

NEWSLETTER INSTITUTE FOR SUCCESSFUL LONGEVITY

Can Technology Aid Those with Cognitive Decline?

Walter Boot and the ENHANCE Center researcher team are developing tech that could help



Why FDA's approval of Aduhelm for Alzheimer's has many medical experts and researchers alarmed

You may have seen news stories about the controversy over the newest Alzheimer's Disease drug, Aduhelm/aducanumab, recently approved by the Food and Drug Administration, https://www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-alzheimers-drug and later defended in a press release by the FDA after intense criticism: <u>https://www.fda.gov/drugs/news-events-human-drugs/fdas-decision-approve-new-treatment-alzheimers-disease</u>. So, what is the ruckus about?

Typically, for new drugs to be approved under the normal process, they must show efficacy. Efficacy is typically defined as a drug treatment group significantly outperforming a placebo group for the registered outcome. In both of the Phase 3 clinical trials, this was not the case. However, a secondary analysis (an unplanned analysis) showed that at a high dose of Aduhelm there was some (weak) evidence of benefit for the drug group over the placebo.

Nonetheless, in this case the FDA changed to a different criterion from the one that their advisory group was told to consider during their evaluation of the request to approve the drug. FDA changed to a criterion allowed for accelerated approval: https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/accelerated-approval.

Accelerated approval is used for early approval of drugs that treat serious conditions. Alzheimer's disease certainly fits that category, as no drugs currently do much to halt the progressive decline and eventual death seen with this form of dementia. For accelerated approval you do not have to show efficacy for the drug. Rather, you only need to show that it works for what is termed an intermediate clinical endpoint. In the case of Alzheimer's disease, the intermediate endpoint was removal of amyloid plaque in the brain. Why? Because one of the hypotheses about Alzheimer's disease, <u>https://www.nia.nih.gov/health/what-happens-brain-alzheimers-disease</u>, is that it is caused by buildup of amyloid plaques and neurofibrillary tangles.

Amyloid plaques form in the spaces between neurons and interfere with cell function (think of them as poisons). However, every drug that has been shown in clinical trials to reduce amyloid plaques in the brain has failed to show efficacy

FROM THE DIRECTOR



Neil Charness, Ph.D., is the William G. Chase Professor of Psychology, FSU Distinguished Research Professor and Director of the Institute for Successful Longevity.

in terms of reducing the rate of decline in cognitive and behavioral function. In fact, the consistent failure to show either reduced decline, stability, or better yet, improvement following reductions in plaque has led many scientists to question the amyloid hypothesis. That is, they question whether amyloid buildup is the primary disease mechanism or a side effect of the actual agent responsible for the disease.

Some researchers have moved on to considering abnormal tau, a different protein responsible for keeping neurons healthy, as the prime culprit. Tau is used to bind and stabilize microtubules in the neuron. When tau starts binding abnormally with other tau molecules, it forms threads that lead to neurofibrillary tangles. These tangles interfere with neuronal firing, blocking the neuron's transport system, hence damaging its ability to communicate information. Other current suspects include chronic inflammation in the brain, perhaps resulting from microglia and astrocyte cells failing to remove cellular debris, or to the effects of vascular disease that interferes with proper brain function.

In this case, the FDA concluded that "this reduction in plaques is reasonably likely to result in clinical benefit." In fact, it did not show clinical benefit so far, but the FDA is hoping that it will once larger numbers of people with Alzheimer's disease take the drug, a Phase 4 confirmatory trial. The company is required to report back (eventually) on whether there is a benefit. If not, the FDA may recall the drug. In response to that decision, three of the advisory committee members, the group responsible for advising the FDA about the clinical trial results. resigned, and some wrote very negative letters about the decision. Why were they so upset? The 11-person committee had voted 10 against, 1 uncertain. Obviously, changing the rules of the game from efficacy to a different endpoint led to frustration. Also, approving a very expensive drug with no demonstrated clinical



efficacy will be costly to society, here Medicare, which will be forced to offer the drug. Biogen plans to charge about \$56,000 a year for treatment.

