TRANSITIONS A JOURNEY IN TIME

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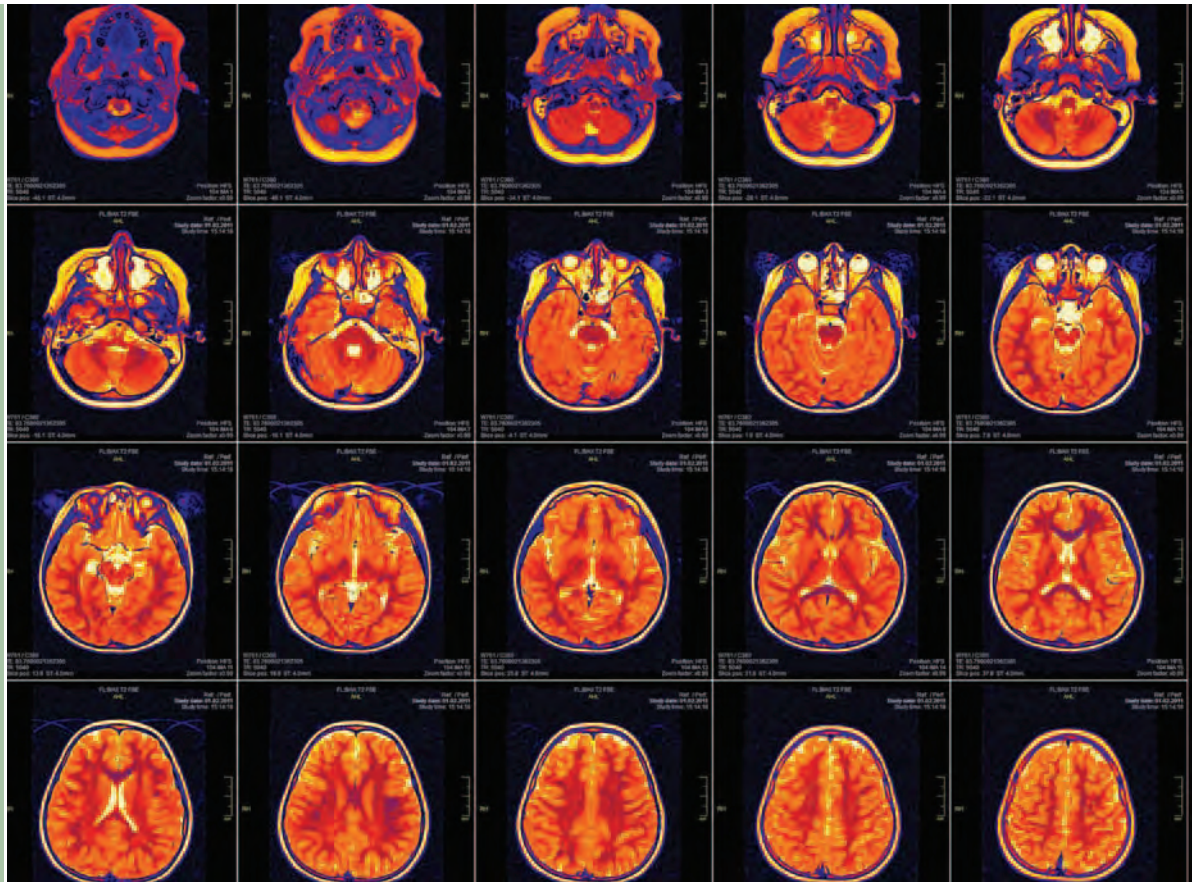

"I wonder if this is how it started for Mom." This sentiment is expressed all too often in the Memory Research Unit (MRU) at UT Southwestern Medical Center in Dallas.

Alzheimer's Disease Neuroimaging

Newest and most innovative imaging techniques

By Mac Miles M.S. and Kristin Martin-Cook M.S., Clinical Research Coordinators Memory Research at UT Southwestern

"I wonder if this is how it started for Mom." This sentiment is expressed all too often in the Memory Research Unit (MRU) at UT Southwestern Medical Center in Dallas. For years, the MRU has researched novel treatments for, and causes of, the brain robbing disease known as Alzheimer's disease (AD). In the past several years however, the MRU has intently focused on the earliest stages of the disease that start with innocent senior moments.

