

This issue features photos from our research studies – to the right, a grip test from the ARMADA study; on Page 3, a pre-PET scan blood pressure reading. (Photos by Clint Thayer/ UW Department of Medicine)



Wisconsin Alzheimer's
Disease Research Center

UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Headlines

FALL 2020

WELCOME

Betthausen joins Wisconsin ADRC as investigator

Tobey Betthausen, PhD, joined the Wisconsin ADRC as an investigator on September 1,



Betthausen

2020. This coincides with Betthausen's new appointment to assistant professor in the UW

Department of

Medicine Division of Geriatrics and Gerontology.

Betthausen's doctoral studies began in 2013 in UW-Madison's Department of Medical Physics. In 2018 he joined the Johnson Lab in the Wisconsin ADRC and was promoted to scientist in 2019.

In Betthausen's new position, he will continue his research as a leading figure investigating amyloid and tau biomarker imaging using PET radiotracers. Much of his work is based on the PET imaging scans study participants undergo as part of their Wisconsin ADRC Clinical Core visits. ♦

DIRECTOR'S MESSAGE

Research continues despite challenges and disruptions from COVID-19

Since March, we have all faced new challenges and disruptions in our lives. COVID-19 has made us focus on our health and the health of the people around us. We have learned this virus is especially deadly in older populations – in Wisconsin, as of November 11, 77% of COVID-19 deaths were in people 70 years of age or older. COVID-19 is burdening our Black, American Indian, and Hispanic and Latino citizens disproportionately. And the disease is especially concerning for people with dementia, disrupting their caregiver routines, increasing isolation, and compounding the symptoms of the disease.

While we understand the importance of physical distancing and avoiding large gatherings, it doesn't make it easier to stay home and miss out on connecting with people. We were saddened to cancel our annual gatherings – namely the appreciation events and the Fall Lecture. Our outreach team is working on new ways to say thanks and communicate important brain

health information to you. We will send updates on those initiatives in the new year, but in the meantime we took a special approach with this issue of the newsletter to offer information on recent studies that utilized data from our Clinical Core participants.

While so much has changed, one thing has stayed the same – the scientists and staff at the Wisconsin ADRC are still working on treatments and programs to lessen the burden of Alzheimer's disease on patients and their families. Researchers continue to examine the wealth of data collected from participants over the last 11 years, and we developed new ways to collect study data over the phone and in shorter in-person visits. Thank you to our many participants who traveled to University Hospital in recent months for in-person visits and those who completed study visits over the phone.

On behalf of the Wisconsin ADRC, I want to say we appreciate you, we miss you, and we hope to see you soon. ♦



Sanjay Asthana, MD
Associate Dean for Gerontology
Director, Wisconsin ADRC & Madison VA GRECC
Professor, UW School of Medicine and Public Health

RESEARCH HIGHLIGHTS

NEWS BRIEFS

The National Institute on Aging awarded **Cynthia Carlsson, MD, MS,**



Carlsson

funding to support recruitment and engagement of Veterans for Alzheimer's disease and related demen-

tias studies. Veterans carry an increased risk for developing dementia. This grant will help Dr. Carlsson's team establish new partnerships with Veterans groups and brain health educational programs for Veterans.

The UW School of Medicine and Public Health was one of four universities with Alzheimer's Dis-



Shah

ease Research Centers that received a grant from the National Institute on Aging to conduct research that could lead

to improved care in emergency departments for people with dementia. **Manish Shah, MD, MPH,** professor of emergency medicine and Wisconsin ADRC researcher, is co-principal investigator for the national project.

The Alzheimer's Association awarded **Gilda Ennis, PhD,** assistant scientist in the Bendlin



Ennis

lab, a grant to study insulin resistance and its relationship to Alzheimer's disease and the degeneration of nerve cells.

The following studies used data collected from Wisconsin ADRC Clinical Core participants. You can read more about these studies on [PubMed.gov](https://pubmed.ncbi.nlm.nih.gov/) – just enter the Pub Med ID into the search bar.

Study finds where you live may impact the brain

A study from the Bendlin and Kind labs found that neighborhood disadvantage may negatively impact the brain in middle to older age. Neighborhood disadvantage is a fundamental social determinant of health that directly reflects the income, employment, education, and housing quality in a precise geographic area.

