

NORTHWESTERN UNIVERSITY FEINBERG SCHOOL OF MEDICINE

Mesulam Center NEWS

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

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Expanding Community Engagement



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.

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On the cover: Phyllis Timpo, Mesulam Center Senior Community Engagement Manager, Janie Urbanic, South Loop Village Founding Director, and Rep. Lamont Robinson, Illinois State Representative for the 5th District, at the 2022 5th District Community Resource Fair.



DEAR FRIENDS AND COLLEAGUES:

After 29 years at the helm, I will step down from the directorship of the Mesulam Center (formerly known as CNADC) at the end of 2022. Although my other research and clinical activities will continue at their current locations (i.e., I am not retiring), I thought this would be the right moment for a brief retrospective.

In July 1994, my wife Sandra Weintraub and I landed on the 11th floor of the Searle Building with 450 boxes containing giant microtomes, half a dozen microscopes, freezers full of specimens, thousands of neuropathology slides, books, and files. The space was unfinished, the laboratory had no distilled water, and the telephones were not connected. We established a "command center" in the library and rigged a telephone line. Within a week of arrival, the neuroanatomy/neuropathology laboratory was established. This was followed by the initiation of the first functional imaging research program at Feinberg. At around the same time, the first neurobehavior clinic at Feinberg opened its doors and led to the establishment of the first behavioral neurology and neuropsychology fellowship programs at Feinberg. In 1996, a P30 application was reviewed favorably at first submission by the National Institutes of Health (NIH) and led to the launching of the first NIH-funded Alzheimer's Disease Center and brain bank at Feinberg. Also in 1996, our application to the Illinois Department of Public Health (IDPH) for designation as an Alzheimer's Disease Assistance Center was successful.

Each of these ventures flourished. I led the NIH-funded Alzheimer's Disease Center for 25 years. During one of the 5-year competitive renewal cycles, our center received a perfect merit score, a feat that, as far as I know, none of the other 29 NIH centers around the country have been able to achieve before or since. The Mesulam Center has brought Feinberg over \$150 million of NIH funding. It is known for clinical research on human beings, basic research on human brains, and personalized multidisciplinary care for patients and their families. Conditions that we identified and named are now part of the NIH lexicon. Our clinic moved to beautiful new quarters with a current staff of over 20. It enjoys an international reputation in diseases of memory, language, behavior, and overall cognition. Northwestern Memorial Hospital receives over \$3 million a year from the State of Illinois for supporting our IDPH Alzheimer's Disease Center. The fellowship programs received formal accreditation and attracted stellar national candidates. Trainees and visiting scholars came from England, Turkey, Korea, Germany, Brazil, Belgium, Japan, Australia, and Canada. The functional imaging program evolved into the Cognitive Brain Mapping Group that now encompasses laboratories throughout Northwestern University. Our programs on the neuropathology of dementia, primary progressive aphasia, and SuperAging have prospered and made Feinberg a world-leader in these fields of research.

Throughout these years, three guiding principles fueled growth: multi-departmental affiliation with governance as a free-standing academic unit, integration of laboratory research with clinical practice, and physical proximity of administrative and research components under a single roof. The resultant formula of heterogeneity with autonomy stimulated innovation and initiative; patients attracted by the reputation of the clinic volunteer for research and, in turn, become beneficiaries of research advances; faculty and students in multiple disciplines rubbed elbows, taught each other, and learned from each other. I feel honored to have served as a catalyst for these developments. They would not have been possible without the loyalty and creativity of past and present colleagues, advisory board members, administrative staff, program managers, research assistants, and students. Some have been my fellow travelers for many, many years and provided pivotal contributions at pivotal points in our history. I will have future opportunities to single out their transformative roles in the history of our center. As I write this letter, the dean of Feinberg has not yet formally announced my successor. By the time this issue reaches you, the chances are that the announcement will have been made. You may want to check our website at www.brain.northwestern.edu. I feel confident that the Mesulam Center has the momentum to maintain its upward mobility and enhance its stature. I will do all I can to help my successor achieve this goal. I wish the Mesulam Center and all its members smooth sailing.

M. Marsel Mesulam, MD

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

Developmental Projects Program Supports Innovative Neurology Research

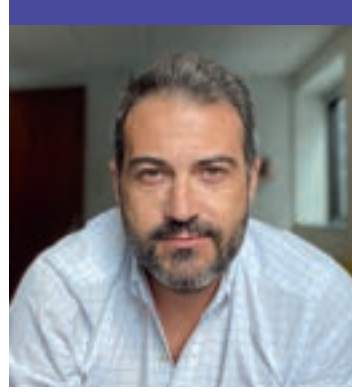
Evangelos Kiskinis, PhD

TDP-43 is a protein mainly present in a cell's nucleus that plays an important role in regulating RNA—a molecule essential for gene coding, expression, and regulation. TDP-43 pathologies have been connected to several neurodegenerative diseases, including amyotrophic lateral sclerosis (ALS), frontotemporal dementia (FTD), and Alzheimer's disease (AD).

ALS is a neurodegenerative disorder characterized by the degeneration of motor neurons in the brain and spinal cord, which causes muscle weakness and impacts voluntary movement. FTD is an early-onset dementia associated with frontal and temporal lobe degeneration, which results in problems with behavior and language. Mislocalization of TDP-43 is a unifying pathological feature of the majority of people with ALS and about 50% of people with FTD.

Evangelos Kiskinis, PhD, assistant professor of Neurology and Neuroscience at the Northwestern University Feinberg School of Medicine, is studying the functional consequences of TDP-43 loss in neuronal nuclei (which contain the neurons' genetic material). Kiskinis is also working to identify other proteins lost in neuronal nuclei in ALS and FTD using human brains donated to him by the Mesulam Center. He found that regulating the voltage-gated potassium channel Kv7.2—a type of channel responsible for returning the cell to a resting state after each nerve impulse—might represent a rational therapeutic approach for ALS and FTD patients with TDP-43 pathology.

Kiskinis has made significant progress in his investigation, which is supported by a grant from the National Institutes of Health (NIH) and a development project of the Mesulam Center. His work has great potential in the study of TDP-43-associated dementia.



Evangelos Kiskinis



David Gate

David Gate, PhD

Cerebrospinal fluid (CSF) circulates around the central nervous system (brain and spinal cord) to protect it from damage. It's tightly regulated, but sometimes, immune cells called T cells can penetrate the barrier and enter CSF. This can result in neuroinflammation—a critical component in the development of neurodegenerative conditions such as Alzheimer's disease.

David Gate, PhD, assistant professor of Neurology at the Northwestern University Feinberg School of Medicine, showed in his 2020 *Nature* paper that a type of T cells called CD8+ T cells is increased in the CSF of people with Alzheimer's disease.

What was still unclear, however, is how the T cells entered the brain. And what mediated the movement of T cells to the brain? Gate has sought the answer to these questions using funding provided through a development project of the Mesulam Center.

In the field of neurodegenerative diseases, understanding the immune response of the CSF is essential. By studying the CSF of both people who are cognitively healthy and cognitively impaired, Gate has learned more about healthy aging and the processes behind Alzheimer's disease. His findings could be used to improve anti-inflammatory therapeutics or to estimate levels of neuroinflammation in cognitively impaired patients. Gate's work can have significant implications on future clinical trials and the fields of aging, neurodegeneration, and immunology.

The Northwestern Alzheimer's Disease Research Center is funded by the National Institute on Aging, and, as part of its program, offers competitive funding for development projects in aging and Alzheimer's disease research. The proposed two-year research project must be relevant to clinical or basic research on Alzheimer's disease, other dementias or cognitive aging. The review committee evaluates the significance of the proposal to the field, scientific innovation, use of NU resources, and probability that the development project will lead to new independent funding.

Center Faculty Share Knowledge and Expertise on Local, National, and International Stages

As the Mesulam Center's work continues to grow, Center faculty continue to take on leadership positions in Chicago and around the world.

Local

- Darby Morhardt, PhD, LCSW, research professor in the Mesulam Center and of Preventive Medicine in the Division of Public Health Practice, was appointed to the Illinois Supreme Court Commission on Elder Law in April 2022.
- Emily Rogalski, PhD, associate director of the Mesulam Center, was endowed as the inaugural Ann Adelman Perkins and John S. Perkins Professor of Alzheimer's Disease Prevention at the Feinberg School of Medicine Spring Investiture Ceremony in May 2022.
- Borna Bonakdarpour, MD, was recently promoted to associate professor of Neurology in the Feinberg School of Medicine at Northwestern University.
- Marsel Mesulam, MD, director of the Mesulam Center, and Morhardt contributed to the writing of the 2023-2026 Alzheimer State Plan as appointees to the Illinois Department of Public Health Alzheimer's Disease Advisory Committee.

National

- Margaret Flanagan, MD, assistant professor of Pathology, served as member of the Alzheimer's Disease Research Center Digital Pathology Working Group.
- Flanagan was the organizer of the Digital Pathology Webinar Series, co-sponsored by the Alzheimer's Disease Research Center Digital Pathology Working Group and National Alzheimer's Coordinating Center.
- Sandra Weintraub, PhD, professor of Psychiatry and Behavioral Sciences, contributed a chapter on Neuropsychological Evaluation in Dementia to a 2022 volume published by the American Academy of Neurology, *Continuum*, which provides continuing education to update neurologists on timely topics.
- Rogalski was elected co-chair of the Imaging Steering Committee for the NIH/NIA Alzheimer's Disease Research Centers program.

