INSIDE:

10 Myths About Aging
Balancing COVID-19, Career, and Children
History of the Adult Children Study and the “ACS Originals”
Blood Test Identifies Alzheimer Disease Before Symptoms
HORIZONS is the newsletter of the Charles F. and Joanne Knight Alzheimer Disease Research Center (Knight ADRC) - a research program in the Department of Neurology, Washington University School of Medicine, funded by grants from the National Institute on Aging and private donations. The Knight ADRC supports and promotes interdisciplinary research on Alzheimer disease. The Memory and Aging Project (MAP) - the clinical research office of the Knight ADRC - provides expert clinical assessments of cognitive functioning in normal aging and dementia. Knight ADRC leadership:

John C. Morris, MD - Director, Knight ADRC; Director, MAP; Administration and Clinical Core Leader
Krista L. Moulder, PhD - Knight ADRC Executive Director
David Holtzman, MD - Knight ADRC Associate Director
Randall Bateman, MD - Knight ADRC Associate Director
Carlos Cruchaga, PhD - Knight ADRC Associate Director; Genetics and High Throughput-Omics Core Co-Leader
Joyce Balls-Berry, PhD - Health Disparities and Equity Core Leader
Tammie Benzinger, MD, PhD - Neuroimaging Core Leader
Andrea Denny, JD, MSSW - Outreach, Recruitment, and Engagement Core Leader
Anne Fagan, PhD - Fluid Biomarker Core Leader
Oscar Harari, PhD - Genetics and High Throughput-Omics Core Co-Leader
Celeste Karch, PhD - Biomarker Core Leader
Richard Perrin, MD, PhD - Neuropathology Core Co-Leader
Susan Stark, PhD, OTR/L - Research Education Component Co-Leader
B. Joy Snider, MD, PhD - Research Education Component Co-Leader; Director, Knight ADRC Clinical Trials Unit
Chengjie Xiong, PhD - Data Management and Biostatistics Core Leader

IN THIS ISSUE

3 Letter from the Director
4 COVID-19, Career, and Children: How One Exceptional Professional Maintains Balance
6 10 Myths About Aging
8 One-on-One with Sushi Sathyan
9 Grant Renewal – By the Numbers
10 Knight Alzheimer Disease Clinical Trials Unit Experiences Growth and Change
11 An Inside Peek at a St. Louis Native: Dr. Joyce Balls-Berry
12 Honors, Awards, and Funding
14 Who Participates in MAP Research?
15 Behind the Acronyms
16 Older People with Early, Asymptomatic Alzheimer Disease at Risk of Falls
17 Resource Center
18 Clinician’s Corner
20 A Special Cohort: History of the Adult Children Study and the “ACS Originals”
21 Welcome New Psychometricians to the MAP Team
22 Blood Test is Highly Accurate at Identifying Alzheimer Disease Before Symptoms
23 Aim High: Striving for 100%
Dear Memory and Aging Project Participants, Family Members, Faculty, Staff, and Friends

Although the COVID-19 pandemic has changed all of our lives in ways none of us could have imagined just a few months ago, some important precepts remain firm:

1. The Knight Alzheimer Disease Research Center (ADRC) and its Memory and Aging Project (MAP) remain firmly focused on our essential mission: to defeat Alzheimer disease.

2. We need our participants to accomplish our goal, as it is YOU who provide us with the data, images, fluid and tissue biospecimens, and support that are the absolute foundation of all that we do.

3. Even with the pandemic, our research efforts proceed and we very much want you, our partners, to be aware of all that is going on. Hence, we are pleased to share this Winter 2020-21 newsletter with you so that you can remain informed of our progress.

All of us at MAP and the Knight ADRC look forward to a future when at least some semblance of personal interactions can safely resume. Until that day, however, we continue virtual contact via mailings, telephone, video-conferencing, or other means. You are always welcome to call us at 314-286-2683 and leave any messages (our staff monitor the voice mail daily) or at our website (knightadrc.wustl.edu) where, under the “Contact” heading, you can access the Feedback Form.

We hope that you enjoy this newsletter, and most of all we hope that you and yours remain safe and well.

With best wishes,

John C. Morris, MD
Friedman Distinguished Professor of Neurology and Director, Knight Alzheimer Disease Research Center, Washington University

We Miss You

Did you catch the Memory and Aging Project faculty and staff sharing their greetings during our recent shelter-in-place video? If you haven’t, check it out online at:

https://knightadrc.wustl.edu/WeMissYou/
COVID-19, Career, and Children: How One Exceptional Professional Maintains Balance

Starting first as a medical student, then a graduate student, then a neurology resident, then the Knight ADRC Postdoctoral Fellow, and now as a faculty member, Suzanne Schindler has experienced many professional transitions during her time at Washington University. Simultaneously, she is among the ranks of working women who are balancing professional and personal lives—and during a pandemic, no less. Read on to see how Dr. Schindler balances her family life and an impressively growing career.

Suzanne Schindler started doing research on Alzheimer disease during college and graduate school over 20 years ago, including research projects with MAP samples and data. She began doing MAP and Memory Diagnostic Center (MDC) assessments during her Knight ADRC Postdoctoral Fellowship in 2012. In describing her path to a research career, she says, “I wanted to do research on Alzheimer disease since high school when I witnessed the devastation it can cause. Developing an independent research program is very difficult. One major obstacle is funding—you can’t do research without funding. My first research grant was relatively small and came at the end of my fellowship, which was a critical time when I had just moved from basic science (involving cells and mice) to clinical (involving people) research. This initial small research grant and the data it generated helped my application for a larger career development grant, which then helped me get the additional training I needed to do clinical research. I took classes in statistics and my mentors gave me opportunities and time to do research, write papers, and develop as a physician scientist. Earlier this year, I submitted my first large ($4.4 million) grant and it was favorably reviewed. If it is funded, this will mark the start of my independent research career. I’m excited that my many years of work are coming to fruition, and that this work may really help patients with Alzheimer disease.”

