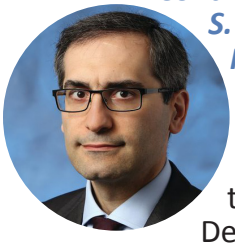
UC Irvine Institute for Memory Impairments and Neurological Disorders

MIND Matters

A quarterly publication of UCI MIND

Spring 2019

Big IDEAS May Improve Clinical Management of Dementia

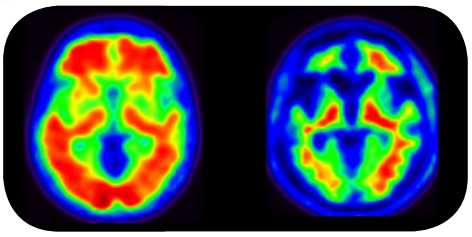


Contributed by S. Ahmad Sajjadi, MD, PhD

The results of a very important and highly anticipated study, the IDEAS (Imaging Dementia – Evidence For Amyloid Scanning) study, were recently published in the *Journal of the American Medical Association*.

This national multi-center study, including UC Irvine, enrolled more than 11,000 Medicare beneficiaries with cognitive impairment to undergo a special type of scan called amyloid positron emission tomography (PET). Amyloid PET scans visualize the accumulation of abnormal amyloid plaques in the brain, one of the two hallmark pathologies of Alzheimer's disease (AD). The study has convincingly shown that amyloid scan results can lead to change in the clinical management of patients with mild cognitive impairment (MCI) and dementia. Based on scan results, physicians involved in the study reported changing their management plan in about 60% of patients. Furthermore, the diagnosis of 25% of patients with presumed AD changed to non-AD, and the diagnosis of 10% of patients with presumed non-AD changed to AD. Further analyses showed that the diagnosis of patients with MCI with a presumed non-AD etiology changed most frequently after amyloid PET.

The study is unprecedented in its scale and importance for clinical management of dementia. It is worth emphasizing, however, that for consideration in the study, patients had to have cognitive impairment for which the etiology was unclear after undergoing appropriate cognitive assessments, laboratory tests, and magnetic resonance imaging (MRI) or computerized tomography (CT) brain scans. These criteria would automatically exclude a large majority of patients routinely assessed in clinics, whose clinical presentation is typical for one of the many forms of dementia. Also, patients were only referred to the study if the referring clinician felt that the outcome of the amyloid scan would lead to a change in either the diagnosis or care. The study also had important limitations, such as only people 65 and older were included, nearly all participants were white, and the study did not compare the value of amyloid PET with other available measures, such as spinal fluid. Currently, the cost of amyloid imaging is not covered by Medicare and other insurance providers. Given the impressive outcome of the IDEAS study, however, perhaps we may see a change in Medicare reimbursement policy for amyloid PET.



Positive (left) and negative (right) amyloid PET scans

Exciting News in Huntington's Disease Research

Contributed by Leslie Thompson, PhD (top) & Joan Steffan, PhD (bottom)

Results from a recent study published by Tabrizi and colleagues and Ionis/Roche Pharmaceuticals in the *New England Journal of Medicine* are very exciting for the Huntington's disease (HD) patient, family, and scientific communities. The researchers showed for the first time that treatment with a *huntingtin* lowering drug called an antisense oligonucleotide, or ASO, is safe in HD patients. *Huntingtin* is the protein linked to the genetic mutation that causes HD. With these results, researchers are planning a large clinical trial to test whether ASO can reduce symptoms in HD patients. The HD community is hopeful this therapy may be the first effective treatment to slow HD progression.

In other exciting news, UCI MIND HD scientist Dr. Leslie Thompson and her team were awarded $6 million by the California Institute for Regenerative Medicine to perform continued testing of promising stem cell treatments for HD. To learn more about HD research and care at UCI, visit the website of our partner organization HD-CARE at **hdcare.org**.

From the Director

Joshua D. Grill, PhD

Dear Friends,

The field of neurodegenerative disease research is evolving with new technologies and promising potential treatments (page 1). At the same time, we continue to encounter challenges as candidate treatments fail. Last month, Biogen halted two large parallel Phase 3 trials of the monoclonal antibody against the amyloid beta protein, aducanumab. This treatment was viewed by many to hold tremendous promise. In an early phase clinical trial, patients with Alzheimer's disease (AD) who were treated with aducanumab showed significant reduction in amyloid plaques in the brain, which appeared to slow disease progression. Disappointingly, the larger more recent trials, in which UCI MIND participated, failed to replicate the earlier findings. At the time of publishing this newsletter, the data for these trials are not yet public.

Multiple drugs, like aducanumab, have now demonstrated to bring amyloid levels "back to normal" in people with AD, if treatment duration is long enough and dose is high enough. Yet, the prevailing unknown is whether any of these treatments can actually slow the course of disease and produce clinically meaningful benefits for patients and their families. Biogen's news suggests that, at least for aducanumab, the answer is no. Like you, we are disappointed by these results. But numerous clinical trials of important candidate therapies remain underway, and a variety of important questions remain unanswered. In particular, many experts believe amyloid-lowering therapies may only be effective if begun very early in the disease process, requiring prevention studies in cognitively healthy people. These trials, as well as trials to test a variety of non-amyloid treatments, will require research participation from volunteers with and without AD. Patients and families are understandably desperate for immediate solutions and may become targets of pseudomedicine (page 3). Only when scientists and families work together to perform careful and rigorous research, however, will we discover effective treatments and preventions for AD and other neurodegenerative diseases.

