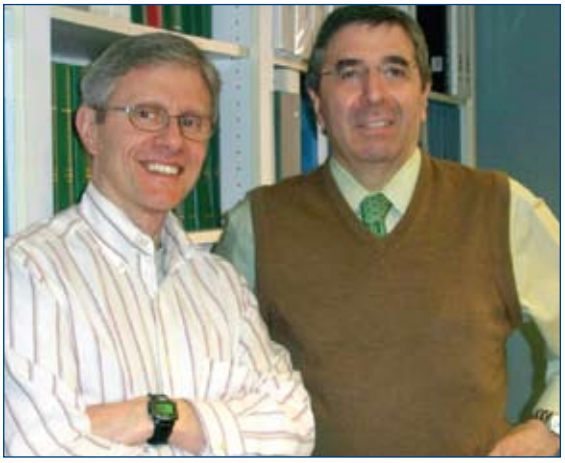
UNIVERSITY OF PITTSBURGH ALZHEIMER DISEASE RESEARCH CENTER

ADRC PATHWAYS

Moving Toward a Cure

Spring 2009

Oscar Lopez and William Klunk Assume Leadership of ADRC



William Klunk (left), ADRC codirector, and Oscar Lopez, director

In the fall 2008 issue of *Pathways*, we announced that Oscar L. Lopez, MD, and William E. Klunk, MD, PhD, would become the new leaders of the Alzheimer Disease Research Center (ADRC) at the University of Pittsburgh. Here is some additional information about the center's new codirectors.

Lopez is a professor of neurology and psychiatry and director of the ADRC. He completed his MD and neurology training in Argentina and a fellowship in behavioral neurology at the University of Pittsburgh. His primary research interest has focused on the distribution (incidence and prevalence), behavioral symptoms, risks, and long-term outcomes of dementia, especially from Alzheimer's disease (AD) and HIV infection.

Lopez's key objectives have been to identify clinical or genetic factors that modify the natural history of dementing illnesses. Lopez has published papers examining the patterns of progression of all clinical forms of AD. Moreover, he also has demonstrated the effects of psychiatric drugs and dementia medications on the progression of AD. Lopez is conducting a large-scale study on the clinical diagnosis of mild cognitive impairment through the Cardiovascular Health Study, and he is principal investigator or coinvestigator of seven National Institutes of Health (NIH)-funded grants.

Lopez has conducted large-scale studies on the clinical diagnosis of AD and vascular dementia, and he published the first integrative overview and outcomes of the clinical diagnosis of Lewy body dementia. He published the first study that linked the presence of Lewy bodies in the amygdala to the development of depression in AD patients. In addition, he is a coauthor of the revised guidelines for clinical and pathological diagnosis of Lewy body dementia.

Klunk is a professor of psychiatry and neurology and codirector of the ADRC. In addition, he is the director of the Laboratory of Molecular Neuropharmacology at Western Psychiatric Institute and Clinic and the director of the National Institute on Aging (NIA)-funded program grant called In Vivo PIB PET Amyloid Imaging: Normal, MCI, and Dementia.

Klunk completed his MD and PhD degrees at Washington University in St. Louis, focusing on neuropharmacology and medicinal chemistry. Klunk then completed a general psychiatry residency and a fellowship in geriatric neuropsychopharmacology at Pitt. He is a member of the Medical and Scientific Advisory Council of the national Alzheimer's Association. He has published more than 100 journal articles and book chapters, is principal investigator of several NIH and foundation grants, and has received a Method to Extend Research in Time Award from NIA.

Klunk is a pioneer in the field of in vivo amyloid imaging in humans. His work ranges from basic synthetic chemistry and neuropharmacological evaluation of amyloid imaging tracers to human PET studies of these tracers. His group's 2004 paper was cited by *Nature Medicine* as the most highly cited research paper published on AD since 2004. He shares with his colleague, Chester A. Mathis, PhD, the 2004 MetLife Foundation Award for Medical Research in Alzheimer's Disease; the 2008 Potamkin Prize for Research in Pick's, Alzheimer's, and Related Diseases; and the 2009 Ronald and Nancy Reagan Research Institute Award for outstanding contributions to the research, care, and advocacy of AD patients and their caregivers.

The Role of the Social Worker

By Amanda Hunsaker, MPH

A social worker is often one of the first people that patients or family members see on a visit to the Alzheimer Disease Research Center (ADRC). The initial goal of Psychiatric Social Worker Thomas C. Baumgartner Jr. and Research Program Counselor Patricia Henderson is to orient patients and their family members to the ADRC.

