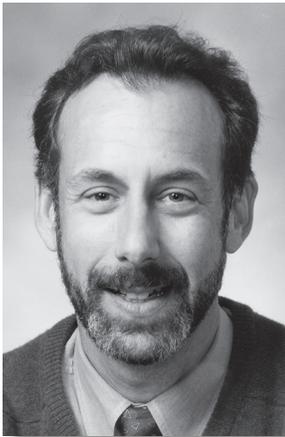


The Aging & Alzheimer's Update

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Marking Milestones in Alzheimer's Research



Fifteen years ago when the OHSU Alzheimer's Disease Center was just beginning to tackle the mysteries of Alzheimer's disease, terms like "senility" and "old-timer's disease" were commonly used to refer to

the memory losses associated with what we now know as Alzheimer's disease. Although Alois Alzheimer first described the now famous first case of "Alzheimer's disease" in 1907, study of this disease did not intensively get under way until the 1990's. In 1990, the OHSU Alzheimer's Disease Center was one of the early federally-funded NIH research centers in the U.S.

These have become a positive example of success in the National Institutes of Health Roadmap for Medical Research initiative, which seeks to improve translation of new knowledge into real improvements in patient care. "We have made considerable progress in understanding Alzheimer's disease," Dr. Elias A. Zerhouni, director of the National Institutes of Health, reports. "Fifteen years ago, we knew none of the genes that cause AD and we had only a limited understanding of the biological pathways involved in the development of brain pathology. Ten years ago, we could not

model the disease in animals. Five years ago, we were not funding any prevention trials and had no way of identifying persons at high risk for the disease. And, as recently as one year ago, we had no way of imaging AD's characteristic amyloid plaques in a living person. Today, we can do all of these things."

Over the course of these 15 years, the Layton Center has become a leader, regionally, nationally, and internationally, in the development of genetic data, animal studies, prevention and treatment trials, and in techniques for identifying individuals at high risk for the disease, such as with neuroimaging technology, all geared toward helping to solve the challenges of dementia. Here is a sampling of the wide range of research conducted at the Layton Center:

Genetics

The Genetics Research Core at the Layton Center has recognized from its inception that genetics provides a powerful tool for understanding the process of brain aging and dementia. The Core supports current research and prepares for the needs of future research by collecting DNA, family history and genotype data on a variety of study populations, including Alzheimer's disease patients and their families, community brain donors, elderly individuals at risk for dementia, and African American elderly.

Two years ago the Layton Center was invited, along with nine other Alzheimer Disease Centers across

the country, to participate in the Late-Onset Familial Alzheimer Disease (LOFAD) Genetics Initiative. This project is funded by the National Institute of Aging, and the primary objective is to maintain a collection of 1000 well-characterized LOFAD families as a national resource for qualified genetics researchers around the world. The Layton Center Genetics Core is a major contributor to this national project.

Animal Models

Animal studies are essential for understanding basic disease mechanisms as well as for research leading to clinical trials in humans. The center has taken advantage of cutting edge technology, which permits the insertion of human genes in rodents, so that human diseases may be “modeled” in mice. Before such models became available, the brains of patients with Alzheimer’s disease were known to harbor lesions including beta amyloid plaques and neurofibrillary tangles, but laboratory studies of these processes could not be conducted because these features do not appear in typical laboratory animals. “Transgenic” animal models with amyloid plaques, neurofibrillary tangles, and apolipoprotein E variants are now available, and are being used by investigators at the Center in order to study disease mechanisms and to evaluate potential treatments for AD. In animal studies, OHSU scientists have found memory-enhancing effects of ginkgo biloba and alpha

lipoic acid. A relatively new model of neurofibrillary tangle pathology is now being studied with funding from Oregon Tax Check-off Program funds (a community-wide research program administered through the Layton Center). This model will be used to evaluate the effects of non-steroidal anti-inflammatory drugs (NSAIDs) on tangle pathology.