One of Dr. Schindler’s research goals is to predict if and when cognitively normal individuals will develop AD dementia. The field has developed very good tests for AD brain pathology, including cerebrospinal fluid testing and amyloid PET scans. In the last three years, several excellent blood-based tests have also been developed. However, the connection between AD brain pathology and dementia symptoms has been difficult to construct. Dr. Schindler’s proposed research will use a combination of blood-based tests to predict both brain pathology and dementia symptoms. A blood test that can predict if and when cognitively normal individuals will develop Alzheimer disease dementia would be extremely helpful in finding drugs that can slow or prevent the onset of dementia symptoms. Hopefully, one day doctors will treat Alzheimer disease like high blood pressure, high cholesterol or diabetes, where early treatment slows or even prevents the major health consequences of the disease.

In addition to her cutting-edge work in research, Dr. Schindler strives to maintain a healthy work-life balance. “I have two sons who are both wonderful: a two-year-old who loves animals and music and a four-year-old who is intensely curious and enjoys building things. They get along most of the time!” Schindler says. In order to maintain balance, Dr. Schindler relies on routine and her supportive spouse. She says, “there are certain hours
that are important to the smooth operation of our family routine, and I try very hard to keep these as family time. I am grateful that my husband is supportive, and we trade off caring for them frequently so that one person doesn’t get too worn out.”

The COVID-19 pandemic has presented unique challenges to the family schedule. “My husband and I work full-time and are very fortunate that we have been able to mostly work from home. During the initial lock-down in the spring, schools and daycares were closed and we cared for our sons by ourselves. I prepared nearly all the meals and learned barbering skills on YouTube. We tried hard to keep the kids stimulated with toys and books, and our couch became a trampoline and slide. It was wonderful to spend so much time with the boys, but it was also exhausting trying to care for them and work—neither my husband nor I were getting enough work time or sleep.”

Dr. Schindler echoes what many other working parents have felt, “it is a difficult time for everyone—kids, parents, and teachers—and we are all trying our best to get through it.” When it comes to managing her time, she says “I have become more organized and efficient. I identify my key goals for the day and work until they are completed. Still, many tasks have taken longer because of competing demands—I have fewer hours in a day that I can work. I often end up working late into the night.”

Dr. Schindler reminds us that the COVID-19 pandemic is probably the greatest public health crisis of our generation, but Alzheimer disease remains a major public health threat. “In recent years we have made tremendous progress in AD research, with major developments that are likely to lead us to effective therapies. We must try to keep our momentum going, despite the challenges presented by the COVID-19 pandemic. This hope is important in sustaining us now.”

Suzanne Schindler enjoys the fall weather with her husband and two young sons. — Dr. Suzanne Schindler
Many people make assumptions about aging, what it is like to grow “old,” and how older age will affect them. But as you age, it is important to understand the positive aspects of aging. Research has shown that you can help preserve your health and mobility by adopting or continuing healthy habits and lifestyle choices. Read on to learn about 10 common misconceptions related to aging and older adults.

1 **Depression and loneliness are normal in older adults.**

As people age, some may find themselves feeling isolated and alone. This can lead to feelings of depression, anxiety, and sadness. However, these feelings are not a normal part of aging as growing older can have many emotional benefits, such as long-lasting relationships with friends and family and a lifetime of memories to share with loved ones. It’s important to remember that older adults with depression may have less obvious symptoms or be less likely to discuss their feelings. Depression is a common and potentially serious mood disorder, but there are treatments that are effective for most people.

2 **The older I get, the less sleep I need.**

A common misconception is that a person’s sleep needs decline with age. Older adults need the same amount of sleep as all adults—7 to 9 hours each night. Getting enough sleep keeps you healthy and alert. Adequate sleep can also help reduce your risk of falls, improve your overall mental well-being, and have many other benefits.

3 **Older adults can’t learn new things.**

Older adults still have the ability to learn new things, create new memories, and improve their performance in a variety of skills. While aging does often come with changes in thinking, many cognitive changes are positive, such as having more knowledge and insight from a lifetime of experiences. Trying and learning new skills, such as playing an instrument or learning to knit may even improve cognitive abilities. Seeking out new social connections with others and engaging in social activities, such as a dance class or book club, can keep your brain active and may also boost your cognitive health.
It is inevitable that older people will get dementia.

Dementia is not a normal part of aging. Although the risk of dementia grows as people get older, it is not inevitable, and many people live into their 90s and beyond without the significant declines in thinking and behavior that characterize dementia. Occasionally forgetting an appointment or losing your keys are typical signs of mild forgetfulness, which is very common in normal aging. Nevertheless, you should talk with a doctor if you have serious concerns about your memory and thinking or notice changes in your behavior and personality. These problems can have a range of different causes, some of which are treatable or reversible. Finding the cause is important for determining best next steps.

Older adults should take it easy and avoid exercise, so they don’t get injured.

Studies show that you have a lot more to gain by being active—and a lot to lose by sitting too much. Often, inactivity is more to blame than age when older people lose the ability to do things on their own. Almost anyone, at any age and with most health conditions, can participate in some type of physical activity. Exercise and physical activity are not only great for your mental and physical health but can help keep you independent as you age.

If a family member has Alzheimer disease, I will have it, too.

A person’s chance of having Alzheimer disease may be higher if he or she has a family history of dementia because there are some genes that we know increase risk. However, having a parent with Alzheimer disease does not necessarily mean that someone will develop the disease. Learn about your family health history and talk with your doctor about your concerns. Environmental and lifestyle factors, such as exercise, diet, exposure to pollutants, and smoking also may affect a person’s risk for Alzheimer disease. While you cannot control the genes you inherited, you can take steps to stay healthy as you age, such as getting regular exercise, controlling high blood pressure, and not smoking.

Now that I am older, I will have to give up driving.

Natural changes can occur with age that may affect a person’s ability to drive, like having slower response speed, diminished vision or hearing, and reduced strength or mobility. The question of when it is time to limit or stop driving should not be about age, rather, it should be about one’s ability to drive safely. These questions may help you determine if you or a loved one needs to limit or stop driving. Talk with your doctor if you have any concerns about your health and driving.

Only women need to worry about osteoporosis.

While men may not be as likely to have osteoporosis because they start with more bone density than women, one in five men over the age of 50 will have an osteoporosis-related fracture. By age 65 or 70, men and women lose bone mass at the same rate. Many of the things that put men at risk are the same as those for women, including family history, not enough calcium or vitamin D, and too little exercise. Low levels of testosterone, too much alcohol, taking certain drugs, and smoking are other risk factors.

