

Cognitive Reserve, Education, and Alzheimer's Disease

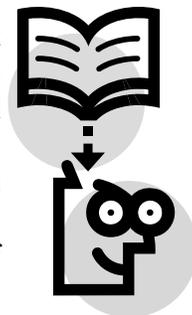
The cognitive reserve hypothesis has been used to explain the fact that some people show less serious outward manifestations of AD than would appear congruent with the extensive AD pathology in their brains. Researchers have suggested that such people, due to the nature of their brains or to the use of skills learned through stimulating intellectual and leisure activities, might be more resilient to neurological damage, or might take longer before exhibiting the symptoms of that damage. One often-used measure of cognitive reserve is education.

The research question recently studied by ADRC investigators was whether or not education has a relationship with participants' CDR ratings and with the amount of AD pathology in the brain. The latter

was measured using "Pittsburgh Compound-B (PIB)," a recent advance in imaging technology that appears to identify areas of amyloid accumulated in the brain. Amyloid is the sticky protein that forms the plaques in the brain associated with AD. As PIB binds to amyloid, more PIB tracer remaining in the brain during the scan suggests higher levels of amyloid, and thus, higher levels of AD pathology.

The study examined the results of PET-PIB scans, as well as CDR rating and several paper-and-pencil tests, of 198 participants. Of these, 161 were rated as nondemented, while 37 were rated as having dementia of the Alzheimer type at the very mild, mild, or moderate level.

Results showed that years of education was unrelated to most test scores for participants without elevated PIB uptake (very little amyloid in the brain). These participants did very well on the tests regardless of their educational level. However, for participants with elevated PIB uptake (more probable AD pathology), more years of education predicted better scores on the CDR, measures of verbal abstract reasoning, and other tests as compared to PIB positive participants with fewer years of education.



Results continued on Page 6

8th Annual Friedman Conference Drives Home a Timely Message

Each year, the Harvey A. Friedman Center for Aging presents the Friedman Conference as a forum for addressing issues related to aging. This year, the increasingly-important topic of transportation and driving issues was highlighted, with presentations ranging from evaluating cognitively impaired older drivers to improving driving skills to establishing reporting laws that keep unsafe drivers off the road.

Cartoonist Mort Gerberg lightened the mood during lunch by sharing some of his humorous depictions of aging and the issues that people face as they grow older as seen in his book, "Last Laughs: Humor in Aging."

Presenters (L to R): Tom Meuser, PhD; Linda Hunt, PhD; Richard Marottoli, MD; Katherine Freund; John Morris, MD; David Carr, MD; Brian Ott, MD; Loren Staplin, PhD; Mike Right



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Congressman William Lacy Clay Visits the ADRC

On May 5, 2008, U.S. Representative William Lacy Clay visited the ADRC to meet some of our investigators and to learn about our research. Stressing to Congressman Clay that he has a world-class Alzheimer's research center right here in his own district, Dr. Morris proceeded to discuss the critical continued need for the federal funding of research.



The effort to have an audience with Congressman Clay was instigated by the ADRC's African American Advisory Board, which is instrumental in advising the ADRC on ways to educate African Americans about the disease and to recruit them into research studies.

The latter is crucial to ensuring that research results are applicable to the African American population, which may be at an increased risk of developing AD.

Volunteers Needed for ADRC Studies

Do you know of someone who might consider volunteering for a research project on cognitive aging?

Two primary projects of the ADRC are in need of new volunteers:

The **Memory & Aging Project** enrolls persons aged 65+, both those with mild memory problems and those who are cognitively healthy.

The **Adult Children Study** needs volunteers between the ages of 45-74 for whom neither parent had AD.

*If you know of a potential volunteer, please ask that person to call the ADRC at **314-286-2683**. Thank you!*

John Morris, MD, Wins Mentorship Award

At their Spring Dinner, Dr. Morris received the Mentor Award from the Academic Women's Network (AWN). The purpose of the AWN is to promote professional and social interactions among the female academic faculty with the intent to discover and support mutual goals and to assist and mentor female junior faculty and trainees in the pursuit of their goals.

Washington University School of Medicine faculty are nominated by the students, post-docs, and faculty who have benefited from the mentor's guidance and role modeling. A winner is chosen who exemplifies outstanding mentorship of a female faculty member or trainee not only through his or her teaching responsibilities but through mentorship in every sense of the word.