During their time with patients and families, Baumgartner and Henderson will provide an overview of the research center and the studies that are being conducted. The social workers will gather information about the patient's memory changes and how those symptoms are impacting his or her everyday activities, such as cooking or getting dressed. They also will assess the patient's mood and how the patient and family are coping with life changes.

The safety of the patient is vital for every family entering the ADRC, and social workers can be the key people to assess safety with patients and their families. They will ask questions about the patient's driving and home environment to see how well the patient is functioning in these areas, what supports are in place, and what additional supports might be beneficial.

Once the initial assessment is complete, the social worker, along with the neurologist or another clinician, meets with the patient and his or her study partners, including family, friends, or a case manager, to review the results of the assessment. After the neurologist or other clinician has explained the diagnosis and provided information about treatment, the social worker offers assistance in helping the patient and family to process the meaning of the diagnosis. He or she will provide a packet of educational materials, direct the patient and family to relevant supportive services, and provide information on research studies in which the patient and family may be interested in participating.

Finally, the social worker is always available by phone to the patient and family for counseling and help with navigating services, including disability, support groups, home-based services, and legal support. Social workers see patients and families annually for follow-up assessments and often have an increased role in assessing the patient's mental and emotional status.

In addition to each of these responsibilities, social workers may coordinate medication studies, screen new patients for the ADRC, and assist with autopsy procedures. The ADRC social workers apply all the advanced tools of social work practice to the diagnosis and treatment of memory loss, providing a service that is central to the mission of the ADRC.

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ADRC Mission

The overall objective of the ADRC is to study the pathophysiology (changes in the brain) of Alzheimer's disease (AD) with the aim of improving the reliability of diagnosis of AD and developing effective treatment strategies. The ADRC is funded by the National Institute on Aging and, as part of its research program, provides a comprehensive outpatient evaluation, including medical, neurological, psychiatric, social, and cognitive assessments. A major focus of the ADRC is a commitment by individuals to participate in additional ADRC research studies. Individuals enrolled at the ADRC are encouraged to participate in additional studies in order to be followed by the center.

Volunteers Needed for Research

Identity Study

Description
This trial aims to see whether it can slow the progression associated with Alzheimer's disease (AD) by inhibiting gamma-secretase. Gamma-secretase is an enzyme that can create amyloid-beta, a sticky protein that is believed to kill off brain cells.

Study Phase
Phase 3

Study Length
24 months

Study Requirements
- Age 55 or older
- Diagnosis of probable AD
- Caregiver or family member able to attend all clinic visits with patient

ICARA Study

Description
Bapineuzumab is designed to bind to and remove the beta-amyloid peptide that accumulates in the brains of individuals with Alzheimer's disease (AD). Bapineuzumab is given as a series of injections, delivering antibodies to beta-amyloid. This approach is called passive immunization because the body is receiving the antibodies via the drug rather than generating the antibodies itself.

Study Phase
Phase 3

Study Length
18 months

Study Requirements
- Age 50 or older
- Diagnosis of probable AD
- Caregiver or family member able to attend all clinic visits with patient

Pittsburgh Compound B (PIB) Study

Description
This study will use PET imaging to determine how amyloid changes across stages of severity in Alzheimer's disease (AD) and whether amyloid is present in elderly individuals without memory problems.

Study Length
Varies

Study Requirements
- 30 years of age or older
- Healthy individuals or diagnosis of probable AD or mild cognitive impairment

If you are interested in participating in the Identity and/or ICARA studies, contact MaryAnn Oakley at 412-692-2721 or oakleym@upmc.edu. If you are interested in participating in the PIB Study, contact Claire McConaha at 412-692-2727 or mcconahacw@upmc.edu.

MEG Study

Description
This is a pilot study investigating the use of an imaging technique called magnetoencephalography (MEG) with Alzheimer's disease (AD). MEG is completely noninvasive and U.S. Food and Drug Administration approved. This study aims to determine how sensitive MEG measures are in identifying early AD. This study will help to determine whether the use of MEG might improve early detection and disease monitoring of AD.

Study Length
One to three visits lasting approximately one to two hours each

Study Requirements
- 55–88 years of age
- Right handed
- Diagnosis of AD

Making Sense of MCI: Patient and Family Perspectives

Description
This study aims to learn how those diagnosed with mild cognitive impairment (MCI) and their family members make sense of—or come to terms with—their symptoms and diagnosis.

Study Length
A one-time interview lasting approximately 45 minutes

Study Requirements
Individuals diagnosed with MCI who have a family member willing to answer questions about them

Neural Accumulation Study

Description
This is a functional magnetic resonance imaging study to learn more about neural bases of perceptual decision making. This study aims to learn more about which areas of the brain are involved in learning, memory, and attention.

