BU ADC Bulletin

Boston University Alzheimer's Disease Center

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In This Issue:

New Outreach Staff
New Faculty
HOPE Appreciation Brunch

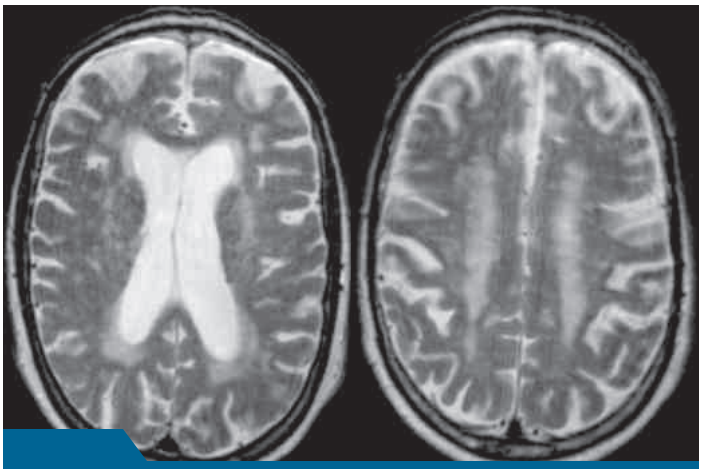
Heart Function as a Risk for Unhealthy Brain Aging

Though much research in the field of Alzheimer's disease (AD) emphasizes new, cutting-edge treatment efforts, another important research area is focused on disease prevention. Prevention first involves identifying risk factors for AD and then managing these risk factors to keep AD from developing among future older adults.

To date, many research studies have found that certain types of heart disease, such as diabetes or high blood pressure, may increase one's risk for developing AD. One exciting new aspect of research being conducted at the Boston University Alzheimer's Disease Center (BU ADC) is the examination of heart function as a possible risk factor for AD. The goal of this new study is to determine if minor abnormalities in heart function are related to an increased risk for developing AD among individuals with mild cognitive impairment (MCI).

Individuals with MCI experience mild impairments in memory and other cognitive or thinking abilities that are not normal for one's age. Some research has

Heart Function and Brain Aging continued on page 3 >



White matter hyperintensities are an MRI sign of vascular changes in the brain.

New Funding to Continue the ADAPT Study

An important area of research in the field of Alzheimer's disease (AD) is identifying methods to prevent the development of AD well before symptoms develop. One particular area of focus in preventative research is the use of non-steroidal anti-inflammatory drugs (NSAIDs). The Alzheimer's Disease Anti-Inflammatory Prevention Trial (ADAPT) was funded by the National Institutes of Health between 2001-2006 to determine if NSAIDs can prevent or delay the onset of AD. The Boston University Alzheimer's Disease Center (BU ADC) was one of six participating sites for this multi-center investigation. When the study began in April 2001, it was the first-ever AD prevention trial using NSAIDs and the largest AD prevention trial in the world. Those individuals over age 70 who had an immediate family member diagnosed with AD, and thus had an increased risk of developing the disease, were invited to participate in the trial. Each participant was randomly assigned to receive a placebo (sugar pill) or one of two NSAIDs: naproxen sodium (Aleve) or celecoxib (Celebrex). Nationwide, 2528 people were enrolled in this study, with over 420 individuals participating locally at the BU ADC site.

In December 2004, the clinical trial was stopped because of an indication that NSAIDs can increase the risk of cardiovascular complications. At that time, all participants discontinued the use of the medications, including both

ADAPT Funding continued on page 3 >

The BU ADC's New Outreach and Recruitment Team

Ms. Silvia Serrano

The Boston University Alzheimer's Disease Center (BU ADC) is pleased to announce the recent addition of Silvia Serrano, MPH, who joined our team in September 2009. Silvia will serve as the new BU ADC Outreach & Recruitment Coordinator, predominantly focused on recruitment efforts for the Health Outreach Program for the Elderly (HOPE) study. She will oversee recruitment and community outreach needs for the broader BU ADC clinical research portfolio. Silvia's primary interests include educating populations at risk for contracting Alzheimer's disease (AD) and increasing their participation in medical research. Prior to working with the BU ADC, Silvia worked with local and state public health agencies, developing chronic and infectious disease prevention programs. Her most recent role was managing cancer prevention screenings and infectious disease programs. Silvia is a recent recipient of a master's degree in public health from Boston University with a concentration in social and behavioral sciences.

