

THE AGING & ALZHEIMER'S UPDATE

THE C. REX AND RUTH H. LAYTON AGING AND ALZHEIMER'S DISEASE CENTER
A NATIONAL INSTITUTE ON AGING ALZHEIMER'S DISEASE CENTER

MAY 2011

How do we know if our brains are fit?

Measuring brain wellness as we age

When it comes to loss of memory and the decline of other mental functions associated with aging, health care providers and their patients need good information to guide proper care and treatment. That is why researchers who investigate brain wellness and aging seek reliable ways to measure brain health. They want to understand the difference between normal, incremental decline and more serious conditions.

Cognitive health is measured in a number of ways. Brain scan (MRI, fMRI and PET) images show structural change and activity the brain tissue. Self-reported problems with thinking or memory provide some clues about brain health. Regularly scheduled memory tests and physical exams at the doctor's office provide snapshots and benchmarks.

Yet, there limitations to all these methods. Is it practical to give everyone a series of brain scans so that we can observe structural changes over time? Are patient perceptions accurate, or do some people worry unnecessarily because they've lost the car keys twice in one week? Maybe your father took memory tests on a particularly stressful day, when the he was not performing at his usual ability.

Can we just look at it?

Brain imaging reveals important information about brain atrophy and the accumulation of pathologies such as the amyloid plaques that are associated with Alzheimer's disease. But scans alone cannot give us a clear picture of an individual's daily health and function. Just one scan does not allow for comparison to what the brain looked like earlier.

Scans may show brain atrophy even though the person does not show any signs or symptoms of cognitive impairment in his/her behavior. Up to 47% of cognitively intact people are found to have moderate to frequent amyloid plaque in their brains.



Adapted from a presentation by Dr. Jeffrey Kaye, M.D. at the American Society on Aging annual conference, April 2011.

Continued on page 2 . . .



OREGON
HEALTH & SCIENCE
UNIVERSITY



Local performance features “Assisted Living”

Retired geriatrician Rich Rubin, M.D. has created a lovely, touching dramatic comedy about the beginning stages of Alzheimer disease. “Assisted Living” will run from June 3rd to July 2nd, 2011 at the Sandy Actors Theatre. The story revolves around Rose, a robust, active woman who resists any help offered to deal with her continued loss of memory. The conflicts with her family are at times hilarious and at other times sad and tender.

Sandy Actors Theatre
17433 Meinig Ave.
Sandy, OR 97055

Performances:
Fridays & Saturdays, 8 p.m.
Sundays, 3 p.m.

Tickets:
General Admission \$15
Seniors (60+) and Students \$12
Children (under 13) \$10

To reserve seats: 503-668-6834
www.sandyactorstheatre.org *

The Layton Aging and Alzheimer’s Disease Center

The Layton Aging and Alzheimer’s Disease Center is one of 30 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.

Volunteering for Clinical Studies

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

How do we know . . .

Continued from front page 1

Can we just ask?

Among self-reported cognitive problems, memory decline is often the first aging concern a patient will report to their doctor. Other common and significant functions that change – reasoning, problem solving, reaction time and effort in learning new things – are often overlooked. Additionally, age-related decline often begins early and changes so slowly as to go unnoticed until a person is older and in worse condition.

Can we just test it?

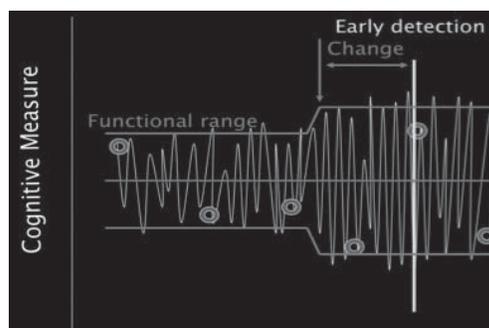
The reliability of cognitive testing is very dependent on when, how and how often it is administered. Frequency, time of day and type of testing can result in variations that do not reflect real differences. Individual variability in cognitive performance testing may also be a marker of accruing problems, yet variability is difficult to capture with infrequent assessment.

Can we just “live it”?

