Northwestern Alzheimer's Disease Center

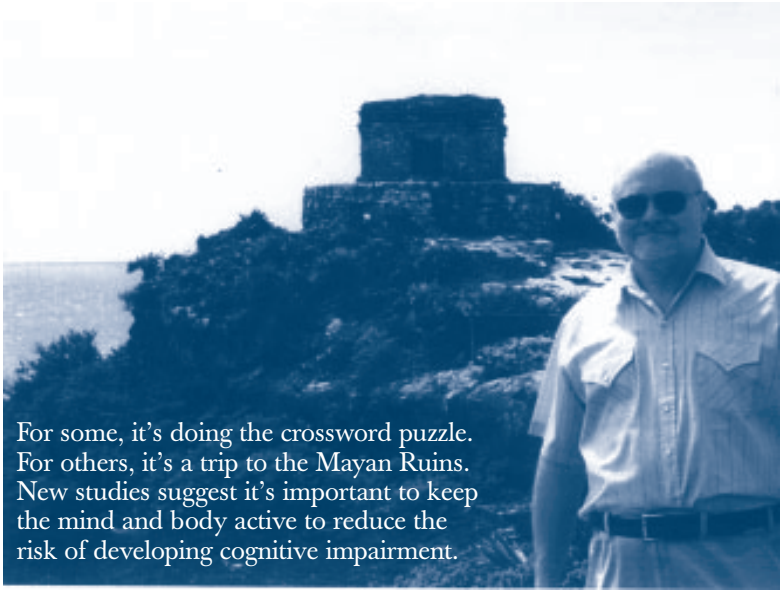
NADC NEWS

Produced by Cognitive Neurology and Alzheimer's Disease Center | Issue 19, Spring/Summer 2002

News Update

Level of Everyday Activity and Cognitive Functioning

by Audrey DiFrancesco, MA and Nancy Johnson, PhD



For some, it's doing the crossword puzzle. For others, it's a trip to the Mayan Ruins. New studies suggest it's important to keep the mind and body active to reduce the risk of developing cognitive impairment.

Recently, the focus of research on aging and dementia has turned to effects of cognitive and physical activity on the risk of developing cognitive impairment or dementia. The results of several of these investigations suggest increased cognitive and physical activities in older adults may reduce the risk of developing cognitive impairment and dementia. A recent study published in the *Journal of the American Medical Association* by Wilson et al., found that more frequent participation in cognitive activities was associated with a reduced risk of being diagnosed with Alzheimer's disease over a period of about 4.5 years. The activities assessed included time spent in everyday mental tasks like reading a newspaper, playing cards or completing crossword puzzles, and watching television. People with frequent cognitive activity (in the 90th percentile) were 47% less likely to develop Alzheimer's disease compared to people who reported infrequent activity (10th percentile). This study also examined the relationship between physical activity and the risk of dementia, but did not find an association, although other previous studies have suggested that physical activity may also be associated with a reduced risk of dementia.

Researchers at the Northwestern Alzheimer's Disease Center have also been investigating the relationship between memory loss and level of daily activity in older adults. The results of a preliminary analysis were recently presented at the International Neuropsychological Society Meeting in Toronto, Ontario. This study was conducted to determine whether reduced activity level was associated with the presence of Mild Cognitive Impairment (MCI). MCI is a term applied to a subset of the older adult population who continue to function normally in their everyday lives, but have impairments on objective testing.

In This Issue

In this study, 352 healthy, non-demented, older adults from the Northwestern Alzheimer's Disease Center Registry were divided into a Normal Control (NC) – those who are healthy and score normally on various neuropsychological tests, and the MCI group. The neuropsychological measures were designed to assess several important cognitive domains including memory, attention, language, visuospatial abilities and executive function. The participants also completed a detailed questionnaire, "The Adelaide Scale," asking them about the frequency with which they typically engaged in 25 common physical, mental, and social activities. The questionnaire asked about participation in everyday tasks like hobbies, entertaining friends and family, attending religious services, and walking outdoors for 15 minutes or more.

