As spring began to emerge last month, we gathered in Detroit for our Beyond Amyloid Research Symposium. This event brings together the top minds from across the state to learn the latest advances in the field of dementia research.

This year’s event was hosted by Wayne State University and held in the heart of the Wayne State campus in Detroit. The day began with a welcome from Peter Lichtenberg, PhD, ABPP, Director of the Institute of Gerontology at Wayne State University, and Co-Lead of our center’s Research Education Component. Following his welcome, Director, Dr. Henry Paulson presented a brief update about the center.

We welcomed keynote presenters, Donna Wilcock, PhD, of Indiana University, who presented about the vascular contributions to dementia from the Diverse VCID study, and Sterling Johnson, PhD, of the University of Wisconsin who presented on the key findings from the Wisconsin Registry for Alzheimer’s Prevention. A third keynote presentation by Wassim Tarraf, PhD, of Wayne State University, discussed the disparities in Alzheimer’s disease and related dementias and their impact on healthcare outcomes. Engaging discussions followed each presentation showcasing the opportunity for future collaborations.

The day also shared the latest research advances from our most recent class of REC mentees. Key presentations included “Bugs, Blood, and Brains,” a presentation by Kelly DuBois, PhD, of Michigan State University, that shared about the bacteria in blood and its potential role in Alzheimer’s disease. Another highlight was a presentation from Xin Wang, PhD, of the University of Michigan, who presented about metals exposure and what it could mean for the long-term trajectory of thinking abilities.

The event was filled with networking from investigators across the three institutions, alongside Central Michigan University, through a vibrant poster session. Poster topics spanned from “Physical Activity Across the Life Course and Risk for Alzheimer’s Disease and Related Dementia” to “The Association of Dementia Caregiver Employment with Sleep Quality: Does Being a Spouse Matter?”, representing the breadth of dementia research and offering an opportunity for making connections between students, trainees, and experienced faculty.

The day closed with three awards for outstanding poster presentations given to Alexis Chargo of Wayne State University, who presented “Age-Sensitive Neural and Cognitive Correlates of Cognitive Mapping: Insights into Wayfinding Deficits,” Yi Chen of Michigan State University who presented “Resting-state functional MRI amplitude of low-frequency fluctuation in hypertensive Alzheimer’s disease rat models,” and Victor Di Rita of the University of Michigan who presented “Network-based HD-tDCS in Posterior Cortical Atrophy” and “Sensitivity of functional Near-Infrared Spectroscopy in Individuals with Posterior Cortical Atrophy.”
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Note from the Director

It has been 15 years since I became associated with the Michigan Alzheimer’s Disease Center (MADC) and about seven years since the MADC received designation from the National Institutes of Health as an Alzheimer’s Disease Research Center. Maybe, then, it’s time to take stock of where we are and where we are going.

When we submitted our NIH grant seven years ago, we aspired to be a statewide center that connected the three major universities in Michigan: The University of Michigan, Michigan State University and Wayne State University. We vowed to learn much more about the causes and treatment of cognitive impairment in people from historically marginalized groups because this has been a major deficiency in the field. We set a lofty goal of training the best and the brightest across our three universities to push for new discoveries and new treatments. And we chose to focus our efforts on a central theme: the “non-beta-amyloid” contributions to brain dysfunction and degeneration in Alzheimer’s and related dementias.

Well, how are we doing? I would say pretty darn well.

Our partnership between the three major Michigan universities has become a new paradigm that other centers across the nation are emulating. I’m so proud of the fact that we support trainees and cutting-edge research. One novel element is our Leaders Initiative which seeks to give leadership opportunities to younger scientists who we think could be next generation leaders. Check out information about our new Leaders Initiative Seminar Series on page 4.

And what about our “non-beta-amyloid” theme? Recall that Alzheimer’s has two pathological hallmarks: the amyloid plaques and the neurofibrillary tangles. While amyloid plaques are essential for the development of Alzheimer’s, we chose to focus on the many other factors that contribute to cognitive impairment, including other disease proteins such as tau, alpha-synuclein and TDP-43, as well as vascular, systemic, and environmental risk factors that underlie various types of dementia. It is exciting that anti-amyloid therapies are beginning to show promise — see for example, our update on the anti-amyloid drug lecanemab on the next page. But truly game-changing therapies are going to require a multi-targeted approach. And that’s what we’re after!

Henry Paulson, MD, PhD

What’s New in RESEARCH

An Update on Lecanemab

On January 6, the FDA granted accelerated approval to lecanemab (Leqembi) citing a biological effect on the beta-amyloid protein in individuals with mild symptoms of Alzheimer’s disease.

