Fall 2013



Alzheimer's

A 'WIN-WIN' UTSW exercise study helped Plano woman in body and mind



Sheila and Ron Jack

Sheila Jack referred to it as her "disconnect"– those odd moments when she'd try and fail to remember the name of an old friend who was speaking to her. Or those times, when sitting at her computer, she would forget how to work the same software program she had been using for a decade.

"I would look at the screen and say to myself, 'Now what do I do?'" said Mrs. Jack, 66. "I'd have to get up and walk around, and I'd think to myself, 'Sheila, what is wrong with you?'

"My mother has Alzheimer's disease, and I knew I definitely had some sort of disconnect." Mrs. Jack learned her symptoms were signs of mild cognitive impairment (MCI), which causes a slight but noticeable decline in cognitive functions such as memory and thinking skills. The declines typically are significant enough to be noticed by those experiencing them but tend not to interfere with daily life or independence.

Thanks to a local newspaper story, the Plano grandmother learned about and eventually enrolled in an exercise study jointly run by the Alzheimer's Disease Center at UT Southwestern and Texas Health Presbyterian Hospital Dallas. The study, which is designed for people with MCI, creates an individually tailored exercise program for each participant. Researchers examine the effects of exercise on cognitive and cardiovascular health and study changes in proteins that damage or protect brain cells.

Individuals with MCI often are at increased risk for Alzheimer's disease or other dementias, said Dr. Mary Quiceno, Assistant Professor of Neurology and Neurotherapeutics who directs the Education and Outreach Core of the Alzheimer's Disease Center. But following the adage that what's good for the heart is good for the brain, researchers are learning that exercise is a likely deterrent for dementia disorders, Dr. Quiceno said.

For example, a 2012 investigation by UT Southwestern and The Cooper Institute published in the *Archives of Internal Medicine*, found that people who maintained healthy lifestyles in their 30s, 40s, and 50s had few chronic illnesses, including Alzheimer's, later in life. People who increased their fitness levels by 20 percent in their midlife years lowered their chances of developing Alzheimer's by 20 percent.

"We know that exercise directly affects the growth of brain cells in a region of the brain called the hippocampus, which plays an important role in storing and accessing memories," Dr. Quiceno said.

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AVERTING ALZHEIMER'S: Mayo Clinic professor says key to treating Alzheimer's disease is prevention



Dr. Clifford R. Jack Jr.

For years, clinical trials for Alzheimer's disease unsuccessfully focused on people with dementia – a stage in the disease now considered by physicians to be too late to represent an ideal time for treatment.

But as modern medicine hones new techniques – primarily brain imaging and biomarker testing – to identify people who do not yet have clinical symptoms but are at risk for Alzheimer's, the focus in clinical trials is shifting from people with dementia to people with no symptoms but who do have imaging and biofluid signs of pathology.

"Treating those with Alzheimer's disease isn't going to be about restoring people with dementia to normal cognitive function. It's going to be about preventing it in those who are at risk," said Dr. Clifford R. Jack Jr., Professor of Radiology at Mayo Medical School.

Preventing Alzheimer's disease through early detection will be one of the key themes of Dr. Jack's lecture on Sept. 16 at the Fall Public Forum. The lecture is titled "The Future of Diagnosing and Treating Alzheimer's Disease."

Dr. Jack's research group at the Mayo Clinic serves as the central MRI

lab for national and international observational and therapeutic studies in Alzheimer's disease. His group heads the MRI section for the Alzheimer's Disease Neuroimaging Initiative, which began in 2005. The Alzheimer's Disease Center at UT Southwestern is one of the research sites for this study.

Dr. Jack said physicians already have developed effective methods of testing for Alzheimer's disease, often turning up signs of its pathology a decade or two before the patient develops any clinical signs of dementia. Through advanced brain imaging and spinal taps that test for the presence of beta-amyloid in the cerebrospinal fluid, it's possible to find and identify definitive evidence of the disease.

"In the past, people have thought of Alzheimer's disease as a condition defined by observable, clinical symptoms," Dr. Jack said. "The reality is that brain pathology that ultimately causes the symptoms precedes those symptoms by many years."

One of the problems with current testing for Alzheimer's disease is expense. Unlike hypertension, in which a clinician can measure blood pressure with a simple blood pressure cuff, testing for signs of Alzheimer's disease remains costly and invasive.

