moment, a quarterly tour and discussion

session hosted at the Art Institute of Chicago, allows for a wide range of conversations surrounding visual technique and historical context. The experience allows participants to enjoy private tours of some of the world's best artworks with their care partner.

"Even when someone is having severe memory problems, they can still appreciate beauty," said Sandra Weintraub, PhD, professor of Psychiatry and Behavioral Sciences. "They can look at art in the moment, and while they may not remember what happened yesterday, they can certainly enjoy this experience while it is happening."

Another program, the Memory Ensemble, uses improvisational performance activities, or "games," to improve participants' ability to listen, observe, and use their imagination to work with others to solve problems. Through this collaboration with Lookingglass Theatre Company, people living with dementia participate in a multi-week program aimed at building skills necessary to navigate moments of anxiety or uncertainty.

"The Miller family had this vision and passion to understand that, in addition to things like research into the biology of the disease, there

# THE GLEN AND WENDY MILLER FAMILY PROGRAM PARTICIPANTS

AUGUST 2019 - AUGUST 2020



Participants in the Memory Ensemble program gain a sense of confidence in their abilities to adapt and cope with a dementia diagnosis.

is a need to do something to strengthen quality of life," said Marsel Mesulam, MD, center director. "We can't just sit and wait until there is going to be a cure."

In addition to these programs, the Miller family funding also supports SEED (Support and Education for Early Dementia), which educates individuals and their families about dementia or mild cognitive impairment, a condition that can evolve over time to dementia. Weekly sessions involve presentations from experts in the field who facilitate emotional and honest peer support groups. Conversations are led by Mesulam Center social workers who can answer lingering questions for members. Exposure to helpful

"Even when someone is having severe memory problems, they can still appreciate beauty."

SANDRA WEINTRAUB, PHD, PROFESSOR OF PSYCHIATRY AND BEHAVIORAL SCIENCES

resources and an understanding support network are highlights of this particular community.

"The Miller Family Quality of Life programs are invaluable," Mesulam said. "What helps families and patients the most are these psychosocial interventions, and they have made a tremendous impact."

Total Participants

305

Care Partner Support Group for Younger-Onset Dementia

76

Support and Education for Early Dementia:

36

Care Partner Support Group for FTD/PPA

119

The Buddy Program

26

Art in the Moment

28

The Memory Ensemble

20

576

patients and their families received diagnosis education and counseling in the Neurobehavior and Memory Clinic with support from the Miller Foundation.

# How the Meaning of the Word Alzheimer's Has Changed

**T**he word "Alzheimer" often evokes dread and anxiety over the incapacitating loss of memory and intellect. But this view is being modified by current research. Investigators now know that the underlying brain disease (known as Alzheimer's neuropathology) emerges many years before symptoms, that it progresses very slowly, that the early stages (also known as mild cognitive impairment) are compatible with nearly normal function, and that the dreaded terminal stages are not always the outcome. Knowledge of the disease is relatively recent. In 1906, Alois Alzheimer reported the case of a patient who died in her 50s following progressive impairment of behavior and cognition. At autopsy, her brain showed easily identifiable lesions that would later be called amyloid plaques and neurofibrillary tangles. For a long time, Alzheimer's disease became known as a "presenile dementia," defined by the presence of these two lesions that make up the core of Alzheimer's neuropathology.

## The most common of neurological diseases

For many decades, Alzheimer's disease and presenile dementia were considered rare conditions. During the second half of the 20th century, it became clear that Alzheimer's neuropathology also caused the much more common condition of late life, which until then was known as senile dementia. This finding brought attention to Alzheimer's disease, and within a few years, Alzheimer's disease was transformed from a rare neurological curiosity into the most common of all neurological diseases.

In the course of this transformation, the term Alzheimer's started to be used as a synonym for late-life dementias related to memory loss, occasionally without documentation of amyloid plaques and neurofibrillary degeneration in the brain. It also became clear that Alzheimer's disease could cause dementias that didn't affect memory, and that there are neuropathologic entities other than Alzheimer's that could cause dementias with memory loss. Needless to say, this complexity led to considerable confusion in terminology.

It is now advisable to specify whether the "Alzheimer" nomenclature is being used in the neuropathologic (changes in the cells of the brain) or clinical (symptoms that bring the patient to clinical evaluation) sense. The combination of amyloid plaques and neurofibrillary degeneration, by itself, is designated "Alzheimer's neuropathology" whereas a neurodegenerative syndrome causing memory loss is known as a dementia (or mild cognitive impairment) of the Alzheimer-type.

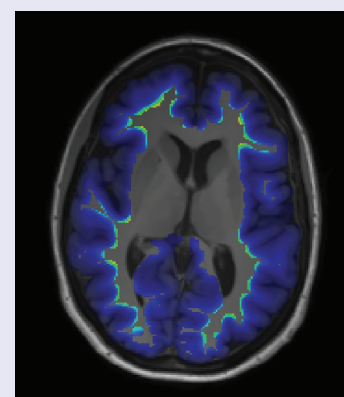
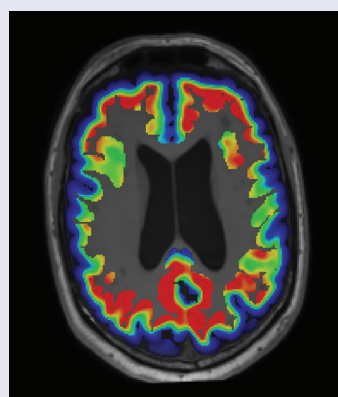
## Early detection now possible

Until recently, Alzheimer's neuropathology could only be detected at autopsy, according to Marsel Mesulam, MD, director of the Mesulam Center. During the past decade, revolutionary advances in biomarkers (such as cerebral spinal fluid and brain scans) have enabled the

detection of Alzheimer's neuropathologic changes in laboratory evaluations. The biomarkers are so sensitive that they can even detect these brain changes at the very early stages of mild cognitive impairment and even before symptom onset.