International

- On June 9, Mesulam was honored at the French Society of Neurology Awards with the designation of "Member of Excellence" in recognition of his important contributions to research in neurology.
- Emily Rogalski, PhD, served as an elected executive committee member for the International Society for Frontotemporal Dementias.
- Sandra Weintraub, PhD, participated in a German translation of a language test for individuals with primary progressive aphasia.
- Weintraub was a member of an international group to harmonize neuropsychological assessment across Europe.
- Mesulam served as the chair of the nominating committee for the International Society for Frontotemporal Dementias.

A Path to Passion for Neurology

Siri Sonty's start at the Mesulam Center helped her find her way to becoming a "family neurologist"

When Siri Sonty, PhD, MD, began working at the Mesulam Center in 2000, she could not foresee the twists and turns that lay ahead in her career. Those twists would ultimately lead her to her current role as a neurology clinician at the Design Neuroscience Center in Doral, Florida, where she treats patients of all ages.

But 22 years ago, her path was uncertain. She had completed her undergraduate degree and two years of medical school at Northwestern, then decided to take time off medical school to find her true passion. She was looking for a place to conduct research as she figured out her next step.

"I knew I wanted to do research, and I knew I wanted it to be in brain with respect to how it makes the human being unique — what guides personality, development, and intelligence. I did a simple web search, and the person who seemed to be doing most of that work was, in fact, Marsel Mesulam," Sonty said. "So, I approached him directly as a second-year med school student and said, 'This is where I want to work and the research I want to be doing.' And that was it. Our relationship was born."

Studying neurodegenerative diseases

Sonty joined the Mesulam Center in 2000 as a Howard Hughes Medical Institute Medical Student Research Fellow, working under Darren Gitelman, MD. In total, she spent seven years with the Mesulam Center. After her first year of independent research under Gitelman, she decided to pursue her PhD in cognitive neurology and remained at the center to study neurodegenerative diseases and their effect on brain function at a network level, working closely with Sandra Weintraub, PhD, and Marsel Mesulam, MD. But it was her research at the center that led to yet another crossroads in her professional journey.

"On one hand, I continued to be extremely interested in the brain and behavior and how fantastic and dynamic those processes were. But on the other hand, my only exposure to neurology was in dementia. It was so disheartening to watch this disease progress and the devastation it causes," Sonty said. "So it was at this point that I decided to go back to med school and take every single specialization seriously to determine what path I wanted to follow."



Sonty applied for residencies in neurology, psychiatry, internal medicine, and family medicine, but ultimately ended up matching in adult neurology, thanks in part to her extensive time at the Mesulam Center. During this time, she became an expert in all disease processes, but it was in her fourth year that she discovered a new passion — pediatric neurology. "I went from geriatrics to pediatrics after four years of residency," she said. "It was working with neurological disorders with children that helped me find my true passion for neurology."

Becoming a family neurologist

Following her residency at the University of Toronto, Sonty accepted a clinical neurophysiology fellowship at the Nicklaus Children's Hospital in Miami, Florida, before beginning her current position at the Design Neuroscience Center, where she has been since 2017.

"I am basically a family neurologist—I see your newborn and I will see your great granddad and I will treat them all differently," Sonty said. "It's fascinating to see the brain at various stages in development or decline, whether it's normal aging or neurodegenerative disease. I am in an extremely unique situation that allows me to see patients at all points of their cognitive journey. Not many people get that opportunity. I am truly the general neurologist, and that has been so awesome."

In addition to her work at the Design Neuroscience Center, Sonty spent the last two years developing curriculum for a new neurology program that was launched by the Larkin Community Hospital in 2020.

"My current work is definitely not where I thought I would end up when I was at the Mesulam Center," Sonty said. "But I think I would be in a very different place if I hadn't spent the time there to really expand my relationship with the brain and even my relationship with my own self. I think fondly of the individuals that I worked and trained with and remain in close contact with many of them to this day. I am eternally grateful to Dr. Mesulam for taking a chance on me and don't think I would be where I am today without his support."

Attracting New Researchers to the Field

EDUCATIONAL INITIATIVES AT THE CENTER ATTRACT FELLOWS AND FACULTY ACROSS DISCIPLINES

Colleen Zaccard, PhD, has studied infectious diseases and microbiology, but now the research assistant professor investigates Alzheimer's disease and related dementias (ADRD) as a Research Education Component (REC) Scholar at the Mesulam Center.

Through the REC Scholars program, postdoctoral fellows and junior faculty who have experience in other fields are selected through a rigorous, multi-step application process to receive training and a stipend to conduct ADRD research for two years. The goal of the program is to attract new researchers to the field as well as supplement the experience of those already engaged in ADRD research.

Taking investigators to the next stage of their career

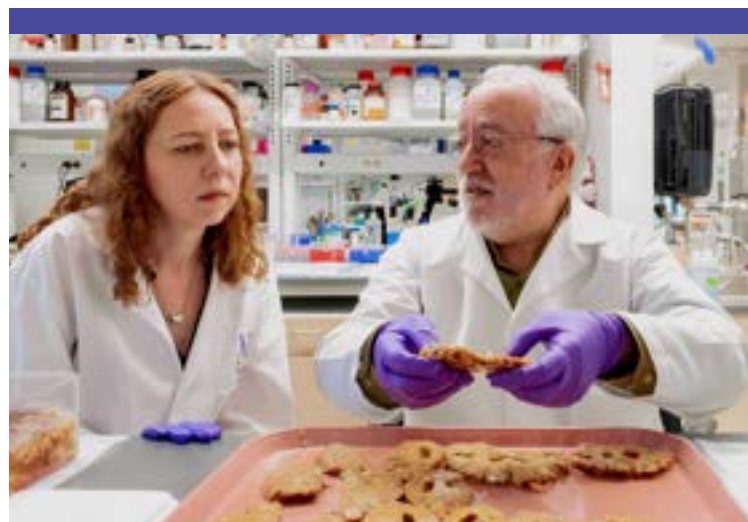
A few years ago, the National Institute on Aging required Alzheimer's disease research centers to have a research education component. It was meant "to enhance the pipeline of professionals working in the fields of dementia, particularly Alzheimer's disease," said Changiz Geula, PhD, director of the REC program at the center.

"There are a lot of brilliant minds, all gathered in one place with all of the tools, and they have the ability to train and mentor me in a way that I would not receive anywhere else."

COLLEEN ZACCARD, PHD

Although the center had already been working on education initiatives for many years, the formal grant allowed the creation of additional programs, such as the REC Scholars program for junior faculty such as Zaccard. "[It] has been integral for my development, making me competitive for major grants that will take me to the next stage of my career," she said.

After her time at the center, Zaccard hopes to establish her own lab focusing on finding ways to reverse chronic microglia activation to slow aging and the progression of Alzheimer's. Microglia are multifunctional immune cells that researchers previously thought of as "the garbage collectors of the brain," but we now know they play a major role in aging and neurodegenerative diseases, according



Colleen Zaccard, PhD and Changiz Geula, PhD study brain tissue in the Mesulam Center wet lab.

to Zaccard. She investigates the differences in microglia from SuperAgers, individuals with Alzheimer's disease, and cognitively normal controls.

Although the subject area of her research differs from her background, she continues to study tunneling nanotubes—dynamic connections between cells used for transport and communication—using the same advanced imaging techniques she honed since graduate school.

Encouraging underrepresented groups to enter the field

The REC Core was recently formalized by a grant from the National Institute on Aging, but the center already had a strong training component. "In the past, we had high school students who conducted research in our laboratories," Geula says. "We have had many visits from middle and high school students to our center, coming to the laboratories, observing various procedures, looking at brains and touching them and exploring them."

Geula loves to help others learn through interactive experiences. He's enjoyed teaching since he was an undergraduate and believes in the importance of building capacity in others. Geula hopes that his efforts at the REC Core will help those who belong to underrepresented groups in ADRD research enter the field.

Zaccard is excited about the opportunity to be part of the Mesulam Center team. "They have a body of expertise that I would not have access to otherwise," she said. "There are a lot of brilliant minds, all gathered in one place with all of the tools, and they have the ability to train and mentor me in a way that I would not receive anywhere else."



Staff Profile: Lauren Dowden, MSW, LCSW

Lauren Dowden, MSW, LCSW, a clinical social worker, is both a veteran and novice at the Mesulam Center. She worked at the center between 2014-18, moved to Los Angeles, CA, for three years, and returned to the center again in March 2022.

Dowden wears many hats in her position. She sees clients at the clinic, facilitates

the Glen and Wendy Miller Family Buddy Program and multiple support groups for care partners of people with dementia, and helps with recruitment, data management and analysis, and planning for events such as the annual Alzheimer Day.

During Dowden's first tenure at the center, she also co-created a storytelling program for people with dementia and their care partners. The couples would create stories and share them with healthcare professionals, students, researchers, and community members—more than 1,000 people in Chicagoland alone. Storytellers would perform at universities, places of worship, and business, and at events such as Alzheimer Day. Although the program is not active today, Dowden and Darby Morhardt, PhD, LCSW, are working on a paper about it to inspire others to continue telling stories.

Prior to working at the center, Dowden worked as an actor for almost 20 years, and for many of those as an improv artist, writer, and faculty

member for The Second City, a comedy theatre based in Chicago. She was inspired to become a social worker when the people close to her went through significant changes, including with their health. "Some of them had tools; some of them didn't and did it on their own. Watching that inspired me to want to be a tool, or somebody who can help people more," she said.

In 2014, Dowden graduated from Loyola University with a master's degree in social work. Her mentor there mentioned the Mesulam Center's improv program.

"It just kind of ended up being this marriage of my improv and creative background with the programs they were doing here," Dowden said. **"I fell in love with the work and the amazing team here. I'm always in awe. They're incredible."**

Staff Profile: Debby Zemlock

Debby Zemlock started as a data analyst associate at the Mesulam Center in January 2022, working for the Data Core. In her position, Zemlock works to eliminate errors by automating data entry features, and she also keeps track of the center's data, such as how many patients are enrolled in a study.

