Blood Tests for Alzheimer’s Disease

Determining whether mild memory problems mark the beginning of an inevitable mental decline is one of the most difficult aspects of Alzheimer’s disease (AD). Researchers at the Stanford University School of Medicine have developed a blood test that is a step toward giving people an answer two to six years in advance of the onset of the disease.

The test identifies changes in a handful of the proteins in blood plasma that cells use to convey messages to one another. The research team discovered a connection between shifts in the cells’ dialog and the changes in the brain accompanying Alzheimer’s disease (AD). They found that the blood test could distinguish who had AD with 90 percent agreement with the clinical diagnoses, and could predict the onset of Alzheimer’s disease two to six years before symptoms appeared.

“Just as a psychiatrist can conclude a lot of things by listening to the words of a patient, so by ‘listening’ to different proteins, we measure whether something is going wrong in the cells,” said Tony Wyss-Coray, PhD, Associate Professor of Neurology and senior author of the study.

“It’s not that the cells are using new words when something goes wrong,” said Wyss-Coray. “It’s just that some words are much stronger and some are much weaker; the chatter has a different tone.”

Listening to cells’ messages may lead to the first noninvasive diagnostic test for Alzheimer’s; it could also lead to similar discoveries about other disorders by focusing on what cells use to talk to each other, said Wyss-Coray, who is part of the Geriatric Research, Education and Clinical Center at the Veterans Affairs Palo Alto Health Care System.

Currently, the clinical diagnosis for Alzheimer’s is one of exclusion – by testing for other causes of memory loss and cognitive declines, such as stroke, tumors and alcoholism. Alzheimer’s disease is now the most common cause of dementia. If all other causes of memory loss can be eliminated, then what remains is most likely Alzheimer’s. Unfortunately, the clinical diagnosis is imperfect; the only definitive diagnosis is by brain autopsy after death.

The blood-test concept began when Wyss-Coray and Sandip Ray, the first author of this paper, collaborated to measure levels of 120 different proteins used by cells to communicate to see if any of them could be indicators for Alzheimer’s.

Ray used blood samples from five people diagnosed with Alzheimer’s, and compared those to samples from five people who didn’t have the disease. He found a number of communication proteins that demonstrated striking differences between the two groups.

Markus Britschgi, PhD, a postdoctoral scholar in Wyss-Coray’s lab, became intrigued with the idea that proteins used by cells to communicate could be measured in the blood to indicate

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what is going on in the body - including the brain.

“This study made me realize that we should get away from this image of a brain isolated from the body,” said Britschgi, who is second author of the paper. “The brain is part of the body and so it’s connected in one huge network.”

By contacting clinics in the United States, Sweden, Poland and Italy, Britschgi obtained a total of 259 archived blood samples from individuals who had symptoms ranging from normal to mild cognitive impairment to advanced Alzheimer’s. Starting with 120 communication proteins, the team developed an analysis procedure to recognize if there was a pattern seen in Alzheimer’s that could be compared with that of people without the condition. They discovered that as few as 18 proteins were sufficient to identify an Alzheimer’s-specific pattern.

Results

Using blood samples from 92 individuals who ranged from no symptoms to full dementia, the protein analysis matched the clinical diagnosis 90 percent of the time.

They then asked if they could predict the development of Alzheimer’s among 47 people with mild cognitive impairment who had been followed from two to six years. The test - done on blood samples taken several years earlier - flagged 91 percent of the patients who developed Alzheimer’s by the end of the follow-up time, as diagnosed by conventional methods.

“Already we have people approaching us at meetings asking if they can give us a vial of their grandfather’s blood for testing,” said Britschgi. Their findings show that it is possible to use factors in the blood to diagnose and even predict the disease, but, the authors emphasized, it must now be confirmed in other labs.

