Washington University St. Louis Alzheimer's Disease Research Center

HORIZONS

Newsletter, Volume 14(1), Spring 2007
ADRC and the Memory & Aging Project (MAP)

In Fondest Remembrance...

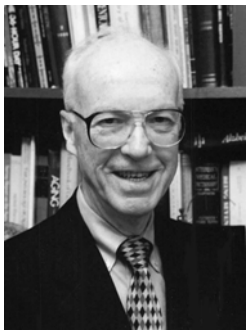
Passing of Leonard Berg, MD (1927-2007)

The Washington University community gathered on March 31st to honor the life and legacy of Leonard Berg, MD, Professor Emeritus of Neurology and founding director of the Memory & Aging Project and the Alzheimer's Disease Research Center (ADRC). Dr. Berg died on January 15, 2007, from complications of a stroke. Current ADRC Director and Dementia & Aging Section Head, John C. Morris, MD, made the following remarks at the March 31st Memorial Service.

I am very honored to be invited to provide a few remarks as we celebrate the life of Leonard Berg. Leonard was my role model, mentor, colleague, and friend.

As we begin careers, most of us wonder if we will ever be successful enough to make a difference, to leave a mark. Leonard not only succeeded spectacularly in making his mark, he did it in many different areas. He was a wonderful physician and teacher, held in the highest regard by his peers and by residents and medical students, and he elicited deep gratitude and affection from his patients and their families. He became a devoted advocate for these families through his tireless work with the Alzheimer's Association, both here in St. Louis and nationally. He always encouraged young clinicians and scientists. I will forever be indebted to Leonard because, for some reason, he took a personal and incredibly supportive interest in my career. I simply would not be where I am today without Leonard.

He was a pioneer, a giant, in Alzheimer's research. Leonard was among the first to appreciate the need to carefully study this terrible disease. At Washington University, he established the Alzheimer research program that culminated in the Alzheimer's Disease Research Center, for which he was founding director. The clinical research methods, including the Clinical Dementia Rating, developed by Leonard and his colleagues for the assessment of Alzheimer's disease, have been adopted as worldwide standards and are used by all researchers. A key to Leonard's leadership of the ADRC was his ability to attract highly accomplished (and sometimes temperamental) investigators and clinicians and mold them into a cohesive team, working together productively toward common goals despite differences in backgrounds and disciplines. He made the ADRC not only rewarding and intellectually stimulating, but fun. It hence is no surprise that many former and current ADRC members are here today in tribute to Leonard.



Leonard's gift in bringing

Cont'd on pg. 3

Inside this issue:

Would you like to make a gift in support of the ADRC?

You may support our research, education and service goals by joining the *Friends of the ADRC*. Members of the *Friends* are entitled to attend periodic *Friends Receptions* featuring presentations on research findings from Dr. John C. Morris, Director of the ADRC, and other investigators, and also receive free admission to various ADRC-sponsored conferences. *Friends* are encouraged to make an annual gift in support of the ADRC.

Donations from *Friends* support both the infrastructure upon which the ADRC depends, as well as specific research and educational projects of the Center. Private donations help to fund promising pilot research projects (i.e., small projects to test out new ideas), educational conferences such as the Leonard Berg Symposium series, the training of medical students and fellows, and other worthwhile projects.

To join, simply contact the Friends Coordinator by phone (314-286-2683) or e-mail *adrcfriends@abraxas.wustl.edu*.

Use of Antipsychotic Medications in Individuals with Alzheimer's Disease

Caregivers for persons with dementia often struggle with decisions regarding the use of antipsychotic medications, which are prescribed to help control behavioral and psychiatric symptoms of Alzheimer's disease. However, studies have shown that these medications increase the risk of death in these individuals. This article will provide information that will help caregivers to weigh the risks and benefits of treating behavioral and psychiatric symptoms of Alzheimer's disease.

Who experiences the behavioral and psychiatric symptoms of Alzheimer's disease?

Behavioral and psychiatric symptoms may sometimes occur, but not all individuals with Alzheimer's disease experience these symptoms. In the early stages of the disease, depression or anxiety may be present. In the later stages of the disease, the individual may have hallucinations, delusions, agitation, or sleep disturbances. These symptoms may be distressing both to the individual with Alzheimer's disease and to their family.

