THE ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE
HELPING TO UNLOCK THE MYSTERIES OF MEMORY CHANGES

Are we on the threshold of developing biological test standards that could detect early changes in memory function before significant symptoms of dementia occur?

Will these standards be useful in improving the effectiveness of future Alzheimer’s disease prevention studies?

We hope to answer these questions as we embark on a landmark research project - The Alzheimer's Disease Neuroimaging Initiative (ADNI) study. The initiative is being undertaken to find the most effective methods for tracking physical changes in the brain and in body fluids during the course of Alzheimer's disease and to establish those methods as clinical standards. These standards would then be used during clinical trials to assess the effectiveness of new Alzheimer's medications, which in turn could lead to more efficient trials and faster approval of medications.

According to Dr. Adam Fleisher, the Principal Investigator of the UCSD site, “This is the first study of its type to develop standardized imaging and biological markers for early diagnosis of memory changes seen in the brain that lead to Alzheimer's disease. This information is..." (Continued on Page 2)

DR. ROBERT KATZMAN HONORED

In 1976, Dr. Robert Katzman, our first Alzheimer’s Disease Research Center (ADRC) Director, wrote an editorial in the Archives of Neurology that identified Alzheimer’s disease as a major public health issue. The editorial was titled “The Prevalence and Malignancy of Alzheimer Disease: A Major Killer” and served as the first significant call to action to find the causes, treatment, and cure for this devastating disease. On the 30th anniversary of this famous publication, the Shiley-Marcos ADRC will honor the legacy of Robert Katzman by hosting a conference on the "Epidemiology of Alzheimer's Disease" on April 28-29, 2006.

Dr. Katzman was raised in Denver, Colorado as the son of a physician. After service in the U.S. Navy as an electronic technician's mate, he attended college at the University of Chicago, where he became interested in the chemistry of the brain. There were no classes on this topic, so he decided to go to..." (Continued on Page 3)
If you feel you may qualify for this groundbreaking study and are interested in participating, call Helen Vanderswag or Deborah Fontaine at (858) 622-5800.
It has long been thought that once people develop Alzheimer’s it becomes very difficult to learn new things or to improve memory and thinking abilities. But this thinking is changing. Although there is no proof that mentally stimulating activities slow the progression of Alzheimer’s, recent research suggests that specific cognitive training may help people with mild Alzheimer’s maintain some abilities for a longer period of time. In one well-designed study conducted at the University of Miami School of Medicine and Mount Sinai Medical Center in Miami Beach, Florida, Dr. David Loewenstein and colleagues found that people with mild Alzheimer’s who participated in two 45-minute sessions of structured cognitive rehabilitation twice a week for a total of 24 sessions could improve in some specific areas of thinking and functioning. The thinking exercises were designed to address specific areas of ability such as recognizing faces, making change, and remembering dates and personal information. During the study, research participants were also asked to maintain a “memory notebook” and encouraged to record appointments, medication schedules, and contact information for relatives, friends, and doctors. They reviewed this notebook twice daily. Although the research findings that people with Alzheimer’s can maintain some abilities for a longer period of time with specific training are very encouraging, we need to see more studies of this kind to further validate the findings.

In the meantime it could be beneficial for a person in the earlier stages of Alzheimer’s to start a memory book. Include a calendar with important dates, pictures of people and places to remember, and specific important personal information. Review the information a few times daily with a care partner or friend.

Other forms of mental stimulation include more general activities and thinking exercises such as puzzles and word games, listening to music, reading, or doing creative or artistic projects. Although Alzheimer’s affects short-term memory, many long-term memories are intact and it can be an enjoyable experience to reflect on positive memories in one’s life and to share them with others. Although participation in these activities may not result in the specific gains found in the cognitive rehabilitation exercises, few would argue with the idea that participating in mentally stimulating activities is good for one’s well-being. Increased mental stimulation may also lead to more social interactions that can maintain personal connections and improve your mood and coping abilities. See next page for programs in the community that could provide some positive mental and social stimulation for people with early-moderate stage Alzheimer’s and let us know what you do to stay mentally active!


