DIMENSIONS
AGING & ALZHEIMER'S UPDATE
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FOCUS ON RESEARCH

Similarities and differences in identical twins with familial Alzheimer's disease.

By Dana Martin

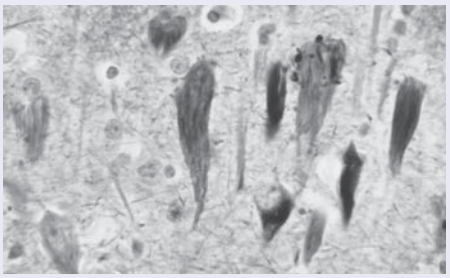
Studies of identical twins with Alzheimer's disease (AD) can reveal a great deal about the disease's genetic and environmental causes. However, identical twin studies are rare and have not looked at all aspects of twin pairs to determine similarities and differences in the disease among twins. These aspects include the disease's clinical presentation (such as information gathered through exams and interviews with the family), epidemiological information (such as education level and occupation), and neuropathology (meaning examining tissue of autopsied brains).

In a recent study, ADRC researchers Dr. Thomas Bird, Dr. James Leverenz, Ellen Steinbart, Malia Rumbaugh and their colleagues, including Kiri Brickell, a neurologist from New Zealand who was completing a fellowship at the ADRC, looked at three sets of identical twins. The ADRC followed all six for a number of years. Each had, or developed, AD during the course of being studied. The diagnosis of AD was based on clinical examinations whenever possible, as well as medical records and family history. Genetics information was gathered as well, and an autopsy was performed when each twin died.

"It turns out that it's really rare in the research on Alzheimer's disease to have three complete sets of identical twins where all of them had had autopsies," says Bird. "We had an opportunity to look at the clinical, epidemiological and pathological aspects of all of them."

The goal of this study was to look at the similarities and differences between identical twins with AD to have a better understanding of how genes and the environment interact and to determine which aspects of the disease seem to be under genetic control and which seem to be influenced by environmental factors. Detailed neuropathology was performed to assess the degree of similarity and difference between each twin pair for each of these variables.

Some of the epidemiological questions the researchers asked for each twin set were if environment, education level, alcohol and tobacco use were the same or different. Clinical questions included whether age of onset and initial symptoms were the same. In terms of pathology, they examined two typical changes in the brain that are seen with AD, neuritic amyloid plaques and neurofibrillary tangles, and if those changes occurred in the same places within the brain.



Neurofibrillary Tangles

Neurofibrillary tangles are an aggregation, or clumping together, of a protein called tau. This change occurs within brain cells. These aggregated tau proteins form long, twisted fibers.

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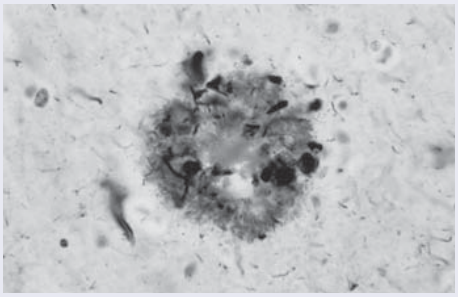
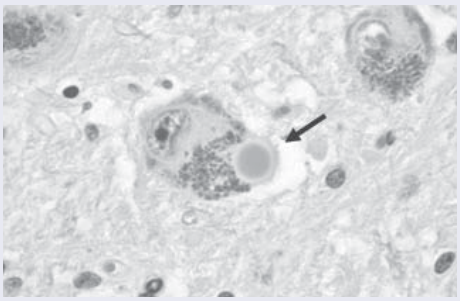


Neuritic Amyloid Plaques

Neuritic amyloid plaques are changes outside the cells but within the brain tissue. These plaques contain the protein that most people are very interested in as a cause of Alzheimer's disease, called amyloid.

"It's the presence of both the plaques and tangles that is required to make a diagnosis of Alzheimer's disease," says Leverenz. "There are some diseases in which you have only the tangles, and that's another disease altogether, not Alzheimer's disease."



Lewy Body

The study also looked at whether both twins in each pair had Lewy bodies. Lewy bodies are changes in the brain associated with Parkinson's symptoms, and they are found in about half of patients with AD.

Dr. Leverenz underscores the importance of neuropathy in understanding AD, particularly the presence or absence of Lewy bodies. "There are things that we just can't tell about the characteristics of the disease by looking at the patient clinically, such as the presence of the Lewy bodies," he says. "When we look at those people with coexistent Lewy bodies, there do seem to be some unique clinical characteristics, but they're fuzzy enough that accuracy based purely on a clinical history, characteristics and examination is not as accurate. Neuoropathological examination improves the accuracy of the characterization of the dementia that the person has."