Results of the analyses, which controlled for possible confounding factors such as age, educational level, and gender, indicated that persons with MCI were significantly less active than the NC group. Further examination of the activity scores suggested that the greatest difference between NC and MCI individuals' level of activity occurred on tasks related to academic/cultural endeavors and household maintenance. In other words, NC and MCI individuals tended to differ the most in the frequency with which they performed activities like heavy housework, gardening, household or car maintenance, educational activities, and attending cultural events. The subset of questions that best distinguished the two groups related to the most demanding physical (household maintenance) and cognitive (academic/cultural) activities of the questionnaire.

This study suggests that everyday activity level may help to identify individuals with Mild Cognitive Impairment (MCI). Because individuals with MCI have a greater chance of developing dementia, this group is being extensively studied by researchers who are exploring ways to possibly delay the progression from MCI to AD. In the NADC study, reduced activity level was shown to accompany even the relatively subtle cognitive decline characteristic of MCI, and suggests that assessment of leisure activities may be an important adjunct in the evaluation of older adults. We are currently in the process of completing additional studies to determine whether activity level can be used to identify individuals who will subsequently develop dementia.

The NADC would like to express its gratitude to the participants in the Memory Disorders Research Core who make studies like this possible. ■

Awards and Honors

Darren R. Gitelman, MD
Associate Professor, Neurology (CNADC)
GRANT AWARDED
Anatomic and Spectroscopic Study of Alzheimer's Disease, Mild Cognitive Impairment and Normal Controls
IL Dept of Public Health $29,952

Madelyn Iris, PhD
Interim Director, Buehler Center on Aging
GRANT AWARDED
Los Caminos: Pathways to Alzheimer's Disease -- Identifying Factors that Promote or Inhibit Early Detection in Hispanic Elders
IL Dept of Public Health $20,000

Pascale Lacor, PhD
Res. Associate, Neurobiology & Physiology
GRANT AWARDED
New Molecular Basis for Memory Loss in Alzheimer's Disease
IL Dept of Public Health $30,040

M.-Marsel Mesulam, MD
Director, CNADC
Recognized by the Institute for Scientific Information (ISI) as one of the most cited researchers worldwide after 19,000,000 articles and source records were categorized into specific areas of research and analyzed for author frequency.

Dana Small, PhD
Research Associate Professor, CNADC
GRANT AWARDED
Neural Correlates of Interactions Between Motivation and Visual Spatial Attention in AD, MCI, and Healthy Aging
IL Dept of Public Health $35,000 (1st yr)

Linda Van Eldik, PhD
Professor, Cell and Molecular Biology
Received a National Institutes of Health Method to Extend Research in Time (MERIT) Award for her research on molecular mechanisms and modulation of glial activation. ■

Editorial Information

The NADC NEWS is funded in part by a grant from the National Institute on Aging -- Northwestern Alzheimer's Disease Center, Chicago, IL.

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http://www.brain.northwestern.edu

Featured Friends

Linda and Robert Mendelson

Linda and Robert Mendelson have been friends of the CNADC since the center was established in 1994. They have been generous supporters of Alzheimer's disease research in addition to their sponsorship of many other health and cultural institutions. Their contributions have funded the Mendelson Fellowship at the Cognitive Neurology and Alzheimer's Disease Center. Recipients of the Mendelson Fellowship are: Nancy Johnson, PhD (1994-96), Zoran Grujic, MD (1996-98), Tina Kwasnica, MD (1999-2000), Alicia Facca, MD (2000-01), and Gabriel Leger, MD (2001-current).

Robert and Linda Mendelson with Mendelson Fellows Zoran Grujic, MD, Nancy Johnson, PhD, and Gabriel Leger, MD

The Mendelsons' generous and steadfast support is far-reaching. They have been supporters from the early days of the National Alzheimer's Association, where Linda serves on the Board of Directors. Following an initial $25,000 gift, their philanthropy led to their inclusion among the Zenith fellows. This distinguished group of individuals fund annual grants to cutting-edge Alzheimer's researchers worldwide. In addition, the Mendelsons support the work of Deborah C. Mash, PhD and her brain tissue bank at the University of Miami, Mr. Mendelson's alma mater, where he is an active alumnus and a member of the president's council.