By Lisa Snyder, LCSW
## Clinical Trials

### Antioxidants

**STUDY DIRECTOR**
Douglas Galasko, M.D.

**DESCRIPTION**
This study will assess the safety, tolerability, and effects related to oxidative damage on cerebrospinal fluid (CSF) biomarkers of two antioxidant treatment regimens in patients with mild to moderate AD. We seek male and female subjects, age 60-85, inclusive, who:
- Have a diagnosis of probable AD (NINCDS-ADRDA criteria)
- MMSE score > 14/30
- Are at least 60 years of age or older who are not currently taking cholinesterase inhibitors and have mild to moderate Alzheimer's disease. Huperzine A is a natural cholinesterase inhibitor, derived from the Chinese herb huperzia serrata, used in China to treat AD. Individuals 55 years of age or older who are not currently taking cholinesterase inhibitors and have mild to moderate Alzheimer's disease are eligible for screening. Treatment with memantine (Namenda) and vitamin E is allowed. Two-thirds of participants will be randomly assigned to receive huperzine A throughout the study; one-third will receive placebo for the first 16 weeks, followed by huperzine A for 8 weeks. An open-label extension study providing huperzine A to all participants for 2 years is sponsored by ONO Pharma, Inc.

**TIME INVOLVED**
Study participation will be 24 weeks.

**COMPENSATION**
Participants will receive $400 upon study completion ($200 per lumbar puncture).

**CONTACT**
Mary Margaret Pay, R.N., C., N.P., at (858) 622-5800 and ask for the "Antioxidant Study"

### Huperzine A

**STUDY DIRECTOR**
Jody Corey-Bloom, M.D., Ph.D.

**DESCRIPTION**
This study to find out whether huperzine A is beneficial in the treatment of mild to moderate Alzheimer's disease. Huperzine A is a natural cholinesterase inhibitor, derived from the Chinese herb huperzia serrata, used in China to treat AD. Individuals 55 years of age or older who are not currently taking cholinesterase inhibitors and have mild to moderate Alzheimer's disease are eligible for screening. Treatment with memantine (Namenda) and vitamin E is allowed. Two-thirds of participants will be randomly assigned to receive huperzine A throughout the study; one-third will receive placebo for the first 16 weeks, followed by huperzine A for 8 weeks. An open-label extension study providing huperzine A to all participants for 2 years is sponsored by ONO Pharma, Inc.

**TIME INVOLVED**
Study participation will be 24 weeks.

**COMPENSATION**
Participants will receive up to $100 for lumbar puncture.

**CONTACT**
Karen Wetzel, M.P.A.S., PA-C, at (858) 622-5822 and ask for the "Huperzine A Study"

### ADNI Alzheimer's Disease Neuroimaging Initiative

**STUDY DIRECTOR**
Adam Fleisher, M.D.

**DESCRIPTION**
This study will measure examine whether imaging of the brain (through MRI and PET scans) every 6 months can help predict and monitor the onset and progression of Alzheimer's disease (AD). We seek male and female volunteers age 55-90 who:
- Have no memory problems (3 year commitment)
- Have a diagnosis of Mild Cognitive Impairment (MCI) (3 year commitment)
- Have a diagnosis of early AD (2 year commitment)
- All participants will undergo repeated brain MRIs and have blood and urine analyzed for biomarkers.
- PET scans and lumbar punctures are a study option.
- Participants must have a study partner (i.e., spouse, relative, or friend).
- Participants must be fluent in English or Spanish.

**TIME INVOLVED**
Study participation will be every 6 months.

**COMPENSATION**
Participants will receive $400 upon study completion ($200 per lumbar puncture).

**CONTACT**
Helen Vanderswag, R.N.C. or Deborah Fontaine, G.N.P., at (858) 622-5805 and ask for the "ADNI Study"

### ONO-2506

**STUDY DIRECTOR**
Jody Corey-Bloom, M.D., Ph.D.

**DESCRIPTION**
This study is a study to find out whether an experimental drug, ONO-2506, is beneficial in the treatment of patients with mild to moderate AD. This study is sponsored by ONO Pharma, Inc.

**TIME INVOLVED**
The safety, tolerability and effectiveness of an experimental drug, ONO-2506, is being studied in individuals with mild to moderate Alzheimer's disease (AD). The study will be conducted at the University of California San Diego. We are seeking participants who:
- Are age 50-90
- Have mild to moderate AD
- Are age 50-90
- Have mild to moderate AD
- Have not taking galantamine (Reminyl), tacrine (Cognex), or memantine (Namenda).
- Treatment with donepezil (Aricept), rivastigmine (Exelon), and/or vitamin E is allowed.
- Participants will be randomly assigned to receive one of two doses of the experimental drug ONO-2506 or a placebo.

**COMPENSATION**
There will be no payment for participation in this study; however, all tests, examinations, and medical care required as part of the study will be provided at no cost.

**CONTACT**
Karen Wetzel, M.P.A.S., PA-C, at (858) 622-5822 and ask for the "ONO-2506 Study"

### Gamma Secretase Inhibitor

**STUDY DIRECTOR**
Dr. Adam Fleisher and Dr. Roy Yaari

**DESCRIPTION**
In the first 16 weeks, while taking the study drug, there are visits every other week. After that, there are 2 visits in the next 12 weeks.

