Quarterly news and updates from the
Stanford Alzheimer's Disease Research Center
and the Healthy Brain Aging Study

MIND MATTERS

2021 Summer Issue

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A·D·R·C
for healthy brain aging

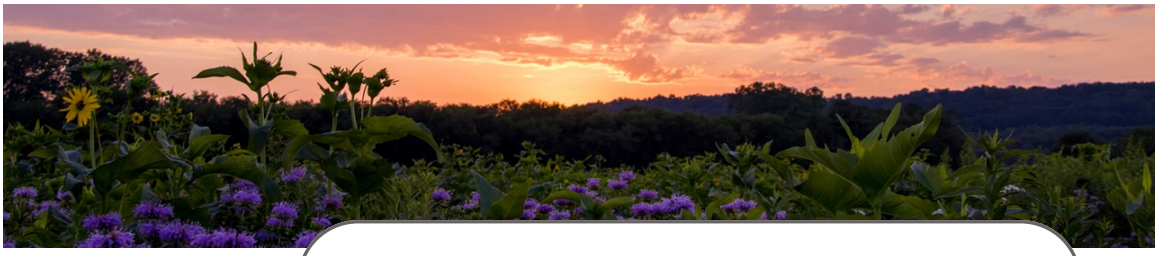
As the state of California begins to fully re-open, we at the Alzheimer's Disease Research Center (ADRC) hope you and your loved ones continue to be safe and well. We appreciate your continued support and patience as we are gearing up for the return of in-person research visits. Your health and safety are our top priority. We are working to create safe procedures for our participants and research staff. As of now, we will be continuing to conduct our study visits virtually and over the phone. We appreciate your willingness to continue to accommodate and support our ongoing effort of improving the diagnosis, treatment, prevention, and care for those with Alzheimer's disease, Parkinson's disease, Lewy Body disease, mild cognitive impairment, and related cognitive disorders.

Save the date

November 3rd, 2021 (Zoom Webinar)

4th Annual Participant Appreciation Day

Details will be provided closer to the date



ALZHEIMER'S DISEASE IN THE NEWS

Aducanumab approved by the FDA

Aducanumab received accelerated approval by the FDA on June 7 for the treatment of Alzheimer's disease. This drug is a monoclonal antibody directed against amyloid, and it is administered as an intravenous infusion every 4 weeks. "Accelerated approval" differs from regular FDA approval and reflects the view that there is an important unmet need for safe, effective forms of treatment for Alzheimer's disease and related disorders. Alzheimer's disease is a dreadful disorder, and we know that patients and families are desperate for treatment that improves its devastating symptoms or halts its relentless progression. Aducanumab approval was based primarily on results from two large clinical trials (phase-3 trials), each lasting one and a half years.

It is clear that aducanumab reduces amyloid plaque in the brain. It was this finding that led to FDA approval. Other monoclonal antibody treatments also reduce brain amyloid but failed to provide clinical benefit and failed to gain FDA approval. We are concerned that the average clinical effect of aducanumab in the first phase-3 clinical trial was too small to be discerned by patients or family members. Results from the second phase-3 trial failed to detect even this very small effect. The principal side effect in these trials was ARIA (Amyloid-Related Imaging Abnormalities). ARIA represents swelling or bleeding in the brain, as detected by an MRI brain scan. This side effect is usually not serious, but it can be associated with headache and confusion.

