



BRAIN INSTITUTE
Oregon Health & Science University

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The C. Rex & Ruth H. Layton Aging & Alzheimer's Disease Center UPDATE

The Layton Aging & Alzheimer's Disease Center is one of 28 NIH Alzheimer's disease centers in the United States and the only one of its kind in Oregon. Our Center is recognized as a national leader in dementia care and research, and is committed to serving the needs of people throughout the Northwest. To find out more about our current clinical studies, contact Lisa Loree: 503-494-7615.

OHSU Brain Institute is a national leader in neuroscience patient care, research and education. We provide the most comprehensive care of the brain, spine and central nervous system in the Pacific Northwest. Our nationally recognized neurological programs and centers offer comprehensive care, advanced research and clinical trial opportunities.

Neurology Research Aided by Health Information Repository

OHSU's Department of Neurology and Layton Aging & Alzheimer's Disease Center are participating in a new information registry. The program will enroll patients who might be willing to participate in research studies focusing on one of a variety of neurological conditions, to be added to the registry. Enrollees will include not only patients with a specific diagnosis, but also those with no disease or symptoms. The purpose of the registry is to add potential research participants to a database that will serve as a primary resource for recruitment to new studies.

Based on the information provided on the consent forms, researchers will be able to quickly identify qualified participants. In addition, those who have signed the consent and are OHSU patients will have the opportunity to check a box on the form indicating their willingness to allow us to review their medical record for confirming eligibility. To date, 196 patients have joined the registry since we started seeking participants in February, 2012.

For information about the Health Information Repository, contact Rhonda Muhly (muhly@ohsu.edu) or Betty Lind (petriko@ohsu.edu).

UPDATE

Adding life to years.

Winter/Spring 2013

A more promising future through dementia prevention

Adapted from the National Institute on Aging booklet, "Preventing Alzheimer's Disease, what do we know?"

Along with keeping our bodies healthy, we all want to keep our minds sharp as we age. Everyone hopes to avoid brain disorders such as Alzheimer's disease (AD).

While there is no definitive evidence yet about what can prevent Alzheimer's or age-related cognitive decline, we do know that a healthy lifestyle can maintain and improve overall health and well-being. Making healthy choices can lower the risk of certain chronic diseases, like heart disease and diabetes, which are risk factors for dementia. As research continues to seek ways to prevent AD, people of all ages can benefit from taking positive steps to get and stay healthy.

Risk Factors for Alzheimer's Disease

Alzheimer's is a complex disease that progresses over many years, like diabetes, heart disease, and other chronic conditions. A number of factors may increase or decrease a person's chances of developing the disease; risk factors include age, genetics, environment, and lifestyle. Research shows that Alzheimer's disease causes changes in the brain years, even decades before the first symptoms appear. One research goal is to find ways to identify who is most likely to develop symptoms of Alzheimer's. Ultimately, we hope to be able to prevent or delay dementia in high-risk individuals.

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Welcome to *Layton Aging & Alzheimer's Disease Center's UPDATE* newsletter. With this first issue of 2013, we introduce a new OHSU Brain Institute format.

We hope you enjoy the new *UPDATE*.



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Exercise and Physical Activity

Exercise and other types of physical activity have many health benefits. We know that physical activities are good for our hearts, waistlines, and ability to carry out everyday activities. Studies also suggest that physical exercise may also play a role in reducing risk for Alzheimer's disease and age-related cognitive decline.

Diet

A diet that includes lots of fruits, vegetables, and whole grains, and is low in fat and added sugar can reduce the risk of many chronic diseases, including heart disease and type 2 diabetes. Researchers are looking at whether a healthy diet also can help preserve cognitive function or reduce the risk of developing Alzheimer's disease.

The Effect of Other Chronic Diseases

Evidence from population-based studies indicates that age-related diseases and conditions—such as vascular disease, high blood pressure, heart disease, and type 2 diabetes—appear to increase the risk of Alzheimer's and cognitive decline.

For example, high cholesterol levels and obesity during midlife—known risk factors for heart

disease—have also been linked to increased risk of Alzheimer's disease. High blood pressure has been shown to be another risk factor.

Keeping Your Brain Active

Staying cognitively active throughout life—via social engagement and intellectual stimulation—is associated with a lower risk of Alzheimer's disease. Several studies link continued cognitive health with social engagement through work, volunteering, or living with others. Mentally stimulating activities such as reading books and magazines, going to lectures, and playing games are also linked to keeping the mind sharp.

Finding Out Who Is At Risk

Several clinical trials of new medications and other therapies have failed to demonstrate improvement in memory and other thinking skills in people diagnosed with Alzheimer's disease.

