If only we could look inside the human brain or understand its chemistry. In the past, detailed study of brain structure and biochemical changes was mainly done by Neuropathologists who examined the brain at the time of death. Now, however, the ability to measure brain structure, function, and aspects of biochemistry is increasingly being used to understand changes that occur in aging and Alzheimer’s disease. These research methods are becoming more refined and powerful, enabling us to increase diagnostic accuracy, push the boundaries of diagnosis earlier, identify people who may be at greatest risk of developing Alzheimer’s, and study the effects of treatment on the brain.

These tools are called biomarkers, and we are increasingly using three of them: brain imaging using new applications of MRI; measuring levels of proteins related to Alzheimer’s in the cerebrospinal fluid (CSF); and imaging deposits of the amyloid beta protein (Aβ) in the brain using PET scanning (a nuclear medicine method).

(Continued on Page 2)

Biomarkers, including brain imaging and spinal fluid draws (also called lumbar puncture or LP) are becoming an essential component of dementia research and clinical trials. Due to their ability to contribute to diagnostic accuracy and to measure the effectiveness of experimental treatments, an ever increasing number of studies are requiring that participants have an LP or brain image (MRI or PET scan). While the potential risks of having an LP are minimal, this procedure has particularly negative associations for many people.

Three research participants from our Shiley-Marcos ADRC, who all consented to have an LP, shared their experiences with us during a brief interview.

Their stories are highlighted in narratives on Page 4.

Research Participants Share Their Experiences

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From the depths of a large, horizontal tube that houses a magnet so strong it could be used to pick up cars, a man grins and exclaims with bravado: “Ready for blast-off!” This man has Alzheimer’s disease, and we are about to embark upon a fascinating journey through his brain. We will glide over every ridge and valley on its surface and plummet through deep internal structures. As he lies in the magnet untouched, this man’s brain will be reconstructed in fascinating detail on the computer before us.

To understand how magnetic resonance imaging (MRI) works, we must return to the 1970s, when scientists discovered that spinning, subatomic particles in the human body called protons tend to align in the presence of a strong magnetic field. Once aligned, the spin of these protons can be manipulated by applying brief pulses of radio wave energy. This phenomenon produces an electromagnetic signal that differs according to tissue density, thereby revealing an image of the body’s internal structure. Since this discovery, MRI has been a mainstay in diagnostic radiology and particularly useful in examining the soft tissue of the brain. Not only does MRI provide a noninvasive look inside the brain, but it does so without exposing patients to radioactivity, unlike many other imaging methods.

In neurology clinics, MRI is mostly used to distinguish normal tissue from pathologic tissue, for example, in ruling out the presence of a stroke, tumor, or bleed. However, such uses of MRI vastly underestimate its power. In fact, the resolution of modern MR technology is so high that the entire brain can be reconstructed digitally within sub-millimeter accuracy. We can analyze this image of the brain with exquisite detail and take advantage of automated computer software to make calculations about the brain’s structure and function. These calculations form the basis for what we call quantitative magnetic resonance neuroimaging, a field that shows tremendous promise in the study of Alzheimer’s disease.

When a person agrees to spend approximately 45 minutes in our MR scanner, we collect an enormous wealth of data about his or her brain. We reconstruct a high-resolution, three-dimensional image that enables us to make measurements across hundreds of regions within the brain, taking particular note of those regions in which Alzheimer’s disease first manifests as the loss of brain volume and thickness. An MRI technique called “diffusion tensor imaging” (DTI) assesses the structural integrity of fiber tracts connecting different regions of the brain. Another technique known as “functional MRI” examines these fiber tract connections to see how well they function when the brain is at rest.

We can not only compare all these measurements to expected values given a person’s age, but using sophisticated methods developed at UCSD, we can also track changes in the same individual over time when he or she returns for follow-up scans. In fact, recent studies suggest that the ability to monitor how the brain actively changes as it ages is one of the most powerful tools in predicting whether a person will develop Alzheimer’s disease.

