Amyloid Imaging and Alzheimer’s Disease Research

Diagnosis of Alzheimer’s Disease

Did you know that doctors currently cannot definitively diagnose someone with Alzheimer’s disease (AD) until after they’ve died? Whether or not the patient’s dementia is caused by AD cannot be known for sure until an autopsy finds the hallmark signs of AD pathology: amyloid plaques and neurofibrillary tangles. Since the symptoms of AD can be similar to those of many other neurodegenerative diseases and disorders, it is not uncommon for patients to be misdiagnosed, rendering treatments ineffective. Thus, finding a way to definitively diagnose patients with AD is absolutely critical.

Alzheimer’s Disease Neuroimaging Initiative

The Alzheimer’s Disease Neuroimaging Initiative (ADNI), a collaborative study with over 60 research centers in the US and Canada, began in October 2004 with an objective of increasing our understanding about the progression of AD. This study utilizes brain scans, genetic profiles, and biomarkers in blood and cerebrospinal fluid to diagnose AD and monitor those who are at high risk for developing AD. There are over 800 participants in this study, including 10 volunteers at the Stanford/VA ACRC. After five years of study, ADNI has developed a standardized approach for the use of neuroimaging, biomarkers, and behavioral tests in the diagnosis and monitoring of Alzheimer’s disease. In addition, ADNI established the feasibility of incorporating a potentially revolutionary technique called amyloid imaging into the ADNI approach.

Amyloid Imaging

Amyloid imaging is a neuroimaging method in Alzheimer’s research that allows researchers to visualize amyloid plaques in the living brain. Amyloid plaques are caused by the accumulation of beta amyloid between brain cells. Beta amyloid is a protein fragment that is produced and subsequently broken down and eliminated in healthy brains. In the diseased brain, beta amyloid is not broken down properly and starts to build up, eventually forming the hard plaques that are characteristic of AD pathology. Along with neurofibrillary tangles, amyloid plaques are believed to be a major indicator of brain cell injury leading to AD. If doctors were able to check for amyloid plaques in a living brain, the absence of amyloid plaques in a demented patient could potentially exclude a diagnosis of AD, making it clear that other courses of treatment would be more appropriate. Additionally, the ability to see these amyloid plaques in a living brain could be a very important step towards providing a definitive diagnosis of AD.

Amyloid imaging involves an injection into the bloodstream of radiolabeled compounds that bind to the amyloid plaques in the brain and can then be visualized using a PET scanner. In 2004, results from the first human study using an amyloid-binding tracer called Pittsburgh Compound-B (PIB) were published (Klunk et al. 2004). This study observed higher
There are issues unique to individuals with memory changes and to their family members. We are trying to learn how to better address these issues by developing new services and providing support groups that meet the needs of individuals with memory problems and their families. We are involved in ongoing development of support groups to achieve these goals. Currently the following groups are available at our center:

Caregivers Support Group
This is a small group designed to provide educational information and answers to individual questions and concerns of caregivers. It also provides a network to offer support and guidance. Since this is a small group we do request regular attendance to the meetings. The group meets on the 2nd Friday of each month from 1:00 p.m.-3:00 p.m. If you are interested in the group or would like additional information, please contact Helen Davies, MS, APRN, BC at (650) 858-3915.

Mild Cognitive Impairment Group
This group is designed for individuals with a diagnosis of mild cognitive impairment (symptoms not meeting criteria for dementia) and their family members or friends. This group focuses on 1) education, 2) communication, 3) management, and 4) psychosocial concerns. The group meets bi-monthly on Wednesdays from 11a.m. - 12:30p.m. For further information, please contact Helen Davies at (650) 858-3915.

Educational Seminars
These are monthly informational/educational seminars given by professional staff addressing a variety of topics pertinent to memory loss and caregiver issues. These seminars are open to all participants and their caregivers and will include a question-and-answer session. Seminars meet on the fourth Wednesday of each month from 10-11a.m. For further information, please contact Helen Davies at (650) 858-3915.

