

Memory and Aging Project Celebrates 25th Anniversary

The Memory and Aging Project (MAP), founded at Washington University in 1979, celebrates its 25th Anniversary this year!

Over its duration, the MAP has enrolled over 2,500 volunteers to participate in annual research evaluations and has supported over 800 scientific papers detailing key aspects of dementing illness.

Origins

The MAP was first funded through the efforts of Founding Director, Dr. Leonard Berg, now Professor Emeritus of Neurology. Others at Washington University made important contributions, including Charles Hughes (Neurology), and Martha Storandt and Jack Botwinick (Psychology).

The collaborators showed they could distinguish healthy subjects from persons with mild dementia with a grant from the National Institute of Mental Health. This grant evolved into two large grants from the National Institute on Aging: a program project grant in 1984 entitled *Healthy Aging & Senile Dementia (HASD)*, and a Center grant in 1985 creating the Alzheimer's Disease Research Center (ADRC). These grants have been continuously funded ever since.

The ADRC & MAP

Under the leadership of Dr. Berg, the ADRC (and the MAP as its clinical research office) grew to become a premier Center for the study of Alzheimer's disease and other neurological disorders.

Dr. Berg stepped down as Director of the Center in 1998, turning

over the reins to Drs. John C. Morris and Eugene M. Johnson as Co-Directors. Dr. Morris became the Director in 2003 with Dr. Johnson and Dr. David Holtzman serving as Associate Directors. A timeline (right and on page 3) highlights important milestones in the Center's development.

Celebration

On Saturday, June 5th, 2004, the MAP celebrated its 25th year by hosting a special Participants Breakfast at the Frontenac Hilton. Many long-time MAP participants and other supporters were in attendance.

Six MAP participants who enrolled in the original project beginning in 1979 were honored for their dedication. These six individuals remain active in the MAP studies 25 years later!

Lifetime Achievement

It is fitting that the many accomplishments of ADRC Director and Friedman Distinguished Professor of Neurology, Dr. John C. Morris, would also be honored in this 25th year of the MAP. Dr. Morris will be one of four recipients of the highly prestigious Lifetime Achievement Award (LAA) from the Alzheimer's Association—National Office. The Association awards the LAA at its biennial international research conference. The meeting this year will be held in Philadelphia in July. Congrats Dr. Morris!



John C. Morris, MD

Milestones in MAP History

- 1979** National Institute of Mental Health awards a 4-year grant to start the MAP.

Founding Director, Leonard Berg, MD, evaluates the first MAP participant.
- 1980** The first brain donation from a MAP participant.
- 1981** MAP participants, Dr. Berg, and others work to form the St. Louis Chapter of the Alzheimer's Association.
- 1982** Berg & colleagues publish MAP research criteria in the *Journal of Neurology, Neurosurgery & Psychiatry*.
- 1984** Berg & colleagues receive National Institute on Aging (NIA) grant to study *Healthy Aging & Senile Dementia*.
- 1985** MAP becomes NIA-funded AD Research Center.
- 1987** The first multicenter clinical trial in the US for an AD drug (Cognex) is launched. MAP is an active study site.
- 1990** First MAP-ADRC Fellow begins training.
- 1992** Dr. Alison Goate is recruited to the ADRC to lead genetic studies.
- 1993** Dr. Morris publishes scoring rules for the *Clinical Dementia Rating* interview for staging dementia-related impairment in *Neurology*.

Alzheimer's May Leave Some Memory Intact

June 9, 2004 -- New research finds that people with Alzheimer's disease might retain the capacity for a specific form of memory, suggesting they may be "trained" to preserve some of their mental functioning.

"I don't want to give the impression that our findings suggest there's a way of reversing Alzheimer's," says researcher Randy L. Buckner, PhD, of the Washington University School of Medicine in St. Louis. "But what they do indicate, and it's surprising to us, is that there are very high levels of memory functions that are more intact in people with Alzheimer's than we previously thought. They have faculties still available that we could take advantage of to help these patients better cope with the disease."

Specifically, Buckner and colleague Cindy Lustig, PhD, found that older adults in the early stages of dementia from Alzheimer's disease retained their capabilities for "implicit" memory. They found that those memories were similar to young and older people without dementia.

Implicit memory is the type of memory that develops as a result of repetitive tasks -- or "priming" the brain -- and relates to past experiences. However, implicit memory is distinct from the "explicit" memory of events and people, which does deteriorate with aging and is affected by Alzheimer's disease.

For their study, the researchers gave word tests to 24 older adults in the early stages of dementia from Alzheimer's, as well as 33 seniors and 34 younger people without dementia.. Each was asked to classify a series of familiar and unfamiliar words based on their meaning, such as either living or non-living objects. While doing these tasks their brain activity was measured with MRI.

With practice, all three groups showed a significant reduction in the time needed to decide on the words -- a characteristic of priming -- although the younger adults were fastest in performing. "But we could see that even people with Alzheimer's didn't have to exert as much effort in terms of brain activity to those words they learned," says Buckner. What was surprising, he adds, was that the brain region with the greatest activity during the word-classification task was the one typically affected in Alzheimer's disease. "These results suggest that despite the damage to these areas in Alzheimer's, certain memory processes that seem to depend on them remain fundamentally intact," he says.