"What I really try to focus on is making the data work for all researchers, from the people that are entering the data to the people who will analyze the data to the professors who will ultimately write up the analysis," she said.

Zemlock graduated from Indiana University in 2016 with a BS in psychology, along with a neuroscience



certificate and a minor in fine arts. Her interest in cognitive neuroscience led her to write her undergraduate

thesis on what makes people creative.

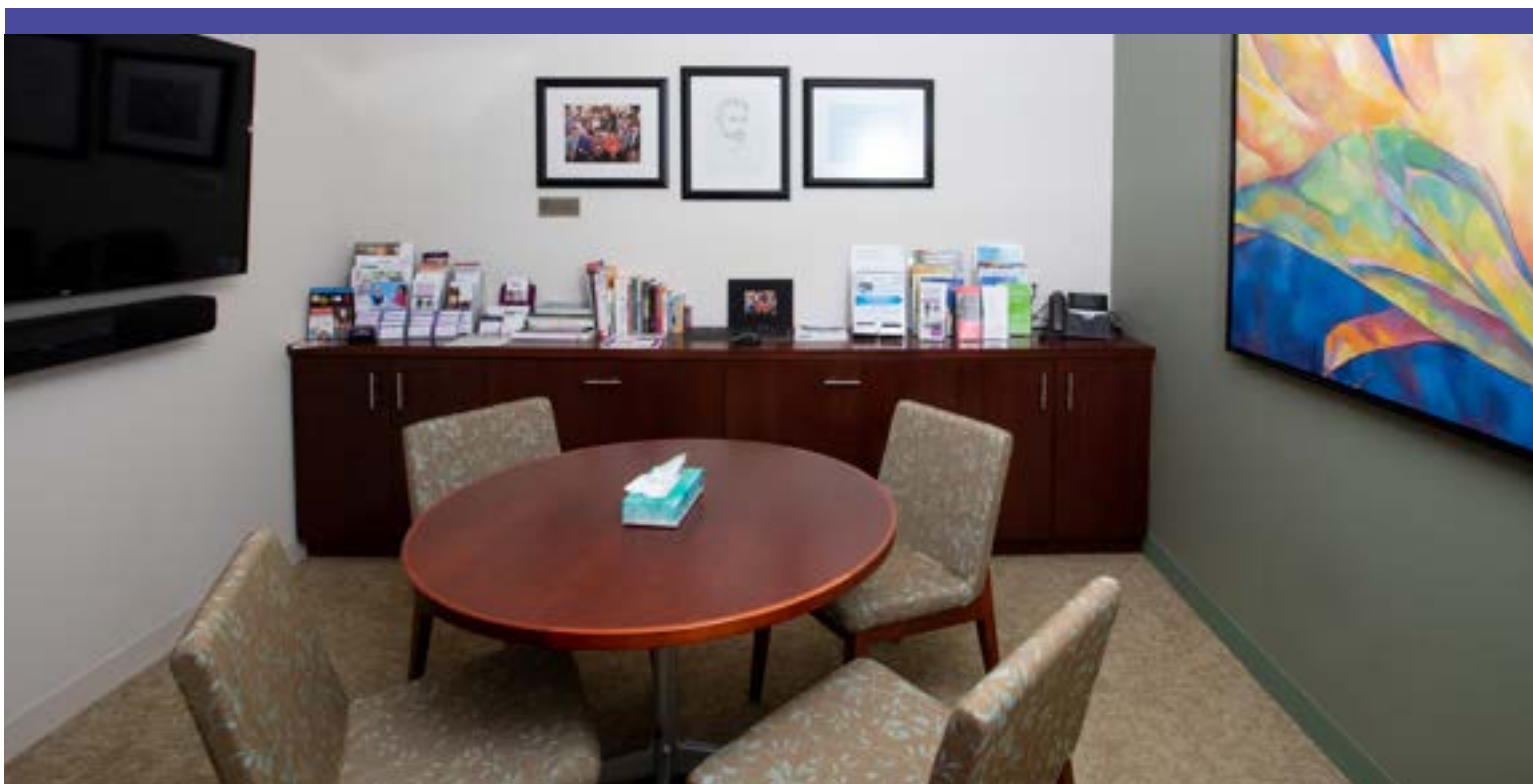
After she graduated, she moved to Chicago and became a research assistant at a child development lab at the Northwestern University Feinberg School of Medicine. In this role, she played with 1-year-olds for two to three hours, then entered the visit data.

"That process for me really seemed like it could be so much more efficient, so much more automated, to where I, as the research assistant, wasn't doing all of the work," Zemlock said. "Those really manual tasks also lead to data entry errors, which is never good. So, I kept being more drawn to fixing these problems in our database."

Eventually, Zemlock became a research data coordinator at the lab, solving the problems she had identified. Then she moved to the Mesulam Center, transitioning from working with infants to older populations.

"I learned, by myself, a lot of the data and the data information that I needed to program databases and how to do what I wanted in R, [a coding language]," Zemlock said. She realized she wanted a more formal education and began a data science master's program last year. She's also excited to be the treasurer for the Staff Relations Committee.

"I love that the Mesulam Center provides me with complex and interesting problems to solve that require that I learn new skills and open my mind to more possibilities," Zemlock said. "I also like the people that I've met and the collaborative culture of the center."



Bob and Linda Mendelson waiting room

Neurobehavior and Memory Clinic Helps Patients Through a Unique, Collaborative Approach

At the Neurobehavior and Memory Clinic of the Mesulam Center, neurologists, neuropsychologists, psychiatrists, and social workers all work in the same space—a unique situation where care providers can talk to their team members down the hall about patients and get immediate answers.

“We really don’t know of many other places where it’s like a one-stop shop,” said Sandra Weintraub, PhD, a professor of Psychiatry and Behavioral Sciences and a neuropsychologist at the clinic. “You may come in and meet with the neurologist first. And then you’ll get referred to the neuropsychologist or the social worker. The same team works with you. It’s a very big strength of ours that we have this multidisciplinary team.”

New clinic enhances patient care

In October 2021, a new clinic opened its doors on the 13th floor of the Arkes Pavilion. It’s double the size of the previous clinic and was designed meticulously through weekly meetings with clinic staff, including Weintraub, Darby Morhardt, PhD, LCSW, and Marsel Mesulam, MD.

Ian Grant, MD, director of clinical trials operations at the Mesulam Center and neurologist at the clinic, welcomed the expanded space for the flexibility it provides. He can see patients on days he wouldn’t normally be in the clinic. “It also helps with privacy,” Grant said. “The waiting areas are more separate. That also helps from a patient standpoint. It’s a little bit less noisy, a little more calm.”

The calming atmosphere of the clinic is intentional. The staff committee and architects wanted to design a space that resembled an office or living room rather than a hospital setting. There are frosted glass panels adorned with flowers, art on the walls, and larger private waiting rooms for patients and their care partners.



The new Neurobehavior Clinic of the Mesulam Center features updated amenities and additional space for patients, clinicians, staff, and their families to come together.

Training the next generation of dementia researchers

The new space is also conducive to training the next generation of clinicians and researchers in cognitive changes with aging, including dementia. Dementia can be caused by many diseases, and diagnosis is presently challenged by the lack of biomarkers for all diseases except Alzheimer's disease. The clinic's providers invite postdoctoral fellows to examine a person who has a less common symptom, such as aphasia (a disorder that affects communication skills), to learn more about unusual presentations of dementia—something in which the center specializes.

"This multidisciplinary bird's eye view is very unusual for people to get in practicum placements," Weintraub said. Clinical practica are offered to predoctoral clinical psychology students who need to complete several of these in the course of their training to qualify for graduation. The practicum provides experience with testing individuals and learning how to integrate the results with the information from neurological evaluation and available tests such as neuroimaging and cerebrospinal fluid tests.

The center regularly employs one or two fellows trained in neurology, psychiatry, or social work who complete their residency at the clinic. They also get exposure to research: For example, the first social work fellow, Debbie Dyslin-Kman, LCSW, who worked with Morhardt, developed her own research protocol to further the center's community engagement mission by investigating why Black research participants were not consenting to brain donation at the same rate as white research participants.

Committing to address the needs of patients

People typically come into the clinic to see a neurologist, who refers them to neuropsychologists for testing and orders diagnostic tests such as MRIs, CT scans, and bloodwork. Sometimes a patient may be referred to the neuropsychologist first and then other consultations are requested as indicated. Once the diagnosis has been made, individuals living with dementia and their care partners are referred to social workers, who can help them understand the diagnosis and plan for the future. The clinic staff are committed to caring for patients and their families through this initial process and follow-ups.

"Just because the disease doesn't have a cure doesn't mean there's nothing that can be done," Grant said. "We can change the responses and reactions of the people around them. Because when they understand it better, and they know how to interact with the person who's experiencing the cognitive issues, things tend to become a lot easier for everybody involved."

The clinic is also where many of the center's research participants find opportunities to participate in clinical trials. People who come into Northwestern often recognize it as an academic medical institution and are already looking for research options in addition to top clinical care.

"We really don't know of many other places where it's like a one-stop shop."

SANDRA WEINTRAUB, PHD

On Wednesday afternoons, the clinic staff and fellows gather to discuss treatment and testing options for new patients and get others' input on atypical cases. They also resolve any issues with existing patients. It's a way for everyone to get on the same page to support holistic care.

"Here, there's this foundation of support," Morhardt said. "We don't abandon them after a diagnosis. This is an illness that goes on for so long, and it's so stressful, and the loss is so great. And, there is a lot we can all do to affect the person's quality of life and that of their family. We want families to have the continuity of care that we provide and know that we are here for them."