Now, scientists want to try some of these interventions earlier in the disease process, in cognitively normal people at high risk of developing Alzheimer's, to see if they can prevent or delay the onset of the disease. However, researchers must first figure out which people without symptoms are in fact at



Brain TLC

A series of free, public presentations on prevention of age related cognitive decline

Coming up: Diet and Brain Health

Joseph Quinn, MD
Tuesday, May 8, 2013 7PM

OHSU Center for Health & Healing
3303 Bond Ave. Portland 97239
3rd floor conference center

increased risk of developing the disease. Because the brain damage caused by Alzheimer's begins years before memory loss and other symptoms may become evident, scientists are developing methods to detect biological changes related to Alzheimer's disease at its earliest stages. Researchers are finding that changes in certain proteins in blood and cerebrospinal fluid, along with evidence shown in brain scans, can indicate early Alzheimer's-like changes in the brain. Understanding more about these "biomarkers" may reveal how Alzheimer's disease begins and develops. The study of biomarkers also may help us track whether certain medications have their intended effects early in the course of the disease.

An NIA-led public-private partnership—the Alzheimer's Disease Neuroimaging Initiative (ADNI)—is examining the relationship between these biomarkers and cognitive changes in older participants who are cognitively normal or have Mild Cognitive Impairment or Alzheimer's disease. The Layton Aging & Alzheimer's Disease Center at OHSU is part of this initiative.

For More Information or to read the full report: "Preventing Alzheimer's Disease, what do we know?," find it, and other resource information from:

Alzheimer's Disease
Education and Referral (ADEAR) Center

1-800-438-4380 (toll-free)
www.nia.nih.gov/alzheimers

What steps can I take?

Participate in Research

Whether or not you have signs of Alzheimer's, you can take one more important action—volunteer to participate in clinical trials and studies.

Volunteers make a valuable contribution that will help scientists, people with Alzheimer's, and their families.

People who participate in this kind of research also have regular contact with medical experts who have lots of experience and a broad perspective on the disease.

Stay Healthy

Many actions lower the risk of chronic diseases plus boost overall health and well-being. As we investigate the role they may play in Alzheimer's disease risk, health experts encourage everyone to:

- exercise regularly
- eat a healthy diet rich in fruits and vegetables
- engage in social and intellectually stimulating activities
- control type 2 diabetes
- control blood pressure levels
- control blood cholesterol levels
- maintain a healthy weight
- do not smoke

While we do not yet know if these healthy habits can directly prevent or delay Alzheimer's disease or age-related cognitive decline, these habits have many benefits for overall health and well-being.

To find out about our current clinical studies, please contact Lisa Loree: **503-494-7615**

Alzheimer's research: disappointments and new hope

Attacking amyloid — is it the wrong Alzheimer's fight?

Not long ago, experts were talking about the next generation of “disease-modifying” drugs that were expected to help treat Alzheimer's disease by attacking amyloid plaque in the brain. In fact, they were arguing that any newly written treatment guidelines were likely to be quickly outdated by the advent of new, powerful drugs. Drug companies were also optimistic, developing all kinds of “anti-amyloid” drugs that were expected to fundamentally alter the course of the disease.

“Amyloid” is the stuff that gets in the brain in Alzheimer's disease. The theory is that amyloid is toxic to the brain, setting up the slow burn we know as Alzheimer's disease. Based on that theory, we've assumed that drugs that prevent amyloid from developing, or that promote its removal, are drugs that would be good for treating Alzheimer's.

So the scientists of the world attacked amyloid with a vengeance, generating drugs to clamp down on the enzyme that produces it, to alter the process that causes it to crystallize in the brain, and developing synthetic antibodies designed to find and remove it like heat-seeking missiles. And they designed

and launched clinical studies to prove once and for all that this would work.

This past August, they reported that the drugs did indeed lower the amounts of amyloid in the brains of living patients. This is amazing all by itself when you consider that extracting amyloid from brain tissue at autopsy requires concentrated acid. And it's also amazing when you consider that the ability to monitor amyloid in living patients was a pipe dream just 10 years ago.

But those findings were still a disappointment — because it turned out that although the drugs basically did as they were told, the patients were no better off as a result. Yes, there was

less amyloid in the brain, but patient's brains did not work any better. So, what does this mean? And what do we do now?

Well, it means either that amyloid is not the problem after all, or it means that anti-amyloid strategies have to be started earlier in the game in order to be clinically useful. It also means that what Alzheimer's researchers will do now — at OHSU and across the nation — is test the drugs in individuals who are at risk of Alzheimer's but have either no symptoms or minimal symptoms. That is going to be the new focus in drug development for Alzheimer's: early diagnosis, early intervention.



The challenge of testing new Alzheimer's drugs

We Alzheimer's disease specialists get a lot of free advice. One of the most common recommendations is that we should work on a way to prevent Alzheimer's in healthy people rather than try to fix people who already have brain damage. As I pointed out earlier, all of our latest research results also point toward prevention as a more plausible goal, and our free advisors ask us: What took you so long?

Here is the scenario: If I had a drug that I was sure would work, I could design a study where one group of people got the drug and a second, similar group of people took a placebo. The proof that the drug worked would be a lower rate of Alzheimer's in the drug-treated group compared to the placebo-treated group. So let's say after two years we take a look to see how the treatment is doing. The likelihood, even with a study population over the age of 70, is that the incidence of Alzheimer's disease will be very low in the placebo group, so that it will be impossible to detect any benefit in the active group. Two options for getting an answer

about the drug are to increase the number of study subjects or to increase the duration of the study. Generally speaking, it will take 4,000 subjects treated for five years at a cost of many millions of dollars to get an answer about one drug. And if the answer is "no," then we start all over again, five to 10 years later.