The study had several important findings. It confirmed that genetics play a strong role in AD. Both neuritic amyloid plaques and neurofibrillary tangles were nearly identical in each twin pair in terms of numbers and locations. Clinically, each twin pair was very similar as well.

However, the study also found that genetics is not the whole story. Age of onset varied considerably, with a difference of between 4 and 18 years within each twin set. Also, in two of the three twin pairs, the twin with the later age of onset did not have Lewy bodies. It appears that disease duration is highly correlated with whether Lewy bodies are present.

"We came to the conclusion that, in these cases, genetics was driving a lot of the clinical and pathological characteristics of the disease but was not in control of everything," Bird says. "There must have been other factors that were playing some role in age of onset, and there probably are other factors playing a role in whether they develop the Lewy bodies or not."

This study is the first to look at the presence of Lewy bodies in identical twins, and the findings provide another piece of evidence that the Lewy bodies, although they are important in Alzheimer's disease, may not be as correlated with the genetics driving the disease as other changes such as the plaques and tangles. "This allows us to begin to think a little bit differently about the Lewy bodies and their relationship to the pathology," Bird says.

Another finding was that one twin pair had a mutation in PS1, known as the A79V mutation. A brother of the twins had remarkably late onset, having been diagnosed at 79 years of age. This is interesting because PS1 mutations are associated with early-onset AD. This relative represents the oldest age of onset in a person with the A79V PS1 mutation.

At this point, it's not clear what environmental factors influence age of onset for AD. The backgrounds of each twin pair were similar. They all had high school educations, grew up in the same environments and had similar professions. Dr. Bird points out that ideas about what environmental factors might be at play aren't well-formulated, and more research is needed to determine what these factors are. He says, "If we knew what could delay the onset of the disease, that would be

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a treatment."

This study also shows how valuable it is for those with Alzheimer's and their families to be involved in this research for the long term. Dr. Bird thanks all these families for donating so much of their time, as well as blood and tissue samples, for this research. It could not be accomplished without them.

If you are interested in participating in genetic studies of Alzheimer's disease, please contact Ellen Steinbart at 206-764-2112 or toll free at 1-800-745-4511.

The results of the study are published in the *Journal of Neurology, Neurosurgery & Psychiatry,* Vol. 78, 2007. ❖

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Dr. Linda Teri gives Lawton award lecture at the 60th Annual GSA Meeting.

The Gerontological Society of America (GSA) held its 60th Annual Scientific Meeting Nov. 16-20 in San Francisco. The theme was "The Era of Global Aging: Challenges and Opportunities." A highlight of this year's conference was the Lawton Award Lecture, delivered by University of Washington Alzheimer's Disease Research Center faculty member Dr. Linda Teri.

Drs. Linda Teri with Nancy Fugate Woods, Dean of the University of Washington School of Nursing

Dr. Teri provided an overview of 20 years of research on identifying and treating behavioral problems in Alzheimer's disease (AD). She described the development of psychosocial treatments to treat these problems, meaning treatments that look at the interaction between social and psychological factors.

In her lecture, Dr. Teri noted that research has come a long way in the past two decades. Just 20 years ago, it was believed nothing could be done to help people with AD – that they would simply have to suffer and worsen as the illness progressed. Now, clinicians have a variety of research-based interventions shown to improve care and quality of life for those living with AD, as well as their caregivers.

In particular, Dr. Teri noted that co-existing emotional and behavioral disturbances cause "excess disability" over and above the cognitive decline that occurs in dementia. In the 1980s, Dr. Teri and colleagues conducted a series of clinical investigations applying behavioral and social learning theory to the treatment of depression in AD. These studies showed that training caregivers to use behavioral skills to increase pleasant events and decrease negative behaviors was as effective as antidepressant medicine in treating depression in the person with AD.

The use of behavioral skills also improved the caregiver's mood. The effects of the treatment were long-lasting: They persisted even after the nine-week treatment program was completed.

Dr. Teri also talked about the role of exercise in reducing excess disability in AD. A 2003 study involving exercise along with behavioral management that lasted 12 weeks and had an exercise and problem-solving focus showed significant decreases in depression at three-month and two-year follow-up.

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Also, those in the study were far less likely to be institutionalized because of behavioral problems.