All groups meet at the
VA Palo Alto Health Care System
3801 Miranda Ave., Bldg. 6,
2nd floor Conference Room (room C258)
Palo Alto, CA 94304

For more information, please call
(650) 858-3915 or (650) 493-5000, x 65051
http://svalz.stanford.edu/groups.html

Continued from previous page

levels of amyloid plaques in Alzheimer’s patients compared to controls. Researchers continue to use this compound to study amyloid plaques, but due to the 20-minute half life of the PIB radiolabel C11, it can only be used at a few sites with the necessary (and very expensive) equipment. Radiochemists have been developing F18-labeled compounds, whose longer half-lives will enable easier and more cost-effective translation into the clinic. Bayer HealthCare is sponsoring a trial at Stanford evaluating the uptake of an F18-labeled amyloid imaging compound in participants who are 55 years and older and healthy, or who have probable AD. ADNI will also be adding a similar F18-labeled amyloid tracer called AV-45 (developed by Avid Radiopharmaceuticals) to its study protocol. ADNI will investigate its potential to contribute to a differential diagnosis of AD when added to the neuroimaging, biomarkers, and behavioral tests already being collected.

Early Detection of Alzheimer’s Disease
In addition to employing amyloid imaging technology, the new ADNI study (ADNI-GO) is focusing on the early detection of AD to examine who is at the highest risk for development of AD. Several studies have shown that amyloid level in the brains of patients with mild cognitive impairment (MCI) is associated with developing AD. A longitudinal study (Wolk et al. 2009) showed that after only 21 months, 5 of 13 MCI subjects with high levels of amyloid at baseline had already developed Alzheimer’s disease. In addition, no one with low amyloid developed AD. Amyloid alone may not cause AD, but this and other research suggests that an increase in amyloid plaques is an essential step in the development of the disease. The measurement of amyloid levels could be an invaluable tool in the early detection of the disease.

Due to the evidence of increased amyloid plaques in many normal elderly subjects, scientists have hypothesized (Jack et al. 2009) that amyloid slowly accumulates over the course of 20 to 30 years, during which time there is little or no evidence of any
Spotlight: Maheen Mausoof Adamson, PhD
Neuroscience Researcher at Stanford Aviation Safety Laboratory/ Deputy Director, Data Core, War-Related Illness and Injury Study Center (WRIISC)/ Instructor, Psychiatry & Behavioral Sciences, Stanford University

Maheen Adamson has been at the Stanford/VA Aging Clinical Research Center (ACRC) since 2005. After completion of her training as a cognitive neuroscientist, she worked as a staff research coordinator at UCLA Alzheimer’s Disease Research Center for six months while teaching as an adjunct professor of cognitive psychology at CSU Fullerton. In 2005, she joined the ACRC as a post doctoral fellow under the research mentorship of Dr. Joy Taylor. Her time as a fellow sparked her interest in the effects of genetic risk, skilled learning, and expertise on brain structure and function of older pilots. This research has led to several publications and presentations.

In her current position as Deputy Director, Data Core of the WRIISC (War-Related Illness and Injury Study Center), Dr. Adamson is involved in several collaborations that utilize state-of-the-art neuroimaging methods, along with clinical and cognitive testing, that improve the diagnosis and treatment of illnesses affecting our veterans, such as Traumatic Brain Injury and Post-Traumatic Stress Disorder. She is also involved in several projects at the Stanford/VA ACRC. For instance, she is designing a functional neuroimaging study of flight simulator performance in older pilots under the guidance of Dr. Jerome Yesavage. She is also recruiting healthy older adults for a behavioral study where she is exploring navigational abilities of older individuals through a computer gaming task (If interested in participating, please call (650) 493-5000 ext.62179.

Dr. Adamson is honored to work with world renowned researchers as her mentors and is equally gratified to work with a patient and subject population that is always keen to participate in her studies. Apart from writing grants in her free time, Dr. Adamson loves to watch movies, cook exotic dishes, travel to foreign lands and play with her 8 month old daughter and six year old son.

---Michelle Farrell

Special thanks to Dr. Ansgar Furst for his assistance and expertise, and to Dr. Minal Vasanawala for her contributions regarding the Bayer study.

References:


RESEARCH OPPORTUNITIES

Memory in Older Adults

This project is designed to look at how mood and worry affect memory in older adults.

It involves 4 hours of testing now and again one year later. Each testing session pays $40 -- a total of $80 for completing both testing sessions (now and a year later).

You may be eligible to participate if:
• You are 65 and older.
• You are interested in memory testing.
• You have not been diagnosed with dementia.