The other problem is what to do with positive test results, Dr. Jack said. The Food and Drug Administration hasn't approved a treatment that slows, stops, or reverses the effects of Alzheimer's disease in more than a decade – and no drug on the market is effective at relieving the symptoms.

Dr. Jack said he is optimistic, however, that a focus on pre-symptomatic patients who show signs that they will develop the disease will lead to better treatments.

"A better understanding of both the basic biology of the disease and of biomarkers obtained from living people will lead to a design of clinical trials that hopefully will demonstrate a therapeutic effect," he said. "If one could intervene earlier, you would be able to exert a much stronger effect at delaying the disease."

WHAT: 2013 Alzheimer's Fall Public Forum

WHEN: 7 p.m., Monday, Sept. 16

- WHERE: Simmons/Hamon Biomedical Research Building, 6000 Harry Hines Blvd.
- LECTURE: "The Future of Diagnosing and Treating Alzheimer's Disease"

NOTEWORTHY: The forum is free to the public, and there is complimentary valet parking. Confirm your attendance by calling 214-648-2344.

Dr. Jack, who has been on the Mayo Clinic faculty since 1985, has been recognized by numerous neurology and radiology groups. His awards include the 2007 American Society of Neuroradiology Award for Outstanding Contributions in Research; the 2008 Potamkin Prize from the American Academy of Neurology; the 2012 International Society of Magnetic Resonance in Medicine Gold Medal; and the 2012 MetLife Foundation Award for Medical Research in Alzheimer's Disease.

Last year he was elected to the inaugural Council of Distinguished Investigators of the Academy of Radiology Research. He also received the Distinguished Mayo Clinic Investigator Award for 2013. *

FROM THE DIRECTOR | Roger N. Rosenberg, M.D.

A remarkable study came out earlier this year that attempted to calculate a dollar figure representing the true costs of Alzheimer's disease.

The study – produced by the nonprofit Rand Corp., sponsored by the National Institute on Aging, and published in *The New England Journal of Medicine* – concluded that Alzheimer's disease is the nation's costliest ailment. The staggering sum, estimated at between \$157 billion and \$215 billion a year, surpasses even bigger killers such as cancer and cardiovascular disease.

The reason why this dreadful illness comes with such a high financial burden won't surprise any physician who has treated an Alzheimer's patient, nor any family member who has cared for one. People with Alzheimer's disease live much longer than cancer patients or heart attack victims – on average eight years after initial diagnosis. All the while, they become desperately ill and often totally dependent on others for their care.

The most expensive costs, we know, don't come from treating or diagnosing the disease. Rather, they stem from the daily care needed to get cognitively impaired people through their daily lives.

The costs of Alzheimer's disease, of course, go beyond the financial. Ask any person in the early stages of dementia what it's like to know their minds and memories are slipping away. Ask the loved ones of someone suffering from Alzheimer's about the emotional toll of caring for a family member. Ask physicians and researchers about the frustrations we feel over our inability to find a treatment. As you've read before in these pages, the problem will only get worse. An estimated 4 million to 5 million people in America suffer from Alzheimer's disease, a number that's expected to increase by as much as half over the next two decades. And yet, federal support for Alzheimer's research remains at about one tenth of what is spent for cardiovascular disease and cancer – roughly \$500 million annually, compared to \$4 billion and \$6 billion, respectively.

At UT Southwestern Medical Center, we're sensitive to the burdens faced by spouses, children, and other caregivers. The Alzheimer's Disease Center offers a support group for dementia caregivers that meets on the third Friday of each month, from 1 p.m. to 2:30 p.m., in the Memory Research Unit, located in the James W. Aston Ambulatory Care Building. (For more information, please call 214-648-9368.) It is open to anyone who cares for a person with dementia and provides valuable support, education, and research information.

Research, of course, remains central to our mission. We continue to benefit from the unwavering generosity of the Friends of the Alzheimer's Disease Center, a far-seeing group that has contributed more than \$1 million since 1996 toward research efforts into neurodegenerative disease. The seed money from the Friends helps junior researchers embark on important investigations into Alzheimer's and other neurodegenerative diseases and attracts additional funding from governmental agencies, advocacy organizations, and other supporters.



Earlier this year, the Friends awarded four \$65,000 grants to UT Southwestern faculty members. In this newsletter, you can read about how Drs. Kevin King, Yun Liu, Steven Patrie, and Martin Woon intend to use those funds to attack neurodegenerative diseases from different angles.