Are there any alternatives to using medication to treat the symptoms?

It is essential to check the patient for another cause of the behavior, such as an infection. Once other causes are ruled out, non-pharmacological options are often recommended prior to starting therapy with an antipsychotic. Non-pharmacological options include adapting the environment. For example, triggers of the behavior may be removed. Depending on the severity of the symptoms, non-pharmacological options may be sufficient to cope with them.

Which medications are used to treat behavioral problems?

There are no drugs that are specifically approved by the FDA to treat the behavioral symptoms of dementia. However, there are drugs approved for other purposes that physicians may prescribe. One group of medications is antipsychotic medications. Although these drugs are approved to treat bipolar disease and schizophrenia, they are also used in the treatment of the behavioral symptoms of Alzheimer's disease.

There are two types of antipsychotics, first generation or conventional antipsychotics and second generation or atypical antipsychotics. See Figure 1 for a list of some of these medications.

Figure 1. Antipsychotics

Conventional antipsychotics
haloperidol (Haldol)
chlorpromazine (Thorazine)

Atypical antipsychotic
risperidone (Risperdal)
quetiapine (Seroquel)
aripiprazole (Abilify)
olanzapine (Zyprexa)
clozapine (Clozaril)
ziprasidone (Geodon)

How do antipsychotics work?

The way in which antipsychotics work is unknown. Generally, the response to an antipsychotic is not rapid. It may take a few days to weeks for an individual to fully respond.

What are potential risks?

In clinical studies, atypical antipsychotics were associated with an increased risk of death in elderly patients with dementia-related psychosis compared to placebo. This conclusion was reached by examining the results of 17 studies that included four atypical antipsychotics. The rate of death in the group receiving atypical antipsychotics was up to 1.7 times the rate of those not receiving an antipsychotic. Most of these deaths were caused by a heart-related problem or an infection.

In 2005, the FDA issued a public health advisory for the use of atypical antipsychotics in elderly patients with dementia-related psychosis. These medications now have a black box warning to advise the public that these drugs may increase the risk of death in elderly patients with dementia. The warning also informs patients that these drugs are not approved by the FDA for the treatment of behavioral symptoms of dementia.

Other potential side effects of antipsychotics include excessive sedation, which could lead to an increase in falls. Extrapyramidal symptoms and tardive dyskinesia (abnormal involuntary movements) may also occur. Usually, atypical antipsychotics are better tolerated than conventional antipsychotics.

What are potential benefits?

Behavioral and psychiatric symptoms may be distressing to the patient as well as the family. In some cases, the behaviors may be dangerous. Often, these symptoms play a large role in determining whether or not the individual will be placed in a long-term care facility. Antipsychotics may help to prevent behavior symptoms and increase quality of life. Thus, caregivers must consider both the risks and benefits of antipsychotic medications.

By Tori Vahle, PharmD candidate, St. Louis College of Pharmacy.

people together was also realized on the national stage. Beginning in 1985, the early meetings of the directors of the first 10 ADRCs established by the National Institute on Aging were ripe for disagreement, even acrimony, as each director put forth his own agenda to more favorably position his Center for the scarce research dollars. Along with other giants in the field, including Zaven Khachaturian, Bob Katzman, and Bill Markesbery, Leonard steered the directors away from debate and dispute. His willingness to share, his sense of humor, and his gracious and gentlemanly leadership soon forged a collegial and collaborative spirit among the ADRCs that continues today.