A 2005 study trained direct care staff in assisted living residences to use compassionate and clear communication with residents who had cognitive impairment. This study also reinforced the values of dignity and respect. In addition, this intervention trained staff to identify and treat common care problems, such as depression and anxiety. Residents in the treatment groups had decreases in both depression and anxiety, compared with increases among the control group.

A similar study focused on family caregivers of individuals with dementia. This program trained community consultants to help family members improve care. Compared with the control group, caregivers in the treatment group had decreased depression and burden. During the treatment program, care recipients (individuals with moderate to severe dementia) also had significantly less decline in overall quality of life than the control group.

What does the past 20 years of research mean in terms of treatment for AD? Dr. Teri explained that for those with AD, it means depression, anxiety and general behavior problems can be reduced. Physical activity can be increased, and disability can be decreased. Also, institutionalization can be delayed. For family caregivers, it means both burden and depression can be reduced. And for staff caregivers, it means skill and job satisfaction can be improved.

At the end of her presentation, Dr. Teri touched on what might be achieved in the next two decades of AD research and treatment. Continued improvement in emotional, physical and cognitive well-being in those with dementia, as well as decreased burden, depression and health problems in their caregivers, are within our grasp. Providing those with dementia, their families and health care workers with easy access to a wide range of research-tested information, education, support programs and interventions is an important "next step" to improving the quality of their lives and maximizing their continued involvement in chosen activities.

Getting there, Dr. Teri said, will require several things: Continued funding for nonpharmacological approaches to patient care, a focus on training those with the most influence in patient care (e.g., families, universal workers, nurses), and identifying untreated sources of disability in people with AD. ❖

Other ADRC Presenters at GSA

Dr. Rebecca Logsdon participated in a discussion on recruiting for diversity in NIH Alzheimer's Disease Centers. She also gave two presentations. The first was on an ongoing investigation which is finding that participants with early-stage AD were able to reliably report on their physical health and their mood. In her second presentation, she discussed research that translates what was learned from two programs, Reducing Disability in Alzheimer's Disease (RDAD) and EnhanceFitness© (EF) to dementia-specific programs within community-based adult day activity programs.

David La Fazia gave a poster presentation on a study that examined the resilience of caregivers and whether that resilience helps protect against depression, stress and burden. The findings indicate that the more resilient a caregiver was, the more protected they were against these adverse outcomes listed, and that it may be important to develop interventions to strengthen resilience among caregivers to improve their lives.

Dr. Susan McCurry gave a poster presentation on a study that examined the factors associated with daytime inactivity and sleepiness in people with AD and their family caregivers. The study indicates that objectively measured daytime inactivity appears to be a product of age and amount of nighttime sleep, whereas self-reports about daytime sleepiness are more influenced by physical health, patient behavioral disturbance and caregiver need for support.

Q&A Winter safety tips

Question:

My wife has early-stage Alzheimer's disease. What can I do this winter to help make sure she stays healthy throughout the colder months and to ensure we're prepared in case of an emergency?

Answer:

During the winter months, everyone should do some basic things to be prepared. In addition, those caring for people with Alzheimer's disease should take extra steps to be ready for the cold weather and for any emergencies that might arise.

Make safety a priority in the home. Make sure fireplaces or woodstoves are in safe working order. Winter is also a good time to check all fire extinguishers and smoke alarms to make sure they work.

Remove any rugs that feet or walkers might get tripped up on, or make sure they are nonslip. Check the living space to ensure pathways are clear of debris and lighting is sufficient. The bathroom and the hallway leading to it should have some lighting at night so your wife does not have to fumble to find her way to the bathroom. Install handrails in bathrooms and halls.

Make sure windows are not drafty, and keep windows closed at night. Even if it's relatively mild during the day, temperatures can plummet at night.

Have home emergency supplies ready. These include flashlights, a battery-operated radio, extra batteries, emergency nonperishable foods that do not require refrigeration, a nonelectric can opener, bottled water, one week's supply of essential medicines, extra blankets and sleeping bags, a first aid kit and manual, and emergency heating equipment.

Make sure all walkways are clear outside before going out. Be especially careful of uneven, slick or dangerous surfaces. For snow and ice, consider sanding sidewalks and driveways to create a safer environment.

Check all clothing and footwear. Make sure your wife has appropriate outdoor winter clothing, including gloves, a hat, a scarf and a heavy winter coat. Check that her shoes are in good shape, have enough tread for the surface (more tread outdoors on rough surfaces and less tread indoors on carpeted or smooth surfaces) and are easy to get on and off. Shoes that are worn out should be replaced with comfortable, high-quality shoes that have a good fit.