On one hand, these advances open the possibility of early interventions that could potentially slow the progression or even prevent the emergence of memory problems. However, these sensitive measures also create a situation where a person with the mildest of memory impairments may receive a biomarker report consistent with the presence of Alzheimer's neuropathology. It is important to explain that this finding does not mean that the person has dementia and that progression from such early stages is extremely variable from person to person.

The word Alzheimer evokes a picture of severe dementia, but its usage and meaning have changed with the evolution of research and medicine. The revolution in early detection makes it possible to launch clinical trials aimed at stopping progression, but the term Alzheimer has also become associated with stages of mild impairment that are nowhere near the dreaded stages of severe debilitation. The added role of the clinician today is to explain these distinctions in order to allay the anxiety evoked by the term, "Alzheimer."



## SEEN ON A SCAN

Recent research has shown that the nerve cell changes of Alzheimer's disease in the brain do not always lead to memory loss. Neurofibrillary tangles and amyloid plaques could be present in the brain before symptoms appear. However, a test would still show up positive and identify Alzheimer's disease being present without memory loss or dementia. Memory loss, the symptom, is not measured on a PET or cerebral spinal fluid test.

# A New Virtual Caregiving Resource: PPA Tele-Savvy

## ONLINE PROGRAM WILL HELP CAREGIVERS BUILD SKILLS, COMMUNITY

Caregiving for people living with dementia is a role that can be both rewarding and challenging. Families face a lot of new responsibilities in this role, and research has shown that they benefit from guidance and training. However, most interventions target the needs of families who care for person with a primary diagnosis of Alzheimer's dementia, when memory loss is the most salient symptom.

One of the most replicated evidence-based caregiver interventions is the Savvy Caregiver program. Developed by Ken Hepburn at Emory University more than 20 years ago, Savvy Caregiver is a six-week educational series designed to help caregivers develop skills to care for their family member with dementia. The program is currently being tested online and is called Tele-Savvy.

"It is exciting to be able to work with this established and effective program model and adapt it to meet the needs of PPA caregivers."

DARBY MORHARDT

During this past year, Darby Morhardt, PhD, LCSW, received a pilot grant from Emory University's Roybal Center to tailor the Tele-Savvy program for caregivers of people living with primary progressive aphasia (PPA), which impairs their language abilities. "Since Tele-Savvy has more of an Alzheimer's and memory-impairment focus, it is not necessarily specific to needs of PPA caregivers," Morhardt said.

In addition to developing a more tailored approach to PPA caregiving, Morhardt hopes to also connect PPA families with each other. "PPA is a rare illness, and people come to us from all over the country, but they don't have the opportunity to meet each other," Morhardt said. "A PPA specific version of Tele-Savvy gives the opportunity for caregivers to connect with each other. With no specific PPA caregiver interventions to date, it is exciting to be able to work with this established and effective program model and adapt it to meet the needs of PPA caregivers."

The PPA Tele-Savvy program is currently in development and will be tested for feasibility within the coming months.



Communication Bridge has continued to enroll participants in the program, which is the country's largest speech language clinical trial for primary progressive aphasia.

## COMMUNICATION BRIDGE: VIRTUAL THERAPY FOR PPA

Communication Bridge is a non-pharmacological clinical trial that evaluates the effectiveness of Internet-based speech language therapy for individuals with primary progressive aphasia (PPA), a dementia syndrome in which a patient's language is affected by the disease.

The online program includes 15 video chat therapy sessions with a certified speech-language pathologist and access to a custom web application to support the intervention. Participants can conduct all sessions from the comfort of their own homes. This year, Communication Bridge passed the halfway mark in its goal of enrolling 90 participants in the trial.

As technology becomes essential in medical care, programs like Communication Bridge have the potential to become the norm rather than the exception. Access to care is critical, and Communication Bridge shows that even without a cure, there is still hope after diagnosis.

*Communication Bridge is recruiting participants. For more information about participating, email [communicationbridge@northwestern.edu](mailto:communicationbridge@northwestern.edu) or call Libby Rogers at (312) 503-4012.*

*If you are interested in participating in the PPA research study, register at [www.brain.northwestern.edu/join/index.html](http://www.brain.northwestern.edu/join/index.html) or email [ppa.research@northwestern.edu](mailto:ppa.research@northwestern.edu) or call Christina Coventry, MS, RN at (312) 908-9681.*

# Clinical Trials Help Find New Treatments

## INTERVENTIONAL AND OBSERVATIONAL TRIALS HELP INVESTIGATORS UNDERSTAND AND TREAT DISEASES

### Interventional trials expand to improve quality of life

**T**he Mesulam Center has always offered several ways for people to get involved in the latest clinical trials. Pharmacological trials, where those enrolled take new pharmaceuticals for their condition, offer the possibility of finding a substance that could safeguard against certain dementia symptoms or prevent Alzheimer's disease changes from taking place in the brain.