As research groups across the world embark upon similar journeys through thousands of brains in various stages of both healthy and unhealthy aging, we have begun to understand the spatial and temporal patterns of changes that occur in Alzheimer’s disease, even before clinical symptoms appear. In the end, we hope to significantly impact the clinical approach to Alzheimer’s by allowing physicians to identify individuals at risk, detect the disease in its earliest stages, and monitor the success of treatments. In the meantime, we enjoy every journey and are thankful for all the individuals willing to “blast-off” in exploration.
Going with the Flow: Cerebrospinal Fluid (CSF) and Alzheimer’s Disease

Luckily for Neurologists, the spinal cord stops growing before the bones of the spine complete their growth. As a result, we can access the membranes and spiny bones that surround the cord in the lower part of the back by inserting a skinny needle, without risking injury to the spine. This procedure is referred to as a lumbar puncture (LP), although it involves no more of a “puncture” than having your blood drawn. The fluid (CSF) that can be collected from the LP flows down after it circulates around the brain and spinal cord. By analyzing the contents of CSF, we can identify certain types of problems that affect the brain. Recently, sensitive biochemical tests have been developed to identify biochemical changes that affect the brain in Alzheimer’s disease and other disorders.

Levels of a protein called A-beta42 (Aβ42 for short) are decreased in the CSF in people with Alzheimer’s, most likely because they aggregate (stick together) in areas of the brain to form plaques and therefore don’t make it all the way down to the end of the lumbar CSF space. Another protein called tau forms clumps (called tangles) within nerve cells and their processes in Alzheimer’s disease. This clumping results in damage and degeneration of nerve cells, and also results in increased levels of tau in the CSF. So, by measuring Aβ42 and tau simultaneously in a CSF sample, we can gain insight into two biochemical processes that are important in Alzheimer’s. Many studies have shown that the profile of decreased levels of Aβ42 and increased levels of tau provides a signature typical of Alzheimer’s.

Lumbar puncture has been around for over a decade, but is gaining more widespread acceptance for several reasons. First, the LP procedure has been simplified and refined by the use of a special flexible needle which can access the CSF with much less discomfort than traditional needles. Second, techniques to measure Aβ42 and tau (called assays) have been standardized; every step from the collection and storage of the CSF to the readout of the assay is carefully controlled. Finally, researchers from centers throughout the world have published studies that confirm this Alzheimer’s signature in CSF. These studies have allowed us to understand how levels of these proteins are influenced by aging and to define cutoff points much more clearly. Recent studies from the Alzheimer’s Disease Neuroimaging Initiative (ADNI), involving over 600 research volunteers across the USA and Canada, identified cutoff levels in CSF that were remarkably accurate at identifying Alzheimer’s. These same cutoffs were applied to people with Mild Cognitive Impairment (MCI), and performed excellently at predicting who were likely to progress to Alzheimer’s.

CSF is particularly attractive for research because many measurements can be obtained from a single sample. In addition to measuring levels of Aβ 42 and tau, collaborators at our Shiley-Marcos ADRC and a similar group at University of Washington recently found that the levels of two proteins, alpha-Synuclein (α-SYN) and DJ-1, both of which are involved in the pathology of Parkinson’s disease, are decreased in CSF in Parkinson’s but not in Alzheimer’s. CSF is increasingly being used to evaluate whether new drugs being developed against Alzheimer’s hit their targets in the brain and bring about desired biochemical changes. For example, drugs aimed at decreasing the production of Aβ can be studied by measuring their effects on levels of Aβ in CSF.

Although CSF is relatively easy to access—which our skilled Neurologists will demonstrate if you agree to undergo the procedure—a blood test would provide an even easier way to try to confirm a diagnosis of Alzheimer’s. Our ADRC investigators and many other groups have been searching for years for such a test, and so far have not found any promising markers. It is possible that our detection methods for blood biomarkers are not sensitive enough. So, for now, we also draw blood from our research participants to use these samples to study new leads or assays.