Clinical Trials Currently Enrolling

Name of Investigational Agent	Inclusion Criteria	Exclusion Criteria	Exclusionary Meds	Study Design	Refer Patient To:
<p>Namenda Study</p> <p>Not actually drug study. Observing brain changes of people on Aricept/ Namenda by MRI.</p> <p>No PLACEBO group</p>	<p>50-80 years old.</p> <p>Alzheimer's disease.</p> <p>Must be on stable dose of Aricept.</p> <p>Memantine to be added.</p> <p>Participants receive Namenda (Memantine) at no cost for the 2 years of the study.</p>	<p>Unable to have MRI.</p> <p>History of LOC or other neurologic disorder that would confound dementia assessment.</p>		<p>Person with mild to moderate AD will be enrolled. Need to be on Aricept. Memantine (Namenda) to be started. MRI scan done before start of Memantine and at the end of study. Participants have cognitive testing once every 3 months for 2 years. Memantine is provided at no cost.</p>	<p>Study Coordinator:</p> <p>Wendy Overkamp, BA</p> <p>314-286-1971</p> <p>Enrollment ongoing</p>
<p>Vitamin D in Older Adults</p> <p>Not a drug study. Observing whether Vit D levels effect mood, cognitive testing or hippocampal volumes.</p>	<p>Healthy volunteers 60+ years old.</p> <p>CDR 0.</p> <p>Ambulatory.</p>	<p>Unable to have MRI.</p> <p>Primary neurological disorder.</p> <p>Malignancy.</p> <p>Severe or unstable medical condition.</p> <p>Renal failure.</p>	<p>Use of prescription Vit D, > 800 international units, daily</p>	<p>Two year study, 2 MRI's, 3 paper and pencil tests, 1 physical exam, 5 questionnaires and 5 blood draws. Much of the above can be done in conjunction with a routine MAP visit.</p>	<p>Study Coordinator:</p> <p>Vicki Weir, RN, MSG, BC</p> <p>314-286-1973</p>
<p>RAGE Inhibitor Trial</p>	<p>50 years old and up.</p> <p>Alzheimer's disease.</p> <p>MMSE = 14-26 at screening.</p> <p>Hachinski Ischemia Score <4.</p>	<p>History of Familial AD or disease causing mutation. History of stroke; uncontrolled hypertension; MI, angioplasty, or bypass in last 6M; pulmonary disease; heart failure; allergic reactions; Cancer in last 5 yrs (skin and prostate ok); Diabetes; Rheumatoid Arthritis or other autoimmune illness; major depression; recent blood donation; low B12; Any unstable medical condition is exclusionary.</p>	<p>Prozac; Erythromycin; Cardizem; Verapamil; Cordarone; Tagamet; Luvox; Tegretol; Dilantin; St. John's Wort; Tamoxifen.</p> <p>Chronic use of nonsteroidal anti-inflammatories or steroids</p>	<p>12 visits over 21 months: PE and Neuro exam at each visit, 9 blood draws, 11 EKGs, 8 paper and pencil tests. May participate in optional MRI, lumbar puncture, and Positron Emission Tomography study.</p>	<p>Study Coordinator:</p> <p>Vivien Gardner, RN, BSN</p> <p>314-286-2433</p>
<p>Wyeth Vaccine Phase 2</p> <p>Vaccine trial to assess the safety, tolerability and immunogenicity of ACC-001 in subjects with mild to moderate AD</p>	<p>Persons with Alzheimer's disease</p> <p>50-85 years old</p> <p>MMSE 16-26</p> <p>RMHI <4</p> <p>Stable on cholinesterase inhibitor for 120 days</p> <p>Namenda ok</p> <p>Collateral source</p>	<p>No neurological disorder</p> <p>Unable to have an MRI</p> <p>Hx of CVA, encephalitis, seizures, auto immune disease, MI recent, uncontrolled BP, alcohol or tobacco abuse, chemo in 3 yrs, multiple allergies</p> <p>Abn physical, neuro, ECG or lab</p>	<p>Stable on meds for at least 30 days</p> <p>Prior tx with immunotherapeutic or vaccine for AD</p>	<p>Two year study, 24 visits for persons with AD. MRI's, ECG's, LP's, 5 injections, blood draws, neuropsych testings</p>	<p>Study Coordinator:</p> <p>Vicki Weir, RN, MSG, BC</p> <p>314-286-1973</p>

FOR YOUR CALENDAR

3rd Annual Norman R. Seay Lecture

October 7, 2008

12:00 pm - 1:00 pm

Reception immediately following

Washington University School of Medicine

Featuring Guest Lecturer

James Jackson, Ph.D.