Study author Jack Hunt, PhD, a student in the Medical Scientist Training Program at the UW School of Medicine and Public Health, examined hippocampal (the center of the brain's emotional and memory system) and total brain volumes of 951 cognitively normal individuals. Results showed that study participants from the most highly disadvantaged neighborhoods had smaller hippocampal areas (4% lower) compared to participants in more advantaged neighborhoods. According to the study, that 4% is the equivalent of 4 to 7 extra years of brain aging.

PubMed ID: 31904767

KLOTHO gene variant found to be potential protective factor against Alzheimer's disease

Research has focused on the relationship between various genes and Alzheimer's disease. A study from the Okonkwo lab looked at a gene that is believed to confer protection against Alzheimer's disease. Claire Erickson, MPA, a graduate student in the Wisconsin ADRC, was lead author on this study, which found that research participants carrying the KL-VS variant of the *KLOTHO* gene had less amyloid buildup in their brains compared to study participants who did not have the KL-VS variant. *KLOTHO* is a well-known anti-aging gene and, in other

studies, the KL-VS variant has been associated with better brain health and increased neural functioning.

Erickson's study looked at how the *KLOTHO* KL-VS variant impacted APOE4 carriers specifically. While age is the greatest risk factor for late-onset Alzheimer's disease, the presence of at least one copy of the APOE4 allele is the second largest risk factor and is associated with brain accumulation of the protein beta-amyloid. The study found that APOE4 carriers who also had the KL-VS gene variant had less amyloid buildup in their brains than APOE4 carriers who did not carry the KL-VS gene variant. This research suggests that the *KLOTHO* KL-VS variant lessens the effect of APOE4 on amyloid burden in people who are at risk for Alzheimer's disease.

PubMed ID: 30867273

REACH trial shows regular aerobic exercise may decrease likelihood of developing Alzheimer's disease

The Aerobic Exercise and Cognitive Health (REACH) trial showed that a lifestyle behavior – regular aerobic exercise – can enhance brain and cognitive functions that are particularly sensitive to Alzheimer's disease, said study author Max Gaitán, MEd, a member of the Okonkwo lab.

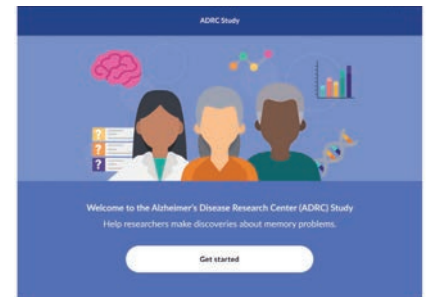
The study investigated 23 cognitively normal, relatively young older adults with a family history or genetic risk for Alzheimer's disease. They underwent measurements of cardiorespiratory fitness, daily physical activity, brain glucose metabolism imaging (to assess neuronal health), and cognitive function. Half of the participants were randomly assigned to receive information about maintaining an active lifestyle but no further intervention. The other half participated in a moderate-to-vig-



NEWS

Center developing electronic consent

Informed consent is critical to performing ethical research. It offers a written explanation of a study's purpose, benefits, risks, and procedures, as well as formal documentation confirming a participant's decision to enroll in the study. But the process is long — 20 pages long in the Wisconsin ADRC Clinical Core — and oftentimes participants find the forms too complicated.



In order to improve the process, a team of researchers from Sage Bionetworks and the Wisconsin and Emory ADRCs are developing an electronic consent process, or eConsent. They hope an interactive eConsent will boost engagement, enhance trust, and improve understanding of the content in the forms. Participants will be able to complete eConsent on a tablet or computer at home or during a study visit. A study coordinator will be available for people who prefer an in-person consent.

A final eConsent process is still a few years away. When it is complete, the team hopes to launch it in ADRCs across the U.S. ◊

orous intensity treadmill training program with a personal trainer, three times per week for 26 weeks.