We have had an active CSF research program at UCSD for many years. We would like to expand our efforts by obtaining CSF from as many ADRC research participants as possible. This will help us to improve our understanding of the protein biomarkers we currently measure, and allow us to search for new markers. The long term goals are to obtain tools to improve our ability to detect Alzheimer changes as early as possible, and to study responses to novel treatments in clinical trials.

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I had my first LP at the ADRC in order to gain additional insight about the underlying cause of my cognitive changes. I understand that there are different proteins in your body that vary depending on your health situation and diagnosis, and that the LP results can provide the doctors with information about what they are likely looking at.

I was concerned about having an LP because I had heard that one of the things that can happen is a real strong headache from loss of spinal fluid. But, I decided to proceed with the request because I believe that if you live in fear and don’t try new things, you won’t get anywhere or grow or get what you want and need in life; you can’t live in fear. During the procedure, I felt nothing more than a prick for the anesthetic in the area where they did the procedure. It was no worse than a simple flu shot; in fact, it was probably less painful than a flu shot because once the anesthetic went in, there was no pain whatsoever. After the procedure was complete, I felt as if the whole thing was done and that was it; I had no pain, no side effects, no nothing except taking it easy for a day or two. I did eliminate my exercise routine for a day or two and drank a lot of water, as they instructed me to do.

I would be willing to do it again if it would help the cause and would recommend that other persons who could benefit from the additional information also consider participation. I would also add that people should not get too whacked out about the concept of an LP. It is totally different from the images that are conjured from the past where a huge needle gets shoved in you. This is so far from the reality.

**VIGNETTES**

**JOSEPH WILER** is a 56-year-old man who recently joined our longitudinal study. Our comprehensive evaluation will lead to a clearer diagnosis of his physical and cognitive (thinking) symptoms.

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**MARGARET COON** is a 79-year-old female who participated in many of our ADRC studies as a control subject (a person without AD). She has had four LP procedures spaced over a four-year period.

I agreed to undergo an LP because they wanted to get biomarkers from my spine to see if the fluid contained trace proteins for Alzheimer’s disease. They are trying to get the disease under control to help people understand how it starts, why it starts, and how to detect it ahead of time, and I wanted to make a meaningful contribution to research. This particular area of research also interested me because my husband is currently experiencing very early changes with his memory.

While I had no prior experience with an LP, I did have two herniated disks in my back and was sure to notify the researchers that this might be an issue that could complicate the process. Prior to agreeing to the procedure, I also had an older woman in the waiting room endorse her experience with it and I figured that if she could do it, I could do it. Of the four LPs that I have had, I only had one slight complication with the first one. At the start of the procedure, I was placed in an upright, hunched over position. That position did not suit me and resulted in a brief wave of nausea and light-headedness at the time that the needle was inserted. Once I notified them of my reaction, they immediately stopped the procedure, gave me some time to normalize and then, with my permission, proceeded with the procedure by having me lay down on my side in a different position. From that point forward, I was completely fine and there were no subsequent reactions or adverse experiences at that LP draw or with the three subsequent draws I had over the course of the following years. After the procedure, on all four occasions, I went about my regular business, driving myself home and engaging in my everyday activities. I would be willing to undergo this procedure again since I’ve had no problems with it.
Congratulations to Jagan Pillai, MD, and Kelly Landy, BA, for receiving honorable mentions for the Alzheimer’s Association’s Young Scholars Award. This award was developed to stimulate new research in dementia by supporting scientists in the early stages of their careers. Awardees are chosen each year by the San Diego/Imperial Chapter’s Medical and Scientific Advisory Board.