In reaction to all the skepticism about the approval process, Dr. Janet Woodcock, acting FDA commissioner, has called for an independent federal investigation into the agency's approval process, and two major health systems, the Cleveland Clinic and the Mount Sinai's Health System in New York City, have said they will not administer the drug: <u>https://www.nytimes.com/2021/07/14/health/cleveland-clinic-aduhelm.html</u>.

Would I consider taking the drug if I were diagnosed, or recommend it for a family member who was diagnosed? The simple answer is no, as it remains unproven in terms of providing clinical benefit. A more cynical view is that the only people who will definitely benefit will be Biogen executives and shareholders.

You can volunteer to help ISL's longevity research

FSU's Institute for Successful Longevity needs research volunteers to help us achieve our mission of improving health and well-being for Florida's aging population.

You can be paid to advance the science of successful longevity, helping your friends and family achieve longer, more productive, and enjoyable lives.

You will be able to choose what studies you participate in.

To volunteer, visit <u>https://isl.fsu.edu/volunteer</u>, or call 850-644-8571, or send an email message to <u>ISL@fsu.edu</u>.

The Institute for Successful Longevity conducts research into how to live longer, stay active and be fully engaged in life. The institute takes a multidisciplinary approach to better explore the complexities of life as an older individual. Learn more at <u>https://isl.fsu.edu/</u>.

Walter Boot and the ENHANCE Center work to create tech to assist older adults with cognitive impairments

The modern technologies at our fingertips — the smartphones and tablets — hold tremendous promise as aids to older adults with cognitive impairment. Now a center co-led by Walter Boot, Ph.D., a Faculty Affiliate of the Institute for Successful Longevity, is working to bring that promise into reality.

With \$4.6-million in support from the National Institute on Disability, Independent Living, and Rehabilitation Research, Boot and a team of researchers that includes ISL Director Neil Charness, Ph.D., are developing novel, cuttingedge technology solutions to help older adults with cognitive impairments live independently and continue to meaningfully engage with their communities.

Boot and researchers at Weill Cornell Walt Medicine and the University of Illinois the I at Urbana-Champaign established a new Med center known as ENHANCE — Enhancing Neurocognitive Health, Abilities, Networks, & Community Engagement — that focuses on older adults living with cognitive impairment, including mild cognitive impairment, traumatic brain injury and post-stroke cognitive loss.

Boot acknowledges that the ENHANCE Center has an ambitious mission. "The center recognizes that as we age there is a diversity of cognitive challenges that older adults face," said Boot, Professor of Psychology at Florida State University. "The center aims to understand those cognitive challenges very broadly, as the issues that people with MCI [mild cognitive impairment] experience may be different from the issues that people with traumatic brain injury experience in older age, which may be different from post-stroke cognitive impairment."

Using a multidisciplinary approach, the ENHANCE researchers are working to both understand these differences and to find similarities among these



Walter Boot, Ph.D., Professor of Psychology at FSU, established the ENHANCE Center in 2019, in partnership with Weill Corness Medicine and the University of Illinois at Urbana-Champaign.



Sara J. Czaja, Ph.D., left, Professor of Gerontology at Weill Cornell Medicine, is co-director of the ENHANCE Center; Wendy A. Rogers, Ph.D., is Director of the Human Factors & Aging Laboratory at the University of Illinois and a principal investigator with ENHANCE.

groups of older adults. "The exciting challenge comes in developing technology to meet the needs of diverse older adults with

cognitive impairment and determining how we can make that technology adaptive and personalized to the problems that that specific person is having," Boot said.

Boot co-directs the center with Sara J. Czaja, Ph.D., Professor of gerontology at Weill Cornell Medicine. Other principal investigators are Charness and Wendy A. Rogers, Ph.D., Director of the Human Factors & Aging Laboratory at the University of Illinois.

The objectives of the ENHANCE Center are to:

- Understand the challenges older adults with cognitive impairments encounter with living activities, determine how these vary according to type of cognitive impairments, and identify needed areas of and preferences for support.
- Identify, develop, and evaluate potential technology solutions.
- Disseminate findings to multiple stakeholders.
- Advance new knowledge in the aging, cognitive disability, and technology space.

Boot's ENHANCE center is working toward those objectives through two research projects and two development projects, as well as a dissemination and training effort.