To sign up for this study, contact:
Sherry Beaudreau
(650) 493-5000 ext. 64119

ICARA study

This research study – ICARA – is now under way to explore a possible new investigational treatment for Alzheimer’s disease. In addition to receiving study-related physical exams and laboratory services at no charge, participants may receive study medication and will be monitored by a medical team, including a nurse or study coordinator and a physician. You may be eligible to participate in the ICARA study if you:
• Are 50 to 88 years old
• Have a diagnosis of probable Alzheimer’s disease
• Have a study partner- a friend or relative who can accompany the volunteer to all clinic visits.

To sign up for this study
Contact: Ansgar Furst
(650) 493-5000 ext. 68652

Citalopram for Agitation in Alzheimer’s Disease

The goal of the study is to learn if Citalopram is helpful to people with Alzheimer’s disease who are experiencing significant symptoms of agitation. Participation is expected to last a maximum of four months.

You may be eligible to participate if you:
• Have a diagnosis of Alzheimer’s disease.
• Are experiencing significant levels of agitation.
• Have a study partner available to attend all study visits.
• Are proficient in written and spoken English.

For more information,
Contact: Jeffery Newell
(650) 493-5000 ext. 23764
RESEARCH OPPORTUNITIES

Longitudinal Sleep Study

This observational study is designed to look at sleep/wake patterns in persons with memory problems over the course of time. Once a year, this study will collect a 1 week record of your sleep, in your own home. No treatment is involved.

Participants should:
- Be 55 years or older
- Have memory impairment or dementia
- Live at home with a caregiver/study partner

To sign up for this study
Contact: Deryl Wicks
(650) 493-5000 ext. 64052

Memory Screening

This project is developing an approach to screen for memory problems in group sessions.
Each screening session:
- Begins with a brief talk on memory & aging
- Involves simple memory games many enjoy
- Reviews your results and concerns with staff

Please call for the next Memory Screening Session.

The Alzheimer’s Disease Neuroimaging Initiative is a nationwide study with the goal of determining whether imaging of the brain (through MRI, PET and amyloid imaging scans) can help predict and monitor the progression of mild cognitive impairment (MCI) and Alzheimer’s disease. In addition to neuroimaging, the study will collect and test blood and cerebral spinal fluid to determine if biomarkers can contribute to disease prediction and monitoring.

Participants should:
- Be between 55 and 90 years of age
- Be in general good health but with memory concerns
- Be fluent in English
- Have a study partner- a friend or relative who can accompany the volunteer to all clinic visits.

To sign up for the study
Contact: Michelle Farrell
(650) 849-0491

ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE
**RESEARCH OPPORTUNITIES**

We are interested in navigation abilities in cognitively healthy adults from the general population. We will be using memory tasks involving objects and words, including a computer game that asks you to “drive” around a town as a taxi driver. Your participation will help us develop memory tasks that can be used in future studies of brain imaging.

Eligible participants:
- Male or female cognitively healthy participants between the ages of 45-75 years.
- No prior stroke, mental illness, major depression or other neurological disorders
- Prior experience using a computer

To sign up for this study
Contact: Maheen Adamson
(650) 493-5000 ext. 62179

This study investigates the use of various support services among patients with Probable or Possible Alzheimer’s disease and their caregivers. Services include: patient and caregiver support groups, adult day care, overnight respite care, and family members for respite.

The study looks at determinants of service use and whether participation in these programs slows the rate of decline and delays time to institutionalization.

This multi-site observational study evaluates the effectiveness of anti-Alzheimer’s medications in patients with Probable AD, Possible AD, and Mild Cognitive Impairment.

Participants are followed for at least one year at one of 11 participating study sites in California. Their treatment regimens are determined by their individual physician according to his or her usual criteria.

Initial findings show a moderate treatment effect in Caucasian patients taking donepezil for 1 year. These findings were similar to those of a landmark Nordic randomized clinical trial. Phase 2 of the Medication Reassessment Study focuses on the 1-year effectiveness of donepezil in minority patients in both community and VA settings.