Darby Morhardt recently had the opportunity to meet with Linda to discuss the inspiration for their support.

What led to your involvement with Alzheimer's disease?
It all started with my mother. After my father died in 1987, we were faced with changes in my mother's mental capacity that we had not noticed before. I realize now that he was trying to protect her—*and us*—from knowing that she was having increasing difficulty with her memory. Several years later, while we were packing some of her books, we ran across a copy of *Newsweek* from 1984 with the cover 'The Tragedy of Alzheimer's Disease.' All I can guess is that my father hid that issue from my mother's sight and used it as a reference for what was happening to her. After evaluations from several doctors, we finally received a diagnosis of probable Alzheimer's disease from Dr. Scott Heller at Northwestern.

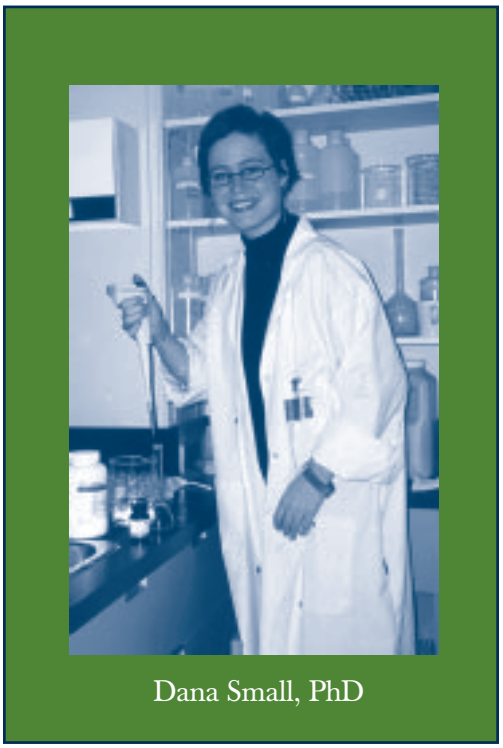
Would you describe some of what you experienced?
I made sure that she was well-cared for at her home and it was clear that I wanted her to remain there. I feel good about the decisions I made about her care and know that I did what I thought was right. The most devastating time came when she no longer recognized me. Then she progressed to where she did not recognize herself. It was an agonizing process to watch.

What led you to become active supporters of Alzheimer's disease research?
After watching how Alzheimer's was destroying my mother's life, my husband and I became intent on fighting back. We came to the realization that we wanted to do our share toward the eradication of this illness for future generations. Due to our commitment to Northwestern and in gratitude for the care my mother received, we were eager to support the work of Drs. Marsel Mesulam and Sandra Weintraub upon their arrival from Harvard Medical School in 1994. After meeting them and hearing about their work, I never doubted for a second we were in the right place.

Is there anything that you would like others to know about you?
I am a great proponent of knowledge and hope. I hope for a cure. In 1995, I was told that a cure was about 10 years away. Now, some say that it may be longer than that, but that is why we are supporting this research and will continue to do so.■

Research Opportunities

Improving Task Performance Through Motivation



Dana Small, PhD

Dr. Dana Small, assistant professor at the Cognitive Neurology and Alzheimer's Disease Center has two related areas of interest. One is to understand how motivation and emotions are represented in the human brain. The second is to understand how the chemical senses are organized in the brain. These two areas of interest (motivation/emotion and chemical senses) come together in the study of feeding and food-reward. Dr. Small has recently published a paper showing that eating chocolate, when it is perceived as pleasant and rewarding, activates different brain regions compared to eating chocolate when it is perceived as unpleasant and aversive.

One specific question of current interest is trying to understand how motivation can interact with attention and other cognitive domains to improve performance. "One important function of emotion and motivation is to enhance cognitive performance" says Dr. Small. For example, facts or events with emotional salience are remembered better than facts and events without emotional salience.