We also are excited to announce that we have a distinguished Alzheimer's expert speaking in September at our Fall Public Forum. I invite all Friends of the Center and readers of this newsletter to come out and hear Dr. Clifford R. Jack Jr., a Professor of Radiology at the Mayo Clinic, discuss MRI techniques for diagnosing and measuring the progression of Alzheimer's.

On a personal note, I'd like to close by acknowledging the generous support of the Darrell K Royal Research Fund for Alzheimer's Disease, a group who's advocacy led to a \$50,000 award to my own research project: a 10-year effort at making a vaccine against beta-amyloid, a protein that forms plaques in the brain and is believed to be both a sign and a cause of Alzheimer's disease. Such contributions bring us closer to better treatments for this disease. *

FUNDING THE FIGHT Friends group awards \$260,000 to four UTSW researchers

SINCE ITS INCEPTION IN 1996, the

Friends of the Alzheimer's Disease Center has donated more than \$1 million toward UT Southwestern Medical Center-led investigations into Alzheimer's and other neurodegenerative diseases. These critical gifts help early-career researchers get started on important projects and attract additional funding from other governmental groups and supporters. Earlier this year, the Friends awarded four \$65,000 grants to UT Southwestern researchers.



2013 Grant Recipient **KEVIN KING, M.D.**

DR. KING, Assistant Professor of Radiology, was awarded a grant for his project "The Role of Cardiovascular Insults on Aging Changes in Brain Structure and Vascular Function and Their Clinical Outcomes." He completed both residency and fellowship training at UT Southwestern before joining the faculty in 2011.

"I have always been interested in how the brain functions and the mechanisms that make it work," he said.

Dr. King hypothesizes that, over time, aortic stiffness makes hypertensive damage to the brain more potent and contributes to cognitive decline. Using new advanced imaging techniques, he plans to explore the specific changes in regional blood flow that cause these insults to brain structure. Dr. King hopes to identify the risk factors most responsible for diseases in small and large vessels that feed the brain and demonstrate how these changes can help predict brain atrophy and cognitive decline.

Dr. Ronald Peshock, Assistant Dean for Informatics and Professor of Radiology and Internal Medicine, said Dr. King is a productive investigator who has developed a specific interest in cognitive impairment, stroke, and microvascular disease in the brain.

"Dr. King is an outstanding candidate for making significant contributions to our understanding of the relationships between cardiovascular disease and cerebrovascular disease, which are of growing importance in the care of patients with Alzheimer's disease and cognitive decline," Dr. Peshock said.

2013 Grant Recipient **YUN LIU, Ph.D.**

DR. LIU, Instructor of Neuroscience, was awarded a grant for her project "The Role of APP, Beta-Amyloid, and LRP4 in Synapse Formation and Function." She came to UT Southwestern from China in 2005, attracted by the Medical Center's reputation for basic science research.

"This institution provides an excellent environment for fundamental research, and that's the kind of research I like to do," she said. Under the mentorship of Dr. Weichun Lin, Associate Professor of Neuroscience, Dr. Liu's research focuses on investigating how motor neurons develop and form synaptic connections to skeletal muscle at the neuromuscular junction and what mechanisms prevent the neuromuscular junction from degenerating. Dr. Liu intends to investigate the role played by two proteins, known as APP and LRP4, in the formation and degeneration of synapses. She plans to study the interaction of these proteins at the neuromuscular junction, the point at which a neuron communicates with a muscle.

Dr. Joachim Herz, Director of the Center for Alzheimer's and Neurodegenerative Diseases and holder of the Thomas O. and Cinda Hicks Family Distinguished Chair in Alzheimer's Research, called Dr. Liu's project "highly innovative."

"It also makes ideal use of several core databases, tissue, and serum collection that only the Alzheimer's Disease Center can provide," Dr. Herz said.





2013 Grant Recipient **STEVEN PATRIE, Ph.D.**

DR. PATRIE, Assistant Professor of Pathology and the John L. Roach Scholar in Biomedical Research, was awarded a grant for his project "Proteotyping L-PGDS Glycosylation Dysfunction in CNS Disorders." He joined the UT Southwestern faculty in 2011.

Dr. Patrie seeks to identify warning signs of Alzheimer's disease long before any symptoms appear by characterizing signs of inflammation at the molecular level. He proposes analyzing changes to protein-bound sugars, which he hypothesizes will function as early warning biomarkers of inflammation in brain tissue.