According to Satoris Inc, the company will develop a commercial Alzheimer’s blood test, initially for use in research labs and, if confirmed as reliable, eventually as a clinical diagnostic test upon regulatory approval.
Spotlight: Joy Taylor, PhD.
Assistant Director, Aging Clinical Research Center; Psychiatry Service, VA Palo Alto Health Care Systems and Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine

As the Assistant Director of the Aging Clinical Research Center, I have a long history with the Center. Dr. Jared Tinklenberg (the Center’s Clinical leader) mentored me when I was fresh out of University of Washington’s Ph.D. program in human cognitive psychology. Over the years here, I have led a longitudinal study as well as two clinical drug trials involving older adults who perceive their memory is declining but are otherwise doing well in their everyday function (neither drug helped; but fortunately, 95% of the study participants showed stable memory functioning over four years of observation).

Facilitating long-term follow-up of our participants from initial evaluation to eventual autopsy has been the most vital Center function I carry out. Through these efforts, I have had the pleasure of supervising the many talented research assistants our Center has recruited, and I have assisted our Director in writing 500-page grant applications to our government funding sources. In addition to these vital behind-the-scenes roles in the Center, our research on aging aircraft pilots landed me squarely in front of the news camera with PBS’s Jim Lehrer NewsHour and NBC’s Nightly News last year. Our longitudinal study of the flight simulator performance of pilots in their 40’s and beyond shines light on the apparent benefits of expert knowledge to gray-haired pilots.

My hope is that more and more people can achieve successful aging through life-long education and new medical knowledge. In keeping with successful aging, my husband and I have taken up ballroom dancing lessons in the past year and we’ve started growing a few veggies at home. It’s nice he likes broccoli as much as I do!

In closing, I would like to express the deep appreciation and admiration I feel toward all of the families who have contributed so much time to our research programs at the Aging Clinical Research Center.

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Britschgi and Wyss-Coray are interested in finding out why the cell communication pathways are altered in Alzheimer’s. In their study, they determined that the 18 proteins that indicate Alzheimer’s are also involved in the production of new blood cells, immune processes and apoptosis, the process of programmed cell death when a cell is no longer needed.

“Our hypothesis is that there is something wrong with the production of certain blood cells, which may be needed to clear that stuff that accumulates in the brain in Alzheimer’s disease,” said Wyss-Coray. “That makes a lot of sense, and it is very exciting to think of immune cells and molecules interacting with the brain.”


-- Stanford News Service
**Sleep Disruption and Modafinil**

To sign up for this Study,
Contact: Ban Ku
(650) 849-1971

**Home-Based Assessments**

To sign up for the Home-Based Assessment study
Contact: Emily Gere
(650) 852-3287

**Light Study**

To sign up for the Light study
Contact: Ellen Kim
(650) 496-2578

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**RESEARCH OPPORTUNITIES**

We are recruiting for a study that examines the usefulness of modafinil (Provigil) in treating sleep problems in Mild Cognitive Impairment or Alzheimer’s disease. We anticipate that this drug will both improve your nighttime sleep and make you less sleepy during the daytime. Modafinil is a drug that is FDA-approved for the treatment of sleepiness in a variety of conditions, but has not been examined in older individuals with memory impairment. The study takes place for 4-weeks in your own home, with weekly visits to the VA. There is also a free screening for sleep apnea that will take place in your home.

You may be eligible to participate if you are:
- Diagnosed with Alzheimer’s disease or Mild Cognitive Impairment
- Live at home with a caregiver or partner
- Willing to take an FDA approved medication (modafinil)

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Older individuals, particularly the very elderly, may have physical, social, and health limitations that make it difficult for them to take part in research trials. This study will examine the use of mail-in questionnaires, automated telephone technology, or computer questionnaires to assess health and memory in the home environment to see how home-based assessments might be used in prevention research programs. Such an approach might reduce the cost and increase participation in these trials.