**TIME INVOLVED**
Inhibitor

**COMPENSATION**
Participants will take the study drug or placebo for 12 weeks, and will have a lumbar puncture (LP), at the beginning and end of that period. Note that LPs are now relatively easy procedures, with rare headaches or other bad consequences. CSF is required to measure the chemical composition of the fluid surrounding the brain, which cannot be measured with a blood test. If you or a family member have AD, and are willing to consider having a lumbar puncture, you may be eligible for this study.

**CONTACT**
Susan M. Frye, G.N.P., at (858) 622-5800 and ask for the "Gamma Secretase Study"

### Passive Immunization

**STUDY DIRECTOR**
Jody Corey-Bloom, M.D., Ph.D.

**DESCRIPTION**
This is a study to find out whether an experimental drug, AAB-001, is being studied in individuals with mild to moderate Alzheimer's disease (AD). Sponsores by Eli Lilly, this study, sponsored by Eli Lilly, will try to determine if blocking the enzyme results in a change of amyloid in the cerebro-spinal fluid (CSF) of people with AD. Also, it is looking at what dose of the medicine works best for safety and effectiveness. Participants will take the study drug or placebo for 12 weeks, and will have a lumbar puncture (LP), at the beginning and end of that period. Note that LPs are now relatively easy procedures, with rare headaches or other bad consequences. CSF is required to measure the chemical composition of the fluid surrounding the brain, which cannot be measured with a blood test. If you or a family member have AD, and are willing to consider having a lumbar puncture, you may be eligible for this study.

**CONTACT**
Karen Wetzel, M.P.A.S., PA-C, at (858) 622-5822 and ask for the "Passive Immunization Study"
**ADNI**
Alzheimer’s Disease Neuroimaging Initiative

**STUDY DIRECTOR**
Adam Fleisher, M.D.

**DESCRIPTION**
This study will examine whether imaging of the brain (through MRI and PET scans) every 6 months can help predict and monitor the onset and progression of Alzheimer’s disease (AD). We seek male and female volunteers age 55-90 who:
- Have no memory problems (3 year commitment)
- Have a diagnosis of Mild Cognitive Impairment (MCI) (3 year commitment)
- Have a diagnosis of early AD (3 year commitment)
- All participants will undergo repeated brain MRIs and have blood and urine analyzed for biomarkers.
- PET scans and lumbar punctures are a study option.
- Participants must have a study partner (i.e., spouse, relative, or friend).
- Participants must be fluent in English or Spanish.

**COMPENSATION**
Participants will receive up to $100 per visit and up to an additional $200 for lumbar punctures.

**Biomarkers in Aging, MCI, and Alzheimer’s Disease**

**STUDY DIRECTOR**
Douglas Galasko, M.D.

**DESCRIPTION**
This study will measure levels of a number of different proteins in cerebrospinal fluid (CSF) and in blood in order to compare these biomarker levels amongst people who have normal cognitive ability, mild memory problems, or early Alzheimer’s Disease (AD).

**TIME INVOLVED**
In the first 16 weeks, while taking the study drug, there are visits every other week. After that, there are 2 visits in the next 12 weeks.

**DETECTION**
Gamma secretase is an enzyme that contributes to making amyloid plaques. This study, sponsored by Eli Lilly, will try to determine if blocking the enzyme results in a change of amyloid in the cerebro-spinal fluid (CSF) of people with AD. Also, it is looking at what dose of the medicine works best for safety and effectiveness.

**STUDY DIRECTOR**
Dr. Adam Fleisher and Dr. Roy Yagi

**CONTACT**
Helen Vandersag, R.N.C.
at (858) 622-5805 and ask for the “ADNI Study”

**Oh My Goodness, His Name Is On the TIP OF MY TONGUE**

"It starts with the letter ‘M’…” It is likely that we have all experienced a “tip of the tongue” episode like this when we cannot recall the name of a person or an object even though the word is very familiar to us. We usually retain the ability to describe the object, tell what it is used for, name what color it is, and relate it to our personal lives, even when the particular word seems to have escaped us. Our ability to communicate clearly with one another is critically dependent upon language. Most often we use words to describe our surroundings and make our wants, needs, and desires known to others. It can be quite frustrating when we cannot come up with a word. Talking about a word’s features when the specific word cannot be retrieved is called circumlocution. This happens to everyone from time to time and is not necessarily a sign of a larger problem. However, language disturbances can be associated with changes in the structure and/or function of the brain.

Brain changes associated with Alzheimer’s disease (AD) are thought to interfere with our word library or our store and organization of word meanings. Numerous language impairments are associated with AD.