Among the latest findings in AD research is that the disease begins long before dementia is recognized. It is with this in mind that researchers now aim to identify the disease early. Currently, a diagnosis of Alzheimer's Disease relies on the identification of symptoms of dementia, defined as a wide range of impaired memory and thinking symptoms. This diagnosis requires that patients have an obvious decline in cognitive function beyond what is expected with normal aging. While this method is still valid it is like waiting for a heart attack to diagnosis coronary artery disease. The damage is already done, and is far worse beneath the surface. Not to mention the difficulty telling apart what is normal and what is not, something with which physicians, researchers and certainly patients and family struggle.

In order to prevent dementia caused by AD, researchers are now looking for ways to identify the disease at the earliest signs of memory and thinking problems; well before dementia has dramatically impacted ones' life. This is why researchers at UT Southwestern are studying a variety of experimental brain imaging techniques to address this concern. One such study is the Alzheimer's Disease Neuroimaging Initiative (ADNI), which is funded by the National Institute of Aging. The purpose of the study is to take a uniform approach to using the newest and most innovative imaging techniques including magnetic resonance imaging (MRI) and Positron Emission Tomography

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Helpful Resources

Local, State and Federal Organizations & Agencies

Alzheimer's Association
Information and referral services. Phone: 1-800-272-3900. www.alz.org. Comprehensive information for family caregivers, healthcare providers, researchers and the media on risk factors, diagnosis and treatment options; day-to-day care; legal and financial planning; insurance coverage; current research; and Association news releases. www.alz.org/findchapter.asp Link to local chapters for available programs and services.

Alzheimer's Disease Center At Baylor College Of Medicine
Phone: (713) 798-6660. Clinical and basic science research; education; and diagnosis and treatment of patients with Alzheimer's disease and related disorders. http://www.bcm.edu/neurology/struct/admdc/admdc.html. Drug trials; research projects; brain donation program; patient appointments and evaluation; and Alzheimer's disease information.

Alzheimer's Disease Center At University Of Texas Southwestern Medical Center
Phone: (214) 648-7444. Scientific research into the causes of Alzheimer's disease; and diagnostic evaluation of adult memory problems. Clinical research studies; patient evaluation process; newsletters; educational events; and caregiver resources.

Alzheimer's Disease Education And Referral (Adear) Center
Phone: 1-800-438-4380 Information about Alzheimer's disease, its impact on families and healthcare providers, and research into possible causes and cures. www.alzheimers.org Research updates; directory of National Institute on Aging Alzheimer's Disease Centers; clinical trials database; recommended reading list for caregivers; and press releases.

Legal Hotline for Texans
The Texas Legal Services Center has established a toll free telephone hotline for Medicaid-eligible persons over age 60 to receive brief legal advice and referrals. Call 1-800-622-2520 or download helpful publications on a range of legal issues at ww.tlsc.org/hotline.html.

MedicAlert + Safe Return
Enrolling in the Alzheimer's Association's MedicAlert + Safe Return program can provide 24-hour immediate assistance when an Alzheimer's patient wanders or has a medical emergency. There is a small charge. For more information, call toll free at 1-888-572-8566 or visit www.alz.org/safetycenter.

Medicare
Phone: 1-800-633-4227 National toll-free number for general information and counseling on Medicare. www.medicare.gov. Official U.S. government site for Medicare information on eligibility, enrollment, and premiums. Search tools for state-specific information on health plan choices; nursing home comparisons; prescription drug programs; participating physicians; and plan coverage.

Texas Alzheimer's Research Consortium
Visit www.txalzresearch.org to find out more about Consortium research opportunities, latest research news and publications, and who to contact at the five participating medical schools and health science centers for more information.

Texas Council on Alzheimer's
The Council oversees the Texas Alzheimer's Research Consortium, provides Alzheimer's news updates, and links to caregiver resources: www.dshs.state.tx.us/alzheimers/council.shtm.