Annual Distinguished Lecture on the Brain

In partnership with UCI School of Biological Sciences and UCI Center for the Neurobiology of Learning and Memory, UCI MIND hosted its annual Distinguished Lecture on the Brain in March at the Irvine Barclay Theatre. Guest speaker Ronald C. Petersen, MD, PhD, Director of the Mayo Clinic Alzheimer's Disease Research Center (below), delivered an insightful lecture on the diagnosis of Alzheimer's disease in the era of biomarkers to hundreds of audience members, both in-person and via live stream. If you missed it, the full lecture is available on our blog and YouTube channel. Stay tuned for announcements of our 2020 distinguished guest speaker!

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Age 60 or older?

Did you know you can receive an income stream for life while supporting UCI MIND?

For more information on how a charitable gift annuity can support research, call **949.824.6233**.

The Rise of Pseudomedicine for Dementia & Brain Health

In January, colleagues at the UCSF Memory and Aging Center published a timely critique in the *Journal of the American Medical Association* on a concerning and increasing practice in the United States. "Pseudomedicine" is a practice whereby qualified healthcare professionals prescribe supplements or other therapies that lack evidence and are not covered by insurance, and therefore require cash payments. Pseudomedicine is especially problematic among older patients and family members concerned about memory loss and desperate for effective therapies to slow or stop the progression of Alzheimer's disease (AD). Other examples of pseudomedicine include recommendations for brain healthy diet plans and exercise programs, which are viewed by many as standard, but in these cases come at a cost to the patient. Here in Southern California, there are also a large number of stem cell "clinics" that circumvent FDA regulations and offer unproven — even untested — treatments at substantial costs to patients with AD and other neurological conditions. In some cases, these scams are even disguised as clinical trials.

In their article, Hellmuth and colleagues outline a few steps that can be taken to try to address this rising problem. Among them is the need for experts to offer honest scientific interpretation of claims such as those outlined above. At UCI MIND, we take this responsibility seriously. If you have questions about claims from individuals offering therapies that stop or reverse memory or cognitive problems, especially at out-of-pocket costs, consider attending a UCI MIND lecture (page 4) or tune in to our new Facebook LIVE Q&A series described below.

Ask Our Docs! On Facebook

As you may know, UCI MIND's quarterly *Ask the Doc* program connects researchers with community members to answer questions about brain health, Alzheimer's disease (AD), and related topics. We hope you join us for our next panel on June 13 at the Bowers Museum in Santa Ana (page 4). In an effort to provide even more people access to this unique opportunity, UCI MIND recently launched its first-ever Facebook LIVE series, *Ask the Doc: Alzheimer's Research Today!* The series features a new topic with a research expert the first Friday of every month at 9AM PST on UCI MIND's Facebook page. Live viewers can type their questions into the comments box and receive an immediate answer from a UCI MIND researcher. So far, topics have included the connection between sleep and brain health, the causes of memory problems as we age, the role of inflammation and immunity

Chelsea Cox, Assoc. Director of Education (left), moderates live Q&A on inflammation and AD with scientist, Andrea Tenner, PhD (right)

in AD, and vaccines as a potential treatment for AD. Together, the first four episodes have been viewed over 4,000 times, and we hope to connect with many more people over the course of the series. To attend live and ask questions, "Like" **@UCIrvineMIND** on Facebook to be notified of upcoming episodes. You can also join our email list at **www.mind.uci.edu/events**. Past episodes are posted on UCI MIND's Blog and YouTube channel for those who do not use Facebook.

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SAVE THE DATE

October 25, 2019 | Irvine Marriott

For 30 years, the Annual SoCal Alzheimer's Disease Research Conference has delivered the latest knowledge in dementia research and care to the Orange County community. In its Pearl Anniversary, join national experts as they explore what we have discovered and charge forward with hope for solutions!

UPCOMING EDUCATION EVENTS

Thursday, June 13 | 1:30-3:30 pm | Ask the Doc @ Bowers Museum in Santa Ana
Open Q&A with Ahmad Sajjadi, MD, PhD, Daniel Nation, PhD & Lindsay Hohsfield, PhD
RSVP requested: **mind.uci.edu/bowers** or **714.567.3677**

Friday, July 12 | 9:00-9:30 am | What medications can I take to prevent or treat Alzheimer's?
Facebook LIVE Q&A with Steven Tam, MD
Login to Facebook on Friday morning & search **@UCIrvineMIND**

Friday, August 2 | 9:00-9:30 am | Can brain scans be used to diagnose Alzheimer's?
Facebook LIVE Q&A with Craig Stark, PhD
Login to Facebook on Friday morning & search **@UCIrvineMIND**

Saturday, August 10 | 10:00 am-12:00 pm | Ask the Doc for Down Syndrome @ AlzOC in Irvine
Open Q&A with Ira Lott, MD, Elizabeth Head, PhD & Eric Doran, MS
RSVP requested: **askucimind.eventbrite.com** or **949.824.9475**