The research projects are:

- ENACT Everyday Needs Assessment for Cognitive Tasks. ENACT is an exploration and discovery project that aims to understand the challenges older adults with different types and levels of cognitive impairment experience in daily and community living. ENACT also seeks to determine needed areas of and preferences for support, technology solutions currently used or considered, and attitudes toward and difficulties with currently available solutions. The needs and challenges of care partners will also be assessed.
- STRUMM Supportive Technology Resources through Usability & Machine-learning Methods. STRUMM is an exploration and discovery project that will design and preliminarily test the efficacy of an innovative intelligent adaptive software package aimed at providing cognitive and social support to aging adults with cognitive impairments. The



WHAT IS COGNITIVE IMPAIRMENT?

Cognitive impairment refers to changes in cognition that result in difficulties remembering, learning new things, concentrating, making decisions important to everyday life, responding to environmental demands, or understanding social cues, and these difficulties can result in significant disability that limits one or more major life activities.

system will serve as an interactive social and cognitive aid that supports everyday activities, new learning, education about resources, and social engagement.

The development projects are:

- AUGMENT Augmenting User Geocoordinates and Mobility with ENhanced Tutorials. AUGMENT will provide proof of concept that a robust instructional package can support successful use of existing, complex navigation applications, such as Google Maps or the Uber rideshare app, by a diverse set of people with cognitive impairments. AUGMENT will provide proof of product by performing evaluations of the developed instructional packages.
- DREAM Digital Reminders for Everyday Activity Memory. DREAM will first establish proof of concept for an
 adaptive cognitive aid to support the prospective memory of older adults with various cognitive impairments. This will
 involve understanding and verifying product requirements through engagement with stakeholders, implementing and
 testing the concept of an adaptive prospective support system, and resolving technical challenges through user testing.
 Two proof of product studies will examine the use of a prototype within the lab and also within participants' homes.

Boot explained that each of the projects begins with a needs assessment study, which he says is critical. "A lot of technology is being designed by people who don't really understand the problems older adults with cognitive impairments face," Boot said. "A developer might think, 'Oh, I'm going to develop an app and this app is going to help people with mild cognitive impairment or traumatic brain injury,' but unless developers first talk to people with those issues they may not be addressing real needs. They might be designing technology to solve imaginary problems." The needs assessment studies, which involve both individuals with cognitive impairments and their care partners, are in place to help the ENHANCE projects avoid this common weakness.

After the needs assessments comes development of prototypes. "It's a user-centered process," Boot said, "where we develop a prototype and show it to the end users. We have them interact with it and give us feedback. Then we take the prototype and refine it. They give us more feedback, and we go through that cycle of iterative user-centered design until the processes ends with what we think will be the final product."

This process is key to developing technologies that address the needs and concerns of older adults with cognitive losses, Boot said. "You have to make sure it actually works, it meets those needs, and it serves its purposes," he said. The technology is then shared with older adults, who are asked to use it to support their everyday lives. ENHANCE monitors whether those activities are improved by access to the ENHANCE technology. "That's a really exciting part of the projects for me," Boot said, "taking it from the very conceptualization of this technology to making it better over time through continuous user input and then to making sure that it works."

Commercial developers often do not go through this process, Boot said, resulting in products that may not address the needs of those with cognitive impairment or that may not be usable.

Charness, the ISL Director, is going through this process now with ENHANCE's AUGMENT project, developing instructional packages for navigation and rideshare apps. The goal is to create instructions that help individuals use these apps so they can navigate their communities without assistance from their caregivers or others.

The project begins with the needs assessment, through survey questions and a large-scale pilot study. "The first



Neil Charness, Ph.D., Director of the Institute for Successful Longevity and Distinguished Research Professor of Psychology at FSU, is a principal investigator with the ENHANCE Center.

thing we need to understand is, what are the mobility needs?" said Charness. "What are the wayfinding difficulties that older adults with cognitive impairment have?"

AUGMENT is also looking for other factors, such as memory, that could hinder an individual's wayfinding. So in addition to developing tutorials on how to use maps and rideshare apps, AUGMENT may work on assisting people's ability to retain wayfinding information, to overcome any memory difficulties. AUGMENT will soon put together draft tutorials, then begin working closely with a small set of people to refine the tutorials to make them easier to use and more effective. "Once we've

honed that," Charness said, "we'll roll it out to a larger set of individuals."