However, the center has always strived to provide support beyond medications. Non-pharmacological intervention trials, which use no pharmaceuticals, have been growing. Rather than testing a drug, these trials test behavioral interventions, counseling, or training to help with symptom management and address issues related to quality of life. One such non-pharmacological clinical trial is Communication Bridge, an intervention for primary progressive aphasia (PPA) that uses video conferencing to offer speech language therapy to affected individuals and those who live and communicate with them. (Read more on page 11.)

When it comes to the future of clinical trials, one prediction is that "we will continue to see pharmacological trials that are aimed at symptom control and management with things like irritability and agitation in people with dementia," said Ian Grant, MD, director of clinical trials operations and assistant professor of Neurology at the Mesulam Center. "As time goes on, we will probably see a shift so that most of the pharmacological interventions, especially in the dementias where we have good biomarkers for them, will be aimed at disease-modifying targets. That means they will try to make an actual difference, or change, in the neuropathology within the brain."

While new drugs will be aimed at disease prevention and pathology, Grant predicts therapies to treat symptoms will move toward non-pharmacological interventions, like behavioral modifications. "There will be a little bit more of a split between pharmacological and non-pharmacological trials as time goes on," Grant said.

### Observational trials to improve dementia diagnosis and care

Beyond pharmacological and non-pharmacological trials, another distinction in clinical trials is the difference between interventional studies and observational studies. Observational studies collect data (information) as the disease progresses, without intervening with

any sort of drug or behavioral exercise. Cognitive tests, MRI scans, blood samples, questionnaires about daily activities, and other types of information are collected at an initial visit, and then at regular intervals thereafter (usually every year).

This information allows the center to understand the natural course of illnesses that cause dementia so that center faculty and staff can stage the illness and provide suitable interventions at different stages. "The goal of an observational trial is to look at a diagnosis and find out how we can better diagnose these individuals," said Brittanie Muse, clinical research project manager. "What kind of things can we find about the progression of the disease that would help us in the development of a treatment that we could use for an interventional study?"

Biomarker data are collected in an observational trial so that if and when an interventional trial comes along (where individuals receive a treatment being tested for its effect on the disease), there will be a "trial-ready" cohort in place for that treatment. The Mesulam Center is currently conducting three observational trials and three interventional trials.

*For more information about participating in a clinical trial, please contact Brittanie Muse at [brittanie.muse@northwestern.edu](mailto:brittanie.muse@northwestern.edu).*

### Putting together a trial-ready cohort

Once an interventional trial has been approved for testing, it is pivotal that a suitable group of patients has been recruited. "Clinical trials are very, very expensive," Muse said. Arguably, the most expensive part of a trial is recruitment, because it takes so many hours of staff time to recruit participants to a study. That is where having a trial-ready cohort on standby comes into play.

A trial-ready cohort means having a prescreened group of people with a specific diagnosis or biomarker findings and imaging results that indicate a certain diagnosis. Once that information has been gathered, "they are already plugged into the system, so if a new trial comes up, we can essentially pull from that group of people to enroll them in a study that we already know they are eligible for," said Ian Grant, MD, director of clinical trials operations and assistant professor of Neurology at the Mesulam Center.

The Mesulam Center has two such trial-ready cohorts underway: The first is the Longitudinal Early-onset Alzheimer's Disease Study (LEADS). LEADS is a multi-center observational study focused on people with early onset Alzheimer's disease (EOAD) and has Emily Rogalski, PhD, professor of Psychiatry and Behavioral Sciences, as the principal investigator at Northwestern. Participants range from 40 to 64 years old and have evidence of elevated amyloid in their brains. The goal of LEADS is to gain a better understanding of EOAD through longitudinal assessments and biomarker data collection. The study also analyzes the relationship of long-term clinical and cognitive assessment with various imaging and biofluid markers.



Emily Rogalski, PhD, is the principal investigator on the Longitudinal Early-onset Alzheimer's Disease Study (LEADS) clinical trial.

Having this information opens a scientific window into how the disease progresses in both early and later stages. LEADS involves three different groups: cognitively normal controls, EOAD participants, and early onset non-Alzheimer's disease participants, who have cognitive impairments that are caused by something other than Alzheimer's disease. Since no intervention is involved with any of the three groups in LEADS, the study can be considered a trial-ready cohort for a future interventional trial for EOAD.

The second trial-ready cohort is ALLFTD, a multi-center observational study that looks at dementia caused by frontotemporal lobar degeneration, a class of neurodegenerative diseases of the brain that are caused by different proteins than Alzheimer's disease.

At present, Northwestern is among more than 15 centers across the country participating in this study. ALLFTD provides observational and longitudinal data on patients dealing with Frontotemporal Lobar Degeneration (FTLD). As an observational clinical trial, with Sandra Weintraub, PhD, professor of Psychiatry and Behavioral Sciences and Neurology as the principal investigator at Northwestern, the goal is to gather information about FTLD and keep participants actively informed about changes in research or their condition. ALLFTD focuses on constructing a FTLD clinical research consortium that can support the development of FTLD therapies and clinical trials.