FACULTY PROFILES

New Faculty Profile: Adam Martersteck, PhD



Though Adam Martersteck, PhD, joined the Mesulam Center this spring as assistant professor of Radiology and assistant director of the Imaging Core, he has a long history with the center. He originally joined the Mesulam Center in 2011 as a research coordinator, and

in 2020, he got his PhD in neuroscience from Northwestern, co-mentored by Todd Parrish, PhD, and Emily Rogalski, PhD, associate director of the center. After a postdoctoral fellowship in California, he returned to the center in April 2022.

Martersteck's research focuses on the heterogeneity of aging and dementia. Using neuroimaging and statistical learning, he studies both successful cognitive aging — also called SuperAging — and dementia syndromes such as primary progressive aphasia (PPA). As the assistant director of the Imaging Core, Martersteck helps build out the critical infrastructure used to process images. "One of the most powerful things about neuroimaging is you can track the brain's progression over time," he said.

He was inspired to pursue research on aging and dementia when he began volunteering at his mother's workplace, an intensive inpatient unit at a hospice. After seeing a range of experiences, including his own grandmother's vascular dementia, he wanted to make a difference in the field of aging and neurodegenerative disease.

In addition to research, Martersteck plans to teach a class on neuroimaging to inspire students in the same way his undergraduate professor had once inspired him, in an undergraduate class on functional neuroimaging.

Martersteck is excited to continue his work in such an interdisciplinary environment. He pointed out how, on the same floor, he can see faculty, trainees, and staff doing neuropsychological testing, neuroimaging, social work, education, and outreach. "I had learned so much about neuropathology because I just ran into people here and talked to them," Martersteck said. **"These little micro-mentorship moments that I experienced all throughout grad school gave me a stronger PhD. It's just a fantastic place."**

New Faculty Profile: Rudolph Castellani, MD



When Rudolph Castellani, MD, began his full-time appointment as a neuropathology professor in the Northwestern Feinberg School of Medicine Department of Pathology in September 2021, he didn't expect to work at the Mesulam Center.

But his colleagues recognized his vast experience with neurodegenerative diseases, and they directed him to the center. Castellani started neurodegenerative disease research in the mid-1990s as a fellow investigating human prion disease—a fatal brain disorder sometimes thought of as a human form of mad cow disease that was epidemic in cattle in Great Britain in the 1990s. "I was involved in some pioneering studies at Case Western Reserve University on the characterization of different protein types that occur in the setting of Creutzfeldt-Jakob disease and related diseases," Castellani said.

Now, in addition to his Feinberg appointment, he serves as the associate director of the Neuropathology Core at the Mesulam Center.

Castellani helps Margaret Flanagan, MD, with her responsibilities managing the brain and tissue bank and preparing for the monthly Clinicopathological Conference (CPC). The CPC is a center-wide presentation about the people with dementia whom the center has worked with and who have donated their brains to research. It starts with a presentation about a patient's clinical story—their symptoms and treatment history—then it's a detailed examination of the condition, necessary to connect the clinical presentation with what happened in the brain to cause illness.

Castellani can examine brains for certain pathologies with the naked eye and is on call to help technicians assess and measure the necessary parts of newly donated brains. He also hopes to help other center faculty with their research in the future.

For Castellani, the Mesulam Center is a beacon for dementia research because faculty consider the clinical symptoms along with underlying pathologies. **"It's important to have a little bit of humility to realize that we don't have any of these cases solved,"** he said. **"So it's important to look in detail at the cases and maybe through one case, we might make a novel observation that leads to disease modification."**

Challenges of Caregiving Q&A with Cheryl E. Woodson

Cheryl E. Woodson, MD, is a seasoned physician, author, and educator. She has taught and practiced geriatric medicine for almost 40 years and experienced the challenges of caregiving for a person with dementia firsthand, having cared for her mother, who had Alzheimer's disease for 10 years. She shared her expertise in the book "To Survive Caregiving: A Daughter's Experience, A Doctor's Advice" and its companion "The Doctor is IN: Answering Your Questions About How to Survive Caregiving."

In your book "To Survive Caregiving," you introduce the Five Keys to Caregiver Survival. What are the main takeaways from this framework?

The most important is that information beats panic. The first key is to find out if you need help, and that means getting an evaluation, or understanding whether you are dealing with dementia or not. The fifth key is also important. It is "put your oxygen mask on first." If you can't breathe, you can't help somebody else breathe. The keys in the middle are more about how you interact with family, with healthcare teams, and how you get people to help you. Many caregivers don't want to tell anybody they need help. There is no way to do this by yourself. You've got to tell people that you need help, and if they don't help, you stop relying on them.

How can people manage competing priorities and responsibilities while providing care?

First of all, they have to understand that there are competing priorities. Try to figure out what the balance is. There's no way for you to do all of this without getting it together, finding out what resources you need, setting up structures and schedules, and making sure that you put yourself on that schedule. Reserving time to just relax and rewind

and rebuild lets you come back as a better caregiver. You deserve some help, and you will burn yourself out if you don't get the help.

What is the most important piece of advice you'd like caregivers to take away from our conversation?

We're nurturers, and we value that part of us, and we want to give until it hurts, but you do not have to give until you are damaged. There are ways to give great care without killing your physical, financial, emotional or spiritual health, without killing your career, your marriage, or your relationship with your kids. You don't have to sacrifice everything to do this. Find out if you need help. Tell people you need help. Let people help, and realize that you can't take care of them, if you don't take care of you.

How can caregivers manage complex feelings of stress, pain, fear, confusion, and guilt?

Guilt is one of the most insidious ones. It's the most dangerous because people feel that they're not doing as good a job as their parents did with their grandparents, but there's a crisis in caregiving today that your grandparents did not have to deal with. Forgiving yourself for not being able to do something that is impossible for you to do — that's one thing. You have to get help, so that you can step back and deal with your grief and deal with your guilt. A lot of times people are afraid because they don't know what they're doing, but some of the fear comes from losing the relationship, or anticipatory grieving. Again, counseling will help. The other thing that helps is to keep your "I love you's" up-to-date and do things with them, not to them. Let somebody else do the dressing changes, and you play a game, or listen to music with them. You're not spending the time with your head down doing stuff; you're interacting with them.



How does caregiving today differ from what it was in past generations?

Each generation has fewer children, so there are fewer potential caregivers. The caregivers have competing responsibilities that previous generations didn't have. And the caregiving season is longer because people are living longer.

What is the most common misconception about caregiving?

That it's easy, and that it is an obligation to do it yourself.

How can caregivers struggling to find time practice self care?

By getting the help you need so that you can step away, whether it's respite care or adult day services. You need people whose shoulders you can cry on who are farther along in the caregiving path than you are. This is why caregiver support groups are essential, because there are people around you who've already been down that path. They may have ideas that you haven't thought of yet. You can't do self care, unless you're willing to step back and let somebody else take care of them on a regular basis. You can't wait until there's a crisis. It ought to be something that you schedule, whether it's monthly, quarterly, or whatever you can afford and tolerate, but it has to be on a regular basis. I'm so passionate about this because I've seen so many people crash and burn, and it just doesn't have to be that way. Self-care is not selfish, it is critical.

Participant Perspectives

Mesulam Center studies help investigators better understand and create future treatments for mild cognitive impairment, Alzheimer's disease, and related dementias. Those who participate in these studies often find both therapeutic resources for themselves and a sense of fulfillment in helping future generations.

PROVIDING HELP TO PEOPLE WITH PRIMARY PROGRESSIVE APHASIA (PPA)

PPA is a rare dementia syndrome that initially affects a person's language and is most commonly diagnosed in people over 65. Marsel Mesulam, MD, the center's director, first described this condition in 1982. Since then, the center has been a premier destination for PPA care and research.

One resource available to those with PPA is the Communication Bridge clinical trial, an internet-based speech therapy intervention for individuals living with PPA and their communication partner (a spouse, relative, or close friend). The first randomized controlled trial of speech therapy for individuals with PPA, Communication Bridge, led by Emily Rogalski, PhD, is available to participants around the world.

For Alexis Martin, the trial offered a way to get therapy during the pandemic after the hospital where she was receiving speech therapy temporarily closed. She and her communication partner Don Martin participated from January 2021–2022 from their home in Kansas City, Missouri. The Martins found the study online.

"We didn't have any other resource available," Don Martin said. "This study sounded very enticing, interesting, and we needed information."

They worked with Leela Rao, a clinical research associate at the center. "That was hard for me," Alexis Martin said. "But she really broke it down. She saved me because I could learn a different way of speaking. And Don and I, we worked really hard."

"We would enthusiastically encourage anybody who has that diagnosis to become involved, to be a participant," Don Martin added.



AJ Olsen, Mesulam Center research study coordinator, meets with SuperAger Carole Book during an annual visit.

LEARNING ABOUT HEALTHY AGING WITH SUPERAGERS

Studying SuperAgers—adults older than age 80 who have the memory capacity of individuals who are at least 30 years younger—allows researchers to understand what factors contribute to remarkable memory performance and how these may potentially be helpful in optimizing healthspan.

SuperAgers participate in studies by completing pen and paper surveys about memory and other thinking abilities, giving blood samples, participating in brain imaging, and committing to brain donation.

Ruth Long has been a study participant for more than 10 years. "I think that it may help others in years to come," she said. "And it's interesting to me to see what my body is doing and how it's holding up."

Long enjoys gardening, going to museums, and trying new foods. She also likes reading, so her favorite part of being a research participant is learning about the results of the study. When asked about the advice she'd give to people considering research participation, Long said, "I would tell them that it has been very interesting to me. I have learned many new things. And it is a way, I feel, to help people yet to be born. Hopefully they will have better, healthier lives than we have."

"I think that it may help others in years to come."