Study Length
One visit lasting approximately one hour

Study Requirements
- 55–85 years of age
- Right handed
- Diagnosis of mild cognitive impairment

If you are interested in participating in the MEG, MCI, and/or Neural Accumulation studies, contact MaryAnn Oakley at 412-692-2721 or oakleym@upmc.edu.

In Memoriam

The University of Pittsburgh Alzheimer Disease Research Center thanks the following individuals and companies for their generous donations received July 1, 2008, through December 31, 2008.

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In Memory of Stanley Bushkoff
In Memory of Nancy Watson
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Your contributions are greatly appreciated and help to support research and education in the area of Alzheimer's disease. You can remember or honor a loved one by using the envelope enclosed in this newsletter to send in your donation.

Volunteer Study for Caregivers

Self-Management and Resource Training (SMART) Study

Description
This study is designed to determine if a self-management (educational) program strengthens the personal resources (physical and/or mental) of men and women living with a family member who has cognitive impairment (MCI or dementia).

Study Length
13 months

Study Requirements
Spouse or living partner of an individual diagnosed with mild cognitive impairment (MCI), Alzheimer's disease, or a related dementia

For more information, contact MaryAnn Oakley at 412-692-2721 or oakleym@upmc.edu.

Visit Our Web Site

For up-to-date information about the Alzheimer Disease Research Center, the autopsy program, clinical trials, and community presentations, please visit www.adrc.pitt.edu.

If you no longer wish to receive issues of *Pathways*, please contact MaryAnn Oakley at 412-692-2721 or oakleym@upmc.edu.

Investigating the Connection between Sensory-based Decisions and AD

By Mark E. Wheeler, PhD

The aim of the research I conducted is to understand how sensory events are transformed into decisions and actions and how the ability to make sensory-based decisions is affected in healthy aging and in Alzheimer's disease (AD).

Sensory-based decisions are a routine part of life. From a distance, the route number on an approaching bus may be visible but not legible. Is it the 500 or the EBO? As the bus approaches, the route number eventually becomes apparent: It is the 500. Time to get in line. Sensory-based decisions like these also occur when matching socks, identifying when it is safe to cross a busy road, and searching for a specific exit sign on the highway.

Early stages of AD are marked most notably by memory impairments. However, research also indicates that perceptual systems are affected, in some cases impairing the ability to make routine sensory-based discriminations effectively. How are these decisions made, and in what ways can AD affect the integrity of brain systems that support them?

Research in my lab investigates these questions using functional magnetic resonance imaging (fMRI). An fMRI measures changes in blood oxygen levels, which are related to changes in neural processing. Studies conducted in young adults indicate that sensory-based decisions involve a series of information processing stages in which incoming sensory details (letter and number forms) are analyzed, evidence related to a goal (identifying the route) is gathered, and a decision about a course of action (get in line) is reached.

These stages are supported by different areas of the brain, including sensory areas that can be affected early in the progression of AD. Atypical function in any of these brain areas could impair the effectiveness of decisions. Ongoing research is investigating how these areas operate in people at risk for developing AD relative to those of healthy younger and older adults. By understanding which systems are affected early in the progression of AD, it may be possible to identify neural factors that differentiate between normal and pathological development.

For more information about this study, please contact MaryAnn Oakley at 412-692-2721 or oakleym@upmc.edu.

alzheimer's association®

Early Onset Support Group Now Available

The Pittsburgh office of the Alzheimer's Association Greater Pennsylvania Chapter is happy to offer a new type of support group. The new group is specifically for individuals who have been diagnosed with early onset Alzheimer's disease (age 65 or younger).

If you, a loved one, or a friend is interested in joining this support group or would like more information, please call Lois Lutz at the Alzheimer's Association at 412-261-5040.

The Greater Pennsylvania Chapter has more than 160 support groups in the 59 counties it serves. Most of these groups aim to educate and help caregivers with family members or friends who have Alzheimer's disease.

Staff Spotlight

Physician Assistant

Carolyn Rickard, PA-C

If you ask Carolyn Rickard what the most rewarding part of her job is, she will tell you that it's the time she spends with Alzheimer Disease Research Center (ADRC) patients and their families.

Rickard has worked as a physician assistant at the ADRC since 1999. Her primary duties are working with the physicians to complete initial evaluations of new patients, performing follow-up interviews and neurological exams, and discussing recommendations with ADRC participants and their families. In addition, Rickard is a study coordinator for clinical medication trials.