Keep an overnight bag packed that has all the necessities in it. This bag will come in handy if a quick trip to the hospital is needed for any reason. It's a good idea to include a sheet of paper that lists your wife's name, address, phone number, Social Security number, medical insurance information, known illnesses and conditions, normal blood pressure, diet restrictions, and emergency contact information.

A detailed list of current medicines, including dosages and instructions for use, should also be included. If an emergency arises, all medicines should be taken to the hospital. Also, place a copy of your wife's living will or health care advance directive in the bag. Keep all information updated and keep the bag in an accessible location.

Keep up (or start) an appropriate exercise program. Since many accidents occur because of muscle weakness and lack of coordination, it's a good idea to help your wife stay strong through exercise. Exercising has been shown to reduce falls and accidents. But make sure to consult with her doctor before starting a program, to start slowly and to avoid outdoor exercise in bad weather. ❖

▼ ADDITIONAL INFORMATION ▼

Home Safety:
www.alz.org/national/documents/brochure_homesafety.pdf

Disaster Preparedness:
www.alz.org/national/documents/topicsheet_disasterprep.pdf

Meet Cat Olcott

When you enter the office of the Northwest Research Group on Aging (NWRGA), you will be greeted by program coordinator Cat Olcott.

NWRGA is the education and information transfer core of the University of Washington's Alzheimer's Disease Research Center (ADRC) and is part of the UW School of Nursing Department of Psychosocial & Community Health. This long-standing research group focuses on interventions to improve the quality of life both for those with dementia and their caregivers – and Cat helps keep everything within the group running smoothly.

When asked about her typical day, Cat says her job allows for a broad range of administrative activities, from travel arrangements to coordinating talks and presentations for the group's director, Dr. Linda Teri. She disseminates program information and training materials to the community and other researchers, as well as responding to requests for referrals to outside agencies or other research studies. She also monitors webmail for the ADRC website.

"One of the things I most enjoy about my position is managing production for the Dimensions newsletter," Cat says. She works on all aspects of this publication, including gathering and writing stories, designing and producing each issue, and coordinating printing and mailing to more than 5,000 readers! She draws from her graphic design background to create dynamic Powerpoint presentations and displays for regional and national conferences and other events. Another high point is the task of coordinating the ADRC's annual Public Forum.

Prior to joining the NWRGA, Cat spent six years with the Reconnecting Youth Prevention Research Program – also at the School of Nursing – which has developed and implemented internationally recognized curricula to help high-

risk junior high and high school youth raise their GPAs and manage their anger, while decreasing drug use, depression and suicide risk.

Cat studied art and French at Eastern Michigan University and after moving to Seattle in 1980 she received her associate's degree in printing and graphics followed by 20 years as a graphic artist and production manager for several in-house advertising agencies.

In her personal life, Cat is a buddhist layperson affiliated with a local Tibetan Buddhist monastery. She says that this discipline has provided her with the healing, stability and the compassion needed in everyday life, as well as with end-of-life issues for those passing and those left behind.

She enjoys spending time with friends and family, being outside, writing, painting and taking silent retreats. She also nurtures interests in modern sculpture, architecture and dance. A longtime amateur environmentalist, she is proud to live in a city that has one of the most innovative and self-sustaining recycling programs in the nation. You might see her out and about on her 80 mpg shiny red scooter doing her bit to reduce her carbon footprint! ❖

ALZHEIMER'S ADVOCACY DAY

Tuesday, Feb. 5
Olympia, Washington

Advocates are people with Alzheimer's and related disorders, caregivers, friends and families whose voices together are a powerful tool for change and hope of a future without Alzheimer's. Join us in Olympia Feb. 5 to educate legislators about issues important to the Alzheimer's community. For more information, contact Nancy Dapper or Patricia Hunter at 206-363-5500 or 1-800-848-7097 or by e-mail at: nancy.dapper@alz.org or patricia.hunter@alz.org

DID YOU KNOW?

One in seven Americans age71 and older has some type of dementia, a NIH-funded study estimates.

Oct. 30, 2007 – A new analysis suggests that about 3.4 million Americans age 71 and older have dementia, and 2.4 million of them have Alzheimer's disease (AD).

To learn more, visit the Alzheimer's Disease Education and Referral (ADEAR) Center News & Events page: www.nia.nih.gov/Alzheimers/

STUDIES SEEKING VOLUNTEERS

University of Washington School of Nursing Northwest Research Group on Aging

To learn more about any of these studies, call Amy Moore at 206-616-5550 or toll free 1-866-292-4464.