I will close with an anecdote from one of those very early meetings of the ADRC Directors. This one was held at the University of Kentucky, where Bill Markesbery was a most gracious host. At the closing dinner, Bill took great pains to offer us only Kentucky's finest food and drink, including mint juleps. Mint juleps, of course, are made with Kentucky bourbon whisky - actually, with a fair amount of bourbon. I seem to remember also that there were a fair amount of mint juleps. Toward the end of dinner, there were the requisite speeches and toasts. Leonard had a habit, listening to talks, of slipping off his wedding band and playing with it absent-mindedly, which he did this evening. When we finally got back to the hotel room, Leonard discovered that somehow he had left his wedding band on the dinner table. A desperate call to Bill Markesbery seemingly resulted in the entire Commonwealth of Kentucky being mobilized because, in the wee hours of the night, police and other officials searched the dining room, entire wait staff, kitchen, even the garbage bags for that band, which unfortunately did not turn up. What makes this story memorable is that Leonard told it himself years later, at the close of the first Leonard Berg Symposium in 1997, held in his honor as he stepped down as ADRC Director. After thanking the organizers and faculty at the Symposium, he recalled his panic at losing his wedding band, then stood at the podium, took off his replacement wedding band, and extended it toward Gerry, seated in the audience, to tell her how much she meant to him and how much he loved her. There wasn't a dry eye in the house.

Leonard lived a full and deeply satisfying life, and he certainly made his mark. The world will remember him as a caring physician, esteemed mentor, and brilliant scientist. He was respected by all and cherished by many. We can never repay Leonard for all he has given us, but part of his legacy is that we will try to live up to his lofty standards. In the end, however, it is relationships that matter more than standards. Here Leonard was truly blessed, because he loved his family and they loved him. That is the greatest mark of all.

African American Outreach

The ADRC African American Advisory Board (AAAB) was established in 2000 to counsel the research team concerning cultural sensitivity and appropriate outreach strategies to encourage active, long-term participation of African Americans in memory and aging studies at Washington University. Our commitment to inclusiveness, diversity and justice (fairness) for research participants is integral to our mission. AAAB members, as pictured here, are members of the community who appreciate the value and importance of clinical research and who are willing to commit their time and energy as liaisons between the ADRC and the community.

(Top L to R): James Williams, Marie Meisel, Dr. Monique Williams, Dr. Donald Nichols, Norman Seay, Myrtis Spencer
(Bottom): Sally Simmons, Bernice Thompson, Dr. Collins Lewis

AAAB members are charged with several important tasks, including:

- Actively representing the research mission and participation interests of the ADRC-MAP in the African American Community;
- Serving as ambassadors and liaisons for the ADRC-MAP in building strong individual and local partnerships to enhance research participation;
- Advising our investigators in the development of culturally appropriate and sensitive education, outreach, recruitment, and retention strategies, products and programs;
- Reviewing print, video and other materials of the ADRC-MAP to ensure the communication of consistent, appropriate, and effective messages.

(L to R): Rev. Doug Petty, Gloria Beard, Dr. Denise Hooks-Anderson, Dr. John Morris, Dr. Monique Williams, Constance Williams

Thanks to the dedicated efforts of the Board, the ADRC has experienced a steady rise in the number of African American participants in its research studies, but we still have room for more improvement. Please contact Myrtis Spencer with questions about the AAAB or African American outreach at 314-286-0930.

Promise in Fish Oil?

Nutritionists have long endorsed fish as part of a heart-healthy diet, and now some studies suggest that omega-3 fatty acids found in the oil of certain fish may also benefit the brain by lowering the risk of Alzheimer's Disease. In order to test whether docosahexaenoic acid (DHA), an omega-3 fatty acid, can impact the progression of Alzheimer's disease, researchers at Washington University School of Medicine and Saint Louis University School of Medicine will evaluate DHA in a clinical trial sponsored by the National Institute on Aging (NIA).

The local effort is part of a nationwide consortium of leading Alzheimer's disease researchers supported by the NIA and coordinated by the University of California, San Diego. The trial will take place at 52 sites across the United States. It seeks 400 participants age 50 and older with mild to moderate Alzheimer's disease. Jospeh Quinn, M.D., associate professor of neurology at Oregon Health and Science University, is directing the national study. James Galvin, M.D., M.P.H., at Washington University, and George Grossberg, M.D., at Saint Louis University School of Medicine, will conduct the study locally.

Researchers will primarily evaluate whether taking DHA over many months slows both cognitive and functional decline in people with mild to moderate Alzheimer's. During the 18-month clinical trial, investigators will measure the progress of the disease using standard tests for functional and cognitive change.