RUTH LONG

Mesulam Center Recruiting for Primary Progressive Aphasia and SuperAging Studies

The Mesulam Center is committed to providing quality care through our affiliated care sites, conducting research on how the brain coordinates mental functions, transferring the benefits of research to afflicted patients and preparing future scientists and clinicians in our field. Two primary areas of focus at the center are primary progressive aphasia (PPA) and SuperAging.

LANGUAGE IN PRIMARY PROGRESSIVE APHASIA

The Language in Primary Progressive Aphasia (PPA) aims to better understand progression in PPA and its link to brain changes, increase awareness of PPA, and identify biomarkers leading to earlier diagnosis and treatment. Participants are asked to undergo tests of language and thinking abilities and have brain scans every two years.

To be eligible for this study, you must carry a diagnosis of primary progressive aphasia, established at a thorough evaluation prior to enrollment. If you think you may have dementia, but have not yet been evaluated, you must first undergo a clinical evaluation. This clinical evaluation is not part of the research. Patients must also meet screening criteria which require the patient to be a right-handed, native English speaker and have the ability to undergo a 3T MRI.

SUPERAGING RESEARCH INITIATIVE

The SuperAging Research Initiative seeks to identify factors that contribute to maintaining superior memory performance in older age (age 80 and above). Researchers are looking at a variety of factors including cognition, personality traits, psychosocial factors, genetic factors, and brain structure. This research may lead to new clues important for protecting against age-related cognitive decline and Alzheimer's disease.

We recently established an international multi-site SuperAging consortium called the SuperAging Research Initiative. Currently the initiative includes five primary recruitment sites across the United States and Canada: the University of Michigan, University of Wisconsin, Emory University, Western University, and Northwestern University. Rush University and University of Waterloo will also provide key referrals.

The goal of the SuperAging Research Initiative is to expand SuperAging research and enroll at least 500 participants from diverse backgrounds, as well as cognitively healthy individuals with similar demographics. Expanding efforts throughout North America will aid in isolating factors that promote successful cognitive aging and perhaps prevent age-related brain diseases such as Alzheimer's disease. To be eligible, you must be aged 80+, cognitively healthy and actively engaged in life, and MRI safe.

Learn more about our research opportunities at brain.northwestern.edu/join

In addition to these studies, the Mesulam Center is currently enrolling for many other research studies. Our research efforts lead to better understanding of and future treatments for age-related cognitive decline and the diseases that cause it. Learn more about all of our active studies at brain.northwestern.edu/join



Jason Boschan crosses the finish line at the 2022 Everest Marathon.

Run4Papa Founder Takes On World's Highest Marathon to Fund Dementia Research

"Everybody has their own Mount Everest they were put on this earth to climb," said Run4Papa founder Jason Boschan. "Mine is running to find a cure for dementia."

Although Boschan is referring to a figurative Mount Everest, his journey towards a cure includes conquering the actual mountain itself. In May 2022, he ran the Everest Marathon, a feat that fewer than 2,000 people have completed in the race's 20-year history.

The endeavor consisted of 11 days of hiking to Everest Base Camp (EBC), an average of more than five hours of hiking per day, and 10 hours, 41 minutes, and 29 seconds running the "world's highest marathon"—all to support dementia awareness and research in the Mesulam Center.

Boschan established Run4Papa in 2011 to honor his grandfather, Louis "Papa" Heyman, MD, who was diagnosed with primary progressive aphasia (PPA) in 2009 and passed away in 2013.



Boschan prepares for marathon during his hike to Everest Base Camp.

PPA is a form of dementia that involves a gradual loss of language function.

When his grandfather sought treatment at Northwestern, Boschan connected with other patients with PPA and caregivers. He has since built a strong foundation of support for PPA research at the Mesulam Center by running 57 races around the world, including 13 marathons.

To date, Run4Papa has raised over \$330,000, and 100% of every donation benefits research within the Mesulam Center. Boschan's fundraising goal for his most recent marathon on Mount Everest was \$17,600 to match the 17,600-foot elevation at EBC where the race began.



Boschan's hiking and running group at Everest Base Camp.

Through generous supporters of Run4Papa, Boschan surpassed his goal and raised \$22,315 to help extend the second round of the global Communication Bridge study at the Mesulam Center, led by Emily Rogalski, PhD. Rogalski's goal through this research is to improve access to high-quality speech-therapy and social work care to maximize communication abilities and quality of life for people living with PPA.

"Thanks to the funds raised by Run4Papa, we have been able to advance important research that will ultimately raise the standard of care for those living with PPA. Jason's passion and determination have truly helped to drive these efforts within the Mesulam Center," said Rogalski, who is the Ann Adelman Perkins and John S. Perkins Professor of Alzheimer's Disease Prevention and professor of Psychiatry and Behavioral Sciences.

Those inspired by Boschan's story might wonder what's next for the marketing professional turned runner and research champion. By the end of 2022, he hopes to have completed half marathons in 30 states to raise awareness for dementia. While he doesn't have plans for another marathon just yet, Boschan is determined to continue running races around the world for the cause until a cure is found.

The growth of the Mesulam Center needs your support. Consider making a gift to support the future of dementia care and research. To learn more about giving, visit brain.northwestern.edu/give

"Thanks to the funds raised by Run4Papa, we have been able to advance important research that will ultimately raise the standard of care for those living with PPA. Jason's passion and determination have truly helped to drive these efforts within the Mesulam Center."

EMILY ROGALSKI, PHD



Boschan crosses the Tenzing Hillary Bridge (above) during his 11 day ascent to Everest Base Camp (left).

Supplement to Research Grant Supports Diversity in the Lab

RECENT HIGH SCHOOL GRADUATE FINDS PATH THROUGH MESULAM MENTORSHIP

Prior to graduating in 2021, Lane Tech College Prep High School student Vivi Lubbat performed lab work solely through a computer screen.

But starting the summer after her graduation, Lubbat got the opportunity to work in a real wet lab (where chemicals and biological matter are analyzed and tested) at the Mesulam Center alongside her mentor, Tamar Gefen, PhD, a clinical neuropsychologist who conducts clinicopathologic studies on dementia syndromes, including primary progressive aphasia (PPA) and behavioral variant Frontotemporal Dementia (bvFTD).

"Vivi came in with passion and interest, but she had no experience," Gefen said. "But when I talk about passion, I'm talking about a burning passion that you don't see in typical 16-year-olds—this real desire to enter the STEM field as soon as possible, diving right in." Gefen committed to mentoring and training Lubbat in techniques for working with postmortem brains and in professional development.

Lubbat was able to work at the lab thanks to a supplement to Gefen's National Institutes of Health (NIH) R01 grant that allows for recruitment of future researchers from groups that are traditionally underrepresented in biomedical, clinical, and social sciences. Lubbat identifies as a proud Palestinian woman. Gefen and she jointly applied for the supplement immediately after they met. "I've been really urging my colleagues to apply," Gefen said. "There's no downside to it."

Learning the research process

At first, Lubbat struggled to follow the anatomical terms and jargon. She'd write down all the terms she could and look them up later. "I would say at first, being in the wet lab, it was a little intimidating, because there was just so much going on all the time," Lubbat said. "But I think my mentors, including Dr. Gefen, and all my co-workers were really welcoming and ensured that I understood the process of how we collect data and how we use brain samples."

After working at the wet lab in person through the summer of 2021, Lubbat transitioned to remote work while she attends Queens University, one of the most prestigious schools in Canada, and majors in health studies. Over the summer, she had prepared scans of the brain that were adequate for remote study. "I look at how the pathology, specifically in primary progressive aphasia, affects neuron sizing," she said. "I take slide samples of specific brain regions and size in neurons by looking at their area, and then we collect that data and understand how the pathology specifically affects regions of the brain."

While Lubbat learned from Gefen's lab members, she influenced them as well. Everyone rallied behind the newcomer to support her growth. "These unsettling times can be particularly disempowering," Gefen said. "And I think when people get together, for the same goal—whether it's research, trying to engage in some form of activism, helping a single person—everyone working collectively empowers not only the receiver, but also the giver. So we've all, including myself, just been empowered by this relationship. It's been so meaningful for all of us."

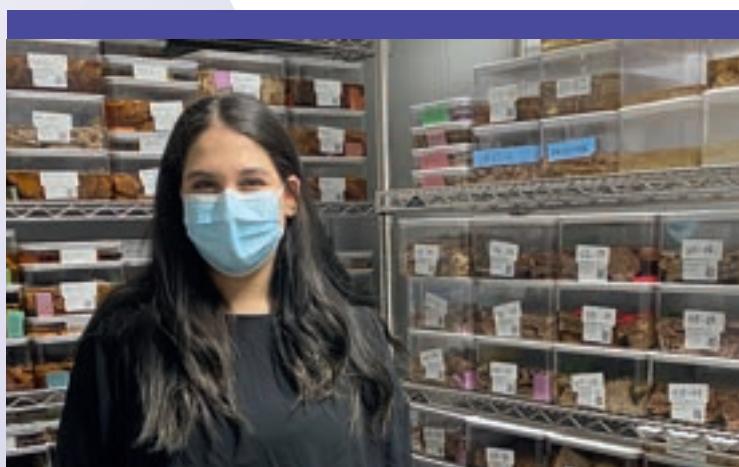
Inspiring women and people of color

"It was really, really inspiring to work alongside all of these strong and really intelligent women, especially as a woman going into STEM," Lubbat said. "Especially because for Dr. Gefen, this is not just a career, this is a passion for her, and just seeing how passionate she is about anything that relates to the brain really makes me excited to work under her and see how she works."

Gefen looks forward to what the future holds for her mentee. "My goal is for her to become part of the next generation of scientists, investigators, and clinicians," she said. "I know she will. That makes it so much fun."