Before joining the ADRC, Rickard was employed in the internal medicine department at Western Psychiatric Institute and Clinic and in a private practice prior to that. She obtained her physician assistant training and degree at Alderson-Broaddus College in Philippi, W.Va.

Rickard has two children, a son in his third year of college studying mechanical engineering and a daughter who will graduate from high school this year. In her spare time, she enjoys spending time with friends and family and going to movies, concerts, and musicals.

New Pilot Study Will Test if Mentally Stimulating Activities Really Do Prevent or Slow Mental Decline

By Beth Snitz, PhD

Many people have heard of the idea that staying mentally active is important for older adults to maintain good health and prevent Alzheimer's disease. "Brain fitness" is getting a lot of coverage in the media these days, and there are now many new books and video games, such as Nintendo's Brain Age, devoted to the idea of keeping the brain fit to ward off disease in older age. But is there scientific evidence for such claims?

Well, there is good evidence from studies of people who have reported on their own daily activities and lifestyle habits that keeping mentally and physically active does indeed appear to reduce one's risk for developing dementia. But, surprisingly, there have been few formal studies done that use mentally stimulating activities as an intervention to prevent or slow mental decline, similarly to the way clinical trials are conducted to investigate new drugs.

A new pilot study at the Alzheimer Disease Research Center (ADRC) aims to test the feasibility of a cognitive stimulation computer program for people with mild memory or cognitive problems. ADRC patients who have been diagnosed with having a mild cognitive disorder and who have previously had a brain scan known as a PIB scan may be eligible to participate.

Participants will play various games having to do with concentration, memory, solving puzzles, and logic on an Internet program from their homes for 12 weeks. They also will undergo a series of neuropsychological tests and complete questionnaires before and after they complete the study. ADRC investigators hope to learn whether this Internet-based kind of program is feasible for patients to complete independently in their homes and whether there seem to be any benefits to thinking and memory, daily functioning, and quality of life. If you are interested in finding out more, please contact ADRC Recruitment Coordinator MaryAnn Oakley at 412-692-2721 or oakleym@upmc.edu.

Supplement Fails to Show Benefit in Preventing Dementia in the Elderly

The dietary supplement ginkgo biloba was found to be ineffective in reducing the development of dementia and Alzheimer's disease in older people, according to a study published in the *Journal of the American Medical Association*.

Researchers led by Steven T. DeKosky, MD, formerly of the University of Pittsburgh and currently vice president and dean of the School of Medicine at the University of Virginia, conducted the trial known as the Ginkgo Evaluation of Memory (GEM) Study at four clinical sites over the course of eight years. GEM is the largest clinical trial ever to evaluate ginkgo's effect on the occurrence of dementia.

For more specific information on the results of this trial, visit the Alzheimer Disease Research Center Web site at www.adrc.pitt.edu.

Klunk and Mathis Receive Ronald and Nancy Reagan Research Institute Award

Chester A. Mathis (left) and William Klunk

Chester A. Mathis, PhD, and William Klunk, MD, PhD, ADRC codirector, have received the 2009 Ronald and Nancy Reagan Research Institute Award for their outstanding contributions to the research, care, and advocacy of Alzheimer's disease (AD) patients and their caregivers.

The Alzheimer's Association—the largest voluntary health organization dedicated to finding prevention methods, treatments, and an eventual cure for AD—presented the award to Klunk and Mathis at an association gala in Washington, D.C., on March 25.

Klunk and Mathis have developed experimental noninvasive methods of detecting and creating images of beta-amyloid proteins (plaques that form in the brain tissue of AD sufferers) using dyes to make the plaques visible through the use of medical imaging equipment. The ability to see amyloid deposits in living patients will enable researchers to measure directly the effects of anti-amyloid therapies now being developed.

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Ask the Medical Professional

Q. Our doctor says that my husband has dementia. What is the difference between dementia and Alzheimer's disease?

A. Dementia is the loss of intellectual functioning—thinking, remembering, and reasoning—to such an extent that it interferes with a person's daily life and activities. Dementia is an umbrella term that embraces a number of conditions. Alzheimer's disease (AD) is one kind of dementia that is caused by physical, nonreversible changes in the brain.

There are many other kinds of dementia besides AD. Lewy body disease, Pick's disease or frontotemporal dementia, and vascular dementia (related to small strokes or transient ischemic attacks) are other types of dementia. Pseudo dementias can occur when other conditions (depression, thyroid disease, malnutrition, infections, or the use of certain medications) are present and similar symptoms are exhibited. These pseudo dementias often are treatable, and when such symptoms occur, a thorough medical evaluation is always a good first step to take.

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