Texas Department of Aging And Disability Services /Area Agency on Aging Information and Assistance
Phone: 1-800-252-9240, which routes calls to 28 Area Agencies on Aging in Texas that provide services for persons 60 years of age and older. Services include healthcare benefits counseling; case management; nutrition services; transportation; in-home help; senior centers; and the Retired Senior Volunteer Program (RSVP).

When the hippocampus is damaged or dying it never registers the event or the knowledge. It doesn't recognize the event, and acts the same as if the event never happened. It never sends the message to the other parts of the brain to store the event.

"First in, last out ... Last in, first out"

You can't retrieve what was never stored

By Carole Larkin MA,CMC,CAEd,QDCS,EICS

I learned a while back how the expression "first in, last out and last in, first out" describes how the loss of memory works in patients suffering from Alzheimer's disease.

The expression, First in, last out ... Last in, first out, is a short way of explaining that the things we learned long ago, like in childhood or when we were young adults, stay in Alzheimer's patients' memories longer than things they learned or experienced recently.

I never knew how this occurred, just that it did occur with persons suffering from Alzheimer's disease and other dementias.

Recently, I went to a lecture given by one of Dallas' most knowledgeable geriatric psychiatrists and I finally found out -- How and Why.

It turns out we form memories in a two step process.

The first step is done by the hippocampus portion of the brain.

When we experience something or learn something the hippocampus takes it in and registers it. Then the hippocampus sends it to other portions of the brain to be stored.

We retrieve the memory from the other portions of the brain when we remember something.

Research tells us that the hippocampus is one of the earliest portions of the brain damaged by Alzheimer's disease. I could never figure out why the doctors made such a big deal of that, but now I know.

When the hippocampus is damaged or dying it never registers the event or the knowledge. It doesn't recognize the event, and acts the same as if the event never happened. It never sends the message to the other parts of the brain to store the event.

You can't retrieve what was never stored can you?

Before the hippocampus is damaged it can register events and send them to storage, so those events are there to be retrieved.

Ever wonder why mom has no idea that she had breakfast, but knows the color of the dress she wore at Easter 40 years ago? Because the old memory was

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Carole Larkin is a Geriatric Care Manager who specializes in helping families with Alzheimer's and related dementias issues.

"Senior Moments" and Exercise

By Kaitlyn White, BA, Research Recruiter, Texas Health Presbyterian Hospital at Dallas

The Alzheimer's Association reports that Alzheimer's Disease ranks 6th for causes of death in the general population. It is the only top 10 "cause of death disease" that cannot be cured, prevented or slowed down at this time. Researchers, worldwide, are in the process of changing that statistic.

Dr Zhang, who is a researcher at the Institute for Exercise and Environmental Medicine at Texas Health Presbyterian Hospital Dallas and an assistant professor at UT Southwestern Medical Center at Dallas, in conjunction with his team members are among the researchers trying to find a way to eradicate the disease. He has been awarded a $ 2 million grant from the National Institute on Aging to research the relationship between exercise and brain function as individuals age. Dr. Zhang's research project, titled "Mild Cognitive Impairment: Cerebrovascular Dysfunction and Exercise Training", could lead to a better understanding as to why people develop cognitive impairment and how the condition worsens. This study tests the hypothesis that regulation of blood circulation within the brain is impaired in those with mild cognitive impairment. The study will also determine whether endurance exercise training improves brain blood flow and if it will slow the decline of brain function in patients with mild cognitive impairment.

Previous studies have led scientists to believe that exercise will improve brain blood flow and possibly ward off the accumulation of brain plaque, which often is the culprit, interfering with brain messaging and could be a cause of AD. At this time, the only existing treatments for AD are symptomatic and do little to prevent or slow the progression of the disease. Dr. Zhang and his team remain hopeful that exercise will have an aggressive impact. His project will study 72 participants with memory concerns/complaints and 30 healthy, elderly subjects. Those patients that qualify for the memory concern group will randomly be assigned to a one year exercise program with either an aerobic fitness component or a flexibility and training component. Dr. Zhang and his team are investigating the connection between exercise and brain function as people age, with the goal of finding better preventions and treatments for AD.

Dr. Zhang's research project is currently searching for volunteers who are 55 years old or older who have memory concerns or complaints but are generally healthy and lead sedentary or relatively sedentary lives. Additionally, healthy elderly subjects with no concerns or complaints are also needed.