Lecanemab is an antibody that is directed at the beta-amyloid protein. It is delivered by an infusion (through a vein) every two weeks. By binding to amyloid, lecanemab allows the immune system to remove the brain beta-amyloid buildup.

This effect was seen in a study of 856 individuals with mild cognitive impairment or mild dementia due to Alzheimer’s disease. More than 300 of the participants had a specialized brain scan called a Positron Emission Tomography (PET) scan to monitor amyloid deposition. Scans were conducted before and after lecanemab treatment and showed that treatment led to removal of brain amyloid.

While the removal of amyloid plaque is important, what is most important is that the drug impacts the symptoms of Alzheimer’s disease.

In a recent study called A Study to Confirm Safety and Efficacy of Lecanemab in Participants With Early Alzheimer’s Disease (CLARITY AD), persons with mild symptoms of Alzheimer’s disease received biweekly infusions of either lecanemab or a placebo. Over time, both groups declined in their thinking and daily function, but the decline was less in the lecanemab group. At 18 months, the lecanemab group had symptoms similar to those of the placebo group at 12 months. This means that decline was slowed by about six months, though decline still took place.

There are side effects with lecanemab. In CLARITY AD, about one in four people had an “inflation-related reaction,” consisting of flu-like symptoms (such as fever, chills, body aches) with the initial infusion(s). Another side effect was amyloid-related imaging abnormalities (ARIA). There are two types of ARIA. One is swelling of the brain (ARIA-E), and the other is small spots of bleeding in or on the surface of the brain, and infrequently larger areas of bleeding (ARIA-H). Though most people do not experience symptoms with ARIA, some people may experience symptoms such as headache, confusion, dizziness, vision changes, nausea, weakness, speaking difficulty, or seizure. Brain Magnetic Resonance Imaging (MRI) scans are done before and during treatment to look for ARIA and to determine if treatment with lecanemab may need to be stopped temporarily or permanently.

There is a higher risk of side effects in some people. The ‘gene variant, apolipoprotein E4, increases the risk of ARIA. Without apoE4, the risk of ARIA-E is around 5%. The risk is around 11% if a person has one copy of the apoE4 gene and 33% with two copies. Understanding your genetic risk will be an important factor in determining if the potential benefits likely outweigh the potential side effects.

The anticipated cost of lecanemab is $26,500 per year, without including the costs of infusion, brain scans, examinations, and other monitoring. At the current time, Medicare does not cover lecanemab outside of a clinical trial.

Lecanemab is currently being reviewed by the University of Michigan to determine if it can be provided to appropriate patients. For more information, please visit our Q&A at michmed.org/mQByG.

Henry Paulson, MD, PhD

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Center Launches Leaders Initiative Seminar Series
Spotlighting Younger Investigators’ Research

During our latest grant cycle, we launched an innovative new initiative to foster the development of next-generation leaders in dementia research. This initiative comprises 11 younger investigators placed within our cores. They interact with core activities and executive committee activities to expose them to leadership opportunities within the center.

This year, Dr. Henry Paulson and Dr. Courtney Polenick launched the Leaders Initiative Seminar Series, highlighting the research of early-career faculty who are part of the Leaders Initiative. Members of the Leaders Initiative also invite guest speakers to present research topics related to dementia and caregiving. The goal of the series is to share key research findings and promote research collaborations across the country and the Alzheimer’s Disease Research Center network.

So far, we have gathered five lecturers, one of which was a Leaders Initiative faculty member, Sheria Robinson-Lane, PhD from the University of Michigan School of Nursing. Dr. Robinson-Lane presented, “Health, Coping, and Family Caregiving: Examining the Support Needs of Family Caregivers.” You can find a recording of her presentation available on our YouTube page at michmed.org/7NM2Y.

In the coming months, we will host presentations from Benjamin Combs, PhD, from Michigan State University, and Amanda Leggett, PhD, of Wayne State University.

Jonathan Reader Receives Research Service Award

On April 26, the U-M Office of Vice President for Research awarded Jonathan Reader, MS, Michigan Alzheimer’s Disease Center Data Core Manager, the 2023 Research Data Management and Analysis Staff Award. This annual award honors staff members for important contributions to the University’s research mission through exceptional performance by going beyond the ordinary fulfillment of position duties. The award was presented at a ceremony at the end of May.

Jonathan was given this award among 12 other recipients across various areas of the University, each focusing on a different area of research service. The awards were selected by Rebecca Cunningham, vice president for research.