My mom agreed to an LP because it was part of a clinical trial she volunteered for. The doctors explained that they were looking for markers of Alzheimer’s that would be visible in the spinal fluid because they thought it would be a more accurate test. I was nervous for my mom because I didn’t know how she would react to the procedure. All of the disclosures and consents bring up every risk, but there just weren’t any issues. I was thinking of an LP like an epidural like they give you for childbirth, but it was nothing like that. In fact, my mom came back out of the room in minutes and she told me she didn’t feel it. In addition, there was no recovery needed; she did not have a headache, pain, or soreness. It was not a big deal at all. We were worried about it beforehand, but it was the most simple, easiest thing – like getting a flu shot as far as how quick and painless it was. My mom had two LPs. The first one, I took the day off of work, took her there, made sure she was rested. I watched her closely, but there was just no effect. The next time, I had a caregiver take her because I just wasn’t worried.

We welcome your comments or questions about the LP procedure. Our neurologists at the ADRC are extremely experienced in conducting these spinal fluid draws and are available to address your concerns. As always, we are truly grateful to all of our research participants who help to advance our efforts in determining early and accurate diagnosis, as well as effective treatments for people with dementia.

Alzheimer’s Association Young Scholars Award Winners

Congratulations to Jagan Pillai, MD, and Kelly Landy, BA, for receiving honorable mentions for the Alzheimer’s Association’s Young Scholars Award. This award was developed to stimulate new research in dementia by supporting scientists in the early stages of their careers. Awardees are chosen each year by the San Diego/Imperial Chapter’s Medical and Scientific Advisory Board.

Jagan Pillai, MD, is a Dementia Fellow at the Shiley-Marcos ADRC under the mentorship of Douglas Galasko, MD. His award was for a project that used Alzheimer’s Disease Neuroimaging (ADNI) data to explore the role of education in the volume changes of specific structures in the brain. He analyzed Magnetic Resonance Imaging data in persons with normal cognition, Alzheimer’s disease (AD), and mild cognitive impairment (MCI) and found that education may protect against AD-related neuropathological changes but not age-associated brain atrophy. His project may help researchers understand how individuals could maintain relatively preserved thinking abilities, despite harboring significant neuropathology. These results may provide a specific marker that could measure the effects of interventions, such as cognitive stimulation and exercise, in persons with MCI and AD.

Kelly Landy, BA, is a doctoral student in the Department of Neurosciences. Her project was completed under the direction of Drs. Joanne Hamilton and David Salmon and examined the relationship between early visuospatial deficits and visual hallucinations in persons with either Dementia with Lewy Bodies (DLB) or AD. The investigators concluded that the level of severity of visuospatial impairment was associated with the presence of visual hallucinations in the DLB group, but not in the AD group. Visual hallucinations can be difficult for both patients and caregivers; knowing which patients are likely to develop hallucinations in the future could inform potential treatment decisions.
**Clinical Trials**

**Participating in Clinical Trials**

A clinical trial is a test or study of a new drug, device, or procedure. The following clinical trials are testing how effectively a medication works in relieving symptoms, diagnosing, or providing treatment for Alzheimer's disease.

Although participation in a clinical trial does require some time commitment with visits to our Shiley-Marcos Alzheimer’s Research Center, in many cases, the visits are infrequent. Some people do not want to participate in a clinical trial if there is a chance of receiving a placebo (a look-alike pill with no medicinal ingredients). It is well-documented, however, that people who are unknowingly taking a placebo sometimes experience feelings of well-being for the therapy they believe they are taking something that could be of benefit to them. Also, the ongoing support of the clinical trial coordinator can be a rewarding experience that increases feelings of well-being for the participants.

Please contact us with any questions or concerns about our clinical trials. We greatly value your participation so that we can continue to make advances in the diagnosis, detection, and treatment of Alzheimer's disease.