A new project that is soon to be underway is designed to look at how motivation may improve performance on a task of attention in patients with Alzheimer's disease (AD). Scientific studies have shown that emotional enhancement of memory and attention is relatively preserved in patients with AD. However, to date, studies have focused upon negative emotional impact, such as looking at frightening images and later recalling these images. The influence of reward upon cognitive function in AD is poorly understood, yet it is this aspect of emotion that is most relevant to the development of strategies to aid cognitive function in AD.

Previous studies from the CNADC and other laboratories have documented visual spatial attention deficits in early AD, but the brain correlates of such changes are unknown. In young subjects, we have developed an attention task that depends upon processing in the posterior cingulate cortex, a region that mediates motivational influences upon attention. This area is affected early in the course of AD and in people with no symptoms who carry two copies of the e4 allele for apolipoprotein E. Moreover, decreased motivation observed early in the course of AD is related to dysfunction in this brain region. In young subjects, we have shown that the opportunity to win money can enhance performance on our task and that this is associated with increased processing in the posterior cingulate and the medial orbitofrontal cortex. This second region is known to be important in processing reward. While decreased motivation in AD may result in a reduced ability to use internally generated motivation to influence behavior, we propose to evaluate the ability of external motivational incentives to enhance visual spatial attention in AD, mild cognitive impairment (MCI) and healthy elderly subjects. We plan to ask patients and healthy control subjects to perform an attention task while being scanned with functional magnetic resonance imaging.

We have the following aims:

1) Evaluate the ability of AD and healthy elderly subjects to use a predictive cue to improve performance on the task.

2) Evaluate the effect of potential monetary gain or loss upon the ability of the spatial cue to enhance performance.

3) Determine brain regions engaged during the modulation of attention by reward.

If you or a family member are interested in participating in this study, please call Dr. Small at 312-503-1834. ■

Alzheimer's Day 2002

Eighth Annual Alzheimer's Day Held

The eighth annual Alzheimer's Day, held on Friday, May 10, 2002 was very well represented by 50 posters from scientists, clinicians, and researchers associated with the CNADC. The purpose of this annual event is to offer the Northwestern community the opportunity to present their research studies, programs and projects in a scientific poster session. These posters synthesize the work of the basic science and clinical faculty and staff spanning the fields of cognitive neuroscience, Alzheimer's disease and other dementias, as well as programs and services for patients and families.

The annual event closed with a dynamic presentation by keynote speaker Dennis Dickson, MD, from Mayo Clinic Jacksonville, Florida, who gave a lecture entitled *The Amygdala in Alzheimer's Disease: Identification of a Real Lewy Body Variant of Alzheimer's Disease.*

The amygdala, an intermediary structure between sensory input areas and deep gray and limbic structures in the brain, is severely involved in Alzheimer disease (AD). Amygdala Lewy bodies (LB) have been seen in brains of persons with familial AD, diffuse Lewy body disease, Down's syndrome with AD, and AD with Lewy bodies. Examining 85 brains at post-mortem, Mayo found that 14 of 69 with sporadic advanced AD had amygdala LBs. An extended study screened 345 AD cases and found LBs in the amygdala in 16% of advanced AD cases. Amygdala LBs increased with disease severity. Clinical features of AD/ALB were not different from typical AD; however, they had a lengthier disease duration. Screening cases with non-Alzheimer degeneration, mostly progressive supranuclear paralysis, they observed that cases with amygdala LB had more Alzheimer-like pathology. The conclusion of the study emphasizes that LBs might arise anew in the amygdala in advanced AD, representing a true Lewy body variant of AD and not the co-existence of Lewy body disease. ■

Caregiver's Corner

We welcome caregivers' stories, ideas, and thoughts for publication. Please send them to the editor for consideration.