Jonathan was nominated for the award by Data Core Leader, Kelly Bakulski, PhD, Bruno Giordani, PhD, Associate Director, and Arijit Bhaumik, BS, CCRP, Research Administrator.

“If it anybody at the University deserves the award, it is without a doubt Jonathan Reader. He has gone above and beyond to earn this honor. His work is always professional and beyond question,” said Bhaumik.

What We’re Learning from your Research Participation: The ELECTRA Study

At any given time, a variety of studies may co-enroll in our center’s University of Michigan Memory & Aging Project (UM-MAP) and contribute to the mission of the whole center. These studies offer opportunities for research participants to partake in multiple studies in one study visit. Many times, the measures taken from an UM-MAP visit are utilized to support the research of other studies.

This was the case with the Encephalographic Computerized Assessment Study (ELECTRA). Many of our participants may be familiar with the ELECTRA Study, which has enrolled African American participants in UM-MAP for many years. Ninety-five of ELECTRA’s participants co-enrolled in UM-MAP, and ten of UM-MAP’s participants also partook in ELECTRA. Although the study is still ongoing, several papers have been published based on the contributions of the participants in the study.

The ELECTRA Study investigated resting state EEG measures before and after participants engaged in a visual movement detection task in hopes of discovering if this technology could differentiate between patients with mild cognitive impairment and those with normal thinking.

Looking at two different EEG markers and varying EEG current densities, ELECTRA and collaborating UM-MAP researchers found that resting state EEG could successfully identify persons with MCI from those without (Pozar, et al., 2020; Kavic, et al., 2020; Martin, et al., 2022).

Most recently, the study compared resting EEG before and after the task had ended – their so-called Aftereffect Model.

“They found that this calculation successfully supported the study’s goal that studying brain activity may be possible in identifying differences between MCI and normal thinking (Pozar, et al., 2023). Their work continues and now links researchers at not only Wayne State University and the University of Michigan, but also colleagues at Michigan State University.”

Jonathan Reader

If you are interested in participating in another co-enrolling opportunity, please consider joining our Diverse VCID, Driving, ALLFTD, STIM, or SuperAging Research Initiative studies.
Finding Meaning with Frontotemporal Dementia

David Werton retired in 2010 and was pursuing his master’s degree in social work when he began forgetting lectures and having trouble with papers.

He saw a local neurologist who ordered an MRI and EEG. At the time, he learned he had frontal lobe atrophy, but his doctor wasn’t exactly sure what that would mean.

After many years, David and his wife, Karen, came to University of Michigan Health where they were ordered an MRI and received a diagnosis of frontotemporal dementia (FTD) from Dr. Henry Paulson.

FTD results from damage to neurons (neurodegeneration) in the frontal and temporal lobes.

Dr. Henry Paulson.

Frontotemporal Dementia (FTD) is a constellation of disorders that affect personality, language, and behavior. It is less common than Alzheimer’s disease, with onset at a median age of 50 years. It tends to occur in younger individuals—usually at age 45-65 years. This diagnosis helped draw connections between the many changes David had been experiencing for years, including visual changes and problems with processing information.

Over the years, David noticed many of the hallmarks of FTD. He became more emotional, sometimes crying uncontrollably. He became less empathetic and more apathetic. His wife described that he used to be laid back and would “go with the flow.” Over time, his “fute” shortened, and he became frustrated quickly, especially at the grocery store when it was busy. Already committed members of the U-M Memory and Aging Project since meeting Dr. Paulson in 2019, this new diagnosis sparked their interest in joining the ALLFTD study—one of the world’s largest ongoing investigations of FTD.

The Longitudinal Frontotemporal Lobar Degeneration Study (ALLFTD) collects comprehensive cognitive and behavior assessments, imaging, blood, and cerebrospinal fluid (CSF) to identify the best clinical measurements and biomarkers for following patients in future FTD treatment trials. The study also identifies clinical measurements and biomarkers that indicate when a person with a high risk of developing FTDL may be at a mutation to begin memory loss.

While the symptoms have certainly been challenging, David explains that now, since he is more aware of the disease, he works to control them. For example, he goes to the grocery store at less busy times.

David also has several hobbies to keep busy. He is an avid gardener, enjoys spending time with his family, and walking their two dogs, Diamond and Ella. Before the pandemic, David really enjoyed going out to eat and volunteering with Meals on Wheels and Angela Hospice. He encourages others who face a diagnosis to do the same.