Charness and his researchers will then take their prototypes to the streets of Tallahassee for a test drive. Working with a group of individuals, they will give half the group a tutorial to help them use navigation apps to find their way and give the other half just a phone or tablet, with no tutorial assistance. The plan is to have the volunteers start at a location on campus (e.g., the Psychology Building) and use Google Maps to walk to a new location on campus (e.g., Dirac Library) and then navigate back. For the Uber app, the goal is to have them summon an Uber ride to go to a target location off campus and then order a second Liber ride to bring them back to the Psychology.

second Uber ride to bring them back to the Psychology Building.

The AUGMENT team will use the results to finetune the tutorials, working toward a final product that is accessible and helps people in their day-to-day navigations. "We didn't design Google Maps, and we didn't design Uber's app, either," Charness said in describing the complexity and hard-to-understand nature of those popular programs. "What we're hoping is that a well-designed tutorial will help people get over the hump and able to use those applications. That's the goal."

ENHANCE is also exploring ways to incorporate social support into its products and to use artificial intelligence to anticipate the needs of individuals over time. While smartphones and tablets are the starting point for its products, ENHANCE is considering alternative means of delivering support. "We could learn throughout our studies that other methods might work better," Boot said. "Perhaps voice interfaces, similar to Amazon's Alexa, but designed considering the needs of people with cognitive impairment might be a better approach." The researchers are open to different forms, he said, and realize that technology changes rapidly. "There could be things on the near horizon that completely change our minds," Boot said.

Throughout their work, the ENHANCE researchers are keeping in mind the problem of design — many products, especially technology products, are not designed to meet the needs of older adults. Boot and Charness have extensive experience and expertise in design for older adults, and ENHANCE has training and dissemination activities to help people understand how to design for older adults with cognitive ENHANCE is part of a network of Rehabilitation Engineering Research Centers supported by the National Institute on Disability, Independent Living, and Rehabilitation Research.

These centers conduct advanced engineering research and development of innovative technologies designed to solve particular rehabilitation problems or remove environmental barriers.

The centers also demonstrate and evaluate technologies, facilitate changes to service delivery systems, stimulate the production and distribution of equipment in the private sector, and provide training opportunities to enable individuals, including individuals with disabilities, to become researchers and practitioners of rehabilitation technology.

impairments. These include webinars for designers and design competitions for undergraduates.

"I think it's the smart thing to do, it's the equitable thing to do, it's the fair thing to do to design technology so that everyone can benefit," Boot said. "But it makes commercial sense, too, when you think about the aging of the population, to make sure that technology benefits everyone of every age." Through its research, development, dissemination and training, ENHANCE is working toward that end.

ISL NEWS BRIEFS

Research center led by ISL Faculty Affiliate Eren Ozguven part of FSU's new Big Bets initiative

A research center led by Eren Erman Ozguven, Associate Professor in the FAMU-FSU College of Engineering and a Faculty Affiliate of the Institute for Successful Longevity, is among three institutes featured in a new Florida State University initiative designed to amplify centers and institutes that are doing high-profile, publicimpact research and connect them with donors interested in pursuing big questions. <u>https://isl.</u> <u>fsu.edu/article/research-center-led-isl-faculty-</u> <u>affiliate-eren-ozguven-part-fsus-new-big-bets-</u> <u>initiative.</u>

Ozguven was recently quoted in the *Palm Beach Post*: <u>https://isl.fsu.edu/article/eren-erman-</u> <u>ozguven-isl-faculty-affiliate-and-director-rider-</u> <u>center-quoted-palm-beach-post</u>.

Brad Schmidt, Distinguished Research Professor, joins the Institute for Successful Longevity

Dr. Norman B. (Brad) Schmidt, Distinguished Research Professor in the Department of Psychology, has joined the Institute for Successful Longevity as a Faculty Affiliate.

His research focuses on the nature, causes, treatment and prevention of anxiety and related psychopathology.