Unobtrusive in-home monitoring can provide a more complete measure of changes in brain and overall health. In-home sensor networks operating in the background measure function directly and regularly. For example, variability in walking speed over time has been shown to be greater in persons with MCI than in healthy older adults.

The future of brain fitness testing has arrived, and it’s right at home!

Technology is now available to bring assessment to the home so that we can measure an individual’s brain fitness in the context of everyday life. Monitoring of activities such as remembering to take medication or playing games on the computer provides continuous and relevant information. Sleep patterns, mood fluctuation, socialization level and physical activity can also be monitored for detection of significant changes over time. Data from such a range of daily activities can be combined for improved continuous assessment of cognitive health and to predict outcomes. The future of brain fitness testing has arrived, and it’s right at home. *



Symptoms may not be reported until well after change has affected function. Variability measurement, which is inherently captured using continuous monitoring technologies may be sensitive to detecting meaningful change, relative to conventional measures.

In pursuing sleep, know this . . .

An ingredient in many sleep aids is known to cause memory problems and confusion in older adults

by Carol Edwards

“A good laugh and a long sleep are the best cures in the doctor’s book,” an old Irish proverb claims. But for some older people, adjusting to age-related changes in sleep is no laughing matter. And those who opt for over-the-counter sleep aids may not realize that these usually include diphenhydramine (Benadryl) — a drug known to have significant side effects in the elderly, including memory problems and confusion.

Understanding that our need for sleep, and the sleep itself changes with age can lessen sleep-related anxiety that fuels insomnia, said Nalaka Gooneratne, MD, DABSM, a Penn Medicine specialist who studies and treats sleep disorders in the elderly.

Older people require less total sleep — about an hour less than in middle age, he said. And the way sleep is produced also changes. “In young people, the body’s core temperature drops slightly a few hours before one’s typical bedtime, signaling the body to rest. As we age, core temperatures don’t drop as much, so there’s less of that physiological drive to sleep.”

But the toughest change for many older people is that “sleep becomes far less ‘consolidated;’ more often punctuated by wakening.” One reason for that is surprising. “Though your general hearing may not be as good as you age, your sleep ‘noise arousal threshold’ drops, Gooneratne said. So those who once slept through the sounds of city traffic or a snoring spouse may now be awakened by it.

Pain from arthritis, heartburn, and other conditions, and the effects of medicines used to treat them, can disrupt sleep. And sleep apnea, abnormal stoppages of breathing that can cause frequent, abrupt wakening “affects nearly one person in 5 over age 60. Muscles in and around the airway slacken with age, especially at rest, blocking air flow,” he said. And sleep apnea is even more common in persons with dementia.

Good information on better sleep for older adults is readily available, Gooneratne said, “and all the basics — keeping your bedroom cool, increasing daily exercise, reducing naps and noise, and no alcohol near bedtime — should be tried before using medications, even OTC ones.”

“If it’s got ‘PM’ in its name, it probably contains diphenhydramine (Benadryl),” said Gooneratne. This drug affects the action of several neurotransmitters in the brain, and is known to cause confusion and other problems in older people. It is cited as a ‘medication to avoid or use within specified dose and duration ranges’ on the Beers Medication list, a guide for pharmacists and physicians to improve medication use in the elderly. “Seniors, especially those with cognitive problems, should be very cautious of medications that affect brain chemistry this way.” ❁



Beware the ‘PM’s’

“As a geriatrician and a memory specialist, I am stunned that diphenhydramine (Benadryl) is still available over-the-counter, in drugs such as Tylenol PM and Advil PM. It may be a reasonably effective sleep aid, but often at the cost of confusion and memory problems for seniors.

Early research in Alzheimer’s disease dosed older adults with diphenhydramine (Benadryl) to mimic the confusion of Alzheimer’s. The data were definitive: diphenhydramine (Benadryl) impaired memory and concentration in the elderly. It can also cause urinary retention, which can lead to infection. Though it’s been around for years, I am convinced that today, if a company applied to the FDA to market diphenhydramine (Benadryl) for over-the-counter use, the FDA would reject the application.”

— Penn Memory Center Associate Director Dr. Jason Karlawish

More on improving sleep at www.nia.nih.gov/HealthInformation/Publications/sleep.htm

This story originally appeared in InSight, the newsletter of the University of Pennsylvania’s Penn Memory Center and Alzheimer’s Disease Center (Fall 2009/ Winter 2010). Reprinted by permission.