I’m “too old” to quit smoking.

It doesn’t matter how old you are or how long you have been smoking; quitting at any time improves your health. Smokers who quit have fewer illnesses such as colds and the flu, lower rates of bronchitis and pneumonia, and an overall better feeling of well-being. Quitting smoking will also lower your risk of cancer, heart attack, stroke, and lung disease. Quitting will also reduce secondhand smoke exposure to other family members or caregivers in the home. It is never too late to reap the benefits of quitting smoking and setting a healthy example for your children and grandchildren.

My blood pressure has lowered or returned to normal, so I can stop taking my medication.

High blood pressure is a very common problem for older adults—especially those in their 80s and 90s—and can lead to serious health problems if not treated properly. If you take high blood pressure medicine and your blood pressure goes down, it means the medicine and any lifestyle changes you have made are working. However, it is very important to continue your treatment and activities long-term. If you stop taking your medicine, your blood pressure could rise again, increasing your risk for health problems like stroke and kidney disease. Talk with your doctor about possibilities for safely changing or stopping your medication.

This content is provided by the National Institute on Aging (NIA), part of the National Institutes of Health. NIA scientists and other experts review this content to ensure that it is accurate, authoritative, and up to date.
Any Memory and Aging Project volunteer who has participated in the Cerebrospinal Fluid (CSF) collection undoubtedly met Sushi Sathyan and experienced her warm demeanor and genuine care. Read on to learn a little more about one of the most beloved members of the MAP family.

Tell us a little about your education and career leading up to your time with the Memory and Aging Project.

Right after completing my undergraduate degree, I moved to the United States from India to pursue my Master’s in Clinical Psychology and Counseling. I worked in the substance abuse field for six years and made a switch to research to be able to spend more time with my two sons. I am passionate about working with people, and after 25 years with the Wash U. community, this has become my second home.

What are some of the most rewarding parts of your job?

I love meeting our participants and working with them. I get to know and develop a rapport with them over the course of scheduling Lumbar Punctures (LP) to the completion and follow-up. I see myself as the ‘liaison’ between the participants, study team and the leadership. I try to make sure all aspects of LP goes smoothly. After weeks or months of coordination, when everything goes smoothly with the LP, that is the most rewarding part of my job. Just spending time with them, getting to know them and gaining their trust is the best feeling.

What are some of the challenges of your position?

I do not consider any situation as a challenge. Each situation is a stepping-stone and a learning experience. Any role, whether in personal or professional setting will have challenges. I strongly believe it is the attitude in which we approach each situation that matters.

What do you enjoy doing in your free time?

I love to read, work out, do yoga, go for walks, spend time with family and play with my son’s dog Louie. I love watching sports on TV and going to sporting events. I strongly believe in and am passionate about giving back to the community. Providing hot meals once a week to homeless shelters, volunteering at Mother Theresa's soup kitchen, going to senior homes once a month, making handmade cards for seniors in nursing homes and hospitalized kids are some of the activities I enjoy doing on a regular basis.

Do you have any last thoughts you would like to share with research participants?

I would like to let them know that we are truly grateful for their participation in this important study and their contribution to research is invaluable for helping us get closer to finding a cure in the future. I admire our participants for their caring hearts, for giving generously their time and effort, and above all for trusting us. I am honored and humbled to play a small role!
Every five years, the Knight ADRC must re-apply to the National Institutes of Health for grant money to fund each of the four main research projects at the Knight ADRC. Those projects are ADRC, Healthy Aging and Senile Dementia (HASD), The Adult Children Study (ACS), and The Dominantly Inherited Alzheimer Network (DIAN).

But what exactly goes into submitting a grant renewal application? In the case of the 2020 ACS renewal, submitted in May to the National Institute on Aging (part of the National Institutes of Health), here are a few details:

Indeed, since Dr. Morris submitted the renewal application of the HASD grant for the first time as Principal Investigator, ALL of the grants under his leadership (ADRC, HASD, ACS, and DIAN) have been awarded and renewed every time!

Special mention and appreciation goes to Krista Moulder, PhD. As Executive Director of the Knight ADRC, her master grantsmanship skills managed all aspects of the grant requirements, key stakeholders at Washington University School of Medicine and the National Institutes on Aging, endless details of the budget, and all the while keeping a large team of contributors on deadline.
Alzheimer disease research continues to expand and innovate through the Knight Alzheimer Disease Research Center Clinical Trials Unit (CTU). The trials unit recruits participants for and implements drug trials of interest to AD research. While the group was originally housed in the Knight ADRC main building at 4488 Forest Park Avenue, they relocated to a newly renovated space just east of the ADRC building on Taylor Avenue in October. While we will miss seeing them in the 4488 Forest Park building, it is incredible to see the group expand their research and work on AD treatments.

B. Joy Snider, MD, PhD, CTU Director and Krista Moulder, PhD, Knight ADRC Executive Director, visit the new space during the renovation.

Front row, left to right: Sonia Simmons, B. Joy Snider, MD, PhD, and Tamara Donahue. Middle row: Jennifer Fisher-Eastep, Becky Fierberg, Bridget Blues, Marta Santos and Wendy Sigurdson. Back row: Amy Evans, Becky Cusanelli, Stacy Schrader and Nicole Elmore.
Joyce Balls-Berry, PhD, MPE, is an Associate Professor of Neurology and the inaugural leader of the new Health Disparities and Equity Core in the Knight ADRC. She is a psychiatric epidemiologist and health educator with primary research focuses on applying community and patient engaged research principles in diverse populations to reduce health disparities and increase health equity.

Much of Dr. Balls-Berry’s research centers on determining ways to increase diversity and inclusion in clinical and translational science. She grew up in St. Louis, Missouri in the Central West End and was in the last graduating classes for St. Francis Xavier and Health Careers High School. She went on to complete her Bachelor’s degree at Xavier University of Louisiana with graduate training at Washington University School of Medicine and The University of Toledo. She completed a post-doctoral research fellowship in health equity, epidemiology, and biostatistics at The University of Florida. “It is wonderful being back home and continuing my career at my alma mater, Washington University,” she says. “My husband Bernard is learning to love St. Louis and my mom is delighted that we are here.”