Ms. Susan Lambe

The BU ADC is also pleased to announce that Susan Lambe, who has been serving as a consultant to the Center for the past year, has joined our team as the Brain Donation Outreach & Education Coordinator. Susan's new role will include conducting focus groups with African American participants in the HOPE study and improving Center efforts to enhance African American representation in the BU ADC brain donation program. The position is being funded by a special supplement grant awarded to Dr. Angela Jefferson and the BU ADC as part of the American Recovery and Reinvestment Act of 2009. Susan is currently a fourth-year doctoral student in clinical psychology at the University of Massachusetts, Boston. Her professional interests include healthcare disparities, culturally relevant mental health services, and psychological effects of racism and discrimination.

New Faculty Members

Dr. Wendy Qiu

Wendy Qiu, MD, PhD, a board-certified psychiatrist and an Alzheimer's disease (AD) researcher, will be joining the Boston University School of Medicine faculty in December 2009 as Assistant Professor of Psychiatry. Dr. Qiu identified the role of insulin-degrading enzyme in the clearance of amyloid-beta peptides while working in Dr. Dennis Selkoe's laboratory at Harvard Medical School. Recently, she and her research team have defined a possible depression subtype for a prodromal (or early) stage of AD. Dr. Qiu has been on the faculty at Tufts University School of Medicine for several years, and she recently received an R01 grant from the National Institute on Aging to support her research examining AD risk factors. Dr. Qiu will be collaborating with the Boston University Alzheimer's Disease Center (BU ADC) to study the role that depression and type 2 diabetes each play in developing AD.

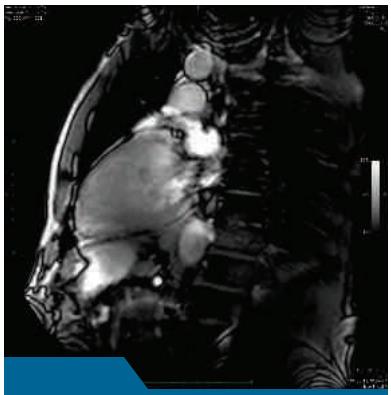
Dr. Brandon Gavett

Brandon Gavett, PhD, recently completed his neuropsychology post-doctoral training at the BU ADC, and he has been appointed to Instructor of Neurology at Boston University School of Medicine. Dr. Gavett received his PhD in clinical psychology from the State University of New York at Albany, and he completed an internship in clinical psychology/neuropsychology at the Veterans Affairs Connecticut Health Care System in West Haven. Dr. Gavett's role at the BU ADC will primarily focus on research and clinical activities. He is seeking career development funding to conduct research and receive training in chronic traumatic encephalopathy as part of Boston University's Center for the Study of Traumatic Encephalopathy. Dr. Gavett will be overseeing new and ongoing research projects within the BU ADC.

< *Heart Function and Brain Aging continued from page 1*

suggested that individuals with MCI are at greater risk for developing AD than individuals without memory or thinking difficulties. However, individuals with MCI continue to live independently in the community and manage their day-to-day affairs without difficulty. Research focused on individuals with MCI may provide important information about risk factors for AD.

The Heart & Brain Aging study, conducted by Dr. Angela Jefferson, a BU ADC neuropsychologist, is investigating the association between heart function and brain aging in individuals with MCI. Funded by the Alzheimer's Association and the National Institute on Aging, the research project includes a study visit at the Boston University Medical Campus in the South End of Boston. During the visit, participants provide a blood sample, participate in a medical history interview, and complete paper-and-pencil tests of memory and thinking abilities. Finally, participants undergo heart and brain magnetic resonance imaging (MRI). Dr. Jefferson and her collaborators plan to combine information from the multiple tests to better understand whether heart function plays a role in the development and progression of early symptoms of AD.