Collaborative effort identifies new genes associated with AD

As recently reported in the national press, and by the Alzheimer's Disease Education and Referral Center (ADEAR) announced that scientists have confirmed one gene variant and have identified several others that may be risk factors for late-onset Alzheimer's disease, the most common form of the disorder. In the largest genome-wide association study (GWAS) ever conducted in Alzheimer's research, investigators studied DNA samples from more than 56,000 study participants in the United States and Europe. Investigators at universities and research centers across the country analyzed shared data sets to detect gene variations that may have subtle effects on the risk for developing Alzheimer's.

The National Institutes of Health funded the part of the study involving U.S. data. The Alzheimer's Disease Genetics Consortium (ADGC), a collaborative body established and funded by the NIA, part of the NIH, initiated and conducted the study. Patricia Kramer, Ph.D., of the Layton Aging & Alzheimer's Disease Center is a member of the ADGC executive committee.

OHSU's Layton Center provided DNA samples from over 800 of our research subjects to the effort.

"New technologies are allowing us to look at subtle genetic differences among large groups of study participants. By comparing people diagnosed with Alzheimer's with people free of disease symptoms, researchers are now able to discern elusive genetic factors that may contribute to risk of developing this very devastating disease," reported Richard J. Hodes, M.D., director of the National Institute on Aging (NIA). "We are entering an exciting period of discoveries in genetics that may provide new insights about novel disease pathways that can be explored for development of therapies."

Joseph Quinn, M.D., leader of the Layton Center Biomarkers and Genetics Core, adds, "people often ask me if we are all working together on Alzheimer's disease, or if rivalries are preventing collaboration. This study is an excellent example of cooperation across many sites for a common effort." ❁



Brain autopsy key to understanding the role of genes in AD

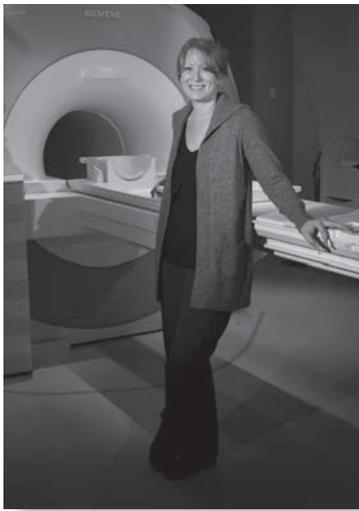
The Layton Center Biomarker and Genetics Core focuses on studies of deceased subjects who have had brain autopsies. For persons who showed cognitive decline (cases), autopsies confirm that subjects have Alzheimer's disease (AD) and not other forms of dementia. For persons who lived out their lives with normal cognitive function (controls), autopsy can be particularly valuable. As many as 30% of individuals identified as controls are found to have AD-related abnormal structures (neuropathology) in their brains. Using autopsy data, we are conducting a genome-wide association study (GWAS) to identify genetic differences between confirmed AD cases and only those controls with no AD neuropathology. This is more specific than the very large-scale study that does not generally include autopsy data.

We are also conducting a GWAS comparing controls with AD neuropathology with controls without neuropathology. These comparisons help us to identify genetic factors that allow some individuals to remain dementia-free even in the presence of AD-related pathology.

Data from research volunteers that includes autopsy is relatively difficult to obtain, particularly for individuals who are cognitively healthy at death. We are fortunate here at the Layton Center that attention has always been given to maintaining a cohort of healthy controls. ❁

Oldest old enter new era of brain research

Dr. Jeffrey Kaye's Oregon Brain Aging Study (OBAS), a longitudinal study of factors related to healthy brain aging, has received a Merit Review Continuation Award from the Department of Veterans' Affairs. The study, now entering its 22nd year, will use the four-year award to focus on understanding the mechanisms related to a major cause of cognitive decline, vascular disease in the brain.



Dr. Lisa Silbert and the Siemens 3T TIM Trio MRI in the Advanced Imaging Research Center at OHSU. A dedicated research-only scanner allows access to new MRI techniques not available in clinical applications.