When asked about her outside interests, Dr. Balls-Berry shares, “I absolutely LOVE to cook. There is a level of joy that happens when I am in the kitchen creating new recipes and having my family and friends give feedback plus share a meal. When I prepare something new, I always end the meal with ‘make it again?’ If I receive a thumbs up then I know it is a go” she said. Additionally, “I’m a huge Prince fan and actually met him on my 24th birthday. A month after Prince passed I gave a TEDx talk, and the sound board was the last sound board he used at Paisley Park.”

Dr. Balls-Berry looks forward to inspiring diversity, inclusion, and belonging in research through her role at the Knight ADRC. It is a hope grounded in her desire to find preventions and a cure for AD. She wants everyone to know that, as an extrovert at heart, her door is always open to chat.

“It is wonderful being back home and continuing my career at my alma mater, Washington University. My husband Bernard is learning to love St. Louis and my mom is delighted that we are here.”

— Dr. Joyce Balls-Berry
Honors and Awards, and Funding

Randall Bateman, MD, has been elected as a member of the National Academy of Medicine (NAM) for discovering the causes of AD, the first highly specific blood test for AD, and initiating the first prevention trial in AD with a public-private clinical trial platform. Membership in the organization is extended to those who have demonstrated outstanding professional achievement and commitment to service and is considered one of the highest honors in the fields of health and medicine in the United States. Dr. Bateman joins David Holtzman, MD, and new member Consuelo Wilkins, MD, (currently at Vanderbilt University Medical Center) as previous Memory and Aging Project clinicians who were selected for membership in the prestigious National Academy of Medicine.

Lubov Ezerskiy, BA, and Jorge Llibre-Guerra, MD were co-recipients of the 2019 Richard & Mildred Polesky Education Award, which supports the career development of promising students or fellows working towards a research, clinical and/or other service career focusing on aging and dementia.

Sarah Hartz, MD, PhD, received the 2020 Alene & Meyer Kopolow Award, which recognizes stellar contributions to the care of older adults by a resident, post-residency fellow, or junior faculty member in neurology, psychiatry, medicine, or related disciplines through direct patient care, education, or research.

Laura Ibáñez, PhD, received a $281,370 grant from the Alzheimer’s Drug Discovery Foundation to study gene products associated with Alzheimer disease that can be found in the blood. The project will use next-generation sequencing to measure gene products known as cell-free ribonucleic acids (cfRNAs) in the blood of Alzheimer patients, pre-symptomatic patients, and cognitively normal individuals to create novel prognostic and diagnostic models of Alzheimer disease risk and age at onset. A coalition of philanthropists, including Bill Gates, Jeff Bezos and Leonard A. Lauder, created the Alzheimer’s Drug Discovery Foundation in 2018. They have committed to funding nearly $50 million in research to improve Alzheimer disease treatments.

Collins Lewis, MD, African American Advisory Board member, was selected by the Global Alzheimer’s Platform Foundation as the 2020 Citizen Scientist Cornerstone Award Honoree. The award celebrates those who participate in Alzheimer disease clinical trials to positively impact the future prevention, diagnosis and treatment of AD.

John C. Morris, MD, has been recognized for his prolific contributions to the body of AD research literature as one of Clarivate’s Highly Cited Researchers, which identifies researchers who produced multiple papers ranking in the top 1% by citations for their chosen field, demonstrating significant influence among his peers. He was also recognized by ExpertScape as among the top 0.1% of scholars writing about Alzheimer disease over the past 10 years, a level labeled as “World Expert.”

Chihiro Sato, PhD received the 2020 Laura S. and John A. Blumenfeld Award, which recognizes a highly promising early-stage investigator at Washington University in St. Louis who is pursuing an academic career that focuses on Alzheimer disease and related dementia.

Congratulations to the following investigators who were selected to receive Knight ADRC Developmental Awards beginning in 2020. This grant program encourages investigators new to Alzheimer disease to initiate research in dementia and aging. Developmental Projects are funded for one year at an anticipated maximum of $100,000 direct costs, and a second year of funding may be awarded pending receipt of an approved progress report near the end of Year One. The funded projects and investigators are:

“CSF Tau Phosphorylation Changes Over the Course of Late Onset Alzheimer Disease”; Nico Barthelemy, PhD
“Haploinsufficiency of Lysosomal Enzymes and Alzheimer Disease”; Mark Sands, PhD
“Adaptive Immune Responses in Alzheimer Disease”; Naresha Saligrama, PhD
Congratulations to the following Knight ADRC-investigators and collaborators who received National Institutes of Health Research Project Grant Program (R01) Awards. An R01 award is considered a mature award that gives newly established investigators four or five years of independent funding to complete a project, publish results, and start writing his/her next grant application in time to get an award before the funding ends.

- Returning Research Results that Indicate Risk of Alzheimer Disease to Healthy Participants in Longitudinal Studies, Sarah Hartz, MD, PhD and Jessica Mozersky, PhD
- Defining the Mechanisms by which MS4A Genes Regulate TREM2 in Alzheimer Disease, Celeste Karch, PhD
- Sleep and Circadian Rhythms in Alzheimer Disease: Potential Bi-directional Relationship with Tau, Erik Musiek, MD, PhD
- Cross-sectional and Longitudinal Racial Disparity in Molecular Biomarkers of Alzheimer Disease, Chengjie Xiong, PhD
- The Impact of Depression and Preclinical Alzheimer Disease on Driving Among Older Adults, Ganesh M. Babulal, PhD, OTD
- Naturalistic Driving as a Functional Neurobehavioral Marker of Preclinical and Symptomatic Alzheimer Disease, Catherine Roe, PhD and Ganesh M. Babulal, PhD, OTD

Congratulations to the following Knight ADRC senior postdoctoral fellows and faculty-level candidates who received a National Institute on Aging Career Development Award (called a K Award). K awards are early-career grants designed to bring investigators to the point where they can conduct their research independently and are competitive for major grant support. Recent awardees include:

- Identification and Characterization of Common Pathways Across Alzheimer Disease Genotypes Using a Multi-Omics Approach, Maria Victoria Fernandez Hernandez, PhD
- Plasma Cell-free RNA as Non-invasive Biomarker for Neurodegeneration, Laura Ibáñez, PhD
- Factors that Contribute to Hearing Handicap and Hearing Loss Treatment Decisions of Older Adults, Kate McClannahan, PhD
- Tau Kinetics in the Human CNS In Vivo and In Vitro, Chihiro Sato, PhD

Fond Farewells and Wonderful Welcomes

Dr. Virginia Buckles, former Knight ADRC Executive Director, retired in June, 2019.