Lubbat acknowledges that it's easy to be intimidated by research, but hopes to inspire others, especially women and people of color, to pursue their dreams. "Everyone deserves to be included in research," she said. "And if they really feel like that's what they have a passion in, then they should really explore that passion, despite barriers that women and people of color might have."

For more information on diversity supplements awarded by the National Institutes of Health, see: grants.nih.gov/grants/guide/pa-files/pa-20-222.html



Lubbat in the Mesulam Center wet lab during a visit to the center.

DOCTORAL STUDENT RECEIVES AWARD FROM THE NATIONAL INSTITUTE ON AGING

Rachel Keszycki, a clinical psychology doctoral student at the Mesulam Center, received the Ruth L. Kirschstein National Research Service Award from the National Institute on Aging, which will help facilitate her training and support the completion of her dissertation.

Keszycki began her doctorate studying neuropsychiatric symptoms in Alzheimer's disease, but over time she decided to broaden her work to other types of neurodegenerative diseases.



With the grant, she will focus on primary progressive aphasia (PPA), a language-related dementia syndrome that can also be accompanied by severe neuropsychiatric symptoms such as apathy and disinhibition, especially in later stages.

Keszycki hopes her research can connect the different underlying pathologies of PPA with these symptoms. She began by

studying a neuropathology called Pick's disease, which is found in brains of those with rarer forms of dementia that typically affect people under 65, and was then inspired to turn that into a larger project and training experience. Because of that, Keszycki applied for the award.

"The hope is that the relationship between certain neuropsychiatric symptoms and pathology might lead to additional insights into how these pathologies contribute to decline and disease in patients outside of studies that have just focused on cognition," she said.

The grant will also help her to network and showcase her research at the International Conference for Frontotemporal Dementia in France later this year. In addition, she won the Marie and Carl Duncan Prize in Memory Disorders and Research at this year's annual Alzheimer Day for her work.

At the Mesulam Center, Keszycki values the opportunity for collaboration most. "There are so many people with different specialties all within this space," she said. "If you have questions or need a consult, there are neurologists, neuropathologists, neuropsychologists, and other interdisciplinary experts within dementia and neurodegenerative diseases to mentor you and collaborate on any clinical and research work."

RESEARCH TECHNOLOGIST RECEIVES PRESTIGIOUS NATIONAL SCIENCE FOUNDATION FELLOWSHIP

Each year, the National Science Foundation (NSF) Graduate Research Fellowship Program recognizes about 2,000 outstanding graduate students in the United States and supports them in their science and engineering research.

Allegra Kawles, research technologist at the Mesulam Center, received this prestigious award in 2022. She is pursuing her PhD in clinical psychology at the Northwestern University Feinberg School of Medicine, in the lab led by Tamar Gefen, PhD.

Kawles studies how different pathologies affect the hippocampus, an area of the brain for memory. Her focus is primary progressive aphasia (PPA), the type of dementia first described by center director Marsel Mesulam, MD, in the 1980s that affects a person's



language. Although people with PPA do not present with memory problems, their brains upon autopsy reveal significant pathologies in the hippocampus.

That brings up the question, "Do you need every part of the hippocampus in order to form memories?" Kawles said. "Every other part of research says yes. Yet, we see people with no memory problems, but pathology

in their hippocampus." With her fellowship, Kawles will look at clinicopathologic correlations, which means she will consider both clinical symptoms before death and the brain autopsy results after.

Kawles hopes that the broader impact of her research will be helping the aging LGBTQ+ population. "I've noticed that this intersection of the two things I'm interested in, which is LGBTQ+ health and aging, is not well studied," she said. "It's this group that's a part of all areas of research, but forgotten."

For Kawles' research, she will receive financial support for three out of five years of membership, along with allowance for her educational institution. She will also access special events, talks, and resources. She is grateful for the support and recommendations of her mentors at the Mesulam Center, including Gefen, Changiz Geula, PhD, and Darby Morhardt, PhD, LCSW.

"I feel very lucky," Kawles said. "I'm really excited to continue this mentorship relationship and continue talking about science with people I admire."



Timpo (center) attends a 1st district walking club event in May 2022.

Building Diversity in Research Through Community Partnerships

CENTER HIRES FIRST SENIOR COMMUNITY ENGAGEMENT COORDINATOR

Studies show that older Black Americans are twice as likely as older white Americans to develop Alzheimer's or related dementias. Racial differences in neuropsychological testing performance, study design, social determinants of health and lack of data are all possible reasons for this unbalanced burden of dementia in Black Americans. Research has increased in recent years but more research is needed to determine the cause behind this disparity.

To help understand this gap, the National Institute on Aging (NIA) has invested in programs that recruit underrepresented groups to participate in dementia research, which has allowed the Mesulam Center to expand its community engagement.

In March, Phyllis Timpo joined the center as its first senior community engagement coordinator. Funded by the NIA, she guides the center's Underrepresented Group (URG) Task Force to develop relationships in Chicago neighborhoods with high populations of Black and older adults.

"Researchers and funding sources are now putting a concerted effort into requiring researchers to have study cohorts that are more reflective of the diversity found in the United States. It is no longer enough to blame institutional distrust for the lack of diversity in samples. The focus on the science of recruitment is key," Timpo said.

"There's a long history of mistrust, especially among the Black community, to participate in research," said Darby Morhardt, PhD, LCSW, research professor and social worker at the Mesulam Center and co-founder of the URG Task Force. "We need to engage the community in trusting partnerships, get to know the community and their needs, and build long-lasting collaborations that are not unidirectional. Our work together needs to be mutually beneficial."

Building on strong community partnerships

Two neighborhoods of focus for the URG Task Force are Bronzeville and South Loop—one of the first neighborhoods in Chicago to be designated as dementia-friendly. The South Loop Village is a nonprofit community-based volunteer organization that provides support for residents to age in those two communities. For several years, the South Loop Village and the Mesulam Center have partnered to provide educational programs and research opportunities.

"The commitment made by the Mesulam Center to the under-resourced communities on the South Side of Chicago has opened doors for us in the South Loop Village," said Janie Urbanic, MA, LPC, the founding director of South Loop Village. "Our partnership benefits both the Mesulam Center and the South Loop Village, but more importantly it benefits the residents in these vibrant but often neglected neighborhoods."

The center has also worked for several years with community engagement consultant Melvin Thompson, the executive director of the Endealeo Institute, a non-profit that focuses on health, education, and community development in Chicago's far South Side Washington Heights and surrounding communities. Thompson has assisted with the center's extensive efforts of recruiting people from underrepresented groups into dementia care, research, and education.

"I feel a duty to keep this partnership going just so there is comfort in our community and in the Northwestern medical community," Thompson said. "This relationship becomes part of the fabric of our community."

Growing efforts to engage the community

In her short time at the center, Timpo has connected with dozens of people and organizations across Chicago. "We're growing our community efforts exponentially as a result of her involvement," Morhardt said. The center has now hired a second community engagement coordinator who is on the research team.

These steps are vital to the success of dementia research. Without diverse cohorts, study results cannot be generalizable, and it's essential to promote trust and provide resources for people in underrepresented groups.

"We need to engage the community in trusting partnerships, get to know the community and their needs, and build long-lasting collaborations that are not unidirectional. Our work together needs to be mutually beneficial."

DARBY MORHARDT, PHD, LCSW

"I really want to develop a strong cohort of Black research participants who are enthusiastic about our work," Timpo said. "And I am excited to develop strong partnerships and relationships with communities who are most impacted with this terrible disease. When I talk to people out in the community, they are often excited and eager to engage on this topic but have not been given the opportunity to do so. I'd like to change that with my work at the Mesulam center. It is time for research to reflect the diverse background and life experiences of all Americans."



Timpo connects with a resident at a South Loop Village Memory Café event.



Timpo meets with residents at Rosenwald Courts Apartments during a recent event.

NORTHWESTERN PREP BRINGS DIVERSE POPULATIONS INTO BIOMEDICAL RESEARCH

The biomedical research workforce lacks gender, race, and ethnic diversity. Part of the problem lies within the industry's pipeline: Many of these jobs require advanced degrees, which first require research experience that sufficiently prepares students for a graduate science program.

The Northwestern University Postbaccalaureate Research Education Program (NU PREP) is aimed at addressing both issues. Housed in the Northwestern University Interdepartmental Neuroscience (NUIN) program, NU PREP is a one-year experience focused on training scholars from diverse backgrounds—students from underrepresented groups, students with disabilities, or students from socially or economically disadvantaged backgrounds.

NU PREP is one of about 30 similar postbaccalaureate programs across the country funded by the National Institute of General Medical Sciences (NIGMS). The program is in its sixth year and has been renewed for five more years. All alumni of the program have been accepted to graduate schools in top-tier universities to pursue PhDs.

"It's something Northwestern is particularly well-positioned to do as a university based in the Chicagoland area, where we have a very diverse population," said John Disterhoft, PhD, NU PREP director and faculty mentor. "It's been one of the more impactful programs in terms of getting a diverse population interested in going to competitive graduate schools, and then actually helping them gain admission and ensuring they are thriving in graduate school."

There is no cost associated with the program: The NIGMS funds six Northwestern scholars to conduct research, learn science communication, and prepare for graduate school through application reviews and mock interviews, and Northwestern's Feinberg School of Medicine funds one additional scholar's experience. The scholars also receive a stipend and medical insurance.

A true first-year experience

Once scholars are provisionally accepted into the program, they pick three labs they would like to conduct research in, out of the 48 labs that have committed to NU PREP mentorship.

Faculty mentors and members of their labs then interview prospective scholars for a mutual match. "We do a matching that combines the selection of the PREP scholar, but also involves the mentors themselves to make sure that there's a fit," Disterhoft said.