Trial-ready cohorts are even more important with disease like Alzheimer's and related dementias, since there aren't many interventions currently available. With these cohorts, the center can continue to respond to the innovative research and hopefully work toward preventing and better understanding Alzheimer's.

## ACTIVE TRIALS

### THREE INTERVENTIONAL TRIALS:

#### LONG-TERM NICOTINE TREATMENT OF MILD COGNITIVE IMPAIRMENT (MIND):

A memory improvement study that uses nicotine dosing to potentially improve mild cognitive impairment. Participants wear either nicotine patches or placebo patches to analyze their effect on memory.

**T2 PROTECT:** An oral medication trial for people with mild to moderate Alzheimer's disease. The drug, troriluzole, is being tested for its ability to protect against, slow down, or potentially improve memory as Alzheimer's disease progresses.

**A4:** An asymptomatic anti-amyloid trial for people who are cognitively normal but who have elevated amyloid in their brain. Participants receive a monthly anti-amyloid drug to test its impact on cognitive abilities.

### THREE OBSERVATIONAL TRIALS:

#### LONGITUDINAL EARLY ON-SET ALZHEIMER'S DISEASE STUDY (LEADS):

A study that observes disease progression in people with early-onset (EOAD) from ages 40 to 64 to collect longitudinal assessments and biomarker data from both people with EOAD and cognitively normal control participants. It is also used to compare results with late-onset Alzheimer's disease data.

**ALLFTD:** A study that observes disease progression in individuals with frontotemporal lobar degeneration causing dementia. It also enrolls individuals with a strong family history of frontotemporal dementia caused by a known genetic mutation.

#### ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE 3 (ADNI):

A trial working to determine the relationships between clinical, cognitive, imaging, genetic, and biochemical biomarker characteristics of Alzheimer's as the pathology evolves from normal aging to dementia. Current participants are 55 to 90 years old with no known neurologic diseases.

**LEARN:** An observational sister trial to the interventional A4 study that looks at participants who were screened for the A4 study but found to not have elevated amyloid in their brain.

**Learn more about joining a study at [brain.northwestern.edu/join](http://brain.northwestern.edu/join)**

# Pilot Program Funds Research in Olfactory, Cellular Systems

## TWO INVESTIGATORS RECEIVE \$35,000 GRANTS FOR NEW ALZHEIMER'S RESEARCH

**P**ilot grants have launched and supported the early careers in the field of Alzheimer's research for 24 years. With funds from the National Institutes of Health (NIH), the Mesulam Center provides two \$35,000 grants to investigators to generate early-stage research data that can be used for larger funding applications down the road. The two recipients have typically included one clinically oriented project and one basic science investigation to further understand dementia.



Thorston Kahnt, PhD

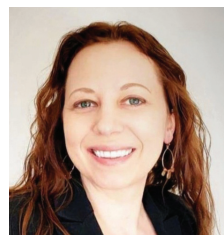
The 2020-21 clinical award went to Thorston Kahnt, PhD, assistant professor in Neurology, for his research on the olfactory system and olfactory learning. Kahnt's laboratory at the Feinberg School of Medicine uses computational modeling to find patterns between behavioral data and neural data from our sense of smell. His research has focused

on healthy younger individuals, but he has recently been interested in learning how these patterns change in older adults, both with and without cognitive impairment. He will be studying if changes in the sense of smell — and in the brain networks that support smell — could serve as a biomarker for cognitive impairment and Alzheimer's disease.

"The observation has been around for a long time that one of the early symptoms of Alzheimer's disease is difficulty with olfaction or smelling," said John Disterhoft, PhD, professor of Physiology and associate director of the Mesulam Center, who directs the pilot grant program. Kahnt is using MRI (magnetic resonance imaging) technology to help view the lateral olfactory tract. This part of the olfactory system "has been somewhat difficult to visualize because of technical challenges having to do with its positioning within the brain and within the skull," Disterhoft said.

While Kahnt has not conducted a large amount of Alzheimer's-specific research, his passionate interest in the field is actually an asset, according to Disterhoft. "One of the things that we try to do with the pilot grants is fund either early investigators or folks who are trying to get involved in the Alzheimer's field, and Thorston qualifies on both counts," Disterhoft said.

## Linking cellular structure to Alzheimer's



Colleen Zaccard, PhD

The second pilot project grant recipient was Colleen Zaccard, PhD, senior postdoctoral fellow in the Department of Physiology, who received funding for her basic science project on tunneling nanotubes (TNTs). TNTs are a newly discovered cellular structure that seem to allow communication between neurons and glial cells. Glial cells surround neurons

and protect them while also providing support and insulation for the brain's communication network. "Such communication is very important for the Alzheimer's disease process, and Dr. Zaccard has been involved with initially describing these TNTs," Disterhoft said.

Zaccard will use her pilot grant funding to explore the role of TNTs in Alzheimer's disease. Zaccard is in the laboratory of Peter Penzes, PhD, professor of Psychiatry and Behavioral Sciences, and is being co-mentored on her TNT project by Changiz Geula, PhD, professor of Cell and Developmental Biology in the Mesulam Center. In order to investigate cellular cross-talk in Alzheimer's disease, Zaccard uses powerful enhanced-resolution, live-cell microscopy techniques.