Two experts not involved in Buckner's study, which is published in the June 10 issue of *Neuron*, say these findings are significant.

"Implicit memory is really, quite frankly, the major way in which we learn and recollect things. It impacts everything from factual knowledge to social relationships, how to interact with someone else," says Molly Wagster, PhD, of the National Institutes on Aging. She says that maintaining certain areas of memory that conditions like Alzheimer's can affect may help prolong a patient's functional independence.

Lars Nyberg, PhD, professor of psychology at Umea University in Sweden who wrote an accompanying article to Buckner's study, says these new findings pave the first steps in developing intervention programs that may someday help elderly patients better cope with aging-related memory loss -- even if they don't have Alzheimer's.

Article by Sid Kirchheimer. Excerpt reprinted with permission from WebMD (www.webmd.com).

NIA Genetics Initiative

The National Institute on Aging (NIA) is greatly advancing the search for genes involved in Alzheimer's disease (AD) with acceleration of the AD Genetics Initiative. Joined by the Alzheimer's Association, the NIA creating a large bank of genetic material, cell lines, and data from families with multiple members with late-onset AD.

The AD Genetics Initiative seeks to enroll 1,000 families in which a pair of living siblings (brothers or sisters) has Alzheimer's disease. Families will often be seen at one of the 29 Alzheimer's Disease Centers located throughout the country. A blood sample collected from each participating individual will be sent to the National Cell Repository for Alzheimer Disease (NCRAD; <http://ncrad.iu.edu>), located at Indiana University, where DNA will be obtained from the blood and used for further genetic studies.

Families interested in participating in this research must meet the following criteria:

1. Two living siblings diagnosed with AD after the age of 60 years.
2. A 3rd family member who is either:
 - A. Diagnosed with memory loss or AD after the age of 50 years, **OR**
 - B. Without symptoms of memory loss or Alzheimer's disease and over the age of 60 years.

Families meeting these criteria and interested in learning more about this important research study may contact the ADRC Genetics Nurse at **314-362-2147**. Or contact NCRAD directly at **800-526-2839**.

HORIZONS is the newsletter of the **Alzheimer's Disease Research Center (ADRC)** — a research program in the Department of Neurology, Washington University School of Medicine, funded by grants from the National Institute on Aging and private donations. The ADRC supports and promotes interdisciplinary research on Alzheimer's Disease. The Memory & Aging Project (MAP) — the clinical research office of the ADRC — provides expert clinical assessments of cognitive functioning in normal aging and dementia.

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 **Washington University in St. Louis**
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Morris Interviewed by Alzheimer's Research Forum

Gabrielle Strobel: Twenty-five years of natural history studies, at Washington University and elsewhere, have persuaded you that dementia is not a normal part of aging?

John C. Morris: It's a challenging and fascinating question for us. Many members of our team, including Joel Price, Gene Johnson, Martha Storandt, Phil Miller, Dan McKeel, Alison Goate, Gene Rubin, Randy Buckner, John Csernansky, and David Holtzman, have contributed importantly to the ideas I'll express here.

Given a long enough lifespan, perhaps the brain would degenerate to a point such that we'd all develop Alzheimer's disease if we lived long enough. There's some basis for this notion; many investigators accept it. But careful analysis shows a differential effect for neurofibrillary tangles and amyloid plaques that we think discriminates aging from AD. There is a slow accumulation of neurofibrillary tangles in vulnerable areas of the brain (entorhinal cortex, hippocampus, and other medial temporal lobe structures) beginning around age 50—if you look hard enough you can find a few tangles in almost everyone of that age or older. Even in people with absolutely normal cognitive abilities, the older they are, the more likely we are to see tangles in these vulnerable regions. It is very likely that the tangles mark neuronal degeneration in these regions.

We postulate that, in the normal human lifespan, this slow accumulation of neurofibrillary tangles does not reach a point where it would cause dementia. If we lived to 200, maybe, but at 100 years I doubt it causes dementia. Could this slow process of neuronal degeneration, marked by tangles, in vulnerable medial temporal lobe structures be responsible for some of the normal cognitive changes that healthy older adults experience, such as, "I can't remember the name of that person" or "I

process information more slowly"? Perhaps so. But in and of itself, this slow process of tangle accumulation does not result in frank dementia.

We believe that there is a disease process that marks the onset of AD that occurs in addition to this very gradual, age-related neurodegeneration in restricted areas such as the entorhinal cortex and hippocampus. This is manifested by the deposition of amyloid in the cerebral cortex. Abnormalities of amyloid generation or metabolism that result in cerebral deposition mark the disease. That's what we think. We find that cognitively healthy older adults can live into the ninth, even the tenth decade of life without cerebral amyloid deposition, so that amyloid deposition is not part of truly healthy aging but instead reflects a disease process. These concepts are open for debate. Perhaps the reason Alzheimer's is so powerfully age-associated is because this age-related accumulation of neurofibrillary tangles predisposes the brain to developing this disease. Nevertheless, our conceptual basis is that age alone is insufficient—even if we all lived to be 100, we would not necessarily develop Alzheimer's. Amyloid deposition triggers the disease.