Mesulam Center faculty mentored two of the seven students in the class of 2022. Bob Vassar, PhD, and Changiz Geula, PhD, both opened



A researcher studies brain tissue in the Mesulam Center labs.

"It's been one of the more impactful programs in terms of getting a diverse population interested in going to competitive graduate schools, and then actually helping them gain admission and ensuring they are thriving in graduate school." "

JOHN DISTERHOFT, PHD

their labs to attract a diverse cohort of future researchers in Alzheimer's disease and related dementias. The year before, Disterhoft, who is also affiliated with the center, served as a faculty mentor.

Scholars spend about three quarters of their time in their mentor's lab, participating in the role of a first-year graduate student. The rest of the time is mostly devoted to science communication: learning how to write grants and graduate school applications, meeting regularly with the program's advisory committee members for mock interviews, and developing a personal statement for their graduate school applications.

Scholars also take graduate or upper-level undergraduate courses to supplement their academic record and attend at least one national scientific meeting, such as the Annual Biomedical Research Conference for Minoritized Students (ABRCMS), the Society for Advancement of Chicanos/Hispanics & Native Americans in Science (SACNAS) conference, or the Society for Neuroscience conference.

"We offer the strengths of Northwestern as a place to do research and graduate studies," Disterhoft said. "We do similar things to programs at other universities, but we do them quite well, because our program has been very successful."

MAJOR PUBLICATIONS BY MESULAM CENTER FACULTY

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Roberts AC, **Rademaker AW, Salley EA, Mooney A, Morhardt D, Fried-Oken M, Weintraub S, Mesulam M, Rogalski E.** **Communication Bridge™-2 (CB2): an NIH Stage 2 randomized control trial of a speech-language intervention for communication impairments in individuals with mild to moderate primary progressive aphasia.** *Trials.* 2022. 23(1):487. PMC9190461.

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PUBLICATIONS AND GRANTS

AUGUST 2021 - AUGUST 2022

Mesulam Center investigators received major grants that advance the field of Alzheimer's disease and related dementias. Notably, the National Institute on Aging awarded the Mesulam Center at \$10 million grant to support the center's ongoing research on primary progressive aphasia. Learn more about that on page 22.

TOTAL NUMBER OF PUBLICATIONS (AUGUST 2021 - AUGUST 2022): 46

NEW GRANTS AND AWARDS: 6

NEW GRANTS:

Margaret Flanagan, MD: Northwestern University Clinical and Translational Sciences Institute (NUCATS) COVID-19 Fund to Retain Dr. Margaret Flanagan as a Physician Scientist

Ian Grant, MD: VIVA Mind (University of Southern California)
A Phase 2A Randomized Double-Blind Placebo-Controlled Trial to Evaluate the Efficacy and Safety of Varoglutamstat (PQ912) in Patients with Early Alzheimer's Disease with a Stage Gate to Phase 2B (VIVA-MIND)

Ian Grant, MD: R56 (University of Southern California)
Long-Term Nicotine Treatment of Mild Cognitive Impairment

Changiz Geula, PhD: University of Illinois Chicago
Hippocampal Neurogenesis in Cognitive Function and Dysfunction in Alzheimer's Disease

Emily Rogalski, PhD and Marsel Mesulam, MD: National Institute of Aging (NIA) Asymmetric Neurodegeneration and Language in Primary Progressive Aphasia

Emily Rogalski, PhD, Changiz Geula, PhD, Marsel Mesulam, MD: National Institute of Aging (NIA) Study to Uncover Pathways to Exceptional Cognitive Resilience in Aging (SUPERAGING)



Brain tissue used for research stored in the Mesulam Center wet lab.

Celebrating Alzheimer's Science and Clinical Care

The Mesulam Center for Cognitive Neurology and Alzheimer's Disease held the 28th annual Alzheimer Day on May 5, returning to campus for the first time in three years.

M. Marsel Mesulam, MD, chief of Behavioral Neurology, the Ruth Dunbar Davee Professor of Neuroscience and director of the Mesulam Center, welcomed attendees to the event, highlighted the recent renewals of several large grants supporting the center and thanked research participants and their families — noting that without them, no center activities would be possible.

"Each one of you and your families deserve gold medals, thank you very much for your contributions to our research," Mesulam said.

The keynote Mendelson Lecture was delivered by Lisa Barnes, PhD, professor of Neurological Sciences at Rush Medical College, who spoke about social and environmental factors that impact cognitive aging in racial and ethnic minority participants.

Impeding progress on this front is poor recruitment of racial and ethnic minority participants into research, according to Barnes, who set out to fix this problem with her Minority Aging Research Study (MARS). MARS is a prospective cohort study of 800 older age Black participants, with the goal of examining how aging may differ in a racial minority cohort.

For example, Barnes discovered that a gene variant thought to have no impact on risk of Alzheimer's was actually protective in Black people, a finding that had been obscured by the low inclusion of Black participants in genetic studies.

"Nobody had noticed this before — you can ask different questions when you include different people," Barnes said.

Barnes also takes a broader view of risk factors, measuring associations between experiences such as racism, unfair treatment and childhood poverty to poor cognition later in life.

"We have to think about policies that will help people mitigate some of this stress to create an equitable society for everyone, so everyone can age in the same way," Barnes said.



Fatima Eldes, Mesulam Center research coordinator, speaks to an attendee during the Alzheimer Day Poster Session.

The scientific poster session showcased dozens of projects, with topics ranging from fundamental mechanisms of neurons to new modalities of speech therapy tailored for an increasingly online world.

Nalini Rao, a student in the Northwestern University Interdepartmental Neuroscience program (NUIN), presented on research into dysfunction in synaptic vesicles, one of the earliest changes yet discovered in Alzheimer's disease. Conducting her work in the laboratory of Jeffrey Savas, PhD, assistant professor in the Ken and Ruth Davee Department of Neurology's Division of Behavioral Neurology, Rao is exploring how lags in protein degradation may lead to buildup of toxic amyloid-beta protein aggregates.

"If we can fix this problem, can we avoid amyloid beta accumulation? That's the question I'm asking," Rao said.

John Disterhoft, PhD, the Ernest J. and Hattie H. Magerstadt Memorial Research Professor of Neuroscience, presented the Marie and Carl Duncan Prize for Memory Disorders, awarded for top-scoring scientific posters. Rachel Keszycki, a student in the Clinical Psychology PhD Program, and Allegra Kawles, research technologist, were awarded this year's top prizes. Both conduct their research in the laboratory of Tamar Gefen, PhD, assistant professor of Psychiatry and Behavioral Sciences in the Division of Psychology.



Mesulam Center staff members connect with community members at Alzheimer Day 2022.

Alzheimer Day 2022 also marked 25 years of the Glen and Wendy Miller Family Buddy Program, which matches first-year medical students with patients diagnosed with early Alzheimer's disease or related illnesses. Each year 10 to 15 medical students volunteer in the program and commit to spending at least four hours a month with their buddy, or mentor. Funded by The Glen and Wendy Miller Family Foundation, the goal of the program is to educate students about the disease outside of the clinic and give persons living with dementia the opportunity to mentor students.

"We have to think about policies that will help people mitigate some of this stress to create an equitable society for everyone, so everyone can age in the same way."

LISA BARNES

Darby Morhardt, PhD, research professor at the Mesulam Center, of Preventive Medicine in the Division of Public Health Practice and director of the program, welcomed Jim Butler, a mentor who's participated in the program for four years. Butler was joined by two of his mentees; Sebastian Otto-Meyer, now a resident in pediatrics at McGaw Medical Center and Brooke Gleason, a first-year medical student.



Buddy Program mentor Joseph Pyle (center) performs at the Quality of Life Symposium with his buddy Melanie Zhang (left) and wife Kimberly Pyle (right).

"The Buddy Program has brought me more joy than I ever would have imagined," Butler said. "I want to thank Darby, and everyone involved with the program."

Mesulam Center receives \$10.4 million grant to fund Primary Progressive Aphasia research

The Mesulam Center has been awarded a \$10.4 million grant from the National Institute on Aging (NIA) to support the center's ongoing research on primary progressive aphasia (PPA).

Marsel Mesulam, MD, director of the Mesulam Center, identified the disease and coined the term in 1982. The center continues to be a global leader in PPA research.

This award will enable the Mesulam Center to continue its 15-year-long study of PPA and focus on enrolling and supporting newly diagnosed persons each year. The grant also will support the Mesulam Center's effort to increase representation of traditionally underrepresented groups in research studies including Black and Hispanic/Latino communities and raise awareness in their communities, a primary goal of the center.

PPA is a relatively uncommon dementia syndrome, in which an individual experiences progressive loss of language and communication, which negatively impacts their daily quality of life. Adults of any age can develop PPA, but it is most often diagnosed in persons under 65. Nearly 40% of PPA is caused by Alzheimer's disease neuropathology.

Mesulam and Emily Rogalski, associate director of the Mesulam Center, will co-lead this new award.

"We will deepen our focus over the next five years, following precision medicine approaches to uncover disease-specific anatomic, cellular, molecular and genetic understanding of PPA," Rogalski said. "We are grateful for the dedication of the individuals living with PPA and their families who continue to help us advance our understanding of the syndrome."

Since Mesulam discovered PPA in the 1980s, research has expanded exponentially, making it possible to accurately define the syndrome and identify key risk factors.

"We are grateful for the dedication of the individuals living with PPA and their families who continue to help us advance our understanding of the syndrome."

M. MARSEL MESULAM, MD

Prior to receiving this grant, Mesulam and Rogalski each led NIH-funded grants to research PPA with different methods, which have been running in parallel for 15 and 10 years, respectively. In 2021, they submitted a combined, comprehensive grant with co-investigators specializing in different disciplines, including innovative methods to characterize clinical trajectories, precision brain imaging, genetic studies and detailed investigations of the abnormal proteins and neuropathologic entities causing this syndrome. Collectively, these investigations aim to inform and improve diagnosis, prognosis and treatment options for PPA and related neurodegenerative dementia syndromes.