"Earlier detection could, in turn, lead to early intervention, and possibly prevention," Dr. Patrie said. "If our hypothesis is correct ... and we can detect them early on, then we may be able to intervene before the inflammation can actually damage the brain." In collaboration with Dr. Benjamin Greenberg, Assistant Professor of Neurology and Neurotherapeutics and Pediatrics, Dr. Patrie will use Fourier transform mass spectrometry as a kind of molecular bar-code scanner to find early signs of brain inflammation. It's a cuttingedge concept called proteotyping that has emerged only in the last few years.

Dr. Diego Castrillon, Associate Professor of Pathology and holder of the John H. Childers, M.D., Professorship in Pathology, said this line of research meshes with Dr. Patrie's efforts to establish a state-of-the-art proteomics lab.

"The proposed work epitomizes a cutting-edge, novel research, the impact of which may resonate throughout science and medicine by showing that protein proteotyping is routinely possible through the power of top-down analytics," Dr. Castrillon said.

2013 Grant Recipient FU LYE "MARTIN" WOON, Ph.D.

DR. WOON, Assistant Professor of Psychiatry, was awarded a grant for his project "Predicting Trajectories of Mild Cognitive Impairment with Medical, Demographic, Neuropsychological, and Neuroimaging Data." He arrived at UT Southwestern in October 2012 having already established a strong research background in neurological and neuropsychiatric disorders. Dr. Woon says mild cognitive impairment (MCI) does not always lead to dementia. Emerging studies suggest the opposite; that, in fact, a majority of patients with MCI either remain stable without additional cognitive decline or recover enough to be considered cognitively normal. Thus the focus of Dr. Woon's research is using existing Alzheimer's Disease Center data to develop a model that will help clinicians determine whether an MCI patient will improve or remain stable.

Dr. Munro Cullum, Chief of Psychology and holder of the Pam Blumenthal Distinguished Professorship in Clinical Psychology, calls Dr. Woon's research proposal "unique, timely, and important."

"Little is known about the neuroimaging, neurobehavioral, and sociomedical factors that contribute to these different clinical trajectories, although understanding this would represent a very significant contribution to the field," Dr. Cullum said.



BRAIN HEALTH

Tips from Dr. Mary Quiceno, Assistant Professor of Neurology and Neurotherapeutics, on how to keep your brain healthy and stave off memory loss

- Talk: Socialization is important to mental health, and participating in social activities may help preserve cognitive function.
- Think: Build your cognitive reserve by continuing to learn, which can help improve processing speed, working memory, and attention.
- Eat: Consuming baked or broiled fish at least once a week helps maintain your brain health. Diets rich in omega-3 essential fatty acids, such as the Mediterranean diet, prevent and slow dementia.
- Exercise: Working out increases brain factors that stimulate brain cell growth and decreases the risk for high blood pressure and diabetes.
- Sleep: Adequate rest and relaxation are important for brain health. Memories are consolidated when you sleep, so sleep will help improve your memory.



Dr. Mary Quiceno

WIN-WIN

Continued from page 1

For Mrs. Jack, her initial participation in the study included MRI and a positron emission tomography scan, blood pressure reading, oxygen levels, a brain blood-flow test, and a full neuropsychological workup that included memory tests.

In addition, an exercise program director put together a workout routine she could do at home that emphasized muscle resistance and stretching. She worked out at least three times a week, sometimes repeating the circuit twice in a day.

"Once I got into it, I really enjoyed it," she said. "It was good for me. It gave me more strength, and it made me feel like I could do anything, like I was ready for the day. And mentally, it made me feel like I was accomplishing something for myself. I could feel myself focus."

After six months, Mrs. Jack had the regimen tweaked. "It was more stretching and a little bit more of a challenge," she said. Overall, she participated in the exercise portion of the study for a total of eight months.

Mrs. Jack completed her involvement in the exercise program in October 2012 and said she found it to be beneficial – for herself and others. "It helped me feel like I was going forward in my life. It's better to get ready and get prepared and maybe get better," she said. "It's a win-win all the way around. You are helping the research, and the research is helping you." *

"IT'S A WIN-WIN all the way around. You are helping the research, and the research is helping you."