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**Nerve Growth Factor**

**Principal Investigator**: Michael Rafii, MD, PhD

**Time Involved**: 24 Months

**Description**: Nerve growth factor (NGF) research is a phase 2 double-blind, placebo controlled study. The purpose is to test the safety, tolerability, and effectiveness of a new experimental gene transfer drug called Cere-110 in those with mild-to-moderate AD. Studies suggest that NGF may help increase the survival of neurons that degenerate in AD. The ability of NGF to prevent brain cell loss in animal models of AD has led to delivering NGF to humans. In this study NGF is delivered directly by surgical insertion into the region of the brain where cell death occurs. Gene therapy is experimental and has not yet been approved by the FDA.

**Requirements**: 55-80 years old

- On stable AD medication for 3 months
- Have a study partner for all visits
- Fluent in English
- Are in general good health

**Contact**: Christina Gigliotti, PhD at (858) 622-5800 and ask for the "Cere-110" study cgigliotti@ucsd.edu

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**BMS-708163**

**Principal Investigator**: Michael Rafii, MD, PhD

**Time Involved**: Minimum of two years

**Description**: Identifying AD in the earliest phase of the disease process offers the opportunity to explore whether the use of potentially disease-modifying agents might alter the long-term course of the illness and prevent the neurodegenerative cascade associated with this disease. No drug therapy is currently indicated for prodromal AD. Studying the effect of BMS-708163, a potentially disease modifying agent, earlier in the disease process may have greater impact in delaying the progression of the illness.

**Requirements**: Age 50 or older

- Diagnosis of Mild Cognitive Impairment (not dementia)
- Have a study partner for all visits
- MMSE scores between 24 and 30 (inclusive)
- Able to read and write English
- Stable health and medications

**Contact**: Elizabeth Ortega, NP at (858) 677-1567 and ask for the "BMS" study ejortega@ucsd.edu

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**AVID-45-133**

**Principal Investigator**: Douglas Galasko, MD

**Time Involved**: 1.5 - 2 Months

**Description**: The purpose is to evaluate two new radiotracers, AV-45 and AV-133, which are used in conjunction with a PET scan to distinguish between patients with Parkinson’s disease and Dementia with Lewy Bodies from those with Alzheimer’s disease and healthy elderly individuals. Participants will undergo two PET scans within four weeks of one another in addition to cognitive testing, a brief physical exam, EKG, and blood work.

**Requirements**: Age 50 or older

- Diagnosis of Dementia with Lewy Bodies or Alzheimer’s disease, or healthy seniors
- Diagnosis of Parkinson’s disease diagnosed within four years, on stable dose of dopamine, and able to endure overnight withdrawal of PD medications prior to scans
- Have a study partner for all visits

**Contact**: Judith Rivera, NP at (858) 622-5800 and ask for the "AVID-45-133" study jrivera@ucsd.edu

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**Alzheimer’s Disease Neuroimaging Initiative Grand Opportunity(ADNI-60)**

**Principal Investigator**: James Brewer, MD, PhD

**Time Involved**: 18 months

**Description**: We are studying the earliest memory changes that occur with aging and are seeking people between ages 55 and 90 who have a concern about their memory. We will screen their memory using a standard memory test, and if it is mildly abnormal, we will examine brain structure and function using Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET). We will also draw blood and cerebro-spinal fluid to determine the best approach for early diagnosis of neurodegenerative disease, such as Alzheimer’s disease.

**Requirements**: Age 50 or older

- Memory complaint by patient and/or study partner
- Mini-Mental State Exam score between 24 and 30 (inclusive)
- Able and willing to undergo lumbar puncture and MRI
- In good general health

**Contact**: Helen Vanderswag, RNC, BSN at (858) 677-1567 and ask for the "IGIV/GAP" study hvanderswag@ucsd.edu

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**Immune Globulin Intravenous (Human) IGIV**

**Principal Investigator**: Michael Rafii, MD, PhD

**Time Involved**: Approximately 2.5 years

**Description**: This study aims to evaluate the novel use of an agent (Immune Globulin Intravenous (Human)), 10% that is approved in the United States to treat various immunodeficiency and autoimmune disorders. IGIV is a biologic agent with anti-inflammatory and immunomodulating properties containing human immunoglobulin G antibodies derived from the blood plasma of healthy donors. Passive immunization could provide a safe and effective alternative to active vaccination for the treatment of AD patients, providing a strong rationale for studying passive immunization with IGIV.