Ms. Linda Amos, Knight ADRC Research Administrator, retired in January, 2020; Ms. Jasmina Kusuran now assumes this role.

Dr. Nigel Cairns, Neuropathology Core Leader, retired in September, 2018; Dr. Rick Perrin now assumes this role.

Dr. Gregg Day departed the Knight ADRC for Mayo Clinic-Jacksonville as of December, 2019.

Dr. Kyle Womack has joined the Knight ADRC from University of Texas Southwestern Medical Center in July, 2020.

Dr. Joyce Balls-Berry joined the Knight ADRC from Mayo Clinic in July 1st, 2020 to lead the Health Disparities and Equity Core.

Ms. Emily Gremminger joined the Data Management & Biostatistics Core as Project Manager as of January 13th, 2020.

In Memoriam

Mary Jean Harper Thomas

The Knight ADRC mourns the passing of African Advisory Board (AAAB) member Mary Thomas who passed away February 18, 2020. Mrs. Thomas was a force in the St. Louis community. In addition to her work with the AAAB, she was the founder and past President of St. Louis Morehouse College Parents Association, Inc., President of the Auxiliary to the Mound City Medical Forum and President of the St. Louis (MO) Chapter of The Links, Inc. She is greatly missed by all those fortunate to know her.
15th Annual Norman R. Seay Lecture

Black Joy Matters in Aging Research
Raina Croff, PhD, Assistant Professor
NIA Layton Aging & Alzheimer’s Disease Research Center
Oregon Health & Science University

If you were unable to join the lecture on Tuesday, October 13, please visit the Knight ADRC website at https://knightadrc.wustl.edu/Education/Multimedia.htm where you can access a rich library of Knight ADRC events, including the recent lecture by Dr. Raina Croff, PhD.

WHO PARTICIPATES IN MAP RESEARCH?

- Total number of active participants: 822
- Volunteers age 65 years and older: 526 (56%)
- Adult Children Study participants (45-64 years): 296
- Women: 56%
- African American: 16%
- Age range = 45 – 96 years old
- Longest length of volunteer participation: 33 years, with another volunteer participating for 30 years.
- Participants residing in 16 states, including: Idaho, Maine, California, and Texas.
Behind the Acronyms

There are many acronyms and abbreviations used in this newsletter and in AD research. Check out the list below to learn more about what just some of these shortened forms mean.

**ADRC**
Alzheimer Disease Research Center, one of 30 centers across the United States conducting longitudinal research and clinical trials in the field of aging and dementia.

**ACS**
Adult Children Study, the study of pre-symptomatic changes in individuals of parents with or without Alzheimer disease.

**DIAN**
Dominantly Inherited Alzheimer Network, an international cooperative of sites to recruit and study Autosomal Dominant Alzheimer disease defined by family history and validated by known causative mutations for Alzheimer disease.

**HASD**
Healthy Aging and Senile Dementia, one of our grant funded research projects

**MAP**
Memory and Aging Project, the clinical research office for the ADRC, HASD, DIAN, and ACS that provides clinical and psychometric assessments for all research participants.

**CTU**
Clinical Trials Unit, the research group that conducts clinical trials of investigational compounds and procedures related to AD.

**Aβ**
Amyloid-beta protein, a 38 to 43 amino acid product of the larger amyloid precursor protein (APP). Aβ is thought to be one of the two main culprits, along with tau protein, in AD pathology.

**APOE/ApoE**
Apolipoprotein E, the gene and protein, respectively (often used interchangeably), the APOE ε4 allele is a polymorphism of APOE that increases AD risk.

**CSF**
Cerebrospinal fluid, collected through a lumbar puncture and used to measure AD biomarkers.

**LP**
Lumbar puncture, procedure to obtain CSF. In the past it was known as a spinal tap.

**CDR**
Clinical Dementia Rating, the staging instrument to determine the presence or absence of dementia, and, when present, its severity.

**MRI**
Magnetic resonance imaging that depicts and measures brain structures and regions.

**PET**
Positron emission tomography, a brain scan which studies brain activity using a low level of radiation, called a tracer. The Knight ADRC uses tracers designed to identify beta amyloid and tau protein aggregates in the brain.

---

Learn More with the Knight ADRC

Our faculty and staff would love to visit your club, organization, neighborhood group, faith community, or social gathering to share information about Alzheimer disease and current research. We always appreciate the chance to talk about disease basics, healthy aging strategies, caregiving and communication, research updates, and more. Contact Jennifer Phillips at phillipsj@wustl.edu or 314-286-2882 to discuss your event and how we can be of service. Programs will be provided over Zoom until the time comes that we can safely meet in group settings again.
Older People with Early, Asymptomatic Alzheimer Disease at Risk of Falls

By Tamara Bhandari

Falls are the leading cause of fatal injuries in older adults, causing more than 800,000 hospitalizations and about 30,000 deaths in the U.S. every year. Some risk factors are well-known—advanced age, problems with vision or balance, muscle weakness—but an under-recognized factor is early Alzheimer disease. Older people in the earliest stages of Alzheimer disease, before cognitive problems arise, are more likely to suffer a fall than people who are not on track to develop dementia.

“In the world of fall research, we generally say that you’re at risk of falling if you lose strength and balance,” said co-senior author Susan Stark, PhD, an associate professor of occupational therapy, of neurology and of social work. “If you lose strength and balance, the recommended treatment is to work on strength and balance. But if someone is falling for another reason, maybe because his or her brain has begun accumulating Alzheimer-related damage, that person might need a different treatment entirely. We don’t yet know what that treatment might be, but we hope we can use this information to come up with new treatment recommendations that will reduce the risk of falls in this population.”

