UCI MIND Institute for Memory Impairments and Neurological Disorders

MIND Matters

FALL 2021

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SPECIAL FEATURE

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Autosomal Dominant Neurodegenerative Diseases (ADND), like Huntington's disease and the rare form of inherited early onset Alzheimer's disease, are particularly challenging brain disorders, in part because they begin to show symptoms when people are mid-career and parenting younger children.

ADND are caused by inherited genetic mutations and researchers can test for these mutations at any age, creating an opportunity to test interventions as possible preventative therapies before even the earliest signs of brain changes.

Yet, many people who are at risk to inherit these mutations choose not to undergo testing and, while there is critical need for these at-risk individuals to participate in prevention trials, significant scientific and ethical complications are brought to bear in these trials. UCI MIND project scientists, Dr. Sarah Hernandez, who works in Leslie Thompson's Lab and Dr. Lindsay Hohsfield in Kim Green's Lab, both in the Department of Neurobiology and Behavior, have spent their careers studying the pathological mechanisms of diseases that affect their respective families.

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Drs. Lindsay Hohsfield (top left) and Sarah Hernandez (top right) consider the issues around fertility for participants in Autosomal Dominant Neurodegenerative Disease prevention trials.

MESSAGE FROM THE DIRECTOR

For the latest news, stories, and resources, visit www.mind.uci.edu/blog

Dear Friends of UCI MIND,

Fall is here and the COVID-19 pandemic is still with us. Though we are seeing signs of improvement, life is not yet back to normal. This fall, the pandemic once again forced us to move several of our major annual activities to a virtual format (page 7) or to cancel them entirely (page 5). But it has not slowed the important work happening at UCI MIND.

In this issue, you will learn about funded work from Dr. Liz Chrastil. She studies the hippocampus, a part of the brain affected early and severely in Alzheimer's disease. Though memory is the predominate role we think of for the hippocampus, it is also essential to our ability to navigate our world and Dr. Chrastil is investigating this aspect of hippocampal function in aging and disease.

You will also learn more about our UCI MIND trainees. Dr. Jean Ho, a UCI MIND post-doctoral fellow was recently featured on National Public Radio for her exciting work on the potential relationship between differing blood pressure medications and cognitive performance (page 6). The work of Drs. Sarah Hernanez and Lindsay Hohsfield is highlighted on page 1. Drs. Hernandez and Hohsfield have authored an important and thoughtful piece on the ethics of moving AD prevention trials into younger and younger participants, in this case in a rare form of the disease that begins in the 3rd, 4th, and 5th decades of life. Dr. Hohsfield has even started a new non-profit organization to support these families (page 3). And finally, we've added to the resources available to support the training of a new generation of investigators to carry the field toward our ultimate goal of discovering solutions for Alzheimer's disease and other age-related brain conditions.

Joshua D. Grill, PhD
Director, UCI MIND

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continued from page 1: Family planning and research participation

In a departure from their bench research, the pair recently published an important perspective article in the Journal of Translational Medicine on one specific scientific and ethical issue that should be considered when enrolling participants in ADND prevention clinical trials—the impact on family planning.

Many of the investigational therapies being studied for neurodegenerative diseases have unknown effects on fertility and pregnancy. Participation in these trials is almost always conditional upon subjects agreeing to practice birth control and not get pregnant during the trial. Yet, the attitudes and ethics around family planning of family members who could enroll in these trials have not been well studied. For this reason, Drs. Hernandez and Hohsfield looked to cancer research to help guide ADND trial design. They highlighted several key areas to consider in ADND prevention research.

Recommendations from Hohsfield & Hernandez, 2021:

- **Interview studies are needed to better understand the attitudes around fertility of people considering ADND prevention trials.**
- **Fertility counseling should be implemented by trials to help potential participants consider their future plans including the possibility of gamete preservation and IVF.**
- **Informed consent should include a detailed discussion about the fertility risks associated with participating in the trial to instruct the potential participant's decision to enroll in the study.**

For more information, visit https://mind.uci.edu/childbearing

Taking these steps would improve participant well-being and the conduct of ADND clinical trials. You can read Drs. Hernandez's and Hohsfield's paper in the Journal of Translational Medicine at the above link.