MRI image of the heart

All participants in the Heart & Brain Aging study receive a copy of their blood test results, including information on cholesterol, blood sugar, and insulin levels. Participants also have the option of having their blood test results and electronic copies of their heart and brain MRI scans sent to their physician(s).

Currently, the Heart & Brain Aging study is recruiting individuals with a diagnosis of MCI. If you have been told by your doctor that you have mild cognitive impairment or MCI and you are interested in hearing more about the study, please contact the study coordinator, **Ms. Amanda Gentile**, by phone (**617-414-1077**) or email (**amgent@bu.edu**) to learn more about enrolling.

ADAPT Study team members (left to right): Patricia Johnson, Dr. Robert Stern, Jane Mwicigi, and Dr. Brandon Gavett

< *ADAPT Funding continued from page 1*

types of NSAIDs and the placebo. However, the study continued and participants were monitored by study staff over the next several years. The results were discouraging at first. It seemed that NSAIDs had no impact on preventing AD. However, examination over a longer period of time eventually demonstrated that the use of NSAIDs, compared to the placebo, might decrease long-term risk of developing dementia. Additional follow-up of these ADAPT participants could provide information as to whether short-term use of NSAIDs can reduce the long-term possibility of developing AD.

As part of the federal economic stimulus package, the ADAPT study investigators have secured funding from the National Institute on Aging to continue researching whether prior treatment with NSAIDs might prevent or delay the onset of AD. The *ADAPT Follow-up Study* will begin soon, and BU ADC staff will re-contact all of our ADAPT study participants to assess any changes that may have occurred in the last four years. The BU ADC is committed to researching possible prevention methods, and we look forward to participating in the *ADAPT Follow-up Study*. For more information on the *ADAPT Follow-up Study*, contact **Patricia Johnson** by phone (617-638-5430) or email (**pattiej@bu.edu**).

Actively Recruiting Studies

Study Type	Study Title	Study Description
BU ADC Research Registry	Health Outreach Program for the Elderly (HOPE)	This longitudinal study examines age-related changes in memory and thinking. It serves as the Boston University Alzheimer's Disease Center (BU ADC) research registry, where participants agree to be contacted about other BU ADC-approved studies. HOPE participants are encouraged to participate in the actively recruiting studies summarized below.
Caregiving Support & Education	Alzheimer's Disease (AD) Care	This one-year study examines a new instrument to assess caregiver burden and the well-being of the person with dementia for whom the caregiver provides support. Participation includes three to five in-person study visits and periodic phone calls.
	CARE-Plus	This study examines whether an educational intervention with caregivers can reduce behavioral problems in AD patients and improve caregivers' well-being. Participation includes a 5-week intervention with weekly sessions on AD and tips to improve interactions. The individual with AD is not involved in this study.
	Health Pathways	This study looks at how caregiving affects one's physical and emotional health among caregivers age 60 and older who currently care for someone with AD. Participants attend four yearly face-to-face interviews where they will be asked questions about their health and about the person they care for.
	Home Safety Education	This study compares two types of education to find out if they help caregivers living with a person with AD or dementia make home safety modifications. This study includes two home visits for data collection and safety education. After three months, each participant is offered the alternative education.
	PAIRS Program	This program pairs first-year Boston University medical students with patients with early-stage AD. The program educates medical students about the care and support-related issues faced by patients with AD. Student-patient pairs meet monthly to participate in activities throughout the academic year.
Evaluation of Daily Living	Functional Assessment in Dementia	This study investigates the relationship between office-based cognitive tests and independent functioning in the home. Individuals with dementia who are not living in an assisted living facility or nursing home may be eligible to participate.
	SAFE Drivers	This study aims to develop a brief, office-based evaluation of driving safety for older drivers that accurately predicts on-road driving performance. Study participation is for drivers with or without memory problems between 55 and 90 years of age. The two study visits involve office-based cognitive tests and an on-the-road driving evaluation conducted by a certified driving instructor.
Memory & Cognition	False Memory in AD	This study seeks to understand why patients with AD and other dementias frequently remember things that never happened. The goal of this study is to provide ways to reduce false memories in patients with dementia.
	Vision & Cognition	This study examines visual change in AD, how it affects cognition and daily activities, and how visual interventions may improve cognitive abilities. Participants perform tests of vision, cognition, and daily functions, and a free eye exam is included.
Neuroimaging	Heart & Brain Aging	This study uses heart and brain imaging and memory tests to better understand relations between heart and brain health among aging adults with mild memory loss, particularly those individuals who have been diagnosed with "mild cognitive impairment." Participants attend a single study visit, and laboratory results are shared with the participants' physicians.