Prevention

Preventing Alzheimer’s disease is, of course, the ultimate goal of AD research. Several NIH-funded studies have or are being conducted in this area. The Center’s dementia prevention study is a 42-month-long research trial investigating whether standardized ginkgo biloba extract may prevent or delay cognitive decline in people age 85 and older, the group at the highest risk for developing mild cognitive impairment, a precursor to dementia. Another study that may have significant implications for prevention is examining the effects of fish oil and a fish oil-ALA combination on people who have probable Alzheimer’s disease, and whether these compounds decrease blood measures of oxidation, inflammation and lipid levels, all of which are believed to contribute to dementia and Alzheimer’s disease.

Risk Identification and Diagnosis

Identifying individuals at risk

for Alzheimer’s disease or cognitive decline as early as possible is a major focus of the Layton Center. The Center has studied a variety of approaches: One ongoing study is measuring the levels of a number of proteins in cerebrospinal fluid and in blood to find out whether the levels of these proteins are altered in people who have normal cognitive ability, mild memory problems or early Alzheimer’s disease. Another study is evaluating the relationship between a stress hormone called cortisol and Alzheimer’s disease.

The ability to accurately classify dementia is fundamental to understanding the cause, clinical presentation, and response to therapy. The Layton Center is a leader in the use of neuro-imaging to diagnose and track Alzheimer’s

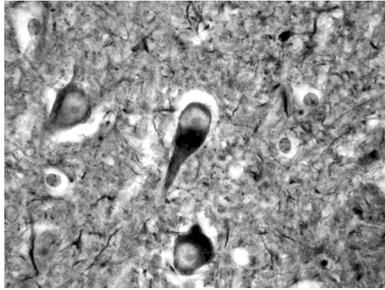
disease. In a study completed this past year, Center scientists found that rates of total brain volume loss may help identify patients with mild cognitive

impairment who are at high risk of developing dementia. It is also one of 50 sites across the country taking part in the NIH Alzheimer’s Disease Neuroimaging Initiative that will compare information from MRI and positron emission tomography (PET) with clinical and neuropsychological assessments.

While numerous advances have been made, pathologic diagnosis based on autopsy tissue remains

The Layton Center is a leader in the use of neuro-imaging to detect and track Alzheimer’s disease

the “gold standard.” The ability of the Oregon Alzheimer’s Disease Center Neuropathology Core to differentiate, characterize, and classify the various forms of dementia has dramatically increased over the last 15 years. For example, we now routinely screen for abnormal accumulations of disease-specific proteins that were unknown a few years ago. In addition, advances in tissue processing allow the characterization and study of several dozen brain regions, or from numerous different patients simultaneously (see figure) further advancing our understanding of the distribution and relationship of certain types of lesions with other types of pathology. Similarly, collaborative studies within OHSU, with other US institutions, and internationally, are helping to further refine our understanding of these diseases with the aim of developing tests that will establish a precise diagnosis early in the disease course to aid in directing appropriate therapies.



In 2003, the Layton Center’s Neuropathology Core joined forces with the University of Washington Alzheimer’s Disease Center to form the Pacific Northwest Dementia and Aging (PaNDA) Neuropathology group. This collaboration will enhance the breadth and scope of research carried out by both centers.

Technology

A relatively new area of research for the Layton Center is the innovative use of technology to enable seniors to remain independent and safe in their homes through the use of computerized, in-home monitoring systems. Center investigators recently received funding for a Roybal Center (see accompanying article in this issue of the Update)

that will allow researchers to assess activity changes in home settings.

As the Layton Center enters the next 15 years, its mission will continue to broaden to encompass the ever-growing number of advancements in clinical care and management of people with dementia and Alzheimer’s disease, as well as the most cutting-edge, productive line of research available to solve the problems related to dementia. The center’s continued success will help it realize its vision of not only adding years to life, but also life to years. We hope you can join us for one of our planned events as we celebrate our first 15 years and what we hope is a brain healthy future.