Exercise study participant Sheila Jack



Research Studies

CLINICAL TRIALS

EXERCISE

People with mild cognitive impairment who do not currently adhere to a regular fitness program are needed for a one-year study that will compare individually tailored, supervised aerobic exercise training with flexibility and stretching. The trial researchers will investigate the effects of exercise on cognitive and cardiovascular health, as well as changes in proteins known to damage and/or protect the brain. Call Kristin Martin-Cook, 214-648-9368, or Candace Hill, 214-345-4665, for more information.

COGNITIVE TRAINING FOR MILD MEMORY COMPLAINTS

People age 60 or older who are in overall good health but who are

noticing more "senior moments" or have been diagnosed with mild cognitive impairment are needed for a study evaluating the effects of cognitive training on brain function. A brief cognitive screening will be given to determine eligibility for the study. Those who qualify will receive eight cognitive training sessions, study-related assessments, an electroencephalogram to measure brain waves, and follow-up testing. For more information, call Kristin Martin-Cook, 214-648-9368, or Audette Rackley, 214-905-3007.

THE TENT STUDY

People with mild memory loss are sought for a two-month study on whether sleeping in an "altitude tent" and exercising at sea level can boost protective protein levels in the brain and blood. Call Kristin Martin-Cook, 214-648-9368, for more information.

SILDENAFIL PILOT STUDY

Men and women age 55 and older with either mild cognitive impairment or early Alzheimer's disease are needed for a one-visit study to determine if the drug sildenafil, which is Food and Drug Administration-approved for other uses, can increase blood perfusion in the brain. The study involves an MRI and a 10-minute cognitive test before and after administration of the medication. Participants will be compensated for their time. Call Gloria Williams, 214-648-9331, for more information. *****

OBSERVATIONAL AND BIOMARKER DEVELOPMENT

While these studies do not require or offer a new treatment, they are the foundation for future research and therapeutic trials.

ALZHEIMER'S DISEASE Neuroimaging initiative – Phase 2 (adni 2)

This study builds on the first ADNI studies. People ages 55 to 90 who have memory complaints but are without impairment on cognitive testing are needed. Participants will undergo MRI, traditional glucosebased positron emission tomography (PET), new amyloid PET scanning to investigate the formation of beta-amyloid plaque formation, and standard neuropsychological and neurological exams. Participants will be compensated. Call Kristin Martin-Cook, 214-648-9368, for information.

CORE AND TARCC RESEARCH STUDIES

People with no memory complaint, mild cognitive impairment, or early Alzheimer's disease are needed for observational studies. The studies usually involve one visit a year for neuropsychological testing, neurological exams, brain imaging, and blood sampling. The data collected from these visits are used by many investigators studying the aging brain and disorders of cognitive function. These visits may involve financial compensation. Call Sarah Hoefs, 214-648-0563, for more information.

LOAD (LATE-ONSET ALZHEIMER'S DISEASE) GENETICS INITIATIVE

The LOAD study began enrolling subjects in 2002, with more than 500 subjects enrolled through UT Southwestern. A new grant, based on previous findings from that study, is facilitating a phone followup for subjects from the first study as well as enrolling new subjects. The goal of this national study is to expand upon the scope of information/ data gathered from subjects already enrolled in the first phase of LOAD as well as to enroll new large families (with three or more living siblings age 60 or older) diagnosed with Alzheimer's disease. The focus is to learn more about the genetic, environmental, and health risks that may contribute to the development of Alzheimer's. For all subjects previously enrolled in the LOAD study, the coordinator will call each person for phone follow-up only. New subjects from previously participating families who are now age 60 or older may also enroll in this study. Call Barb Davis, 214-648-9367, for more information. *



Join Us SUPPORT THE QUEST FOR PREVENTION, TREATMENT, AND A CURE



JOIN THE FRIENDS OF THE ALZHEIMER'S DISEASE CENTER

The Friends of the Alzheimer's Disease Center provides crucial support to UT Southwestern Medical Center's most promising and passionate researchers working to unlock the mysteries of Alzheimer's disease.

In addition to funding research through generous annual grants, the Friends sponsor a community-wide public forum every fall and spring, where the latest breakthroughs and best information on Alzheimer's disease are presented by leading experts from UT Southwestern and major medical centers nationwide.

Membership begins at \$500 per year, per individual or couple. Your donation is tax deductible and truly makes a difference in the fight against Alzheimer's disease.

To join the Friends of the Alzheimer's Disease Center, call 214-648-2344. Your support safeguards vital research into enhancing quality of life through early detection and improving the lives of patients and their families who live courageously each day with Alzheimer's disease.

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