In 1987, John C. Morris, MD, and his colleagues at Washington University discovered that older people with Alzheimer dementia are more than twice as likely to suffer a traumatic fall than people of the same age without dementia. Since Morris’ discovery, scientists have learned that the brains of Alzheimer patients start undergoing changes decades before memory loss and confusion become apparent. First, plaques of amyloid proteins form, then tangles of tau protein. Some brain areas begin to shrink, and communication networks between distant parts of the brain start to decay. Stark and colleagues have shown that the link between Alzheimer disease and falling holds true even during the silent phase of the disease: People with preclinical Alzheimer disease are at increased risk of falling despite having no apparent cognitive problems.

To better understand why people without cognitive symptoms are at risk of falling, first author Audrey Kelemen, a graduate student in Stark’s lab, and colleagues followed 83 people over age 65 for a year. All participants were assessed as cognitively normal by a qualified neurologist at the beginning of the study. Each participant filled out monthly calendars recording any falls and underwent brain scans for amyloid and for signs of atrophy and impaired connectivity.

The researchers discovered that the presence of amyloid in the brain alone did not put people at increased risk of falling, but neurodegeneration did. Participants who fell had smaller hippocampi—brain regions that are devoted to memory and that shrink in Alzheimer disease. Their somatomotor networks—webs of connections that are...
involved in receiving sensory inputs and controlling movement—also showed signs of decay. The researchers concluded that falling is most likely to occur in the neurodegeneration phase of preclinical Alzheimer disease—the last five years or so before memory loss and confusion arise.

“Since I started working on this project, I’ve started asking my patients about falls, and I can’t tell you how often that has helped me start understanding what is going on with the individual,” said co-senior author Beau M. Ances, MD, PhD, the Daniel J. Brennan, MD, Professor of Neurology and a professor of radiology and of biomedical engineering. “When a person’s mobility is being diminished, even though the person looks very normal, that could be a sign that something needs further evaluation. It’s actually a really important potential marker that should make us say, ‘Wait a minute. Let’s dive into this more. Are there other things that go along with it?’”

The researchers have begun further experiments to better understand why brain changes in Alzheimer disease put people at risk of falling, so they can develop fall-prevention recommendations. In the meantime, simple changes could go a long way toward protecting older people from devastating falls.

“You can prevent a lot of falls just by making the environment safer,” Stark said. “Simple changes could help and can’t hurt: making sure the tub isn’t slippery; making sure you can get up easily off the toilet; balance and strength training; reviewing your prescriptions to see if certain medications or combinations of medications are increasing the risk of falling. Until we have specific fall-prevention treatments for people with preclinical Alzheimer disease, there are still plenty of things we can do to make people safer.”

Resource Corner

The St. Louis and surrounding areas are fortunate to have many outstanding resources for both healthy older adults and families affected by Alzheimer disease and related dementias. If you find yourself with questions or looking for quality programming, the following are some great places to start.

Knight Alzheimer Disease Research Center – In addition to research, our center has an outstanding website that features AD in the news, upcoming events, updates on investigators and research studies, links to AD resources, and more. Connect with us online at http://alzheimer.wustl.edu, via Facebook at https://www.facebook.com/KnightADRC or on Twitter at @WUADRC.

Alzheimer’s Association, Greater Missouri Chapter – Serves 86 counties in Missouri and 10 in Illinois, the Alzheimer’s Association supports over 110,000 people in the region currently living with Alzheimer disease and their care partners through support, research, advocacy and education. Contact the organization to learn more about support groups, care consultations, telephone support, education, and more. https://www.alz.org/greatermissouri

Memory Care Home Solutions – Aims to extend and improve quality time at home for families supporting and caring for loved ones with memory loss, dementia, and Alzheimer disease. Goals are to reduce family care partner stress, provide tools that increase confidence to handle difficult situations, improve quality time at home, and help prepare for the future. memorycarehs.org

Project Present – Improves the quality of life for individuals living in the early stages of Alzheimer dementia and their caregivers through engaging improvisation workshops to encourage interpersonal connection, creative expression, and joyful collaboration. Project Present provides workshops for individuals living with dementia, caregivers, shared joint improv sessions, professional trainings, and general presentations. https://projectpresent.org

STL Village – Enhances the quality of life and well-being of people age 50+ who want to continue living at home and stay active in their communities. stlvillage.org

The Friedman Center for Aging at Washington University – Connects individuals and organizations to conduct innovative research, expands education on issues relevant to individual and population aging, and supports aging initiatives throughout St. Louis and around the world. https://publichealth.wustl.edu/aging

OASIS – Promotes healthy aging through lifelong learning, active lifestyles and volunteer engagement, and ensures that adults age 50 and older have opportunities to pursue vibrant, healthy, productive and meaningful lives. www.oasisnet.org
Maria Carroll, MSN

Gerontological Clinical Nurse Specialist
BSN, Southern Illinois University in Edwardsville, 1987
MSN, Saint Louis University, 1994

Career:
I worked for the Memory and Aging Project from 1995 to 1999 and returned to MAP in 2010. I worked as an oncology nurse and in staff education before becoming a clinical nurse specialist in gerontology. I love working with our participants and their families! It’s fun to get to know people from different backgrounds, hear their stories, and benefit from their wisdom.

Personal:
I am married and have three sons—one finished with college (currently enrolled in graduate engineering classes) and married, one a senior in high school, and one in 8th grade. We are privileged to be caring for my 94-year old mother in our home. I enjoy gardening and my screened porch for reading and relaxing; I can even do some of my work from there now! I like to bike, hike, and travel—when time allows and it’s safe!

What is something you would like the research participants to know?
You are absolutely invaluable to scientific progress toward more simplified diagnosis, better treatment, and ultimately a cure of this disease. While it may not seem like it, we have already learned so much in a relatively short period of time—all thanks to volunteers who are willing to spend time with us each year, take cognitive tests, have MRIs and PET scans, and give blood and spinal fluid samples.

We miss seeing you in-person. In the meantime, many thanks for participating by phone and Zoom. We appreciate your willingness to go beyond your comfort zone with technology as we continue our rigorous research despite social distancing. We look forward to the day when everyone feels safe being together again.
My name is Kelly Larkin, and I was born and raised in St. Louis, although I spent 10 years of my childhood living just outside of Chicago. I am an energetic dog, so I do a lot of hiking and walking. From a young age I wanted to work in the field of nursing with older adults. Growing up I lived next door to a very important man, my grandfather, Gentry, who lived to be 99 years old. He was a very knowledgeable and loving man—he always had a word of the day and was always telling me that he was the best kisser in the world.