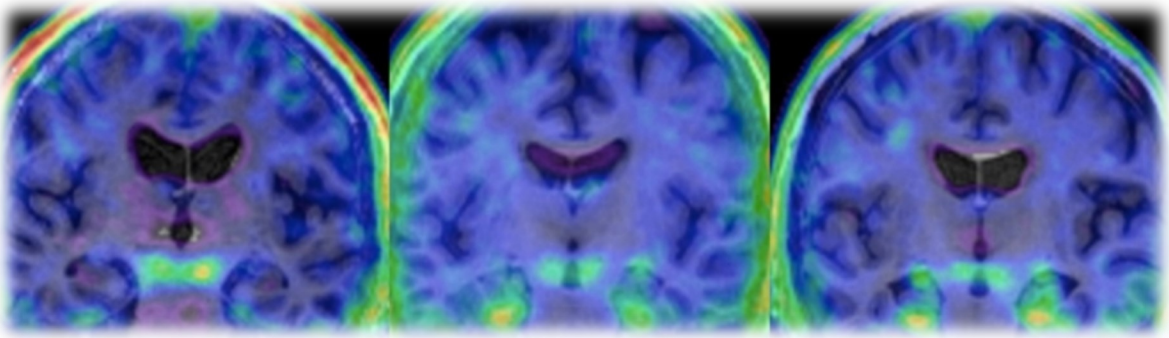
We view FDA accelerated approval of aducanumab as a symbol of hope. We are pleased that the FDA announcement states that the manufacturer will be asked to conduct post-approval studies to verify clinical benefit, which was not clearly evident in the two large phase 3 trials. This drug is not yet available at Stanford or elsewhere but will be soon. We will provide updated information as it becomes available. We continue the search for better, more effective means of prevention and treatment through NIH-sponsored research in the Stanford Alzheimer's Disease Research Center. It remains to be seen whether aducanumab is a helpful step along this arduous pathway.

ADRC CORES

Imaging Core

The Imaging Core provides researchers with user-friendly molecular, structural, and functional brain imaging of Stanford Alzheimer's Disease Research Center (ADRC) participants. The Core has particular expertise in PET imaging of amyloid and tau proteins, as well as MRI metrics of blood flow and functional connections between brain areas affected by Alzheimer's disease and related disorders. Imaging data can be analyzed in conjunction with other ADRC data, including results of neuropsychological testing, spinal fluid measurements, and blood biomarkers.

The Imaging Core is led by Elizabeth Mormino, PhD and co-led by Michael Greicius, MD. Other faculty and staff in the core include Guido Davidzon, MD, SM; Gregory Zaharchuk, MD, PhD; Michael Zeineh, MD, PhD; Gabriel Kennedy, BS; Tyler Toueg, BS; Hillary Vossler, BS; and our PET/MRI technicians Dawn Holley and Kim Halbert.



Early Tau accumulation is detected within the medial temporal lobe using Tau PET imaging.
Photo credit: Mormino Lab

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Core Leader

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Associate Core Leader

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Gabriel Kennedy, BS

Tyler Toueg, BS

Hillary Vossler, BS

Dawn Holley
PET/MRI Technician

Kim Halbert
PET/MRI Technician

ADRC FACULTY HIGHLIGHTS

Elizabeth Mormino, PhD
Assistant Professor (Research) of Neurology and Neurological Sciences

Dr. Mormino obtained her doctorate in neuroscience at the University of California at Berkeley and completed postdoctoral fellowship training in neuroimaging at the Massachusetts General Hospital and Harvard Medical School. She is a neuroscientist who uses multimodal brain imaging to understand the development of Alzheimer's disease in older adults without dementia. This work involves amyloid PET imaging, tau PET imaging, structural MRI, and functional MRI. Her research may help to identify people at risk before widespread neuronal damage has occurred. Many older adults without cognitive impairment have brain amyloid. Dr. Mormino has found great variability in the rate of decline among those who eventually progress to Alzheimer's disease, and she is examining genetic factors that influence the risk of decline.