**Requirements**: 50-89 years old, (inclusive)

- Diagnosis of probable AD
- MMSE scores of 16 to 26 (inclusive)
- Have a study partner for all visits
- Able to read and write in English
- Stable health and medications

**Contact**: Elizabeth Ortega, NP at (858) 677-1567 and ask for the "IGIV/GAP" study ejortega@ucsd.edu

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**Clinical Trials Registry**

Are you interested in clinical trials but don’t find one that suits you? You can now join our Shiley-Marcos ADRC registry to be placed on a list for future studies.

**Participants Can Be:**

- Normal Controls
- Have a mild memory problem
- Be diagnosed with early-to-moderate Alzheimer’s

**Call the Shiley-Marcos ADRC at (858) 622-5800**
Researching Ways to Reduce Caregiver Stress

As the Baby Boomer generation ages, the prevalence of Alzheimer’s and the number of family caregivers will dramatically increase. The chronic stress associated with caregiving can have a harmful impact on physical and mental health, resulting in caregivers requiring medical services at a greater rate than the general population.

The UCSD Alzheimer’s Caregiver Project recently examined many social and psychological effects of caregiving. Researchers compared stress, mood, coping, use of anti-depressants, and health outcomes of 125 Alzheimer’s caregivers with those of 60 non-caregivers. Forty percent of caregivers experienced significant clinical symptoms of depression, compared to only 5% of non-caregivers. Caregivers utilized greater negative coping strategies (e.g., avoidance; wishful thinking) compared to non-caregivers and reported less access to resources (e.g., social support). They felt less confident in their ability to solve problems, and reported greater health symptoms and reduced sleep quality. Also, while 25% of caregivers reported taking anti-depressant medication, 69% of these continued to experience significant symptoms of depression. These results suggest that caregivers may need help in learning more effective methods of coping.

Brent Mausbach, PhD, is conducting a new research project intended to help caregivers improve their emotional and physical well-being. Participation in the study is approximately 6 weeks and takes place in the home (4 home visits and 2 phone calls). Before and after the study, caregivers will participate in an interview and receive a visit from a study nurse who will check blood pressure and take a blood sample.

For more information or to enroll in this research, contact Jenni Ceglowski at (858) 822-2534 or Brent Mausbach, PhD at (858) 822-5925.

New Non-Alzheimer’s Dementia Caregiver Support Group

When many people hear the word “dementia,” they associate it with Alzheimer’s disease. Although Alzheimer’s is the most common form of dementia, frontotemporal dementia and Lewy Body dementia (including Parkinson’s disease with dementia) are responsible for up to 30% of dementia cases. These dementias share common symptoms with Alzheimer’s, but also pose unique challenges early on including significant behavioral, language, visuospatial, and motor symptoms that are less pronounced in early Alzheimer’s. Caregivers of persons with these dementias sometimes struggle to have their unique concerns and needs met in caregiver support groups.

The UCSD Shiley-Marcos Alzheimer’s Disease Research Center (ADRC), the San Diego/Imperial County Chapter of the Alzheimer’s Association, and Advanced Neurobehavioral Health of Southern California (ANH) are co-sponsoring a new non-Alzheimer’s dementia caregiver support group to try to address the needs of families caring for someone with Frontotemporal dementia, Lewy Body dementia, or Parkinson’s with dementia. This group will be facilitated by Shannon Foster, PhD (ANH) and Alisa Cox, MS (Alzheimer’s Association).