To qualify, you must be:

- Be between the ages of 55 and 80
- Be without chronic health conditions such as uncontrolled high blood pressure, diabetes or obesity with a BMI > 35
- Be WITHOUT any metal implants in your body
- Exercise less than or up to 3 times per week
- Be willing and able to complete a 12 month exercise intervention

To learn more about participating in this study or if you have any questions regarding your eligibility, please call Kaitlyn White, Research Recruiter at 214-345-4629.

For more specific information for Dr. Zhang's study, please go to the following website: http://clinicaltrials.gov/ct2/show/NCT01146717

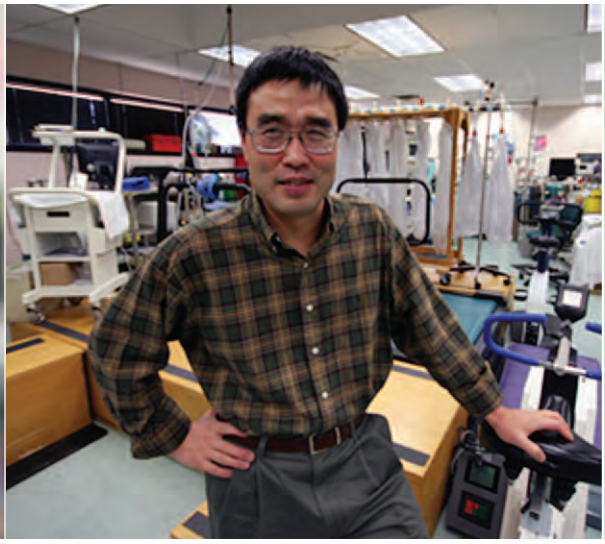
How Clinical Trials Work

"Studies proceed in phases"

The U.S. Food and Drug Administration (FDA) has established a rigorous sequence of testing for experimental drugs. The system gradually builds evidence for a drug's effectiveness and determines that a drug has an acceptable "safety profile" (that is, the risks associated with its use are reasonable, given its potential benefit). Experimental drugs must perform well enough in each phase to be allowed to progress to the next one.

Preclinical studies in laboratories establish a scientific basis for believing a drug is reasonably safe and may be effective.

- Phase I trials, the first stage of human testing, typically enroll fewer than 100 volunteers. These studies are primarily concerned with assessing risks and side effects associated with a drug.
- Phase II trials enroll up to a few hundred volunteers with the condition the drug is designed to treat. These studies provide further information about safety and focus on determining the best dose of a drug. Scientists also watch for signs of effectiveness.
- Phase III trials enroll several hundred to thousands of volunteers, often at multiple study sites nationwide. They provide the chief evidence for safety and effectiveness that the FDA will consider in deciding whether to approve a drug.
- Phase IV trials, also called post-marketing studies, are often required by FDA after a drug is approved. The trial sponsor must monitor the health of individuals taking the drug to gain further insight into its long-term safety and effectiveness and the best way to use it.



Dr Zhang, who is a researcher at the Institute for Exercise and Environmental Medicine at Texas Health Presbyterian Hospital Dallas and an assistant professor at UT Southwestern Medical Center at Dallas and research nurse Estee Brunk, RN, BSN,

Memory Loss. Rx: Exercise?

By Kaitlyn White, BA, and Estee Brunk, RN, BSN

It's not a secret. Exercise has significant benefits for your physical health and your mind. It seems as though the news media has a new article out daily regarding what exercise can do for you. The New York Times published an article on March 23, 2011 that found physical activity keeps your mind sharper. A recent study at the University of Illinois at Urbana-Champaign showed that athletes performed better on a street-crossing task than non-athletes, indicating that sports help to focus your mind. If physical activity can be beneficial to help with focusing in a younger population, can it help older adults with cognitive decline? Fortunately, researchers are in the process of answering this question right now, and the answer is likely a favorable one.