A new resource for families affected by rare form of Alzheimer's disease

In 2020, Dr. Lindsay Hohsfield, a UC MIND scientist in Dr. Kim Green's lab studying the role that microglial cells play in Alzheimer's Disease (AD), started a non-profit organization to provide support to patients and families affected by the early onset inherited form of Alzheimer's Disease, Autosomal Dominant Alzheimer's Disease (ADAD), also known as Early Onset Familial Alzheimer's Disease (EOFAD).

Although rare, ADAD is devasting. Dementia-related symptoms begin when people are in their 30s and 40s. Those affected face a unique set of challenges including difficult decisions about genetic screening, family planning, and financial considerations. The genetic nature of the condition allows researchers to study the earliest brain changes associated with disease and studies in these families have produced key findings for the general Alzheimer's Disease community.

The burden of young onset Alzheimer's Disease, however, is heavy for families and few resources are available to address the unique challenges felt in this community.

Youngtimers®

To address this gap, Dr. Hohsfield founded Youngtimers. It is the mission of Youngtimers to create a supportive and inclusive space to share stories and struggles, to provide education and to encourage research participation for ADAD patients and their families.

> To learn more about this rare inherited form of Alzheimer's Disease and to support Youngtimers, visit **www.youngtimers.org**

To learn more, visit the Chrastil lab website: https://faculty.sites.uci.edu/spatialneuro

Spatial navigation, sex, and Alzheimer's

Dr. Elizabeth Chrastil is an Assistant Professor in the Department of Neurobiology and Behavior at UC Irvine. Dr. Chrastil's lab studies the learning and memory processes related to spatial cognition and navigation. In 2019, she was awarded a UCI MIND / Women's Alzheimer's Movement grant to better understand how sex, spatial navigation and Alzheimer's disease interact.

What is spatial navigation?

Spatial navigation is the ability to understand where you are on the planet and then how to get to other places.

How do you measure a person's ability to navigate?

We use several methods in the lab. For our virtual reality tests, we put people in a big empty room where they walk around with a helmet on and we create virtual environments including mazes, city environments and virtual deserts, or spaces void of any landmarks.

What are people doing in these virtual environments?

We ask them to do certain tasks like walk in a circle or navigate to a certain location. For instance, when we ask them to reproduce a distance, we measure how far off they undershoot or overshoot the length. Alternatively, if we have people find a location, we measure whether they get to the right place and how efficient their path was.

Do males and females navigate differently?

Yes and no. There's a lot of individual differences in spatial navigation that sex differences don't account for. Spatial navigation consists of both the ability to get to a place and a term called spatial strategy, or the specific path you take to get to a place. Women tend to follow the same route that they know, while men are more inclined to take the shortcut. This doesn't mean that men know the environment better they just tend to have different strategies for getting around. We know that there are structural and hormonal differences in the brain between men and women but there are also social factors that aren't necessarily driven by biology and are hard to disentangle.

Do women vary in their ability to navigate across the lifespan?

We know that the brain, especially the hippocampus, which is critical to spatial navigation, has a lot of estrogen receptors. During menopause there is a huge change in estrogen levels. We are currently conducting a study to see if menopause leads to changes in spatial navigation.

How do changes in estrogen affect navigation?

We are still early in our study so we don't have results yet. We might expect postmenopausal women to behave more like men in their navigation strategy. On the other hand, estrogen is associated with better memory so if it is decreasing during menopause, then we would expect spatial navigation to get worse. You also have to consider long-term exposure to hormones occurring early in life that help shape the way that people navigate long-term. In addition, as people age, they tend to take the known routes instead of shortcutting. The sex differences we see in early life tend to disappear as people age into mid and late life.