STUDY SUBJECT	DESCRIPTION	CANDIDATE CRITERIA	TIME / PROCEDURE
NITE-AD Study: Sleep Difficulties in the Home Setting	Evaluates 4 treatments to improve insomnia and nighttime behavior problems in AD patients.	Individuals have a diagnosis of AD or severe memory problems and live at home with a family caregiver.	Treatment visits during 2 months. 3 interviews during 6 months. All study activities are done in the home.
NITE-AD in AFH Study: Sleep Difficulties in Adult Family Homes	Evaluates a treatment to improve insomnia and nighttime behavior problems in AD patients.	Individuals have a diagnosis of AD or severe memory problems and live in an Adult Family Home.	Treatment visits during 1 month. 3 interviews during 6 months. All study activities are done in the Adult Family Home.
Sleep Description in AD Patients	Assesses sleep of AD patients. No treatment is provided.	Individuals have a diagnosis of AD or severe memory problems and live at home with a family caregiver.	3 interviews during 6 months. All study interviews are done in the home.
Early Stage Memory Loss Seminar and Study	Evaluates individuals with early-stage memory loss and their caregivers who attend the Alzheimer's Associations Early Stage Memory Loss Seminars.	Individuals have early-stage memory loss and their caregivers attend the Early Stage Memory Loss Seminar.	3 interviews during 6 months. All study interviews are done in the home.
RALLI Study: Mild Cognitive Impairment (MCI) and Exercise	Evaluates two exercise programs provided to individuals with MCI.	Individuals have MCI and are 70 years or older.	Exercise programs last 2 months. Study interviews are done in the home over a 36-month period.

Alzheimer's Disease Research Center, University of Washington and VA Puget Sound Health Care System

Genetic Studies of Dementia

The Genetics Program of the Alzheimer's Disease Research Center at the University of Washington and the VA Puget Sound Health Care System is studying the role of genetics in dementia. It seeks to identify the genes responsible for various forms of dementia. Families are being sought with two or more living affected individuals. Participation could involve an interview, examination, review of medical records and a blood sample. For further information, please contact Ellen Steinbart, RN, at 206-764-2112 or toll free 1-800-745-4511.

UPCOMING EVENTS

MAINTAIN YOUR BRAIN

Wednesday, March 19 - 10:30 a.m. - 12 p.m. Redmond Senior Center

If you are interested in the latest information on maintaining your brain and delaying the symptoms of dementia, you should consider this seminar. We will have a quick review of normal aging and dementia followed by:

- The brain – how it works and changes with age.
- The body – how the heart and brain are connected.
- The person – how social connections and emotional health affect the brain.

For reservations and directions call Charlene Runio at 425-688-5806.

Alzheimer's Association of Washington 23rd Annual ALZHEIMER'S EDUCATION CONFERENCE

Friday, April 4 - Washington State Trade and Convention Center

Mark your calendars now for the 2008 Annual Education Conference being held on April 4 at the Washington State Trade and Convention Center. The Alzheimer's Association Regional Conference is a dynamic and multi-disciplinary forum dedicated to the care of people with dementia and their families. This conference showcases the latest and most innovative evidence-based practices and programs designed for both beginning and advanced practitioners, as well as family caregivers.

Check back in mid-January for more information. You'll find details on conference registration and how to nominate your favorite caregiver for the "Excellence in Caregiving" awards.

http://alzwa.org/education_training.htm

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THE ALZHEIMER'S DISEASE RESEARCH CENTER (ADRC) PROGRAM SUPPORT FUND

The University of Washington ADRC Support Fund is used to help support new junior faculty investigators with strong credentials in the field of Alzheimer's disease research. This fund also helps enhance the research infrastructure of the ADRC by providing funding for the purchase of scientific equipment, supplies, training and numerous other opportunities that would otherwise not be available, as federal dollars are not able to fully support the growing research in Alzheimer's disease.

For more information regarding the Alzheimer's Disease Research Center Program Support Fund, please contact Victoria Hoyt, ADRC Program Coordinator, at 206-764-2749, or toll-free at 1-800-329-8387, ext. 6-2749. E-mail: Victoria.Hoyt@va.gov

Checks should be made out to ADRC and addressed to:
VAPSHCS (S-116-MIRECC) Attn: Viki Hoyt
1660 S. Columbian Way, Seattle, WA 98108