Compared to the participants maintaining their usual level of physical activity, individuals assigned to the exercise training program improved their cardiorespiratory fitness, spent less time sedentary after the training program ended, and performed better on cognitive tests of executive function, which is responsible for attention and planning. Improved cardiorespiratory fitness was linked to enhanced executive function and to brain glucose metabolism in a brain region known to decline early in the progression to Alzheimer's disease.

PubMed ID: 32587945

Researchers examine relationship between cardiovascular risk factors and brain health among whites and African Americans

Lindsay Clark, PhD, and Heather Johnson, MD, MS, are investigating midlife cardiovascular risk factors, such as tobacco use, insulin resistance, hypertension, and obesity, to determine whether they increase the risk of Alzheimer's disease by altering blood flow to the brain. Their team is also assessing whether these relationships vary across race, specifically between African Americans and whites — African Americans have a higher prevalence of vascular risk factors compared to whites as well as a higher incidence of Alzheimer's disease. Their research aims to improve the treatment and prevention of Alzheimer's disease by identifying unique risk factors or disease mechanisms across races. Clark and Johnson recently published two articles that examined two facets of cerebrovascular health

using MRI: arterial blood flow through larger blood vessels to the brain and cerebral perfusion, which is how blood is filtered into brain tissue.

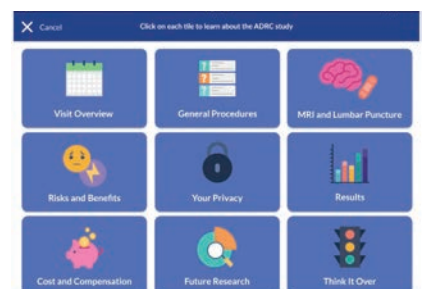
In the first paper, the research team found that increased blood glucose (sugar) negatively impacted blood flow to the brain, and that African American participants overall had decreased blood flow to the brain compared to white participants. Paired with previous research results that tied brain blood flow to memory function, these results suggest that elevated blood glucose may be a modifiable risk factor for the development of dementia.

In the second paper, Clark and Johnson's team found that higher diastolic blood pressure (the lower number in a pressure reading) was significantly associated with lower perfusion within brain tissues. And while this association did not vary by racial group, African American participants exhibited lower perfusion rates than white participants. Perfusion is an important marker for brain health because the process is how key nutrients and hormones are delivered to vital brain regions. If perfusion rates fall, less nutrients are delivered to the brain, which can cause cell loss and brain shrinkage.

Clark says there is more to be done in studying mechanisms for increased dementia risk in white and African American populations. More studies are planned that evaluate cognitive function as it relates to brain blood flow, and future studies could also look at whether reduced blood flow in the brain contributes to amyloid deposits, an early hallmark brain change of Alzheimer's disease.

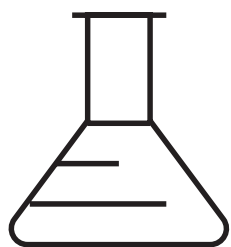
PubMed ID: 31658057

PubMed ID: 32310160



Wisconsin ADRC By the Numbers

The Wisconsin Alzheimer's Disease Research Center (ADRC) studies the causes, diagnosis, treatment, and prevention of Alzheimer's disease, as well as related topics such as caregiver stress and patient care. The following is a summary of our accomplishments since the center was formally established in April 2009 through March 31, 2020.



33
SCIENTISTS



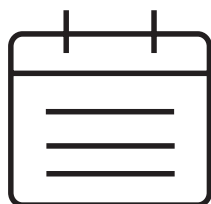
981

participants in
Clinical Core

25%

from underrepresented
groups (URGs)

266
community
outreach and
educational
events in 2019



77%
overall
Clinical Core
retention rate



66
podcast episodes of
Dementia Matters

104,380
episode downloads

13% international
listenership from
88 countries



61
**RESEARCH
PAPERS
PUBLISHED**
last year



789
participants received
Magnetic Resonance Imaging
(MRI) scans

543
participants received
Lumbar Punctures (LPs)

519
participants received
combined MRI and LP

80
participants received
biomarker Positron Emission
Tomography (PET) exams



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Stay Connected!

600 Highland Avenue, MC 2420
Madison, Wisconsin 53792
(608) 265-0407 | www.adrc.wisc.edu