Powerful Tools for Caregivers

It is well known that caring for a family member with a chronic illness such as Alzheimer's disease, Parkinson's disease or stroke is stressful and takes an enormous physical and emotional toll on caregivers. Mather LifeWays, a non-profit organization based in Evanston, has received a three-year grant from the U.S. Administration on Aging to test an innovative training program to enable family caregivers to better care for themselves by improving their self-confidence and problem solving skills. Dozens of professionals from healthcare and social service organizations throughout northeastern Illinois have been trained as Class Leaders to teach family caregivers a set of self-care skills through a six-part course known as *Powerful Tools for Caregivers.* Classes are now being held at various times and locations in Cook and the collar counties. Any family member who cares for a relative at home, in a care facility or at a long distance is welcome to participate. A nominal fee is requested for participation but no one will be turned away due to inability to pay. If you know of any family caregivers interested in registering for classes at sites in their local communities, please refer them to Mather InfoPlus at 1-888-600-2560. All class schedules and locations are updated weekly and can be found at the Mather Institute on Aging Web site at: *http://www.matherlifeways.com*

Contact: Daniel Kuhn, Mather Institute on Aging (847) 492-6813

Alzheimer's Association Expands Services to Caregivers

To better meet the needs of all caregivers, the Alzheimer's Association Helpline recently expanded its services. Prior to this time, the Helpline was available Monday through Friday from 9:00am – 5:00pm. Now, support and assistance is available 24 hours a day, seven days a week. Trained volunteers and staff offer emotional support and information on Alzheimer's disease and related dementias throughout the continuum of care. Information on dementia, caregiving and local community resources can be shared by phone or mailed upon request. Callers of different cultural backgrounds are able to connect with their trained volunteers and staff, along with translators who can offer assistance in 140 languages.

For 24 hours a day, seven days a week assistance, call the Alzheimer's Association-Greater Illinois Chapter Helpline at 1-800-272-3900. For those outside Illinois call the National Alzheimer's Association at 1-800-272-3900 for the chapter nearest you.

Caregivers Can Make a Difference

With new funding from the federal government, The National Family Caregiver Support Program is now taking shape in suburban Cook County. The Buehler Center on Aging at Northwestern University is working with the Suburban Area Agency on Aging (SAAA) to find out about the needs and concerns of family and friend caregivers in suburban Cook County. Caregivers are people who care for or assist an older adult with personal care and/or various daily tasks, such as shopping and choosing health care. To learn more about what caregivers want and need, a series of focus groups and personal interviews will be held with caregivers at various locations in suburban Cook County. If you care for someone 60 years or older who lives in the suburban Cook County area and are interested in participating in either a focus group or interview, please call Ellen Navarro at the Buehler Center on Aging at 312-399-6275. However you may help, your input is very valuable to the community at large!■

Inside each one of us is a piece of the puzzle...

You can help solve the Alzheimer's disease mystery.

The Healthy Aging & Memory Study needs volunteers who are **75 years of age or older**, in good physical and mental health, who will help us test new ways of measuring and tracking memory changes over time.

We're looking for volunteers who speak English or Spanish, and who have a friend or relative willing to participate with them in the study. Participants will be assessed regularly by qualified health care providers over the course of the 4-year study.

...By working together, we can solve it.

Call Laura Herzog at 312-695-2343

News In Brief

Current Studies & Research

by Serpil Demirci, MD

Targeted pharmacological depletion of serum amyloid P components for treatment of human amyloidosis.

MB Pepys and others. Nature May 2002.

Amyloidosis is a systemic disease that arises from misfolding and aggregation of normally soluble globular proteins in the tissues as abnormal insoluble fibrils. Amyloid protein build-ups are also associated with Alzheimer disease and type II diabetes. The normal nonfibrillar plasma protein serum amyloid P component (SAP) is universally present in amyloid deposits. SAP itself is highly resistant to proteolysis. It covers amyloid deposits and protects them from being destroyed and cleared from the body. The new drug, CPHPC, a proline derivative, inhibits binding of SAP to amyloid fibrils and dissociates SAP that is already bound to fibrils. It has been shown to be safe and efficient in experimental animal studies. Administering the drug to patients with amyloidosis, researchers observed a rapid fall in plasma SAP levels that remained low after stopping the drug. Depletion of SAP from amyloid in the organs was traced by whole-body scintigraphy. Radioactively labeled SAP disappeared from the blood and decreased in spleen with significant accumulation in the liver, identifying this organ as the site to which the drug caused clearance of SAP. Researchers gave the drug to 19 patients with amyloidosis up to 10 months and observed no adverse effect that could be attributed to it. The researchers propose that efficient removal of SAP would reduce the stability of amyloid deposits and promote their regression, and absence of SAP may retard new amyloid deposition. They say that their drug may provide a new therapeutic approach not only for primary amyloidosis, but also for Alzheimer's disease and Type-II diabetes, in which local amyloid depositions are implicated in pathogenesis.