After college I came home to work on the neurology floor at St. Luke’s Hospital before beginning this new opportunity at the Memory and Aging Project. It has been great getting to know everyone and seeing how much time and effort the participants put into growing this research initiative. Even though we have been working remotely through this difficult time, it is the highlight of my day when I get the opportunity to talk with our participants. Getting to know them over the phone shows me I am in the right place, and I can’t wait to meet you all in person when it is safe for us.

Kelly with her grandfather, Gentry.
A Special Cohort: History of the Adult Children Study and the “ACS Originals”

A number of studies in the Knight ADRC during the 1990s indicated that the brain changes of Alzheimer disease (AD) were present in older adults who had no evidence of AD symptoms during life. Eventually, we determined that approximately 30% of cognitively normal older adults over the age of 65 (which then was the lower age limit of our research participants) already had AD brain changes. We considered this to be “preclinical AD” and thought that, if a person with preclinical AD continued to live, eventually symptoms of AD would appear. We also thought that preclinical AD would be an ideal target for drug trials to prevent AD symptoms.

Our problem was that we did not know at what age the brain AD changes first appeared, as all of our participants were 65 years and older. So, we developed the idea of studying middle age persons, 45 years and older, who were at elevated risk for AD because they had an affected parent—that is, they were “adult children” of a parent with AD. To detect the appearance of AD brain changes, we used amyloid PET scans and the examination of cerebrospinal fluid, obtained by lumbar puncture. We committed to study such individuals for two decades or longer to learn whether the symptoms of AD eventually developed and what we might do to prevent those symptoms.

Our scientific peers seriously doubted that such a demanding study could be accomplished. There had never been a group of perfectly healthy middle age individuals who would agree to regularly undergo all kinds of procedures, including PET scans and lumbar punctures, for two decades or more. We thus aimed to demonstrate the feasibility of our plans. Without any support from the National Institutes of Health (NIH), in 2002 we asked the adult children of our over-65-year-old participants in the Knight ADRC whether they would agree to participate in this preliminary “pilot” study. We were so pleased that 93 participants signed up. After demonstrating that it was possible to enroll healthy people who indeed completed all the procedures, including the lumbar punctures, we applied to the NIH for substantial funding to move the ACS study full steam ahead. Our application was successful, and in 2005 the grant-supported ACS study officially began.

None of what has been learned about preclinical AD from the ACS study would have been possible without the ACS Originals. Even more inspiring is that of the 93 ACS Originals, 44 are still active in the study—over 18 years later. The story of the Adult Children Study, and of the pioneering volunteers involved, reminds us that none of the work of the Knight ADRC is possible without the support of our participants.

Potential New AD Treatment

Biogen and Eisai, Co., Ltd. announced in July, 2020, that the U.S. Food and Drug Administration (FDA) accepted the Biologics License Application for aducanumab, an investigational treatment for Alzheimer disease, in order to determine whether the drug should be approved as an Alzheimer therapy. If approved, it would mean that the FDA believes that aducanumab reduces the clinical decline of Alzheimer disease and that the drug’s effects in removing amyloid beta from the brain results in better clinical outcomes.

Aducanumab is an investigational human monoclonal antibody that targets brain deposits of amyloid beta. Based on clinical data from patients with very mild Alzheimer disease dementia who were administered the drug, the sponsors (Biogen and Eisai) believe that aducanumab has the potential to impact underlying disease pathophysiology and to slow cognitive and functional decline. However, many Alzheimer disease investigators, including those on an FDA Advisory Committee that met on November 6, 2020, believe that more evidence of the drug’s benefits is needed before it merits approval. The FDA’s decision is expected by March, 2021.
Welcome New Psychometricians to the MAP Team

The Knight ADRC continues to be an engaging and exciting place for professionals to expand their skills and knowledge in the field of older adult research. Please join the Memory and Aging Project in welcoming two new faces to the staff.

**Megan LaRose, BS**, graduated from The Ohio State University in May of 2019 with a double major in psychology and neuroscience, and she joined the Knight ADRC just a week after graduation. LaRose says “the most rewarding part of my job is working with all of our amazing participants. Whether they are personally affected by Alzheimer disease or volunteering their time for research, it is amazing to see so many people who are dedicated to ending this disease. I’ve enjoyed having great conversations and meeting people from all different backgrounds.” In her free time, Megan loves to play tennis, read, and spend time with friends, family, and her cat, Bowie. She says, “it’s been great being back in St. Louis the past year!”

**Hannah Wilks, BS**, graduated from Saint Louis University in May, 2020 with a degree in Neuroscience. In her spare time she enjoys working out, hiking, icing sugar cookies, and spending time with her friends and family. If you have completed your cognitive assessment with Hannah over Zoom, you might have noticed her profile picture (at right). It was taken in May as she backpacked in Custer State Park near Mount Rushmore to catch an early morning sunrise at Black Elk Peak. Wilks says of her work, “I appreciate knowing I am part of a large group of people dedicated to furthering our understanding of Alzheimer disease.” And to our volunteers, she says, “thank you so much for participating in our research studies! We couldn’t do it without you!”

---

**MAP Assessment Aids COVID-19 Patient**

People volunteer for Memory and Aging Research for a variety reasons, but one participant never anticipated that it would help during a global pandemic. The daughter of a MAP participant shared that when her father was admitted to the hospital to be treated for COVID-19, he was listed with a diagnosis of dementia. With the documentation provided by MAP to the participant following his annual research assessments, the daughter was successful in establishing that he had normal cognition, which expedited his COVID-19 therapy. The daughter expressed many thanks to the MAP program and credits her father’s participation as the means that saved his life.
Blood Test is Highly Accurate at Identifying Alzheimer Disease Before Symptoms

By Tamara Bhandari

Up to two decades before people develop the characteristic memory loss and confusion of Alzheimer disease, damaging clumps of protein start to build up in their brains. Now, a blood test to detect such early brain changes has moved one step closer to clinical use.