Recent work from the Imaging Core:

True ultra-low-dose amyloid PET/MRI enhanced with deep learning for clinical interpretation

PET/MRI scans can be used to understand the pathology of proteins in the brain involved in dementia. This method assists in identifying at-risk individuals and indicating the optimal time point for early interventions in potential anti-amyloid therapies. However, the radioactive exposure and the cost of these scans can be limiting factors for both patients and research centers. In an effort to reduce these factors, Dr. Chen and colleagues used deep learning methods to show that PET/MRI images collected using lower doses of the radioactive tracer ^{18}F-Florbetaben are of valid, diagnostic quality. This provides evidence for the feasibility of reducing radiation exposures and cost.

https://pubmed.ncbi.nlm.nih.gov/33416955/

Tau PET imaging with ^{18}F-PI-2620 in aging and neurodegenerative diseases

Accumulations of the protein amyloid-beta and tau tangles in the brain are considered to be the hallmark pathological features of Alzheimer's disease (AD). The ability to assess and measure amyloid-beta plaque accumulation through PET/MRI has been reliably available for decades, whereas tau tangle measures have only become available recently. Dr. Mormino and colleagues set out to experimentally provide validation for ^{18}F-PI-2620, examining its distribution throughout the course of AD. Preliminary results suggest differences in medial temporal lobe and cortical brain regions known to be impacted in AD. This work provides evidence to confirm ^{18}F-PI-2620 holds promise as a tool to visualize tau tangle aggressions in AD.

https://pubmed.ncbi.nlm.nih.gov/32572562/

Additional Opportunities to Participate in Research

The Stanford ADRC Research Education Component (REC) is a formalized training program to prepare the next generation of researchers for careers in aging, Alzheimer's disease, and Alzheimer's disease-related disorders. We currently have 4 active REC fellows, one of whom is Joe Winer, PhD, a postdoctoral fellow working with Elizabeth Mormino, PhD and Kathleen Poston, MD. Joe is interested in looking at the impacts of sleep on the development and progression of neurodegenerative disorders. He is currently looking for interested ADRC participants who are willing to participate in the following study:

Sleep and Physical Activity Study
Sleep and daytime activity are known to change across the lifespan, and both are affected in neurodegenerative disease. New research suggests that these changes are not only symptoms of disease, but may affect cognition and disease progression. We are looking for participants to wear a motion-sensing wristwatch for a period of two weeks.

The watch will measure 24-hour patterns of sleep-wake activity which may advance our understanding of the role of sleep and daytime activity in disease processes. Participants will be given a prepaid envelope to mail the watch back after the two-week period. We greatly appreciate the volunteerism and involvement of all of our participants. We have already begun to collect this data on ADRC participants and will continue to collect data throughout the next few years. Please contact Dr. Joseph Winer, jwiner@stanford.edu if you have questions.

Stanford ADRC Affiliated Studies

Study: Healthy Brain Aging Study **Study status:** Open, enrollment ongoing

Contact: Veronica Ramirez vramirez1@stanford.edu or (650) 721-5354

Study: Pacific Udall Center **Study status:** Open, enrollment ongoing

Contact: Maria-Lucia Campos udallcenter@stanford.edu or (650) 721-5351

Study: Health IQ Study **Study status:** Open, enrollment ongoing

Contact: Tlesa Meadowcroft tmeadowcroft@stanford.edu or (650) 308-9269

Study: Alzheimer Gut Microbiome Project **Study status:** Open, enrollment ongoing

Contact: Veronica Ramirez vramirez1@stanford.edu or (650) 721-5354

Study: Sleep and Physical Activity Study **Study status:** Open, enrollment ongoing

Contact: Joseph Winer jwiner@stanford.edu

Clinical Trials

Sponsor: NIA (PEACE-AD) **Study status:** Open, enrollment ongoing

Contact: Amanda Ng amandang@stanford.edu or (650) 485-9560

For more information on the trial, please visit: https://clinicaltrials.gov with identifier **NCT03710642**

Sponsor: Genentech/Roche (Digital Biomarker) **Study status:** Open, enrollment ongoing

Contact: Viktoriya Bourakova viktoriya.bourakova@stanford.edu or (650) 709-9041

Sponsor: Eisai and NIH (AHEAD 3-45 Study) **Study status:** Open, enrollment ongoing

Contact: Amanda Ng amandang@stanford.edu or (650) 485-9560

Anthony Velasquez anthgv@stanford.edu or (650) 206-0963

For more information on the trial, please visit: https://clinicaltrials.gov with identifier **NCT04468659**