The Home-Based Assessment study needs volunteers who:
- Are over the age of 75
- Have normal mental function
- Are fluent in English
- Live independently
- Are willing and able to take multivitamins provided by the study
- Are able to answer and dial a telephone, have access to secure mail, and willing to learn computer skills

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This study is testing light treatment to improve daytime alertness and nighttime sleep. It is designed to benefit both the individual with memory impairment and their caregiver. A Stanford research team will set up light equipment for the treatment in your home and assist in making your participation in the study as convenient as possible.

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

There is evidence that physical exercise can protect and enhance cognitive functions in aging populations. This multi-site study, which is part of the Alzheimer’s Research Centers of California, will ask caregivers to fill out questionnaires about the amount of activity the individual with cognitive impairment participates in on a weekly basis. The questionnaires will be administered once a year, for two years, either in person or over the phone. Each session will take 1-3 hours.

Participants should:
- Be older than 60 years
- Be English or Spanish speaking
- Have someone who has frequent contact (3-4 days per week)

Exercise and Alzheimer’s Disease

To sign up for the Exercise study
Contact: Christine Coughlin
(650) 858-3915

RAGE Inhibitors

Researchers are conducting studies on an experimental medication to block nerve damage and inflammation in the brain that can lead to progressive memory loss and behavioral changes in people with Alzheimer’s disease. Researchers will test an experimental drug that seeks to stop amyloid beta from binding to a receptor in the brain called RAGE (receptor for advanced glycation endproducts).

You may be eligible to participate if you are:
- Aged 55 – 90 years
- Diagnosed with Alzheimer’s disease
- Live at home with a caregiver or partner
- Willing to take medication

To sign up for the RAGE study
Contact: Emily Gere
(650) 852-3287

Memory Screening

This project is developing an approach to screen for memory problems in group sessions.

Each screening session:
- Begins with a brief talk on memory & aging
- Involves simple memory games many enjoy
- Reviews your results and concerns with staff

To sign up for the Free Memory Screening
contact: (650) 852-3287
Scientists Seek to Block Progression of Alzheimer’s Disease with Novel Medication that Targets the Source

Researchers are conducting studies on an experimental medication to block nerve damage and inflammation in the brain that can lead to progressive memory loss and behavioral changes in people with Alzheimer’s disease. Current Alzheimer’s disease therapies focus on improving symptoms versus attacking the root of the disease progression; 400 volunteers with mild to moderate Alzheimer’s disease are needed to further test this new approach.

The buildup of plaques can trigger inflammation in the brains of people with Alzheimer’s disease (AD). A protein called amyloid beta builds up in plaque deposits and may promote damage to nerve cells. Researchers will test an experimental drug that seeks to stop amyloid beta from binding to a receptor in the brain called RAGE (receptor for advanced glycation endproducts). Douglas Galasko, M.D., Professor of Neurology at UCSD, is directing the study.

“The evidence from basic research studies is compelling and merits further evaluation in a rigorous human clinical trial,” Galasko said. “While most current Alzheimer’s disease therapies focus on the various symptoms of cognitive impairment, this trial is testing whether we can modify actual progression of the disease itself by targeting the interaction between amyloid beta and an important receptor in the brain.” The industry-sponsored study is being conducted by the Alzheimer’s Disease Cooperative Study (ADCS), a consortium of leading researchers supported by the National Institute on Aging (NIA), part of National Institutes of Health (NIH). The ADCS at the University of California, San Diego (UCSD) will coordinate the 18-month, double-blind, placebo-controlled clinical trial. The drug, which has been tested in animals and in preliminary human studies, is being studied in this Phase II clinical trial to determine if it will slow the progressive decline associated with Alzheimer’s disease.

“Progress in treating and preventing Alzheimer’s would just not be possible without the dedication of the patients and families who volunteer for clinical trials,” said Neil Buckholtz, Ph.D., chief of the NIA Dementias of Aging Branch.

Physicians and nurses will monitor the participants during regular visits and measure the severity and progression of disease using standard tests of functional and cognitive abilities. To ensure unbiased results, neither the researchers conducting the trial nor the participants will know who is receiving the study drug and who is getting the placebo.