Researchers from Washington University School of Medicine in St. Louis report that they can measure levels of the Alzheimer protein amyloid beta in the blood and use such levels to predict whether the protein has accumulated in the brain. When blood amyloid levels are combined with two other major Alzheimer risk factors—age and the presence of the genetic variant APOE4—people with early Alzheimer brain changes can be identified with 94% accuracy, the study found.

The findings, published in August 2019 in the journal Neurology, represent another step toward a blood test to identify people on track to develop Alzheimer disease before symptoms arise. Surprisingly, the test may be even more sensitive than the gold standard—a PET brain scan—at detecting the beginnings of amyloid deposition in the brain.

Such a test may become available at doctors’ offices within a few years, but its benefits will be much greater once there are treatments to halt the disease process and forestall dementia. Clinical trials of preventive drug candidates have been hampered by the difficulty of identifying participants who have Alzheimer brain changes but no cognitive problems. The blood test could provide a way to efficiently screen for people with early signs of disease so they can participate in clinical trials evaluating whether drugs can prevent Alzheimer dementia.

“The right now we screen people for clinical trials with brain scans, which is time-consuming and expensive, and enrolling participants takes years,” said senior author Randall J. Bateman, MD, the Charles F. and Joanne Knight Distinguished Professor of Neurology. “But with a blood test, we could potentially screen thousands of people a month. That means we can more efficiently enroll participants in clinical trials, which will help us find treatments faster, and could have an enormous impact on the cost of the disease as well as the human suffering that goes with it.”

The test uses a technique called mass spectrometry to precisely measure the amounts of two forms of amyloid beta in the blood: amyloid beta 42 and amyloid beta 40. The ratio of the two forms goes down as the amount of amyloid beta deposits in the brain goes up.

The current study involved 158 adults over age 50. All but 10 of the participants in the new study were cognitively normal, and each provided at least one blood sample and underwent one PET brain scan. The researchers classified each blood sample and PET scan as amyloid positive or negative, and found that the blood test from each participant agreed with his or her PET scan 88 percent of the time, which is promising but not accurate enough for a clinical diagnostic test.

In an effort to improve the test’s accuracy, the researchers incorporated several major risk factors for Alzheimer disease. Age is the largest known risk factor; after age 65, the chance of developing the disease doubles every five years. A genetic variant called APOE4 raises the risk of developing Alzheimer disease three-to-fivefold. When the researchers included these risk factors in the analysis, they found that age and APOE4 status raised the accuracy of the blood test to 94%.

Further, the results of some people’s blood tests initially were considered false positives because the blood test was positive for amyloid beta but the brain scan came back negative. But some people with mismatched results tested positive on subsequent brain scans taken an average of four years later. The finding suggests that, far from being wrong, the initial blood tests had flagged early signs of disease missed by the gold-standard brain scan.

There is growing consensus among neurologists that Alzheimer treatment needs to begin as early as possible, ideally before any cognitive symptoms arise. By the time people become forgetful, their brains are so severely damaged no therapy is likely to fully heal them. But testing preventive treatments requires screening thousands of healthy people to find a study population of people with amyloid build-up and no cognitive problems, a slow and expensive process.
AIM HIGH: STRIVING FOR 100%

The Knight ADRC is proud to maintain one of the most comprehensive libraries of participant data in the field of AD research. We are grateful to our volunteers who contribute their time, energy, and samples to enrich the field of research. Let’s continue striving for 100% together! Participation in AD study procedures:

- **Amyloid PET Scan**: 80% participation
- **Lumbar Puncture for CSF Collection**: 72% participation
- **MRI Scan**: 87% participation
- **Tau PET Scan**: 60% participation

**2020 Knight ADRC Participants’ Meeting**

Although we could not gather together in person to thank our participants and share a research update over breakfast, be sure to visit the Knight ADRC website at https://knightadrc.wustl.edu/Education/Multimedia.htm to enjoy recorded research presentations on just some of the exciting research happening at the Knight ADRC.

Topics and speakers for the 2020 Virtual Participants’ Meeting include:

- **Overview of the Knight ADRC: Progress and Proposals**, by John C. Morris, MD
- **Alzheimer Disease Clinical Trials**, by Joy Snider, MD, PhD
- **Microbiome – What it is and Relevance for AD Research**, by Beau Ances, MD, PhD
- **Exercise, Growth Factors, and AD Risk**, by Denise Head, PhD
- **New Racial Disparities and Equity Core**, by Joy Balls-Berry, PhD
- **Lifecourse Influences on Alzheimer Disease (LIAD)**, by Marissa Streitz, LCSW
- **Return of Individual AD Risk**, by Jessica Mozersky, PhD
New! Support Groups Offered

The Knight ADRC is excited to offer new memory loss support groups: one for individuals diagnosed with younger-onset memory loss, which is memory and thinking change that begins before the age of 65 years—with a breakout group for care partners and supportive friends, and a second group for research participants in clinical trials and/or longitudinal research. These confidential groups meet monthly for discussion, support, education, and to build connections among members. Meetings are currently being held on Zoom, with the hopes of transitioning to in-person meetings in the future. One member of the group for individuals diagnosed with younger-onset memory loss said, “I can’t tell you how much I appreciate our support group. I have no sense of being judged…and realize that I don’t even question their abilities. They are all smart, funny, and compassionate people.” To learn more or schedule a visit, please contact Jennifer Phillips at phillipsj@wustl.edu or 314-286-2882.

MAP Wants to Hear From You

Your participation and feedback are the most important tools in the research to find a treatment and prevention for Alzheimer disease. Your opinions, satisfaction, and suggestions help us maintain the highest quality research program possible. Please contact us any time to share your feedback or questions at https://knightadrc.wustl.edu/Feedback

Time to Schedule?
Call Colleen!

Everyone at the Knight ADRC looks forward to the time when we can resume safely meeting in person for research visits. When it nears time for your annual MAP cognitive assessment, keep an eye on the mailbox for a postcard reminder. You’re also welcome to contact Colleen Duchild who can help you schedule your telephone visit and/or in-person assessment at colleend@wustl.edu or 314-286-2478. Colleen is also a great person to contact if you have changes in your address or phone number so we can keep your file up-to-date.