The Alzheimer's Association has estimated that 5.4 million have Alzheimer's Disease (AD) in the United States, which equates roughly 1 in 8 older Americans. The Chicago Health and Aging Project (CHAP), a population-based study of chronic health diseases of older people, has found that nearly half of the people older than 85 years old have been diagnosed with AD. The Alzheimer's Association reports that Alzheimer's disease costs the U.S. $183 billion annually. On a global scale, Alzheimer's Disease International reported that for 2010 the total estimated cost of dementia was $604 billion. Clearly, Alzheimer's disease has a staggering impact on economies both domestic and abroad.

Building evidence suggests that physical activity can help slow cognitive decline and thereby reduce the risk of dementia. With recent findings, such as the one mentioned above, researchers are trying to see if an exercise intervention program would benefit those with Alzheimer's Disease (AD), or who are within the early stages of AD, beginning with memory loss. Cognitive decline includes problems with memory, language, thinking and judgment. So you may be inclined to ask, how does exercise improve cognition? We know that as we age, the brain begins to shrink. Exercise has been found to increase the size of the hippocampus in another study recently released by the University of Illinois. The hippocampus is responsible for short-term memory, long-term memory and spatial navigation. The individuals who engaged in the physical activity component of the study not only increased their aerobic fitness, they also increased their memory performance to a substantial degree.

The incidence of Alzheimer's Disease is only expected to increase within the next couple of decades. Research related to the slowing or prevention of the disease is vital as the cost of public health will increase as well; a fact clearly evidenced by the $604 billion dollar price tag referenced a bit earlier. However, aside from the financial burden, AD can greatly reduce quality of life and is devastating to friends and families alike which is why an exercise intervention program holds great potential benefit. Even if you do not have any memory concerns or a family history of dementia, physical activity is still beneficial to overall health for a myriad of reasons. However, it is recommended that you receive medical clearance from your personal physician prior to the start of any exercise program.

1. Reynolds, Gretchen. (23 March 2011). How Sports May Focus the Brain. The New York Times. http://well.blogs.nytimes.com/2011/03/23/how-sports-may-focus-the-brain/?ref=health
2. Alzheimer's Disease International. World Alzheimer Report 2010: The Global Impact of Dementia. http://www.alz.org/documents/national/World_Alzheimer_Report_2010.pdf
3. Alzheimer's Association. 2011 Alzheimer's Facts and Figures - www.alz.org/alzheimers_disease_facts_and_figures.asp

Kristin Martin-Cook M.S., Clinical Research Coordinator, Memory Research Unit at UT Southwestern

Alzheimer's Disease Neuroimaging *cont. from pg* ***1***

(PET) techniques to identify the brain changes that occur from normal aging, Mild Cognitive Impairment and early AD over time and how they relate to changes seen in spinal fluid, the fluid of the brain, and blood samples.

In addition to brain imaging studies, researchers at UT Southwestern are also looking for ways to identify the body's natural response to AD. Up to very recently, the only measurable way to identify AD was to look at the brain. This has long been a great roadblock to investigation because of the necessary caution taken when dealing with this highly sensitive part of the body. Historically, less intrusive measures of the human body, such as blood sampling and skin tissue biopsy, have not yielded consistent results. However, Dr. Dwight German of UT Southwestern has recently had early success with identifying disease respondent anti-bodies through a blood test. In another study called the Texas Alzheimer's Research Care and Consortium (TARCC), UT Southwestern researchers along with researchers at sister universities throughout the state have had similar results, albeit through different methods. Lastly, researchers have recently begun a study looking to identify biological markers of the disease by sampling living skin tissue.

It is hoped that these biomarker studies will not only lead to better and earlier detection but more importantly serve as a marker of disease progression and therefore responsiveness to new therapies that are under development at UT Southwestern and other medical institutions. These are just a sampling of several studies conducted at the Memory Research Unit at UT Southwestern targeting early memory problems as well as Alzheimer's disease. Research is necessary and on going. Studies are continually enrolling. Research is progressing, and major breakthroughs are very near, thanks to the efforts of many participants who have contributed to dementia research over the years. You can find out more about local research at www.utsouthwestern.edu/alzheimers/research.

First in, last out *continued from page* ***3***

stored, while the newest memory is no longer stored because the hippocampus is no longer doing its job.

It actually makes sense that mom repeats herself over and over, because her brain never registered the fact that she already asked the question or told the story before.