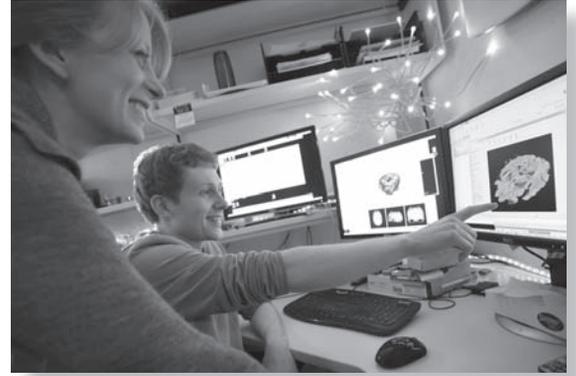
OBAS is a study that tracks cognitive health among a group of "oldest old." The oldest old, defined as persons 85 years or better, are the fastest growing segment of the population. Persons in this age group are also at highest risk for developing dementia.

Thanks to study participants, the OBAS team has examined the trajectory and meaning of aging change for 21 years. Researchers track a range of markers such

as brain volume, clinical profile, genetic data and brain pathology (diseased structures in the brain). As a result, they've identified a latent period of a decade or more during which some individuals appear to have disease markers in the brain, but without showing the outward symptoms of dementia, such as difficulty with daily activities. Images of a person's brain may show, for example, the plaques and tangles associated with Alzheimer's disease, though the person remains very capable of independent living.

Among factors that have been found to lead to cognitive decline, those related to vascular disease stand out. A prominent marker of vascular disease associated with aging, called white matter hyperintensities (WMHs), is often seen on magnetic resonance images (MRI) of the brain. These WMHs show up as bright patches on MRI scans, and are indicative of white matter injury from unknown sources.

During this next research phase, OBAS will focus on improved understanding of these indicators. New, cutting edge brain imaging techniques will allow us to see aspects of the vascular system that could not be seen using older technology. The objective is to identify how and when changes in cerebral blood flow lead to damage of the aging brain, and ultimately, what changes in the blood vessels underlie these changes.



Dr. Lisa Silbert and her research assistant examine WMHs visualized in a 3D model to gain a better understanding of their interconnection.

Comparing new imaging information with the rich history of data from 100 OBAS participants will enable researchers to identify markers that best predict rates of age-related cognitive decline. ❄

Take brain health to heart

Research suggests that what is good for your heart is good for your brain, and may lower your risk of developing Alzheimer's disease.

- **Your numbers count!**
Keep body weight, blood pressure, cholesterol and blood sugar levels within recommended ranges
- **Work your body!**
Physical activity keeps the blood flowing
- **Feed your brain!**
Eat less fat and more fish, fresh fruits and vegetables
- **Jog your mind!**
Engaging in activities that stimulate the mind builds reserves of brain cells and connections

Adapted from Alzheimer's Association's Maintain Your Brain®

Oregon Health & Science University
Mail Code CR-131
3181 S.W. Sam Jackson Park Road
Portland, OR 97239-3098

NON-PROFIT ORG.
U.S. POSTAGE
PAID
PORTLAND, OR
PERMIT NO. 722

THE AGING & ALZHEIMER'S UPDATE

THE C. REX AND RUTH H. LAYTON AGING AND ALZHEIMER'S DISEASE CENTER
A NATIONAL INSTITUTE ON AGING ALZHEIMER'S DISEASE CENTER

LAYTON CENTER DIRECTOR
DR. JEFFREY KAYE, M.D.

EDUCATION DIRECTOR
LINDA BOISE
BOISEL@OHSU.EDU

NEWSLETTER EDITOR
MARY RUHL
RUHL@OHSU.EDU
503-494-6370



OHSU includes the schools of dentistry, medicine, nursing, and science and engineering; OHSU Hospital and Doernbecher Children's Hospital; numerous primary care and specialty clinics; multiple research institutes; and several outreach and community service units.

OHSU protects the privacy of its patients' and research participants' personal health information. If you would like a copy of the OHSU Notice of Privacy Practices, please call 503 494-0444.

OHSU is an equal opportunity, affirmative action institution. 0306(5)

CHARITABLE GIVING
LORI SWEENEY, 503-494-7455
NICOLE GOOD, 503-494-7504