When: 1st Wednesday of every month from 2:00-3:30 beginning January 5th, 2011

Where: UCSD Shiley Marcos ADRC
8950 Villa La Jolla Drive, Suite C-129
La Jolla, CA 92037

Contact: Lisa Snyder, LCSW
Shiley-Marcos ADRC
(858) 622-5800
ON JUNE 19, 2010, THE LATINO FORUM, as part of the development of California's State Plan for Alzheimer's disease for the expected Alzheimer's epidemic, was brought to fruition with the driving force from San Ysidro Health Center's CEO, Mr. Ed. Martinez and Ana Melgoza, Director of Community Relations. The forum's emphasis was to bring various community professionals together to collaboratively address the Alzheimer's epidemic, described by Mr. Martinez as a "tsunami" (which paints a clearer picture of this devastating condition). According to the Alzheimer's Association, 1.1 million Californians now provide unpaid care for people with Alzheimer’s.

The event started with a Latino Alzheimer’s Presentation by the National Alliance for Hispanic Health with a Leadership Dialogue Session comprised of 20-30 professionals. Susan DeMarois, State Plan representative, was present and participated in the group discussions. Over 55 family caregivers participating in 10 focus group discussions were quite candid with their opinions when answering the questions set forth by the state (table at left). The process was moving in light of the fact that this is exactly the outcome the state was hoping the forums would accomplish. With as much as a caregiver attends to in a day’s work, they are to be commended for making these focus group discussions possible and successful.

Committee members who served as group facilitators and contributed to this accomplishment are from the following organizations:

- San Ysidro Health Center
- Shiley-Marcos Alzheimer's Disease Research Center
- Alzheimer’s Association, San Diego/Imperial Chapter
- Southern Caregiver Resource Center
- Casa Familiar

Aging and Independence Services, La Maestra Community Health Centers, and those associated with the Fotonovela Study from San Diego State University also participated and Maxim Companion Services provided no-cost respite care on the day of the event.

Forums like the one held on June 19, 2010 along with an action plan are a must for the good of our community. The Forum results have been tabulated and will be presented and discussed at a follow-up leadership dialogue session where I look forward to representing our Shiley-Marcos ADRC.
The Neuroscience Community in San Diego has been a leader in basic and clinical research into the cause, effects, and treatment of Alzheimer’s disease and related neurodegenerative disorders. In order to continue and enhance this tradition of cutting-edge research, the Shiley-Marcos ADRC hosted our second “Data Blitz” on Monday, October 25th. Twenty-five research scientists from leading laboratories at UCSD, Scripps Research Institute, and the Salk Institute gave very brief presentations describing their most recent findings related to Alzheimer’s disease. It was our hope that this event would help investigators become familiar with the breadth and depth of Alzheimer’s disease research being carried out in our community, and identify potential collaborations that would enhance everyone’s research efforts. In addition, it allowed Drs. Douglas Galasko (Director of the UCSD Shiley-Marcos ADRC) and Paul Aisen (Director of the UCSD Alzheimer’s Disease Cooperative Study) to describe the resources and research support available to Alzheimer’s disease researchers through our large, nationally-funded centers. Hosted by Dr. Eddie Koo (Co-Director of the UCSD Shiley-Marcos ADRC), the Data Blitz was organized around several themes of clinical and basic research being conducted in our local scientific community.

Researchers interested in neuroimaging and other biomarkers of early Alzheimer’s disease presented evidence that loss of cortical gray matter volume in specific areas of the brain occurs early in the course of the disease and predicts the future development of dementia in those who are in a “preclinical” stage known as Mild Cognitive Impairment (MCI). New imaging methods for measuring the adverse effects of Alzheimer’s disease on the ability of different brain regions to actively work together were also described. In addition, an important biomarker for Alzheimer’s disease was described that is based on measuring the constituents of the plaques and tangles of the disease in cerebrospinal fluid. These measurements might provide a way to more definitively diagnose the disease in mildly demented patients.