The relationship of hypertension in the elderly to AD, vascular dementia, and cognitive function.

HB Posner and others. Neurology April 2002.

Hypertension is as important a health issue in the elderly as dementia. Association of high blood pressure with Alzheimer's disease (AD) is controversial, although it is one of the proposed culprits in vascular dementia (VaD). In this study, the relationship between hypertension and dementia was investigated in a group of 1259 dementia-free subjects who were followed over seven years. Of these subjects, 731 had a history of hypertension associated with diabetes, stroke and/or heart disease. During the follow-up, AD developed in 12.5% of the participants and VaD in 4.4%. A history of hypertension was not associated with an increased risk for AD whereas it was associated with an overall increased risk for vascular dementia. They observed threefold increase in risk for vascular dementia when hypertension was accompanied by heart disease and a sixfold increase when associated with diabetes. Hypertension did not adversely influence memory, language, or general cognitive functioning in those without dementia. The authors conclude that the association between hypertension and VaD is weak and may be related to concurrent vascular-related disorders so prevalent among the elderly.

Localization of Neurofibrillary Tangles and Beta-Amyloid Plaques in the Brains of Living Patients with Alzheimer Disease

K. Shoghi-Jadid and others. American Journal of Geriatric Psychiatry, February 2002

Neurofibrillary tangles (NFTs) and amyloid plaques (APs) are the main pathologic hallmarks of Alzheimer's disease (AD). Clinicians have no means to determine the amount of NFTs and APs in the living patient. In most cases, the initial diagnosis of AD is made after significant pathological changes have occurred in the brain. In this study, investigators report the use of a new molecular imaging probe, FDDNP, in conjunction with positron emission tomography to determine the localization and amount of NFTs and APs in the brains of living AD patients. This study potentially offers a noninvasive technique for monitoring the amount of NFT and AP which could facilitate the longitudinal evaluation of the disease process and therapeutic effects.

Serious side-effect kills highly promising experimental Alzheimer's vaccine

www.nlm.nih.gov/medlineplus/news, March 2002

Discovery of a vaccine against Alzheimer disease (AD) was a promising therapeutic approach. In mice it was shown that immunization with b-amyloid, the core material of amyloid plaques seen in AD, helped to block the production of plaques, clean up the brain tissue and prevent the symptoms of Alzheimer disease. Initial human studies were reported to be safe. However, studies were suspended when it was discovered that 4 people suffered from an encephalitis-like brain inflammation. Later, 11 more patients were observed to have the same symptoms. Recently, the manufacturer halted development of the compound, named AN-1792. The company is continuing to develop a vaccine to slow worsening of AD.

Upcoming Events

If you would like to be added to our mailing list or relate a change of address, please notify us. The editor welcomes your comments and letters. Please address them to:

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Online: d-morhardt@northwestern.edu

When you have finished reading this issue, please pass it along to someone else who might be interested.

The following are sponsored by Northwestern Alzheimer's Disease Center, Northwestern Memorial Hospital –Geriatric Evaluation Service, and the Greater Chicagoland Alzheimer's Association.

Alzheimer's Caregiver Support Group
First Monday of Each Month, 6:30 pm
Call Jeanne Hutchinson at 847-492-7599.

Alzheimer's Spouses' Support Group
Fourth Monday of Each Month, 10:00 am
Call Helene Raidl at 312-926-3344.

Early Stage Memory Loss Support Groups for Patients and Families
Ongoing weekly groups
Call Darby Morhardt at 312-695-7913.

SAVE THE DATE!

The 2nd Annual

Best Practices Day

Friday
October 4, 2002
Town Hall Meeting
Poster Session
Keynote Speaker
Luncheon
Northwestern University

Memory Walk

September 22, 2002
9:00am

Chicago Lakefront

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