Is spatial navigation related to Alzheimer's disease?

Some labs have shown deficits in spatial navigation in people at significant risk for developing Alzheimer's. We are starting to examine how navigation might be an early marker for Alzheimer's disease. It would be exciting for the field to be able to identify a behavioral marker decades before any symptomology onset for early detection, but this is challenging due to the huge individual differences that we see in the population. We need to understand more about these individual variations at a young age, and then see how that extends to older groups and follow these changes over time.

A message from Virginia Naeve, UCI MIND Gala Committee Chair:

We need your help!

It has been my privilege to volunteer for UCI MIND's annual gala planning committee since 2015. The *A December to Remember* Galas have offered an opportunity for friends of UCI MIND to come together for a festive evening to raise vital support for Alzheimer's research. This year, facing uncertainty about what the winter months would bring amid the COVID-19 pandemic, and after giving thoughtful consideration for the health and wellbeing of our community and our supporters, UCI MIND has cancelled the 2021 Gala.

As you think about your end-of-year giving, please consider making a gift to UCI MIND.

It is important to note that during the past year and a half under the impact of COVID-19, UCI MIND did not pause research but in fact, adapted to the changing landscape. Protective measures were added to ensure that participants could safely continue research activities. Similarly, animal and other laboratory studies progressed in a safe but steady way and several important scientific advancements have been made since COVID began. Education and outreach went virtual and events like the annual research conference were held over video to record audiences. These adaptations had costs, and fundraising has remained key to UCI MIND pursuing its mission. I am continually impressed, actually amazed, to see the dedication, commitment and hard work being done by the scientists and clinicians at UCI MIND. Please rest assured that the team involved with this work deeply appreciates the funding they receive because of people like you. Without your gifts, some vital research would be delayed or would have to stop.

In light of the cancellation of the annual gala, I would like to respectfully urge you to consider making a special end-of-year gift to support Alzheimer's research at UCI MIND. We all look forward to seeing you in person at the Gala next **December 3, 2022**. Please save the date! Until then, stay healthy and happy. Thank you again for your consideration and support.

Thank you to our donors

To make a gift, call 949.824.3251 or visit www.mind.uci.edu/donate

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Brethren Commuity Foundation
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Gifts of $50,000+ (Sept. '20-'21)
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Mrs. Karen Rockel Speros

* Indicates multiple donors

UCI MIND is home to the next generation of dementia researchers

New training grant to attract nation's brightest scientists

UCI MIND's Drs. Elizabeth Head and Joshua Grill and a core group of faculty members were recently awarded a prestigious National Institute on Aging T32 training grant to help recruit and prepare the next generation of predoctoral and postdoctoral scientists to study Alzheimer's disease and related dementias.

The training grant will support several promising early-stage scientists for a renewable one-year appointment, as they learn from UCI MIND's renowned faculty. This collaborative opportunity for UC Irvine bridges scientists from the Schools of Medicine, Biological Sciences, Physical Sciences, Information and Computer Sciences, and Social Ecology to help support young dementia researchers.

Rising scientist featured on National Public Radio podcast

Dr. Jean Ho, a postdoctoral scholar in Dr. Daniel Nation's lab was interviewed for NPR's, Academic Minute, a podcast that connects with experts from different universities to discuss a range of subjects.

She was featured as part of UC Irvine Week to discuss her research on blood pressure medications and memory loss. Listen to Dr. Ho's episode to learn which drugs were shown to preserve memory function in her study:

https://mind.uci.edu/npr-podcast

Watch the conference on youtube.com/ucimind or facebook.com/UCIrvineMIND

Annual conference attracts record audience

On Friday September 10th, 2021, UCI MIND and Alzheimer's Orange County held their annual Southern California Alzheimer's Disease Research Conference. Due to the COVID-19 pandemic, the event, which was titled "Alzheimer's From All Angles," was held virtually on Facebook and YouTube. This year's conference was moderated by **Dr. Joshua Grill** and included talks from esteemed experts in the field of Alzheimer's research.