Several researchers interested in clinical aspects of Alzheimer’s disease and related disorders presented data on how Alzheimer’s disease and Parkinson’s disease can interact to produce unique learning and visual processing deficits. Severe deficits in the ability to visually detect and identify objects and their direction of motion were described in patients with a condition called Dementia with Lewy bodies (DLB), a disease that has the pathology of both Alzheimer’s disease and Parkinson’s disease. This feature of their clinical presentation may allow these patients to be differentiated from those with “pure” Alzheimer’s disease early in the course of the disease. A unique deficit in learning to categorize visual stimuli was also shown to be a specific feature of Parkinson’s disease that predicted the development of dementia. This deficit may eventually help to distinguish between Alzheimer’s disease and Dementia with Lewy Bodies in clinical evaluations. Another presentation showed that people who are bilingual and have used two languages most of their life may have a delayed onset of dementia. It was hypothesized that the extra cognitive processing that occurs in managing two languages confers a cognitive “reserve” that protects against the neural decline associated with Alzheimer’s disease.
Researchers interested in the basic biological mechanisms that cause Alzheimer’s disease presented data showing that the transport of important cellular proteins inside neurons (nerve cells in the brain) is disrupted in animal models of Down’s syndrome and may be similarly disrupted in Alzheimer’s disease. They also showed that the development of Alzheimer’s disease pathology might be hastened by cellular processes associated with diabetes. Progress in identifying causes of other neurodegenerative diseases that cause dementia such as Huntington’s disease and prion diseases (e.g., Cruetzfeld-Jakob disease or “Mad Cow” disease) was also described with the hope that this information might provide important clues about the causes of Alzheimer’s disease. The production of an abnormal form of the amyloid protein (i.e., beta-amyloid) in the brain has been proposed as a primary cause of Alzheimer’s disease. A number of researchers presented data on molecular mechanisms that contribute to the development of beta-amyloid and how it interferes with the normal function of neurons and synapses that allow neurons to communicate with each other. This new knowledge may lead to ways to block the production of beta-amyloid and its dreadful impact on brain function. Indeed, several presentations described ways in which beta-amyloid’s adverse effect on the cellular activity underlying learning and memory could be measured and reduced in animal models of Alzheimer’s disease.

An important area of research that was discussed involved efforts to develop new therapies for Alzheimer’s disease. Several researchers described new methods to effectively block the production of beta-amyloid in mouse models of Alzheimer’s disease and to remove misfolded proteins (including beta-amyloid) from the brain. Another researcher showed that the death of neurons due to Alzheimer’s disease in animal models could be prevented or slowed by introducing a growth factor known as brain-derived neurotrophic factor (BDNF). Better methods to administer and test potential drug therapies were also described. These included new ways to deliver therapeutic proteins across the blood-brain barrier that usually protects the brain from blood-borne abnormalities, and how human stem cells from patients with Alzheimer’s disease can be developed into neurons and used to test new potential therapies for the disease.

A highlight of the Data Blitz was a keynote presentation by Dr. Dan Skovronsky, the founder and CEO of Avid Radiopharmaceuticals. Dr. Skovronsky and his colleagues have developed a new imaging method to detect amyloid in the brains of living people. This technique involves injecting a molecule that will attach to amyloid in the bloodstream so that it will be carried into the brain. Before injection, the molecule is tagged with a small, harmless amount of radiation so that it can be detected with a PET (Positron Emmission Tomography) scan. In this way, any amyloid in the brain can be visualized until the tracer decays away. This methodology is likely to have very important uses in making an accurate diagnosis of Alzheimer’s disease and in tracking the effectiveness of new therapies that are designed to remove beta-amyloid from the brain.
YOU'RE INVITED!

January 12, 2011
10:00 AM - 12:00 PM

Sheraton Hotel
3299 Holiday Court
La Jolla, CA 92039

(Across the street from the ADRC, behind the gas station as you're coming up the hill)

To RSVP for this event, please call (858) 622-5800