If you are interested in participating in this study, please contact: Emily Gere (650) 852-3287

10th Annual Updates on Dementia Conference

You are invited to attend the 10th Annual Updates on Dementia Conference: Translating Research into Practice. The conference will be held on Wednesday, June 4, 2008, from 8:00 am to 4:00 pm, at Dinkelspiel Auditorium, Stanford University.

This year’s topics include:

-- Emerging Research
-- Frontotemporal Dementia
-- Mild Cognitive Impairment
-- Enhancing Care in the LGBT Community
-- Bathing without a Battle
-- Love, Sex and Alzheimer’s
-- Accessing Resources in the Multicultural Community
Updates on Dementia, continued from previous page

This year’s Moderator, Victor Henderson MD MS, Stanford University Department of Neurology, opens the morning session with two of the nation’s leading experts, who explore the latest developments in dementia research and practice. Bruce Miller MD, Department of Neurology and Psychiatry, University of California, San Francisco, describes medical treatments for frontotemporal dementia and how it can be differentiated from Alzheimer’s disease. Ronald Peterson MD PhD, Professor of Neurology, Mayo Clinic College of Medicine discusses the clinical manifestation and characterization of MCI, the harbinger of dementia. Wrapping up the morning session, Dolores Gallagher-Thompson PhD ABPP, Stanford University School of Medicine and Edie Yau MA, Alzheimer’s Association discuss resources in the multicultural community, many of which will be represented by an expanded exhibit area that runs throughout the day.

The afternoon session opens with Ann Louise Barrick PhD, Director of Psychology and Clinical Director, Umstead Hospital, University of North Carolina, Chapel Hill, who will present on techniques to improve personal care with respect and emotional sensitivity. Donna Schempp LCSW, Family Caregiver Alliance, facilitates an expert panel that will increase awareness of perceptions of dementia and their impact on caregiving practices. Using lecture and film excerpts, Elizabeth Edgerly PhD, Alzheimer’s Association explores the sometimes controversial subject of intimacy and sexuality in the long term care setting in the closing session.

Regular registration: $80; VA Employee: $60; Senior/Student: $35

Register online or download the brochure at www.alz.org/norcal
Advance registration recommended For further information, contact education@alznorcal.org

Make a difference: Help end Alzheimer’s Disease!

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

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

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

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

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

Updates on Dementia Conference
10th Annual Updates on Dementia Conference: Translating Research into Practice
Wednesday, June 4, 2008, 8:00 am – 4:00 pm
Dinkelspiel Auditorium, Stanford University
Register online or download the brochure at www.alz.org/norcal
Advance Registration Recommended
For further information, contact education@alznorcal.org

Memory Screening Sessions available this year:
Dr. J. Wesson Ashford, MD, PhD, is a Senior Research Scientist who has been part of our Aging Clinical Research Center (ACRC) since 2003. He is available to give free talks and conduct Memory Screenings in the local community. His presentations are interactive, in a layperson’s language, and give people ways to encourage healthy memory. You can view his web site at www.medafile.com, and to see a clip of him speaking, click on “See Dr. Ashford talk…” (it will take a couple of minutes to come up).

As part of his lecture format, Dr. Ashford demonstrates a Memory Screening game. It involves a 5-minute slide show of pictures of common objects, some recurring. The participants are asked to indicate whether they have seen the object before. This gives a general idea of memory function. After the screening, Dr. Ashford and a staff member can review results and discuss concerns.

Upcoming lectures:
May 29, 9am-4pm, Active Older Adults Day, El Camino YMCA, 2400 Grant Road, Mountain View
June 25, 1–2:30pm, Sunnyvale Senior Center, 550 E. Remington Dr, Sunnyvale
August 18, 10-11:30am, San Mateo Senior Center, 2645 Alameda de las Pulgas, San Mateo