To sign up for this study
Contact: Helen Davies
(650) 493-5000 ext. 65051
Research Results

Since 1989, the Stanford/VA Alzheimer’s Research Center has been studying changes in marital relationships when one partner is diagnosed with Alzheimer’s disease. Our past research has looked at erectile dysfunction, communication problems after diagnosis, and inappropriate sexual behaviors, among other topics. Research findings have indicated that older adults continue to be sexually active well into later life and more professionals need to be trained to discuss sexual issues openly.

We are currently working on a manuscript evaluating gender differences in sexuality and intimacy in marital relationships affected by Alzheimer’s disease. This study is different from our previous research because it takes into account both caregiver well-being and various patient factors, including cognitive, psychiatric, and behavioral issues.

Analysis is still underway, but our results thus far show that male patients had more trouble than female patients staying engaged in sexual activity without getting distracted or losing arousal. Overall, male patients were more easily distracted than female patients. As difficulties with sexual performance and levels of distraction in male patients increased, sadness in female caregivers also increased.

Our study highlights the importance of improving sexual and intimate relations among AD patients and their caregivers, particularly early in the course of disease progression. Health care professionals should be aware that both male and female patients and caregivers may have different needs and should address them accordingly. Helping caregivers cope with these changes may delay nursing home placement, as sexual and emotional dissatisfaction may play a significant role in a caregiver’s decision to relocate their spouse.

Make a difference: Help end Alzheimer’s Disease!

A contribution to the Aging Clinical Research Center is a gift to future generations in our quest to cure Alzheimer’s disease. Your generous support ensures that the Center continues to conduct top-quality clinical research to improve treatment options and to provide education and support for patients and families. With your help, our clinical researchers investigate the causes of memory loss and neurodegeneration, develop and test better treatments for Alzheimer’s disease, and share these discoveries with the local community and with scientists around the world.

Tax-deductible contributions can be made by check, payable to: Stanford University
Please indicate Stanford/VA Aging Clinical Research Center in the memo line.

Mail your contributions to:
Jerome Yesavage, MD, Director (151Y)
Stanford/VA Aging Clinical Research Center
3801 Miranda Avenue
Palo Alto, CA 94304

Gifts may be made in honor of someone’s special occasion or in memory of someone who has passed away. Please provide the name of the person you wish to honor, as well as the name and address of anyone whom you wish to receive an acknowledgement of the gift.

For additional information about the Stanford/VA Aging Clinical Research Center and opportunities to contribute, call (650) 852-3287. All donations are tax-deductible.
UPCOMING EVENTS

Updates on Dementia Conference
When: Tuesday, May 18, 2010, 8am - 4pm
Where: Crowne Plaza Hotel, Foster City, CA
Register at: http://edconference.kintera.org/fostercity

Speakers this year include William Jagust, MD on “New Models for Diagnosis and Treatment of Alzheimer's Disease”; Elizabeth Brawley, AAHD, on “Raising the Bar in Environments for Alzheimer's”; Sandra Black, MD on “Vascular Cognitive Impairment”; and a panel discussion on “Risk Factors for Dementia in Latino Populations”.

Memory Walk
There are two Memory Walks in the Bay Area this year: September 11, 2010 in San Francisco, and September 25, 2010 in San Jose. More information will be in the Fall issue. Plan to join our team at one of these walks!

Memory Screening Day
Tuesday, November 16, 2010 10am-11:30am, VA Palo Alto Health Care System, 3801 Miranda Avenue, Palo Alto, CA in Building 5, 4th floor conference room.

National Memory Screening Day is part of a national effort to promote early detection of Alzheimer’s disease and related illnesses, and to encourage appropriate intervention, including medical treatments, social services and other resources. Memory screenings are a significant first step toward early diagnosis. To register for a memory screening at the Stanford/VA Aging Clinical Research Center, call (650) 852-3287.

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650-852-3287
Visit us on the web:
Aging Clinical Research Center (ACRC): http://alzheimer.stanford.edu
Stanford/VA California Alzheimer’s Center: http://svalz.stanford.edu
Sierra-Pacific MIRECC: http://www.mirecc.va.gov/visn21/

To add or remove your name from our mailing list, call (650) 852-3287 or visit the ACRC web site.

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This newsletter is supported in part by grants from the National Institute on Aging, the Sierra-Pacific Mental Illness Research, Education, and Clinical Center (MIRECC), the Alzheimer’s Disease Program of the State of California, and the Department of Veterans Affairs Medical Research Service.