"Evidence to date in various research studies that have examined the effect of omega-3 fatty acids on Alzheimer's disease merits further evaluation in a rigorous clinical trial," Galvin says. "Our hope is that we may find out that DHA plays a role in slowing the progression of this destructive disease."

In recent European studies and the Framingham Heart Study, scientists reported that people with the highest blood levels of DHA were about half as likely to develop dementia as those with lower levels.

For the clinical trial, the Martek Biosciences Corporation of Columbia, MD will donate a pure form of DHA made from algae devoid of fish-related contaminants. Participants will receive either two grams of DHA per day or an inactive placebo pill. About 60 percent of participants will receive DHA, and 40 percent will get the placebo. Doctors and nurses at the 52 research clinic sites will monitor the participants in regular visits throughout the trial. To ensure unbiased results, neither the researchers conducting the trial nor the participants will know who is getting DHA and who is receiving the placebo.

In addition to monitoring disease progression through cognitive tests, researchers will also evaluate whether taking DHA supplements has a positive effect on physical and biological markers of Alzheimer's, such as brain atrophy and proteins in blood and spinal fluid.

To learn how to participate in the study, call (314) 286-2683 at Washington University School of Medicine or (314) 268-5385 at Saint Louis University School of Medicine.

NOTABLES

Eugene Johnson, PhD, was elected as a Fellow in the American Association for the Advancement of Science. This distinction, which recognizes scientifically or socially distinguished efforts to advance science, is the highest honor awarded by the AAAS.

Brian Carpenter, PhD, was granted tenure and promoted to Associate Professor of Psychology.

Effective July 1, 2007, **Rohit Pappu, PhD**, is promoted to Associate Professor with Tenure in Biomedical Engineering. He also received an RO1 grant funded by the NINDS entitled "Atomistic studies of nucleation and oligomerization in polyglutamine aggregation."

Debra Siegel received her BA in Psychology from WU with departmental honors and has transitioned from undergraduate student to full-time MAP employee.

Jim Galvin, MD, MPH, has been promoted to Associate Professor of Neurology.

Joanne Norton received the Friedman Award from the Center for Aging.

Within the ADRC, **Cathy Roe, PhD,** is moving from a staff position in Biostatistics to a faculty position in Neurology.

In September of 2006, **Kevin Black, MD**, received the Hope Award from the St. Louis chapter of the Huntington Disease Society of America. Also in September, Dr. Black was in the first group of people to be certified in Behavioral Neurology and Neuropsychiatry by the United Council for Neurologic Subspecialties (UCNS).

Margaret Perkinson, PhD, was elected treasurer of the Association for Gerontology in Higher Education (AGHE).

Monique Williams, MD, was named one of the "Volunteers of the Year" for the St. Louis Chapter of the Alzheimer's Association.

Keoni Kauwe and **Karen Browning's** posters were co-selected as "Best in Show" at the Alzheimer's Disease Biomarkers Conference in Washington, D.C.

FOR YOUR CALENDAR

The **6th Leonard Berg Symposium** is quickly approaching!

Novel Therapies for Protein Misfolding Disorders

Friday - Saturday, September 28 - 29, 2007

Eric P. Newman Education Center

Washington University School of Medicine, St. Louis

The symposium, which honors ADRC founding director Dr. Leonard Berg, will focus on *new and potential therapies for protein misfolding disorders, Alzheimer's disease and others*. A call for posters was issued in January. As during past Symposia, accepted poster presenters may attend at no charge and have an opportunity to share their work with researchers from across the US and the world.

Presented by:

Alzheimer's Disease Research Center

Department of Neurology

John C. Morris, MD, Director & Principal Investigator

With special co-sponsor:

The Hope Center for Neurological Disorders

View program information, apply to present a poster, and register at:

http://Alzheimer.wustl.edu/education/berg/berg2007

2nd Annual Norman R. Seay Lecture

October 16, 2007

12:00 pm - 1:00 pm

East Pavilion Auditorium,

BJH South

Featuring Guest Lecturer

Peggye Dilworth-Anderson, Ph.D.

University of North Carolina

Associate Director for Aging and Diversity

Director, Center for Aging and Diversity

Memory Walk 2007

Memory Walk is the Alzheimer's Association's signature event to help those battling Alzheimer's disease. Memory Walk proceeds support programs, services and research.