Neuropsychologists evaluate language in a number of ways — by observing conversational speech, assessing word-finding ability with picture naming, by recording how quickly one can produce words, and/or by asking a patient to describe the meanings of words. Although spontaneous speech in people with AD is usually fluent, word finding difficulties and circumlocutions are common. That is, people with AD often have difficulty producing the names of common objects, people, and places. For example, when presented with a picture of a cow, a person with early AD might say “animal that produces milk, usually found on a farm” rather than the specific name. This type of language impairment is referred to as anomia and can become more noticeable as the disease progresses. In addition, people with AD tend to have more difficulty coming up with specific items within meaningful categories of words (e.g., naming animals) compared to producing words that begin with a particular letter (e.g., naming words that begin with P). This is thought to be related to a breakdown in their organization of how words are stored in the brain, referred to as semantic knowledge.

In spite of their difficulty retrieving words, people with AD are often able to provide adequate definitions of words indicating their overall vocabulary remains intact.

Tara Milbrandt is our newest staff member who joins the ever-growing team of ADRC psychologists. Tara earned a Bachelors degree in Psychology from the University of California, San Diego and went on to receive a Masters degree in Social Work from San Diego State University. She comes to us with extensive experience performing neuropsychological testing. She most recently served as a clinical research coordinator with Affiliated Research Institute of San Diego for a period of five years before taking a hiatus to spend time with her busy family of five. Tara is returning to the 9-to-5 workforce on a part-time basis to explore professional options for the future.
Congresswoman Susan Davis Visits Shiley-Marcos ADRC For A Weekly Support Group

On January 25th, 2006, Congresswoman Susan Davis visited with 15 participants and family members of the Shiley-Marcos Alzheimer's Disease Research Center's (ADRC) weekly support group for people with Alzheimer's. Staff from the Alzheimer's Association and the ADRC were also present. The meeting was organized by Kassandra King of the San Diego Chapter of the Alzheimer's Association's Public Policy division as a means of informing Ms. Davis of the issues facing Alzheimer's families. The families identified three key concerns that they shared with Ms. Davis:

- They feel there should be a public awareness and education campaign about the earlier stages of Alzheimer's so that people feel less stigma about the disease and are more likely to seek an evaluation or possible treatment. They think early-detection is important and feel doctors also need to be better trained and informed about AD.
- They would like to see more funding for research, particularly genetics and family risk factors. The federal government is currently reducing its funding for AD research and this is a concern given the growing number of people with the disease.
- They are concerned about people with Alzheimer's or a related disorder who live alone, are homeless, or live in remote areas, and have no family to care for them. They discussed the difficulties people with Alzheimer's have in accessing services (specifically transportation) and the importance of not overlooking these at-risk groups.

Congresswoman Davis listened attentively to the concerns that were expressed and shared that Alzheimer's disease has personally touched her own family. The meeting provided an excellent opportunity to reinforce the importance of continued advocacy work in Sacramento and Washington DC, contact Kassandra King at the Alzheimer's Association (858) 492-4400

Florence Byerly Covell was born at home.

That's because she was born on November 4, 1905 when home birth was still the norm. She remembers the parks of her native Chicago, and moving out to the suburbs shortly before her baby brother was born. She studied art at a women's college in Milwaukee, where most of the students married the week after graduation. She took a road less traveled, teaching art, then working as a decorator, and then as the Home Furnishings editor of Better Homes and Gardens Magazine. This career entailed a lot of travel, which is one of her great joys.

At age 60, after 16 years of travel, she was ready to stay put, and moved to St. Louis to work for the May Company. There she was greeted by a brother of a friend of hers, who had been instructed to make her welcome to her new home. He did such a good job of it that they got married! When her husband, Dr. Covell, retired she did too, and they spent the next year traveling around the world on freighters. He died after 11 happy years of marriage, and Florence moved to White Sands, where she has lived ever since. In addition to the social group there, she also has a circle of friends from her volunteer teaching of English Conversation at UCSD. This is one of her tips on how to age successfully: stay connected to people. Her other strategies are to be always curious, to look forward to change, and to keep learning.

Fondly,
Florence Byerly Covell
BULLETIN BOARDS IN THE ADRC WAITING ROOM

Did You Ever Wonder If There Was Any Organization To Our Bulletin Boards?  
Well, There Is.

BULLETIN BOARD #1— next to our front door—posts Resource Information and Educational Opportunities. These include classes, lectures, support groups and our resource packet. It changes frequently so please check it often.

BULLETIN BOARD #2— next to the front desk—posts Research Studies exclusively. Some are clinical trials and some are not. All are affiliated with the ADRC in some way.