University of Michigan, Ann Arbor

Professor and Director
Institute for Social Research



**Alzheimer's Association
International Conference on Alzheimer's Disease
2008**

**July 26-31, 2008
McCormick Place, Chicago, IL**

Visit
<http://www.alz.org/icad/>
for more information.

**A poster reception will be held to highlight the
research of ADRC investigators that will be
presented at the ICAD:**

When: July 18, 2008 -- 11:30 am - 1:30 pm

**Where: The atrium of the Farrell Learning and
Teaching Center, Washington
University School of Medicine**



Memory Walk 2008

The Alzheimer's Association's Memory Walk is the nation's largest event to raise awareness and funds for Alzheimer care, support, and research. Volunteers of all ages are called on to become champions in the fight against Alzheimer's.

St. Louis Walk
Forest Park
Saturday, September 13

The Memory and Aging Project forms a Memory Walk team each year to support the event and to raise money. Register online to join our team, or contact Barbie Kuntemeier at 314-286-2882 for more information about the MAP team.

Please visit www.alzstl.org for more information and to register to walk.

Friedman and Kopolow Award Winners

Did You Know?

It's not all just science.....

Josiah Gerdts, a medical student who participated in the ADRC's 1st year selective course on Alzheimer's disease, showed off a different facet of his talents when playing the lead male role in the School of Medicine's spring production of "Bye Bye Birdie."



Each year at the Annual Friedman Conference, two awards are bestowed upon deserving individuals who have made outstanding contributions to the field of aging and have shown a commitment to research and/or patient-oriented care.

The **Kopolow Award** recognizes a resident, post-residency fellow, or non-tenured junior faculty member in Geriatric Neurology, Geriatric Psychiatry, or Geriatric Medicine.

This year's Kopolow awardee is **Consuelo Wilkins, MD**, Assistant Professor of Medicine in Geriatrics. Dr. Wilkins received a plaque and award money for aging-related educational endeavors. The award is supported by Barnes-Jewish Hospital Foundation from the Alene and Meyer Kopolow Fund for Geriatric Psychiatry, Geriatric Neurology, and Geriatric Medicine.



COMINGS

Ray Thierry - Accounting/Purchasing Assistant

Mary Weis - Center for Aging Administrator

GOINGS

Debra Siegel - left to pursue a fully-funded Ph.D. program in Clinical Psychology at the University of Michigan - Ann Arbor

Karolina Piotrowicz - transferred to a Grants/Budget Specialist position in the Physical Therapy program at Washington University.

The **Friedman Award** recognizes a non-physician who has made outstanding contributions to patient-oriented care, education, or research on aging or aging issues.

This year's awardee is **Marie Meisel, RN, MSN**, who works with the St. Louis Area Agency on Aging and the Memory and Aging Project Satellite. Ms. Meisel received a plaque and award money for aging-related educational endeavors. The award is supported by Barnes-Jewish Hospital Foundation from the Dorismae and Harvey A. Friedman Fund.



The ADRC congratulates Dr. Consuelo Wilkins and Marie Meisel!

Cognitive Reserve, cont'd

This study supports the cognitive reserve hypothesis because it suggests that among people who have AD pathology in the brain, greater cognitive reserve may delay the expression of dementia symptoms. The ADRC investigators used years of education to measure cognitive reserve, but other life experiences and activities, such as reading, visiting friends and relatives, and walking for pleasure, are also believed to be related to cognitive reserve.

This result is encouraging in that it suggests that there may be ways in which people with AD can enjoy more time with a lesser degree of symptoms. However, it is possible that cognitive reserve applies to some cognitive processes more than others. Furthermore, it is likely

that the benefits of cognitive reserve to people with AD decrease as the AD pathology reaches a certain threshold.

The research manuscript has been submitted for publication.

Catherine M. Roe, PhD,^{1,2} Mark A. Mintun, MD,^{1,3} Gina D'Angelo, PhD,^{1,4} Chengjie Xiong, PhD,^{1,4} Elizabeth A. Grant, PhD,^{1,4} John C. Morris, MD,^{1,2,5,6}

¹Alzheimer Disease Research Center, ²Department of Neurology, ³Department of Radiology, ⁴Division of Biostatistics, ⁵Pathology and Immunology, and ⁶Physical Therapy; Washington University School of Medicine, St. Louis, Missouri, USA

Notables

Qiang Liu, PhD, received the Hope Center Award in May. Each year, an award goes to a graduate student and a postdoctoral fellow whose work best fulfills the mission of the Hope Center.