This year, the program received 16 applications for funding, the highest number ever. "As the years have gone on there has been more and more interest in Alzheimer's disease and more and more interest in Alzheimer's disease within the Northwestern community," Disterhoft said.

The process may become even more competitive in the next cycle, when the program changes from a pilot grant to a development grant and increases funding to as much as \$100,000 per year for two years. "I think it is an important change," Disterhoft said. "That should allow a young professor who is developing a new Alzheimer's disease approach, or a postdoctoral fellow like Dr. Zaccard, to get data that she can use when she gets an independent position." This change in the funding program, prompted by the National Institute on Aging, allows the work at the Mesulam Center to continue being highly productive and innovative.

*"As the years have gone on there has been more and more interest in Alzheimer's disease and more and more interest in Alzheimer's disease within the Northwestern community."*

JOHN DISTERHOFT



# New Insights from the Northwestern Alzheimer's Disease Research Center

The Northwestern Alzheimer's Disease Research Center (ADRC) in the Mesulam Center is supported by a P30 grant from the National Institute on Aging and is one of more than 30 centers in the United States.

Understanding the different causes of Alzheimer's disease can be daunting, but it is the life's work of Bob Vassar, PhD, the director of the ADRC P30 and director of the behavioral neurology laboratory in the Department of Neurology.

"The overarching goal of our lab is to understand the different molecular and cellular events that lead to Alzheimer's disease and how it progresses in the brain," Vassar said. The P30 grant helps support the major research initiatives on Alzheimer's and related disorders in the Mesulam Center.

## Recent findings examine pathology

As director of the ADRC, Vassar conducts research at a basic molecular level that complements the clinical and cognitive neuroscience research at the Mesulam Center. A major publication in January 2020 explored the commonly held thought that the source of amyloid beta (Abeta), which is an essential component of amyloid plaques found in the brain of people with Alzheimer's, came from excitatory glutamatergic neurons in the brain.

However, another important cell in the brain, GABAergic interneurons, had never been tested for their contribution to the cerebral Abeta involvement, according to Vassar. His study, in collaboration with Heather Rice, PhD, at the University of Oklahoma, showed that GABAergic interneurons are an important source of Abeta that contribute to amyloid pathology in the brains of people with Alzheimer's disease. "These results suggest that therapeutic approaches targeting Abeta production, specifically in GABAergic interneurons, may be beneficial for developing drugs for Alzheimer's disease."

Recently, Vassar also investigated a medication that was initially intended to help patients recover from strokes to discover the impact it might have on treating Alzheimer's disease. In a recent study published in the *Journal of Experimental Medicine*, Vassar and his co-authors showed that the drug, called 3K3A-activated protein C



Bob Vassar, MD

(3-APC), significantly slowed the production of dangerous proteins in mouse models of Alzheimer's disease.

Vassar, in collaboration with Berislav Zlokovic, MD, PhD, at the University of Southern California, administered a daily treatment of 3-APC to mice that had been genetically engineered to have symptoms that mimicked

Alzheimer's disease. After four months, these mice had 40 to 50 percent less amyloid protein development in comparison to mice who received a placebo treatment.

Mice treated with 3-APC performed better on cognitive testing than mice who had received a placebo treatment and nearly as well as healthy mice, leading scientists to believe that decreasing amyloid buildup could help reduce cognitive symptoms.

## Moving toward a clinical trial

Vassar's research interests typically involve "studies that are trying to translate what is understood about the basic research of disease and how we can translate that from the bench to the bedside." One of his papers recently accepted for *Science Translational Medicine* investigates the link between blood pressure medication and Alzheimer's disease. "We really think it could be a game changer for the prevention of Alzheimer's," Vassar said.

With collaborators at Harvard, Vassar used whole genome sequencing to discover a rare mutation in ACE, a molecule commonly found in blood vessels that regulate blood pressure that is associated with Alzheimer's disease in families with late onset Alzheimer's. Vassar's lab then introduced the same ACE mutation in mice using genetic engineering to investigate how the mutation causes Alzheimer's. They found that it led to increased neurodegeneration over time. In addition, breeding the ACE-mutated mice with another group of mice that had mutations for higher levels of amyloid doubled the rate of neurodegeneration. That cross "sped everything up," Vassar explained. "It was like throwing gasoline on a fire."

Administering blood pressure medications, which block ACE, reduced neurodegeneration in mice. "It looks like ACE is producing angiotensin in the brain itself, and that this ACE mutation is causing too much angiotensin," Vassar said. "The high levels of angiotensin may be leading to brain degeneration in Alzheimer's."

The blood pressure medication both blocks the function of ACE in the brain and decreases angiotensin in the body to help control blood pressure. The inhibitor acts on neurons to reduce the amount of angiotensin and therefore preserves the neurons.

Vassar predicts these drugs could potentially serve as a prevention strategy for Alzheimer's disease. "I'm hopeful that we can get some of our colleagues who are interested in clinical trials interested in performing this clinical trial," he said. "Then we can test this hypothesis in people."

# 'Connecting the Dots' Through Brain Donation

## GIVING THE ULTIMATE GIFT HELPS INVESTIGATORS UNDERSTAND DEMENTIA

**B**rain donation may not be an easy conversation topic for some families, but the potential such a gift can give to future families is immeasurable.