continued on page 5 >

Actively Recruiting Studies < *continued from page 4*

Study Type	Study Title	Study Description
Treatment	CONCERT *new study	This multi-center treatment trial will evaluate a new oral medication, Dimebon. Dimebon may stabilize unhealthy changes in brain cells in individuals with mild or moderate AD. Participants must be 50 years of age or older and need a study partner to accompany them to study visits.
	IDENTITY	This multi-center treatment trial will evaluate if an oral medication, "LY450139," can slow the progression of mild or moderate AD. This new compound attempts to reduce amyloid-beta (Abeta) in the brain. Abeta has been linked to AD. Study participation is for adults over 55 years of age with a diagnosis of AD.
	Investigational Clinical Amyloid Research in Alzheimer's	This multi-center treatment trial will evaluate whether a new medication, Bapineuzumab, increases the clearance of Abeta from the brain. Abeta is believed to be the initial cause of AD. This treatment study is for adults 50-89 years of age with an AD diagnosis. Participants will need a study partner to accompany them to study visits.

For more information, please contact the BU ADC Outreach & Recruitment Coordinator, Silvia Serrano, at 617-414-1078 or sserrano@bu.edu

Research Updates

An Optical Test for Early Detection

Building on their exciting discovery that amyloid-beta protein associated with Alzheimer's disease (AD) can be detected in the lens of an eye, **Drs. Lee Goldstein** and **Juliet Moncaster** and their team are developing new non-invasive optical tests that can detect and track the disease process in its earliest stages. Such tests are being developed and tested in mice. At the recent 13th meeting of the International Conference on Alzheimer's Disease in Vienna, Austria, Drs. Goldstein and Moncaster presented a corresponding finding that amyloid-beta is also found in the lenses of patients with Down syndrome.

Envisioning Future Events is Impaired in AD

It is well-known that patients with AD have trouble remembering information from the recent past, but do they have difficulty imagining the future as well? This question is exactly what Boston University Alzheimer's Disease Center (BU ADC) researchers **Drs. Andrew Budson** and **Brandon Ally** investigated in their paper, "Episodic simulation of future events is impaired in mild AD," published in *Neuropsychologia* earlier this year. Patients with AD and healthy older adult controls were given a series of cue words and asked to either remember events from the past or imagine future events related to that word. Not only did the patients with AD have difficulty with both past and future tasks compared to the controls, the findings suggest that the same brain system responsible for remembering the past is also in charge of envisioning the future.

Ibuprofen & Cognitive Performance

In a collaborative project across several cores of the BU ADC, **Drs. Ann McKee**, **Neil Kowall**, and **Alpaslan Dedeoglu** recently published findings in *Brain Research* on the effects of ibuprofen on cognitive deficits, amyloid-beta, and tau accumulation in young triple transgenic mice. Learning performance of the mice was significantly improved with ibuprofen treatment compared to mice who did not receive the treatment. Ibuprofen-treated transgenic mice showed a significant decrease in intraneuronal oligomeric amyloid-beta and hyperphosphorylated tau immunoreactivity in the hippocampus, a part of the brain responsible for learning new information. Additional data suggest that intraneuronal amyloid-beta may be a cause of cognitive impairment. These findings support the idea that pathological alterations of tau are associated with intraneuronal oligomeric amyloid-beta accumulation.