"Our PPA research program includes key experts covering topics from cells to social work who are sharply focused on improving diagnosis, care and interventions for those with PPA and related dementias," Rogalski said.

"The identification of PPA initiated three pivotal insights that still dominate this field of neurology — namely that dementia can be caused by entities other than Alzheimer's disease, that not all dementias impair memory and that dementias can arise well before old age, in the 40s and 50s," Mesulam said. "Advances in PPA also stand to make the pejorative term 'dementia' obsolete by showing that it is both too inclusive and too ambiguous for research and patient care."

CONFERENCE PRESENTATIONS

In addition to the work and research that Mesulam Center faculty have been doing in Chicago, various faculty members have presented at conferences locally and internationally, showcasing the research of the Mesulam Center on the world stage.

Emily Rogalski, PhD, presented a lecture titled “The Many Ways to Age” at the Northwestern University Lawrence B. Dumas Domain Dialogue event in December 2021. **Rogalski** presented a keynote speech entitled “Why do some people show resistance to cognitive aging?” at the 13th Annual McKnight Brain Research Foundation Inter-Institutional Meeting March 2022.

Borna Bonakdarpour, MD, presented at the 2022 American Academy of Neurology Annual Meeting in Seattle, Washington in April 2022.

Marsel Mesulam, MD, delivered the Brenda Milner Lecture, titled “Behavioral Neurology of the Temporal Pole” at the 23rd Annual Neuropsychology Day on May 16 in Montreal, Canada.

Shadi Ghourchian, former postdoctoral fellow in the Flannagan Lab, had a platform presentation at the June 2022 American Association of Neuropathologists meeting in Bonita Springs, Florida.

Margaret Flanagan, MD, presented the invited “What Every Neuropathologist Needs to Know” Lecture at the June 2022 American Association of Neuropathologists meeting in Bonita Springs, Florida.

Mesulam delivered a talk titled “Exploring the Temporal Regions of the Human Brain” at Journées Internationales de la SFN (International SFN Days) in Paris, France on June 8, 2022.

Sandra Weintraub, PhD, co-presented “Multidimensional Aspects of Health in a Cognitive Aging Sample” at the International Neuropsychological Society 2022 meeting in Barcelona, Spain on July 8, 2022.

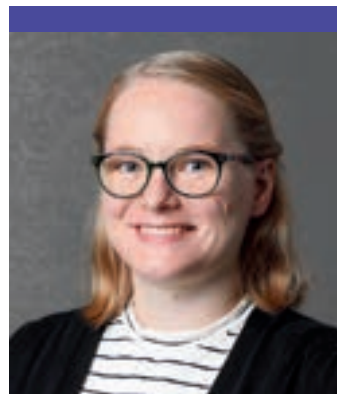
Multiple faculty and staff members from the Mesulam Center presented at the Alzheimer’s Association International Conference in San Diego, California in August 2022. Notably, Sandra Weintraub, PhD was a presenter on the “Dementia Nomenclature: We Can Do Better” panel and Robert Vassar, PhD, was on the “BACE Inhibition for the Prevention of AD: From Pre-Clinical Insights to Clinical Opportunities” panel.

Various members of the Mesulam Center will be presenting at the biennial congress of the International Society for Frontotemporal Dementias (ISFTD) in Paris, France in November 2022. Keep an eye on our website and social media for more information about their presentations.

Darby Morhardt, PhD, was an invited speaker at the NASW (National Association of Social Workers) National Conference in Washington, D.C. in June 2022. She co-presented a pre-conference symposium on “A Person-Centered Approach to Working with Individuals Living with Alzheimer’s Disease or Other Dementias.”

Morhardt was a panelist in the 2022 DIAD (Dominantly Inherited Alzheimer’s Disease) Family Conference in July 2022 in San Diego, California.

Postdoctoral Fellow Profile: Molly Mather, PhD



Molly Mather, PhD, applied for the Neuropsychology Postdoctoral Fellowship because it combined research and clinical work. She enjoyed both while pursuing her graduate degree in clinical psychology at the University of Massachusetts Amherst, where she studied early

neuropsychiatric symptoms in Alzheimer’s disease and how emotions change in older adulthood.

“The person-to-person connection and being able to hopefully help individual patients and families is the more emotionally meaningful piece of the work and has been for me, throughout my training,” Mather said. “And the research side of it is a bigger picture, longer term, trying to build understanding around how we can actually best help people.”

Mather received her undergraduate degree in psychology from Pomona College, graduating Cum Laude with Distinction in 2012. After college, she worked as a full-time clinical research assistant, where she learned how to administer cognitive tests. During graduate school, she completed a year-long practicum in neuropsychology in New York City. She also interned at the University of Chicago, primarily in outpatient and memory disorders neuropsychology rotations. “[It] was a great sort of happenstance that allowed me to stay in the Chicago community. There’s a really wonderful neuropsychology community here,” Mather said.

In the future, she would like to focus on early neuropsychiatric symptoms in Alzheimer’s disease and how they relate to neurodegenerative changes. Finding the underlying cause of these symptoms can lead to a better understanding of their management and treatment.

Mather has a personal connection to her research. Her father had Parkinson’s disease, so she knows firsthand how difficult it is for families to adjust to and cope with neurodegenerative diseases. She wishes her dad could have been seen clinically at an interdisciplinary place such as the Mesulam Center.

“I find it very amazing to be working in a place where we have behavioral neurologists and neuropsychologists and social workers all working together, and we’re able to offer those kinds of services to people, and a clear diagnostic process, and biomarker testing,” Mather said.

2022 Research Breakthroughs

BIOMARKER PREDICT COGNITIVE DECLINE IN ALZHEIMER'S DISEASE

According to a recent study published by lead author, Adam Martersteck, PhD, the buildup of tau protein in the brain predicts the amount of future cognitive decline over one year in individuals with Alzheimer's disease. The higher the level of the damaging form of tau in the brain, the worse a person's cognitive performance, the study showed. "These tau-based biomarkers may help predict the pace of progression of the disease. They may eventually help us treat AD before we see symptoms," said senior study author Emily Rogalski.

PRIMARY PROGRESSIVE APHASIA

There are five different diseases that attack the language areas in the left hemisphere of the brain that slowly cause progressive impairments of language known as primary progressive aphasia (PPA), a recent study by lead author Marsel Mesulam, MD, discovered. The study is based on the largest set of PPA autopsies — 118 cases — ever assembled. The patients had been followed for more than 25 years, so this is the most extensive study to date on life expectancy, type of language impairment and relationship of disease to details of language impairment. The underlying disease specifies the type of medical treatment or clinical trial that is appropriate whereas the symptoms determine the optimal non-pharmacologic interventions. "The trick is to approach PPA at both levels simultaneously," Mesulam said.

NOT ALL TAUOPATHIES ARE ALIKE

Changiz Geula, PhD, and colleagues investigated the response of basal forebrain cholinergic neurons to two diseases associated with abnormal tau, Alzheimer's and Corticobasal Degeneration. Both led to abnormal tau accumulation in the cholinergic neurons but only those in Alzheimer's destroyed the cholinergic fibers that supply the cerebral cortex. This study showed that different tauopathies have different effects on the function of the nerve cells they invade.

THE FRONTOTEMPORAL DISEASES OF TDP-43

One of the most important causes of dementia is associated with abnormalities in a protein known as TDP-43. A subtype is known as TDP-C and leads to severe impairments of word comprehension and social conduct. Alegra Kawles and colleagues in Tamar Gefen, PhD's laboratory investigated the distribution of abnormal TDP-43 in patients who died of this disease and had autopsies. One surprising finding was that the TDP-43 abnormalities were lighter in areas that had the most neural cell destruction. This study showed that in TDP-C the abnormal protein starts by destroying neurons but then is removed from the tissue as the disease progresses.

Read more about the latest research at
brain.northwestern.edu/about/news

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Follow us on your social media channels to have the latest updates on Alzheimer's disease and related dementia research at your fingertips. We also share the human stories of people behind the research, testimonials from our research participants, and invitations to our unique educational events and conferences. Check us out!

"We have to think about policies that will help people mitigate some of this stress to create an equitable society for everyone, so everyone can age in the same way."

M. MARSEL MESULAM, MD



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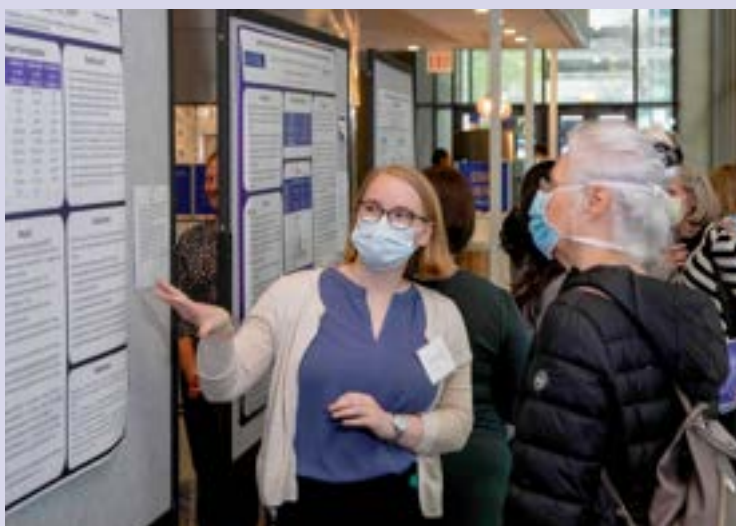
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