“This disease can be overwhelming. You need hobbies so that you don’t feel depressed and wallow in self-pity.”

In addition to David’s committed participation in research, he also agreed to donate his brain to science in the future. “I want to be able to help others,” he shared.

Agreeing to participate in brain donation is never an easy decision, but we are grateful that David is willing to provide such a gift to further our understanding of FTD.

The ALLFTD Study is currently enrolling participants in the frontotemporal lobar degeneration spectrum. If you are interested in learning more, please visit allftd.org or contact Kiren Chaudhry at chaudhki@med.umich.edu.

Donor’s Gifts Expand Storage for Michigan Brain Bank

Phyllis was a woman with an incredible personality, her wife, Sara, remembers. She was the oldest of four sisters, meticulous with the finances and chatty. After growing up with a stutter, she committed to conquering it and pursued a successful career in sales.

She worked for Co/Op Optical in the Detroit area for many years, agreeing to assist a family friend’s business at the request of her father. Because of her success, she was recruited to a role that would take her to New York, where she met her wife, Sara Mayes. Sara was a customs broker and CEO of the Gemini Shippers Association. The two lived happily together for 25 years, eventually joining forces in Sara’s consulting business.

They traveled the world for work many times over the years. On their travels, Phyllis was described as finding connections and friends everywhere. Sara describes the time she befriended someone with a University of Michigan jacket while in an airport in Thailand.

As the years progressed, Sara noticed that Phyllis began to make little mistakes, even with the finances, when she was usually so meticulous. When they traveled, she also expressed concerns about the time—almost excessively—a new behavior that was not typical of her.

At New York—Presbyterian in 2014, Phyllis was diagnosed with probable Alzheimer’s disease. As the years went on, the disease grew more challenging. A woman who had once spoken so exuberantly eventually went a month without speaking. She lived with the disease for five years before passing on October 19, 2019.

Upon her passing, Sara established the Phyllis T. Glanz Fund for Research. She asked friends and family to make contributions in her memory. Sara gave generously at her wife’s passing and has continued her commitment to giving many times since.

This past fall, with funds from Sara reaching $50,000, we were able to purchase a new freezer for the Michigan Brain Bank. The Michigan Brain Bank holds the brain donations of hundreds of past research participants and patients who gave their brains to science, with the hopes that scientists at U-M and across the country could advance our knowledge of the disease.

Sara’s gift expands the storage capabilities of the Brain Bank to hold the tissue of over one hundred additional brain donors, expanding our footprint for years to come.

Would you or a family member be interested in brain donation?

Brain donation is one of the greatest gifts to further dementia research.

Brain autopsies are an important source of information about how disease affects the brain’s anatomy. This information is used to direct future research into the cause of memory loss, their progression over time, and clues about effective treatment approaches. What we know today has only been possible because of the commitment of patients and research participants who donate their brain to science.

When a patient or research participant passes away, our staff work alongside families to ensure autopsies are carried out thoroughly, and funeral arrangements are accommodated.

If you are interested in learning more, contact Matthew Perine, Michigan Brain Bank Coordinator, at 734-615-7868 or matthewperine@med.umich.edu.
We want your feedback!
We are considering making adjustments to our newsletter. Share your thoughts with us in a survey.

Save the Date for our Speaker Series!
Join us at the University of Michigan Detroit Center (3663 Woodward Ave, Detroit) for our upcoming Speaker Series presentations. Lunch is provided and registration is required. Please register by contacting Stephanie Nava at senava@med.umich.edu or 734-615-1755.

“New and Exciting Research at the Michigan ADRC”
Wednesday, July 26 at 10 a.m.
Join us to hear from three of our study teams - You’ll hear more about our new studies, have an opportunity to get your questions answered, and learn if you might qualify to join.

“The Latest in Alzheimer’s Research”
Wednesday, August 23 at 10 a.m.
Bruno Giordani, Ph.D., University of Michigan Department of Psychiatry will present the latest discoveries from the Alzheimer’s Association International Conference.

Are you interested in watching videos from our past Speaker Series events?
Find recordings at michmed.org/AY7m7

About Us
The Michigan Alzheimer’s Disease Center is dedicated to the discovery of new ways to diagnose, treat, and prevent Alzheimer’s disease and related dementias. We promote state-of-the-art clinical care, conduct memory and aging research, and provide education, support, and wellness programs.

Visit our website at alzheimers.med.umich.edu

Support
Gifts from generous donors are critical to support our work. If you are interested in giving, please contact Mike Harders at miharder@umich.edu or 734-763-1402.

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