Data collection from PET scans, MRIs, qualitative questionnaires, and quantitative exams is important to understand the brain, but it's enriched by looking at the brain post-mortem.

"To be able to share the full picture of how Alzheimer's or other types of dementia affect people, both inside their brain and externally in their lives and caring relationships, is really valuable, and makes our research more powerful," said Debbie Dyslin, LCSW.

### Understanding the importance of donation

One man who made the ultimate gift of giving his brain to Mesulam Center was Don Tenbrunsel. Tenbrunsel passed away on April 29, 2020 in Chicago. He was part of the original cohort of SuperAgers (Read more about SuperAgers on page 1) and was 71 when he signed up to be part of this group of older adults who have intellectual capabilities on par with people decades younger.

As a part of the SuperAger longitudinal study, Tenbrunsel had agreed to donate his brain at the end of his life. It was his daughter Ann Tenbrunsel's responsibility to ensure his final wish was carried out. "He definitely made it known to me that should he pass away, that was the first thing I needed to do," she said. In his list of instructions for his family to prepare for his burial, the first item underlined was getting in touch with the Mesulam Center about his passing. "There was no doubt. It was always assumed that if brain donation was feasible, that was the first thing we should do," she said.

When she realized her father was not going to make it to the morning, she called the Mesulam Center, even though it was after normal business hours. "Someone called me back right away and told me what to do," she said. "It was incredibly easy and handled very professionally."

Tenbrunsel never had any hesitations about his decision to donate once he signed on for the SuperAger study. "He felt very strongly about the project and the importance of it," his daughter said.

The SuperAger study allowed Tenbrunsel and his family to learn more



SuperAger Don Tenbrunsel and his daughter Ann Tenbrunsel enjoyed time together at a Chicago Cubs game.

about his unique brain patterns, while also providing investigators across the country with more data on this exceptional subset of older adults. "As SuperAgers started to pass away, you could really see the richness of the data that they were getting from the brain donations," Ann Tenbrunsel said. "The potential benefits of understanding brain aging and Alzheimer's is incredibly important when it comes to donation, because you get an in-depth look and can go deeper into the issues that are being studied."

### Increasing awareness among communities

Without a commitment to brain donation, that final missing piece in a person's dementia story is hard to understand. "Our understanding of the longitudinal data during a person's lifetime is greatly enhanced by being able to connect that data to our actual examination of the brain tissue," Dyslin said. "You're basically connecting the dots."

There are individual and institutional barriers to brain donation, from ensuring family (or next-of-kin) will carry out brain donation to representation of minority (or marginalized) groups in health care and research. Dyslin works to increase awareness and understanding about brain donation, especially in racially and ethnically diverse communities.

"People of color have historically not been as involved in Alzheimer's research," she said. "Part of my own investment in this topic is about making sure our research sample is as representative of the entire population as it can be. How can we best support all our participants and the entire population that is affected by Alzheimer's and other dementias, especially during this time and in this context? Brain donation is a really powerful way that participants can help researchers hopefully get one step closer toward treatments and cures."

**Learn more about brain donation at [brain.northwestern.edu/join/brain-donation.html](https://brain.northwestern.edu/join/brain-donation.html)**



Sandra Weintraub, PhD, working to better identify older adults with dementia in the emergency department (ED) and provide them with a tailored care plan.

## Dealing with Dementia in the Emergency Department

A trip to the emergency department can be terrifying for anyone, but for someone struggling with undiagnosed dementia, a hospital visit can be even more challenging.

A new collaboration between the Mesulam Center and Northwestern Memorial Hospital is working to change that. Called the Geriatric Emergency Department Innovations (GEDI) program, it aims to better identify older adults with dementia in the emergency department (ED) and provide them with a tailored care plan.

“The problem is if you don’t know that someone has dementia, you are going to send them home with a list of recommendations that they cannot follow on their own,” said Sandra Weintraub, PhD, professor of Psychiatry and Behavioral Sciences and Neurology and a consultant on the program. “Our population is aging rapidly, so this is going to become a bigger problem.”

In February 2019, GEDI accredited Northwestern Memorial Hospital as a Level 1 Geriatric Emergency Department, the first Illinois hospital awarded this level from the American College of Emergency Physicians’ Geriatric Emergency Department Accreditation.



Scott Dresden, MD

The GEDI multifaceted approach works to cut down on dementia ED return visits. The protocol can be simple. A trained geriatric ED transitional nurse asks older adults logic questions like, “Does a stone float?” or “What weighs more: one pound or two pounds?”

If their answers reveal a potential concern for dementia, the GEDI team then regularly checks in on the patient via phone. The team can also call a social worker or pharmacist to help formulate an achievable plan for the patient’s care once they leave the ED.

The GEDI proposals involve increased staffing and education on best geriatric practices. The program also aims to provide patients with quality of life improvements and transitions to rehabilitation or long-term care facilities.

The initiative was spearheaded by Scott Dresden, MD, assistant professor of Emergency Medicine and director of GEDI at the Feinberg School of Medicine. Dresden and his team also collaborated on the GEDI program with Mount Sinai in New York, Washington University in St. Louis, and University of Wisconsin - Madison.



Borna Bonakdarpour, MD, was interviewed on NBC Nightly News with Lester Holt on September 14 to discuss his music therapy initiative at Northwestern Medicine.