The day kicked off with a presentation from **Dr. Sid O'Bryant**, Professor of Pharmacology and Neuroscience from the University of North Texas, on the current state of diagnostic blood biomarkers. He explained the process needed to get a blood-based biomarker accepted for use in a clinical setting.

Dr. Dena Dubal, Associate Professor of Neurology at the University of California at San Francisco spoke next about sex and genetic resilience. Her lab is conducting experiments to better understand why women tend to live longer with Alzheimer's than men and has found that a gene called *Kdm6a* might be the answer.

Dr. Thomas Lane, a Chancellor's Professor in the Department of Neurobiology and Behavior here at UC Irvine, spoke on the effects of coronaviruses, like the one that causes COVID-19, on the neuropathology of Alzheimer's disease. Dr. Lane's work suggests that Alzheimer's pathology may be more severe in virus infected mice.

Next, **Dr. Amy Kind**, Professor in the Department of Medicine at the University of Wisconsin, presented her research on social disparities in Alzheimer's disease and the link between where you live and your risk for developing dementia later in life.

The conference concluded with a lively talk from **Dr. Gregory Jicha** from the University of Kentucky on the current state of investigational therapies for each stage of Alzheimer's disease.

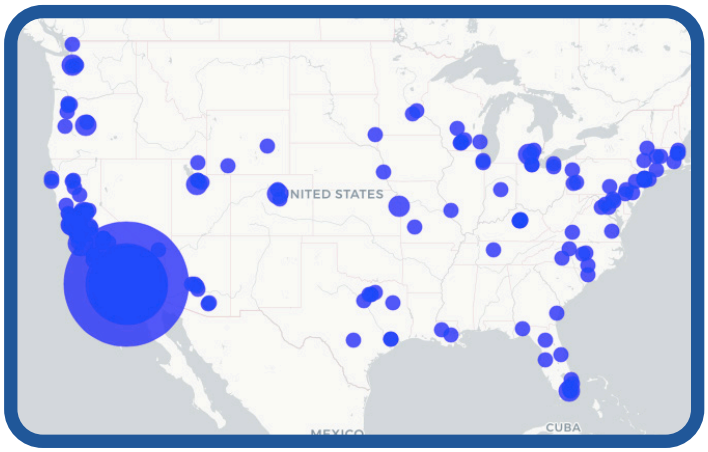
As with past conferences, live viewers had the opportunity to engage with the speakers after each talk. If you missed the conference, no problem; you can watch it anytime on our Facebook and YouTube channels.

Conference viewers by the numbers:

more than 1250 registrants

2,600+ views on Facebook and YouTube

Nationwide conference viewership:



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Connect with us on social media!

OC COVID-19 RESOURCES

Facility for COVID-19+ Dementia Patients
Alzheimer's OC | covid@alzoc.org

ASSIST Program for Isolated Seniors
UC Irvine | 714.497.0315

Virtual Caregiver Support Groups
Alzheimer's Association | 800.272.3900
Alzheimer's OC | 844.435.7259

Food, Housing, Financial Support
211OC | Call 211 or Text Zip Code to 898-211

In Home Supportive Services (IHSS) Hotline
OC Social Services Agency | 714.825.3000 (Dial 4)

Mental Health Support
NAMI Warm Line | 877.910.9276
New Hope Crisis Hotline | 714.639.4673

Upcoming events

Ask the Doc Video Series
Guest Experts from UCI MIND
New Episodes Monthly
UCI MINDcast | mind.uci.edu/mindcast

Spotlight on Care Podcast Series
Steve O'Leary, Virginia Naeve, & Guests
New Episodes Regularly
UCI MINDcast | mind.uci.edu/mindcast

Past education sessions are archived on UCI MINDcast and youtube.com/ucimind