Biologically, the brain cannot do its job because the hippocampus is damaged.

You cannot teach mom to not repeat herself because the hippocampus cannot register the teaching or send it to the storage units of the brain -- this is caused by damage to the hippocampus.

Do yourself a favor -- think about this when an Alzheimer's patient keeps asking the same question over and over, or engages in behaviors like insisting you did not call this morning.

Recognizing why this is happening might help you overcome feelings of anger and frustration.

Carole Larkin MA,CMC,CAEd,QDCS,EICS
is a Geriatric Care Manager who specializes in helping families with Alzheimer's and related dementias issues. She also trains caregivers in home care companies, assisted livings, memory care communities, and nursing homes in dementia specific techniques for best care of dementia sufferers. ThirdAge Services LLC, is located in Dallas, TX and can be reached at Carole_Larkin@tx.rr.com or through www.thirdageservices.com

Healthy Volunteers Needed for Memory Study

Study Title: Telecognitive Assessment in Underserved Elders

Protocol Number: 032008-043

Department(s) involved in the Study: Neurology, Psychiatry

Purpose of the Study: This study is comparing the effectiveness of performing neurocognitive testing via a new medium, videoconferencing, and the standard method of the patient and examiner sitting across the table from each other. The video is not recorded. The study takes approximately 2 hours.

Participant Eligibility: Criteria For Inclusion Of Subjects: 1. Minimum age of 50 years 2. Capable of hearing well enough to maintain a regular conversation (with or without the use of hearing aid) 3. Able to read simple sentences in large print (with or without vision correction, glasses, contacts, etc) 4. English fluency

Disease/Condition Under Study: Alzheimer's Disease, Mild Cognitive Impairment, Healthy Volunteers

Study Doctor: Dr. C Munro Cullum
Location of Study: Aston Ambulatory Care Center, University of Texas Southwestern Medical Center, Dallas
Contact Phone: 214-648-4642
Other Information: Healthy volunteers are needed for this and many studies on an ongoing basis. If you are interested in working with our Alzheimer's Disease Center to contribute your time to participating in other studies, please call 214-648-9376.

Researchers at UT Southwestern uncover preliminary new blood test to detect Alzheimer's disease

By UT Southwestern News Department

UT Southwestern Medical Center scientists have helped develop a novel technology to diagnose Alzheimer's disease from blood samples long before symptoms appear.

This preliminary technology, which uses synthetic molecules to seek out and identify disease-specific antibodies, also could be used eventually in the development of specific biomarkers for a range of other hard-to-diagnose diseases and conditions, including Parkinson's disease and immune system-related diseases like multiple sclerosis and lupus, the researchers predict

"One of the great challenges in treating patients with Alzheimer's disease is that once symptoms appear, it's too late. You can't un-ring the bell," said Dr. Dwight German, professor of psychiatry and an author of the paper published in the Jan. 7 edition of Cell. "If we can find a way to detect the disease in its earliest stages – before cognitive impairment begins – we might be able to stop it in its tracks by developing new treatment strategies."

Because patients with Alzheimer's disease (AD) exhibit immune system activation and neurodegeneration in several brain regions, researchers in the study hypothesized that there may be numerous antibodies in the serum of affected patients that are specific to the disease and can serve as a biomarker.

Antigens – substances such as protein from a virus or bacteria that triggers an immune response – traditionally have been necessary for the discovery of antibody biomarkers. It has been impossible previously to identify an antibody (a type of targeted immune molecule) without first knowing the antigen that triggers its production.

The new study, however, challenges conventional wisdom and uses synthetic molecules (peptoids) rather than antigens to successfully detect signs of disease in patients' blood samples. These peptoids have many advantages; they can be modified easily and can be produced quickly in relatively large amounts at lower cost.

The adaptive immune system is thought to be a rich source of protein biomarkers, but diagnostically useful antibodies remain undiscovered for a large number of diseases, Dr. German said. This is, in part, because the antigens that trigger an immune response in many diseases are unknown. The technology behind this discovery is essentially an immune-system reader, which is designed to pick out antibodies without knowing in advance which ones to look for.