John Morris, MD, received the AWN Mentor Award. See page 2 for more details.

Henry "Roddy" Roediger III, PhD, received the Howard Crosby Warren medal, the highest honor awarded by the Society of Experimental Psychologists, in April.

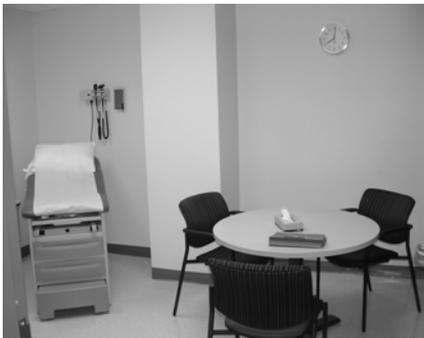
Gene Rubin, MD, PhD, received the 2008 Alumni/Faculty Award from the Washington University Medical Center Alumni Association on May 10th.

MAP West Location Open for Business

To offset the inconvenience of the Highway 40 closure and make our research studies more accessible to our participants, a Memory & Aging Project satellite location opened in March at Barnes Jewish West County Hospital located at 1040 N. Mason Rd. Any participant wishing to be seen at the MAP West office can make that

request when setting up their next appointment. The facility can handle clinical memory assessments and psychometric testing.

We thank Virginia Buckles, Mary Coats, the WUSM Business Office, and all the other people who worked so hard to get this beautiful space up and running!



Questions from the Adult Children Study Participant Appreciation Brunch

Lumbar puncture and Dr. Bateman's 36-hour LP study:

What information do you get from the weekend-long study that you don't get from the more common (1-2 hour) study?

We get kinetic information on the rate at which proteins are made and cleared by the brain. The 2 day study provides information about the speed of clearing amyloid away that can not be obtained in a 2 hour study. An analogy is the difference between a motion picture (images over time) vs. a still photo (a single time point).



Randy Bateman, MD

What is a vasovagal reaction?

A normal reaction that causes the blood pressure to drop, sometimes leading to fainting. It usually occurs during certain activities associated with stress, hunger, dehydration, urination or defecation, or even coughing.

Disclosing test results to patients:

If the PET PIB shows a significant quantity of AB plaques, will the individual be informed?

At present, there is no proven test that can definitively diagnose Alzheimer's disease. Although experimental procedures such as the PET PIB scan have great promise to become such a test, until we are certain that they function accurately, we cannot share the results of the scans with our participants. It would be terrible, for example, if we indicated to a participant that their PET PIB scan revealed amyloid plaques only to discover later that it was a "false positive." We would have created needless worry.



John Morris, MD

If an indication of AD is found at an early stage, will this be shared with the subject?

The best diagnostic procedure to determine the absence or presence of Alzheimer's, even when it is in its earliest symptomatic stages, is a careful evaluation by an experienced clinician. Our clinicians share their research assessment findings with our participants. This is meant to help the participant in communicating with their private physician, who rightly provides the "official" evaluation and determines therapy. Even when disease symptoms are very mild, it is appropriate to undergo evaluation.

If alarming/possibly grave medical findings or issues (other than AD) appear during the battery of tests (MRI/PET/LP), what is the procedure to 1) alert the participant, 2) notify the participant's primary physician, and 3) expose the findings?

We strive to balance our obligation to fully protect the confidentiality of the research participants as they go through our various studies with our obligation to inform them of any potentially important medical findings. All abnormalities from research test procedure are reported to the Clinical Core leader (John C. Morris, MD). Dr. Morris reviews the abnormal findings and then communicates the results to the participants. Only with the participant's permission, and only when the findings warrant further evaluation or treatment, Dr. Morris communicates the abnormalities to the participant's personal physician.

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.

John C. Morris, MD, Director, ADRC, & Director, MAP

Eugene M. Johnson, PhD, Associate Director, ADRC

David M. Holtzman, MD, Associate Director, ADRC

Martha Storandt, PhD, Psychometric Core Leader

Nigel J. Cairns, PhD, MRCPATH, Neuropathology Core Leader

Alison Goate, DPhil, Associate Director and Genetics Core Leader

Mark Mintun, MD, & Denise Head, PhD, Neuroimaging Core Leaders

J. Philip Miller, MA, Biostatistics Core Leader

Monique Williams, MD, African American Satellite Leader

James E. Galvin, MD, MPH, Education Core/Rural Satellite Leader

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SCHOOL OF MEDICINE

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