The other way to find out if a prevention drug is working is to start with study subjects who are known to be at high risk for developing dementia. That way, the placebo group's rate of new dementia will be high enough to have a chance of detecting a treatment effect of the drug.

One indicator of increased risk is a memory impairment that is more severe than average (but not as severe as that in dementia, since we are still aiming for prevention). The term now used for people in the category is "mild cognitive impairment", or "MCI", and at first we thought we could test prevention strategies in this population.

Unfortunately, the Alzheimer's rates were still too low in the first several MCI studies, so the research community has worked to identify "biomarkers" that might be used as risk indicators and as criteria for participation in prevention studies. The most common practice now is to restrict participation in prevention studies to people who initially qualify as having MCI based on memory testing, and then also qualify as "high risk MCI" on the basis of biomarker testing. The biomarker may be a gene, a brain scan, or test of spinal fluid. At present, the spinal fluid test is the most practical, even though it involves the volunteer having a spinal tap.

We are now recruiting for several studies for the prevention of Alzheimer's disease, with each study taking a slightly different approach to recruiting people who are at increased risk of developing Alzheimer's.

These articles are adapted from blog posts on the OBI blog (<http://www.ohsu.edu/blogs/brain/>) by Layton Center neurologist, Joseph Quinn, MD.

A big boost for ORCATECH

In December, Oregon Center for Aging and Technology (ORCATECH) leaders presented a business proposal to OHSU's Executive Leadership Team (ELT). In January, the ELT approved and distributed a \$2 million investment to ORCATECH under the Unlocking Value initiative. This investment in ORCATECH recognizes its strong track record of innovative research addressing the health needs of our aging population.

With the home health market estimated at eight billion last year and predicted to triple in size by 2020, the proposal aims to capitalize on ORCATECH's novel and well-established "Living Laboratory" research. The new plan will enable the center to license technologies, test products and provide unique data to developers. The end goal is to commercialize aging-care and health promotion technologies developed by ORCATECH, which could drive significant long-term revenue opportunity.

ORCATECH will build on its relationships with health technology companies to create evidence of what works in the real world, while at the same time expanding the Living Laboratory for further research. In-home home and personal monitoring technologies will be tested with cutting-edge companies, using ORCATECH infrastructure to fast-track development. Continuously collected data for all projects will itself be an important resource for the growing predictive health care, personal medicine and "Big Data" enterprises.

The goal of the Unlocking Value initiative is to generate new revenue by investing in OHSU research areas that demonstrate commercial potential. This new revenue will, over time, help support scientific, educational and other initiatives throughout the university.

For information on technologies for healthy aging, visit:
<http://www.leadingage.org/high-tech/>



Jeffrey Kaye, M.D., is ORCATECH director and director of the Layton Aging & Alzheimer's Disease Center, as well as the Layton professor of neurology and biomedical engineering at OHSU.

"Traditional, current models of research and development are not sustainable. We need to move not only toward novel, more enduring funding structures, but to methods that increase the pace of discovery and translation into practice."

Help Oregon discover new treatments for Alzheimer's disease!



When filling out your tax return this year, please **check the designated box** to donate a portion of your state tax return to fighting Alzheimer's disease.

Every dollar of **Tax Checkoff** donated funds goes to researchers in Oregon. Funds are administered through Oregon Health & Science University under the direction of Oregon Partnership for Alzheimer's Research (OPAR).

The Oregon State Charitable Tax Check-Off fund for Alzheimer's Research, established by the Oregon State Legislature in 1990, helps make it possible for over 100 Oregon scientists to establish their research focus. Donations to The Oregon Alzheimer's Research Tax Check-off Fund come mostly from tax refund amounts, designated by Oregon taxpayers on their state income tax form.

The Fund has typically provides support of up to \$30,000 for one-year projects. Priority is given to investigators just entering the field of dementia research, enabling junior investigators to develop their ideas and gather pilot data. Small pilot grants are critical to securing subsequent research grants from the NIH National Institute on Aging and other national programs.

As an example, the initial Tax Check-off pilot provided the key data to support the VA funding of the Oregon Brain Aging Study, which has gone on to be one of the major longitudinal studies of brain aging in the US. The study has contributed fundamental insights into changes in the brain associated with healthy aging and the earliest signs of Alzheimer's disease. This would never have been possible without the early data showing the feasibility of this approach.

The Alzheimer's Tax Check-Off program is administered by the Layton Aging & Alzheimer's Disease Center in collaboration with the Oregon Partnership for Alzheimer's Research (OPAR). The OPAR advisory committee—volunteer representatives from statewide research and health care institutions—oversees the granting of donated funds each year.

You can support grants to Alzheimer's disease researchers in Oregon by donating directly to the Oregon Partnership for Alzheimer's Research. To do so, visit www.opar.ohsufoundation.org.

For more information about the check-off grant program and the Oregon Partnership for Alzheimer's Research, visit www.ohsu.edu/alzcheck.