September 15

- Tower Grove Park

September 22

- St. Peters
- Franklin County/Washington
- Cape Girardeau
- Edwardsville, IL

For more information and to register, go to:
http://www.alzstl.org

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 this year. The **Memory & Aging Project** enrolls persons aged 65+ with mild memory problems. The **Adult Children Study** needs a few additional adult volunteers, age 55 or older, with a family history of Alzheimer's disease (AD) in at least one parent, as well as adult volunteers 45 and older 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!*

Comings

- Vicki Weir - MAP Nurse Clinician
- Myrtis Spencer - Community Outreach Coordinator
- Barbie Kuntemeier - Education Core Coordinator
- Karthik Nandagopalan - Psychometrician
- Cathy Roe (as of July) - Research Instructor

Goings

- Jessica Lester left in May to attend medical school.
- Abbey DeWeese also left in May to pursue a BSN.
- Michelle Burack, M.D., left for the University of Rochester in New York this June.
- David Johnson leaves for the University of Kansas at the end of June.
- Joy Kurz will leave to complete her clinical doctorate in nursing.
- Jan Palmer will leave at the end of August to begin a fellowship and finish her dissertation.

Current Research Studies Conducted Through the ADRC

Name of Investigational Agent	Inclusion Criteria	Exclusion Criteria	Exclusionary Meds	Study Design	Refer patients to:
Namenda Study Not actually drug study. Observing brain changes of people on Aricept/Namenda by MRI. NO PLACEBO Group.	50-80 years old. Alzheimer's disease. Must be on stable dose of Aricept. Memantine to be added. Participants receive Namenda (Memantine) at no cost for the 2 years of the study.	Unable to have MRI History of LOC or other neurologic disorder that would confound dementia assessment.		Persons 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.	**Study Coordinator:** **Wendy Overkamp, BA** **314-286-1971** overkampw @abraxas.wustl. edu Enrollment ongoing HRPO# 04-1167
Docosahexaenoic Acid (DHA) 18 month Randomized, Double - Blind Placebo Control Clinical Trial	Are over the age of 50, male or female, excellent health, reliable study partner, daily DHA consumption ≤200mg/day, mild to moderate AD, stable dose of standard AD treatment for 4 months, MMSE (14-26)	Non-AD dementia, Resident in long-term care facility, history of epilepsy, seizure, focal brain lesion, head injury with loss of consciousness, major psychiatric disorder including psychosis, major depression, bipolar, alcohol or substance abuse, use of another investigational agent within two months, Active neoplastic disease	DHA containing supplements, most benzodiazepines, lithium, agents with central anticholinergic effects, antiparkinsonian medications, and narcotic analgesics	18-month, Randomized, Double-Blinded Placebo Controlled. Monitoring visits are every 3 months. Cognitive & laboratory testing at screening, baseline, 6, 8, 12, and 18 month visits.	**Study Coordinator:** **Pamela Jackson RN, BSN, MA (314) 286-2409** Enrollment ongoing
F-AV-138 Imaging Trial 2 visit imaging trial testing the amyloid binding properties of a radiotracer. **Not a treatment trial. Imaging session must occur within 30 days of screening.*	*Two groups needed*: • Healthy volunteers 50 years and older without memory complaints and a stable health history • Persons with Alzheimer's disease 50 years and older; stable health history; MMSE score of 10 - 24 on testing; reliable study partner	• Unable to have MRI; • History of LOC or other neurologic disorder that would confound dementia assessment; • Have current clinically significant cardiovascular disease (EKG changes); •Have a currently unstable health condition or history of an infectious disease. •Participation in an experimental study with an amyloid targeting agent	• Any medication with a narrow therapeutic window, such as coumadin or theophylline • Gingko Biloba	*Two Day Study Design for Healthy Volunteers and Individuals with Alzheimer's Disease:* -Day One: Screening: eligibility reviewed, safety labs, memory testing, physical/neurologic exam; EKG and MRI - Day Two: Imaging: PET imaging of brain for approximately 3.5 hours with safety measures. Imaging session allows for multiple breaks.	**Study Coordinator:** **Angela Oliver, RN, MSG (314) 286-2407**

19th Annual Participants' Meeting

Each year, the ADRC invites all the people who have participated in its research studies to a breakfast gathering, where they mingle with ADRC faculty and staff members, hear about some of the newest Alzheimer's-related research, and have the opportunity to learn about and sign up as participants in new and upcoming research studies. Along with providing updates on current research studies, ADRC presenters spoke about topics ranging from the relationship between alcohol and dementia to peoples' reactions to receiving a dementia diagnosis.