Read all of Gabrielle Strobel's interview with Dr. Morris on-line at <http://www.alzforum.org>. Excerpt reprinted with permission.

Support for AD Research

We are grateful to the *Friends of the ADRC* for their generous financial support over the years. Donations from the *Friends* and others help to fund promising pilot research, educational conferences, training of medical students and fellows, and other worthwhile projects. Membership in the *Friends* group is open to anyone. *Friends* are invited to periodic receptions & educational events. **To learn more, call the Friends Coordinator at 314-286-2881.**

Milestones in MAP History

- 1994 The Alzheimer List, an e-mail based support group for caregivers, is launched.
- 1995 The ADRC moves into the old Health Key Building at 4488 Forest Park.

Dr. David Holtzman is recruited to Washington University and MAP.
- 1997 Biennial Leonard Berg Symposium is inaugurated.
- 1998 Dr. Eugene Rubin and colleagues publish a paper in the *Archives of Neurology* showing that, in the absence of disease, older adults maintain stable cognitive functioning over time.
- 2001 Dr. Morris and colleagues publish a paper showing that Mild Cognitive Impairment represents the earliest stage of AD (*Archives of Neurology*) and that brain changes associated with AD begin years before the onset of clinical symptoms (*Journal of Molecular Neuroscience*).

Dr. Morris becomes Editor-in-Chief of *Alzheimer's Disease and Associated Disorders*.
- 2003 Dr. Morris invites scientists from across the US to discuss the development of biological tests to detect pre-clinical AD. Recommendations are published on-line by the Alzheimer's Research Forum (see <http://www.alzforum.org/res/enab/workshops/biomarkers.asp>).
- 2004 A new PET imaging tracer, developed at the University of Pittsburgh to detect amyloid plaques, gets its first use at Washington University. A 5-year study of this detection method is now underway in St. Louis.

Alzheimer List 10th Year

In 1994, when the Internet was still in its infancy, Dr. Kathy Mann-Koepke, then Education Director for the ADRC, had a bold idea to serve isolated caregivers: *Why not use the internet to provide 24/7 e-mail support focusing on the special needs of families struggling with Alzheimer's disease?*

With funding from the National Institute on Aging (P50-AG05681) and a lot of effort, the Alzheimer List (AL) was born. A small group of caregivers and professionals joined in 1994 and began talking, sharing and leaning on each other. Soon, a unique community formed with its own etiquette, abbreviations, etc. Over the coming years, caregivers from all over the US and World joined. More than 4,000 individuals have joined since and thousands of other web-browsers have benefited from the AL's searchable archive.

To learn more about the AL and how to become a member, visit <http://alzheimer.wustl.edu/adrc2/alzheimerlist>.

Notables

ADRC researchers will present 45 posters and presentations for the 2004 *International Meeting on Alzheimer's Disease* to be held in Philadelphia, July 17-22. View the abstract booklet at <http://alzheimer.wustl.edu>.

Consuelo Wilkins, MD, ADRC Investigator, was named *Volunteer of the Year* by the St. Louis Chapter of the Alzheimer's Association (4/04).

Elizabeth Grant, PhD, ADRC Biostatistician, received the Harvey and Dorismae Friedman Award during the Center for Aging's annual Friedman Lecture in May. This award is presented to a non-physician for outstanding contributions to patient-oriented care, education, and/or research focusing on healthy aging.

Joy Snider, MD, PhD, ADRC Investigator, received the Alene and Meyer Kopolow Award from the Barnes-Jewish Hospital Foundation at the Center for Aging's Friedman Lecture (5/04). The award provides \$3,000 in recognition of exemplary achievement in geriatrics by junior faculty or trainees, and honors the Kopolows' efforts to improve geriatric care through Barnes-Jewish Hospital.

Virginia Buckles, PhD, ADRC Executive Director will be promoted to Research Associate Professor in the Department of Neurology in July.

John C. Morris, MD, ADRC Director & Principal Investigator, will receive a Lifetime Achievement Award for Research Excellence in AD Research from the Alzheimer's Association in July 2004. This prestigious honor was also received by ADRC Founding Director, Dr. Leonard Berg, in 2000.

Alison Goate, D.Phil., has been named the holder of the Samuel and Mae S. Ludwig Chair in Psychiatry. Goate, professor of psychiatry and of genetics, is a key member of the Department of Psychiatry's Genetics Research Program and the Genetics Core Leader for the Alzheimer's Disease Research Center. The appointment was recently announced by the Barnes-Jewish Hospital Foundation Board of Directors.

David Holtzman, MD, ADRC Associate Director and Head of Neurology, became a member of the American Society for Clinical Investigation (ASCI) at the ASCI Annual Meeting in 4/04. The ASCI is an honor society of physician-scientists, those who translate findings in the laboratory to advance clinical practice.

Randall Bateman, MD, new ADRC Fellow, received a 2-year research fellowship award from the American Academy of Neurology at the Annual Meeting (4/04).



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