## Music to Clinician's Ears

### PROGRAMS USE MUSIC TO INCREASE QUALITY OF LIFE FOR THOSE WITH DEMENTIA

**W**e all have likely experienced the power music has to influence our emotions. Feeling sentimental, melancholy, or excited during a song is hardly revolutionary. But harnessing and quantifying the effect of music as a medication has been the goal of classically trained pianist Borna Bonakdarpour, MD, also assistant professor of Neurology at the Mesulam Center.

Throughout his career as a neurologist, Bonakdarpour has been referring people with dementia to music and dance therapists to improve their quality of life. "At some point I went to one of the group-based music intervention sessions offered through Institute for Therapy Through the Arts to see the effects of music," he said. "It was amazing! I saw individuals who had moderate to severe dementia and were not quite functional in terms of communication,



Borna Bonakdarpour, MD

but they could sit very well and listen to music and get engaged through music."

The biological impact of listening to music has great potential for people with dementia. In recent years, music has been linked to improving focus and reducing stress.

"Instead of using medication in nursing homes to calm down people who become agitated, we can use music to do the same thing," Bonakdarpour said. "Then, you save them from all the medications they are taking and those side effects." This realization sparked the beginning of several musical and research collaborations for Bonakdarpour.

### Everyday therapy with music

Songs By Heart is an ongoing program with Nancy Gustafson, a former soprano opera singer who became a professor at Northwestern's Bienen School of Music. After performing in premier opera houses around Europe and the United States, Gustafson noticed the positive impact singing could have in memory care for her own mother, who had been diagnosed with dementia.

Beginning in 2018, Bonakdarpour and Gustafson began to study the efficacy of daily singing for individuals with dementia over a one-month period. "The higher dosage in this approach is very interesting," Bonakdarpour said. "We wanted to see if we could show scientifically whether this method works for persons with dementia." One round of intervention in two different memory care facilities has been completed, and data analysis is underway.

"Instead of using medication in nursing homes to calm down people who become agitated, we can use music to do the same thing."

BORNA BONAKDARPOUR

### Symphonic support

Bonakdarpour has also partnered with the musicians of the Civitas Ensemble, a chamber ensemble formed by a group of Chicago Symphony Orchestra musicians and led by Yuan-Qing Yu. Civitas Ensemble specializes in bringing music to communities who might not have access to live performances. Anyone from hospital patients to economically disadvantaged youth have had the pleasure of hearing the ensemble's music. Now, individuals with dementia will have the chance to hear them in an online format. In June, the center and Civitas Ensemble hosted a virtual concert for people with dementia and those affiliated with the Mesulam Center through participation in research and Miller Family Quality of Life programs.

Similarly, Bonakdarpour has been collaborating with Clara Takarabe, who also plays viola with the Chicago Symphony Orchestra, to bring therapeutic music to patients admitted in the neurology unit at Northwestern Memorial Hospital. Both of these projects have been very well received during the COVID-19 pandemic.

### Where it all began

Bonakdarpour started research in music and dementia through his collaboration with Institute for Therapy Through the Arts. They studied how a weekly music intervention for three months impacted the relationship between someone with severe dementia and their care partner or spouse. "So far we have shown that 20 persons with dementia who got the intervention did better in terms of their general psychiatric well-being," Bonakdarpour said. "They were less agitated. They had less depression. They could also engage in communication, socially, with their spouses and with their care partners better than the group that didn't get the intervention."

"The point of these focus groups is to respond to what the needs in communities actually are, rather than what we think they are," said Debbie Dyslin, LCSW. "I have every hope that this will translate to real impact on the work we do with people who are considering brain donation."



This summer the Center hosted the first Northwestern Civitas Music Café to bring music to dementia patients and research participants.

# From Chicago to Shanghai

## LEARNING ABOUT OLDER ADULT AND DEMENTIA SERVICES IN CHINA

International collaboration has always been a cornerstone of the Mesulam Center. To continue this global work, Darby Morhardt, PhD, research professor, traveled halfway across the globe to Shanghai in October 2019 to hear more about emerging trends in the city's rapidly aging population.

Morhardt was selected as one of eight delegates for the Chicago-Shanghai Social Services Committee who spent a fruitful week in Chicago's sister city, where officials have developed several new programs to treat and care for people with dementia.

As part of the trip, Morhardt and other delegates visited community centers, homes, and programs for older adults throughout the city, such as community gardens that were being tended to by multiple generations. They also visited the headquarters of the Civil Affairs Bureau offices for discussions with Chinese government officials. Conversation topics included best practices for healthy aging, caregiving, legal decision-making, dementia, and end-of-life care.

### A shortage of caregivers, new technological initiatives

Shanghai officials' plans for the coming years include studying current challenges, such as a lack of caregivers (they estimate that they will need 80,000 to 100,000 more caregivers) and a waning desire of local citizens to work in the big city. To help with this, the government has established a new program with opportunities for growth and promotion to help incentivize those interested in this work.

Morhardt was impressed by the Chinese government's integration of social and person-centered practices with medical aspects of care, focusing on ways to decrease social isolation and improve overall function. Initiatives included introducing robots in elderly homes that can sing, broadcast news, and engage in simple communication. "They are also working on establishing dementia-friendly communities in Shanghai in a centralized and organized way," Morhardt said.