Angelina Sutin quoted in article on how maintaining cognitive abilities

Professor Angelina Sutin of FSU's College of Medicine is quoted in a *Time* article on steps older adults can take to maintain their cognitive abilities. Sutin, a Faculty Affiliate of the Institute for Successful Longevity, tells *Time* of the dangers of social isolation and how hearing loss, common among older adults, can magnify the problem: <u>https://time.com/6053519/how-to-keep-brainsharp-aging/</u>.

ISL Brown Bags for Fall Semester 2021

The Institute for Successful Longevity holds Brown Bag sessions so ISL Faculty Affiliates can share their research on living better, longer lives. These Brown Bags are open to the public and available via the Zoom online meeting platform. For links to the Brown Bag sessions, please send an email message to ISL@fsu.edu.

Here are the Brown Bag sessions for the Fall 2021 semester.

"Who We Are Shapes How We Cognitively Age? Personality & Cognitive Health in Late Life," by Damaris Aschwanden, Ph.D. Monday, September 20, at noon. Dr. Aschwanden is a post-doctoral researcher in the College of Medicine.

"Alzheimer's Disease and Brain Function During Sleep: What Mouse Models Suggest Regarding Memory Loss and Impairments," by Aaron Wilber, Ph.D. Monday, October 4, at noon. Dr. Wilber is Assistant Professor of Psychology & Neuroscience.

"Gender Difference and Medical Factors in Postoperative Outcomes Among Older Patients Undergoing Open-Heart Surgery," by Amy Ai, Ph.D. Monday, December 6, at noon. Dr. Ai is Professor in the College of Social Work.

If you have never used Zoom, the Institute for Successful Longevity has developed guides that show you how to set up a Zoom account and join a meeting.

The guides are easy to follow and are free.

You can read or download our Zoom guides at <u>https://isl.fsu.edu/article/</u> isl-launches-zoom-initiative-help-older-adults-fight-socialisolation.



Damaris Aschwanden, Ph.D.



Aaron Wilber, Ph.D.

ISL Faculty Affiliates Robert Hickner, Michael Ormsbee and team win NIH grant to study resistance training and type 2 diabetes in women

A multidisciplinary team of Florida State University researchers, led by two Faculty Affiliates of the Institute for Successful Longevity, has received a \$3-million National Institutes of Health grant to examine how resistance training may help older

women struggling with obesity to potentially prevent type 2 diabetes.

Professors of Nutrition and Integrative Physiology Robert Hickner and Michael Ormsbee, both ISL Faculty Affiliates, will co-lead the project, which also will include colleagues from the FSU College of Health and Human Sciences and the Pennington Biomedical Research Center in Louisiana as well as the University of Arkansas.

The co-investigators at FSU are Claire Berryman, Ph.D., from Nutrition and Integrative Physiology and Thomas Ledermann, Ph.D., from Human Development and Family Science, in the College of Health and Human Sciences; and Michael Sweeney, M.D., from the Department of Clinical Sciences, in the College of Medicine.



ISL Faculty Affiliates Michael Ormsbee, left, and Robert Hickner have received a National Institutes of Health \$3-million grant to examine how resistance training could help prevent type 2 diabetes.

"Although there are clear health-related

benefits of physical activity, little is known about how resistance exercise, as opposed to endurance exercise, can reduce the risk of metabolic disorders, particularly in women," Hickner said.

Excess body fat can cause insulin resistance, which is the driving factor behind type 2 diabetes. The researchers will investigate how effective resistance training is in improving the metabolic health of postmenopausal women with obesity and pre-diabetes.

The team will work with a group of study participants who will undergo regular training sessions at the university's Functional Movement Clinic. Hickner and Ormsbee designed the resistance training program to target all of the major muscle groups and to expend approximately 300 calories per training session.

"The important piece to understand is that the common exercise prescription for controlling not only body weight, but also body fat, is aerobic (endurance) exercise," Ormsbee said. "However, we also know that resistance training increases fat metabolism and improves body composition.

"The issue is that very few studies have been completed to directly compare endurance to resistance exercise when energy expenditure is equated between the types of training. In addition, due to many changes that occur with menopause and as a result of type 2 diabetes, there is a huge need to understand the most impactful form of exercise to recommend."

More than 34 million Americans have diabetes and about 90 to 95 percent of them have type 2 diabetes. Another 88 million Americans have pre-diabetes, according to the Centers for Disease Control.