The researchers used a combination library of several thousand peptoids to screen serum samples from mice with multiple sclerosis-like symptoms as well as from healthy control mice. The particular peptoids that retained more antibodies from the blood samples of the diseased animals were identified as potential agents for capturing diagnostically useful molecules.

The investigators then examined serum samples from six AD patients, six healthy patients and six patients with Parkinson's. Three peptoids were identified that captured six times the IgG antibody levels in all of the Alzheimer's patients when compared to the control group or to the Parkinson's patients. Two of the peptoids were found to bind the same IgG antibody, while the third was shown to bind to different antibodies – meaning there are at least two candidate biomarkers for AD. Using an additional set of 16 normal control subjects and 10 subjects at the very early state of AD, the three candidate biomarkers identified AD with 90 percent accuracy.

"The results of this study, though preliminary, show great potential for becoming a landmark," said Dr. German.

Other UT Southwestern researchers involved in the study were Dr. Ramon Diaz-Arrastia, professor of neurology and neurotherapeutics; Steven Connell, research technician; and Dr. Linda Hynan, professor of clinical sciences. Others include senior author and former UT Southwestern faculty member Dr. Thomas Kodadek, now at Scripps Florida Research Institute; Dr. Anne Gocke, former postdoctoral fellow in translational medicine; and researchers with Opko Health Laboratories.

Funding was provided by the National Institutes of Health.

Visit http://www.utsouthwestern.org/neurosciences to learn more about UT Southwestern's clinical services in neurosciences, including psychiatry.

Need answers and a starting point?

Make your first call to the 24-hour Helpline:
1-800-272-3900 www.alz.org
Greater Dallas Chapter:
214-827-0062 www.alzdallas.org
North Central Texas Chapter:
817-336-4949 www.alz.org/northcentraltexas

To identify other genetic factors that could affect the risk of late-onset Alzheimer's, NIH's National Institute on Aging (NIA) established the Alzheimer's Disease Genetics Consortium (ADGC).

New Genetic Risk Factors for Alzheimer's Disease

By NIH Research Matters, Office of Communications, National Institutes of Health

In 2 massive studies involving thousands of DNA samples, scientists from around the world identified a number of new genes and confirmed several others that may be risk factors for late-onset Alzheimer's disease.

Until recently only one gene, APOE, had been significantly linked to the risk for developing late-onset Alzheimer's disease. In 2009 and 2010, researchers identified 3 additional genes as possible risk factors. Although these new genes don't predict the development of late-onset Alzheimer's disease as strongly as APOE, their identification gives researchers an idea of the biological factors that may contribute to the disease.

To identify other genetic factors that could affect the risk of late-onset Alzheimer's, NIH's National Institute on Aging (NIA) established the Alzheimer's Disease Genetics Consortium (ADGC).

A similar research effort was underway involving groups of investigators from the United Kingdom, the United States, France and other European countries. Funding for both studies came from several NIH institutes and other organizations. The results were published in 2 papers on April 3, 2011, in the online edition of Nature Genetics.

The ADGC conducted a genome-wide association study on DNA samples collected from more than 54,000 participants. By comparing genetic variations in Alzheimer's patients to those of cognitively normal individuals, the researchers were able to discover variants that were consistently associated with the disease.

The genes identified by these studies suggest that pathways involved in inflammation, the movement of proteins within cells and lipid transport may have a role in the disease process. These new insights will affect how scientists study Alzheimer's and develop new strategies to prevent and treat the disease.

"This is the culmination of years of work on Alzheimer's disease by a large number of scientists, yet it is just the beginning in defining how genes influence memory and intellectual function as we age. We're all tremendously excited by our progress so far, but much remains to be done, both in understanding the genetics and in defining how these genes influence the disease process," said ADGC's director, Dr. Gerard Schellenberg of the University of Pennsylvania School of Medicine.

TRANSITIONS A JOURNEY IN TIME

AVALON ALZHEIMER'S CARE

Is brought to you quarterly by: Avalon Alzheimer's Care, Inc. a Texas based not-for-profit corporation that believes in taking a whole new approach in caring for those with Alzheimer's Disease and related dementias. Our genuine concern for the quality of life of seniors with dementia has motivated us to redesign the standards of development, management, and operational criteria for senior living environments.

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