Darby Morhardt, PhD, LCSW, gained valuable insights during her trip to China as a delegate for the Chicago Shanghai Social Services Committee.

### Historical respect, cross-cultural communication

This is the sixth annual exchange, which rotates between sending delegates to Shanghai and hosting them in Chicago.

Unfortunately, the Chinese delegation will be unable to travel to Chicago this year due to the pandemic; however, plans to create a virtual meeting are in discussion. "I want to share with my Shanghai colleagues the innovative work we are doing at the Mesulam Center that they may be able to take back to their community," Morhardt said.

It is an experience Morhardt won't soon forget. In Shanghai, "there is historical respect and honor given to older people," she said. "It was a fantastic and inspiring experience."

## MESULAM CENTER EDITORIAL COMMITTEE

Mesulam Center News is published annually for research participants and friends of the Mesulam Center for Cognitive Neurology and Alzheimer's Disease.

Editorial Advisors: Sandra Weintraub, Emily Rogalski, Darby Morhardt  
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Paula Basta, director of the Illinois Department of Aging, and deputy director Lora McCurdy visited the Mesulam Center in winter 2020.

## Illinois Department of Aging Director Basta Visits Mesulam Center

Working together with state officials is key to furthering the mission of the Mesulam Center to conduct research and develop personalized diagnostic and clinical care. On February 3, Paula Basta, director of the Illinois Department of Aging (IDoA), along with her deputy director Lora McCurdy, visited the center to learn more about its work.

Since being appointed IDoA director by Governor J.B. Pritzker in the spring of 2019, Basta's work has focused on improving the lives of senior citizens in Illinois through statewide programming and with the support of medical centers such as Northwestern. Basta's visit allowed the state officials to better understand the clinical services the Mesulam Center provides, the Miller Family Quality of Life Programs that the center offers, and the community engagement center faculty and staff are involved in both locally and statewide.

In addition to getting to know Basta, the center was able to learn about the IDoA priority areas and potential areas of collaboration. "It was an important exchange of information and an opportunity to maintain our connection and to let her know that we are available to help support her and her work," said research professor Darby Morhardt.

# AWARDS AND PUBLICATIONS

Mesulam Center investigators continue to receive several awards and publish cutting-edge research on dementia and Alzheimer's disease.

August 2019 - August 2020

## 36 PUBLICATIONS

### 5 NEW GRANTS:

#### **Rogalski, Geula, Mesulam R56 AG045571**

*Exceptional Cognitive Aging: Neuropsychologic, Anatomic and Pathologic Correlates*

#### **Rogalski, Geula, Mesulam R01 AG067781**

*Cognitive SuperAging: A model to explore resilience and resistance to aging and Alzheimers disease*

#### **Morhardt P30AG064200 (Pilot)**

*Primary Progressive Aphasia (PPA) Tele-Savvy: A Pilot Study of an Online Intervention for Caregivers of Persons Living with PPA*

#### **Gefen R01AG062566**

*Clinical, Neuroanatomic, and Pathologic Signatures of FTLD-tau in Dementia Phenotypes*

#### **Geula R01NS085770**

*Concordance of TDP-43 Inclusions with Cortical Atrophy and Clinical Phenotype*

### SUPPORT THE MESULAM CENTER

**Generous individuals are catalysts in enabling innovative medical research to flourish. To propel new discoveries at the Mesulam Center, we seek private funds to help defray expenses related to the research process. If you are interested in making a gift to support the work of the Mesulam Center, please contact Jordan Sund (Jordan.sund@northwestern.edu or 312.503.2706) or make a gift online at [brain.northwestern.edu](http://brain.northwestern.edu)**

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## UNPRECEDENTED TIMES

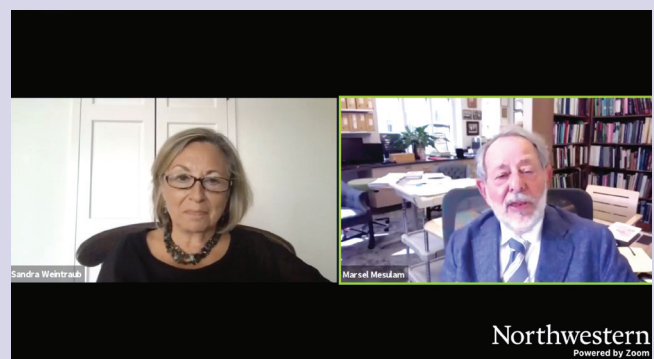
This year we adapted our annual Alzheimer Day for a virtual platform. For the past 25 years, we have held this event on campus to share the important research breakthroughs that are happening at Northwestern, but this year we had to change plans to host this event in a safe way.

The pandemic has only brought more urgency to our work, and we continue to be committed to better understanding the complexity of Alzheimer's and other dementias.

Read more and watch a recording of this year's virtual event at [brain.northwestern.edu/about/newsletter](http://brain.northwestern.edu/about/newsletter)

## SAVE THE DATE FOR OUR 27TH ANNUAL ALZHEIMER DAY May 6, 2021

For more event information, visit:  
[brain.northwestern.edu/about/events](http://brain.northwestern.edu/about/events)



More than 350 people joined us for our virtual Alzheimer Day in September.