Layton Center to develop Roybal Center for Applied Gerontology

The National Institute on Aging (NIA), part of the

National Institutes of Health (NIH), recently awarded a unique collaborative group of investigators led by Jeffrey Kaye, MD, Director of the Layton Center, an Edward R. Roybal Center for Research on Applied Gerontology grant. The Center will join five new Centers — at Indiana University, Princeton University, Stanford University, RAND — and four existing Roybal Centers. The OHSU Roybal Center will use new technologies and input from academics, health providers, and community and industry leaders to develop a unique senior community from the ground up, one in which the activities within this community can be studied unobtrusively to examine, in particular, the cognitive well-being of older people as they age.

Using technology to support aging in place is not a new concept. Demonstration houses or laboratories, built by partners in OHSU’s Roybal Center and by others, suggest how technology may transform the aging experience. Studying technology in the real world carries the discoveries of research closer to older people’s true experiences and enhances the relevance of such research.

The Layton Center has become part of a multidisciplinary workgroup, called ORCATECH (Oregon Roybal Center for Aging, Technology, Education, and Community Health). On the public and academic side, OHSU’s Biomedical Engineering Department, Hartford Center for Geriatric

Nursing Excellence, Center for Ethics in Health Care, Center for Healthy Aging, and Oregon National Primate Research Center are key participating members. Industry partners include Intel Corporation, General Electric, Hewlett-Packard and several small companies serving older adults in a variety of ways, including Spry Learning, The Fountains, and Elite Care.

Authorized by Congress in 1993 and named for former House Select Committee on Aging Chair Edward R. Roybal, Roybal Centers are designed to move promising social and behavioral basic research findings out of the laboratory and into programs, practices and policies that will improve the lives of older people and the capacity of society to adapt to societal aging. Established for 5 years, the Centers will receive a total of \$1.8 million in funding in their first year. "Building on a foundation of strong basic findings, this new group of Roybal Centers has the potential to develop highly innovative and practical solutions for a number of very real and pressing problems," said Richard Suzman, Ph.D., Associate Director of the NIA for Behavioral and Social Research.

More information on the national Roybal Center programs, as well as consumer-oriented publications on healthy aging, can be found on the NIA's web site www.nia.nih.gov or by calling 1-800-222-2225.

Pilot study of home monitoring to detect cognitive decline

The Oregon Alzheimer's Disease Center recently funded a pilot study to investigate the use of continuous monitoring to detect changes in activity that may provide early

The Layton Center's continuing mission will be to encompass the ever-growing number of advancements in clinical care and management of people with dementia and Alzheimer's disease

indicators of cognitive decline. This study, conducted by Dr. Tamara Hayes in the OHSU Department of Biomedical Engineering, is part of a larger effort to develop technology and tools which provide for health and wellness assessment in the home setting, and which enable the elderly and chronically ill to remain independent longer.

Prior research has suggested that simple motor measures such as walking speed may be predictive of the later onset of Alzheimer's

disease. However, there could be many reasons that a person has a slower walking speed in the clinic on any particular day. Therefore, it is difficult to assess long-term changes by simply comparing a measure like walking speed from visit to visit. However, if we measure walking speed continuously, then we can understand what is normal daily or

weekly variation for an individual, and are better able to recognize long term trends.

The current study is examining daily activity in the home environment. It uses unobtrusive wireless motion sensors and contact sensors

distributed around the home to detect activity in different rooms. The study will investigate how the variance in walking speed, in total activity, and in patterns of movement around the home differ between healthy elderly and those who have mild cognitive impairment. Early results indicate that daily variability in these measures is much greater for those with cognitive loss than for healthy controls.

If you are interested in learning more about research and clinical drug trials at the Layton Aging & Alzheimer's Disease Center, check our web site (www.ohsu.edu/research/alzheimers) or call Joyce Lear at 503.494.7615.