- 856 men and 1,366 women have participated in MAP longitudinal studies.
- 663 participants are currently active in MAP.

Q & A: MAP Stats

Some participants were curious about the statistical breakdown of our research participants.

- From 1979 to the present, there have been 2,222 participants enrolled in longitudinal studies.
- Participants range from 23 to 103 years old at the time they enter MAP.
- The number of annual assessments per MAP participant ranges from 1 to 27.
- 804 participants have given brain donations since 1979.

The next issue of Horizons will feature more answers to participants' questions!

Congratulatory Farewell

Tom Meuser, who had been working in the Department of Psychiatry at St. Louis University and exploring grief reactions in older adults with his collaborator, Sam Marwit, from the University of Missouri, St. Louis, joined the Alzheimer's Disease Research Center (ADRC) in October 1999. As the new leader of the ADRC's Education Core, he quickly was immersed in learning the many activities and the broad scope of the Core and had to transition from a researcher into an administrator and educator. He succeeded spectacularly. During his eight years as leader, our Education Core has grown into one of the very best such programs across the 29 Alzheimer's Disease Centers in the United States. The Education Core now organizes a vast array of educational programs and materials that focus on increasing awareness about Alzheimer's disease, including the highly successful Leonard Berg Symposia held every two years at Washington University. The Core partners very successfully with the St. Louis Chapter of the Alzheimer's Association to coordinate and facilitate efforts of mutual interests. Under Tom's leadership, the Core has pioneered the use of technology to deliver its message with the use of video- and web-based methods and shares these technologies with investigators throughout Washington University. The Core actively supports the African American Advisory Board in its efforts to improve diversity in the ADRC. Tom also capitalized on an applied research activity in the ADRC to expand knowledge of the problems associated with demented drivers and has seen these efforts grow into a highly visible research program that itself has become increasingly well-funded. Perhaps the signature program of the Core developed by Tom was the provision of mini-residencies for health professionals in both rural and urban areas of Missouri to enable them to better detect and manage dementing disorders.

Educator, innovator, administrator, researcher: Tom Meuser has grown remarkably in all these areas during the eight years of his tenure as leader of the ADRC's Education Core. Correspondingly, the Core also has grown in stature so that it now is the model for all Alzheimer's Disease Centers. We shall miss Tom's creativity, energy, and citizenship as he departs for his new career opportunity and wish him the very best in his new endeavors.

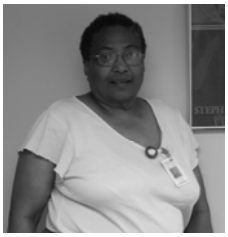
~Dr. John Morris

Farewell to Dr. Dorothy F. Edwards

(L-R): Monique Williams, MD, new African American Satellite Leader, with Dorothy Edwards at her Farewell Reception on June 14th.

Dorothy F. Edwards, PhD, long-time Leader of the ADRC's African American Outreach Satellite Program (known by the acronym "MAPS") is leaving Washington University this summer after a 30+ year career beginning as a student in the 1970s. Dorothy is now an Associate Professor of Kinesiology at the University of Wisconsin – Madison, teaching in the Occupational Therapy Program. Dorothy plans to continue her research on health in minority elders, the impact of stroke on well-being and daily life functioning, and dementia. All in the ADRC Family wish Dorothy all the best in her new position!

39 Years with Washington University



Shirlene Taylor received an award in June for having devoted 39 years as an employee at Washington University. She began in the Division of Biostatistics, later moved to the Medical Computing Services Group, and finally joined the ADRC as a Data Entry Operator, where she has been for the past 16 years. We truly appreciate all of her hard work and dedication to the university!

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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