BRAIN AWARENESS SEASON 2005
**Gray Matters: New Ways of Understanding How the Brain Powers
Life, Love and Society**

OHSU Brain Awareness Season 2005, co-sponsored by OMSI, features a variety of events that reveal and explore how our brains quite literally create our everyday lives. For information on times, locations, and tickets, go online at www.oregonbrains.org, or call 503-418-2515.

Free talks (Registration required)

January 22, 1 – 3 p.m. “A Meeting of the Minds on Stem Cell Research.”

February 26, 8:30 – Noon “The Brain In the Classroom Teacher Workshop”

February 26, 1:30 p.m. “Growing Healthy Young Brains”
(Workshop for parents)

Gray Matters Lecture Series (Tickets required.)

February 1: Music & The Brain

February 8: Emotion, Mood & The Brain

February 15: Computer Technology & The Brain

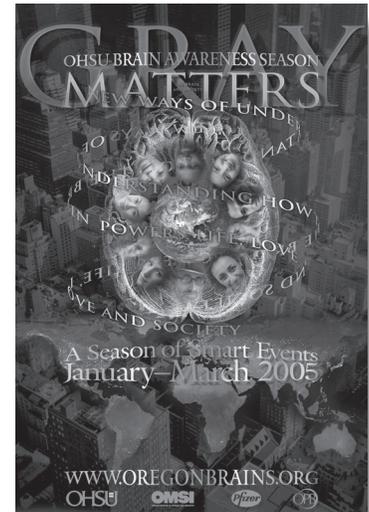
February 22: Sex, Drugs, Rock N’ Roll & The Teenage Brain

March 1: The Once & Future Brain

March 8: Developing Your Child’s Brain

OHSU Brain Fair at OMSI. March 12 and 13, Noon – 5 p.m.

Free. No registration necessary. Fun for the whole family!



Remember Alzheimer’s Research when you do your taxes!
(Charitable Check-offs are at the end of form 40)

The Oregon Tax Check-Off Alzheimer’s Research Fund provides funding for research that will improve our understanding of dementia or that will advance health care treatment or prevention strategies. These funds are made available by Oregonians through the Oregon income tax check-off program.

Applications are evaluated on the basis of scientific merit, with priority given to investigators just entering the field of dementia research and to new or innovative projects. Special attention will be paid to projects that foster collaboration. The program is administered by the Oregon Partnership for Alzheimer’s Research (OPAR), a community-wide research support program that is administered by the Layton Aging & Alzheimer’s Disease Center Education Core. For more information, check out our website (<http://www.ohsu.edu/research/alzheimers/pdf/opar.pdf>) or call Linda Boise at 503.494.6320.

Layton Aging & Alzheimer's Disease Center

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**Please Join Us as the Layton Center Celebrates
15 Years of Research, Education and Patient Care**

The Layton Aging & Alzheimer's Disease Center at Oregon Health & Science University is marking its 15th year with a series of events. We hope you can join us! For information on the Layton Center's 15-year celebration events, call 503 494-6370.

Reception and Celebration at the Layton Center

February 4, 2005,
12:30 p.m. to 2:30 p.m.
13th floor Hatfield Research Center, OHSU

**Buffet lunch and recognition ceremony
Photography exhibit, theater scenes, and
displays**

"Sky....Diamonds"

March 7, 2005, 7 pm
Coho Theater, 2257 NW Raleigh Street, Portland.

A brand new play by Kate Hawkes about living with Alzheimer's disease. For tickets, please call 503-494-6976. Tickets \$10. The play is open to the public.

OHSU Healthy Talk: "Healthy Brain Aging and Alzheimer's Disease"

Saturday, February 5, 2005,
9 am – 12 noon
Old Library Auditorium, OHSU

A panel of experts including Dr. Jeffrey Kaye, MD, Layton Center Director, present current understanding of the aging human brain, who may be at risk for Alzheimer's and what may help delay its onset.