Psychological Effects of Genetic Disclosure

Dr. Robert Green and the REVEAL study group recently published a study in the *New England Journal of Medicine* on the psychological effects of disclosing the AD risk-increasing apolipoprotein (APOE) ε4 genotype to adult children of patients with AD. Dr. Green and his colleagues found there were no significant increases in levels of anxiety, depression, or test-related distress for those who learned they were ε4-positive compared to those who did not receive their genotyping results, suggesting that disclosure of APOE genotype does not result in short-term psychological risks.

BU ADC Happenings

Welcome

The Boston University Alzheimer's Disease Center (BU ADC) welcomes new staff members: Nicole Cantwell, research assistant to Dr. Angela Jefferson and PAIRS Program Coordinator; Patrick Curtis, administrative assistant to Drs. Robert Green and Robert Stern; Fareesa Islam, administrative assistant to Dr. Angela Jefferson; Patricia Johnson, psychometrician on the ELAN and ADAPT studies; Denise Lautenbach, MS, Genetic Counselor and REVEAL Project Manager; Theresa McGowan, psychometrician on the ELAN study; and Silvia Serrano, MPH, BU ADC Outreach & Recruitment Coordinator.

We also extend a warm welcome to our new student trainees: Michael Dombek, a senior at Boston University, and Bhaavika Patel, a junior at Boston University, who are both working with Dr. Jefferson; and Brittany Masatsugu, a Boston University graduate student who is working as a HOPE psychometrician.

Congratulations

Dr. Alpaslan Dedeoglu, Director of the Translational Neurotherapeutics Laboratory and BU ADC Translational Core Associate Director, recently received an R01 grant from the National Institute on Aging. Dr. Dedeoglu's project, "*Cyclohexanehexol Therapy in Transgenic Models of Alzheimer's disease (AD)*," assesses transgenic mouse brains and the correlation between amyloid-beta and neurofibrillary tangles with magnetic resonance imaging, magnetic resonance spectroscopy, and cognitive function. Dr. Dedeoglu is also investigating the effect of non-steroidal anti-inflammatory drugs and inositols that may alter amyloid-beta aggregation.

The BU ADC would like to congratulate Dr. Gwendalyn King, a biochemistry postdoctoral fellow with Dr. Carmela Abraham, who was awarded a prestigious K99 award from the National Institute on Aging for research on the anti-aging/protective gene Klotho. Dr. Abraham's group found that Klotho levels are decreased in the aged brain and more so in models of AD. Dr. King's award will allow her to continue studies to determine why Klotho is decreased with age and how its production is regulated in the brain. In parallel studies, Dr. King has identified potential novel drugs to elevate the Klotho protein. Experiments in animals will establish whether increasing this molecule is protective against neurodegenerative diseases, such as AD.

Goodbyes

Many thanks and best wishes to the BU ADC staff who have recently left to pursue new directions: Susan Hiraki, MS, who left the REVEAL Study in May to pursue a master's degree in public health in New York; and Stephanie Sikora, who left the BU ADC in September to relocate to Arizona.

Thank you and best wishes to our recent student trainees: Monique Pimontel, who completed her master's degree at Boston University and has since moved to New York to pursue a psychometrician position; and Morgan McGillicuddy, who has left to pursue her PhD in clinical psychology at the University of Maine.

Greater Boston Memory Walk

The Memory Walk is the Alzheimer's Association's largest fundraising event. Walks take place annually in more than 600 communities nationwide. On Sunday, September 27th, the faculty, staff, participants and friends of the Boston University Alzheimer's Disease Center (BU ADC) participated in the Greater Boston Memory Walk in Cambridge, MA. This year, the BU ADC team welcomed staff and friends of one of our continuing care retirement community affiliates, Senior Living Residences, and together we raised over $11,000 for the Alzheimer's Association!

The BU ADC team raised $11,000 for the Massachusetts Alzheimer's Association as part of its annual Memory Walk fundraiser.

HOPE Participant Appreciation Brunch

HOPE Study Participant Mary Carroll and HOPE Psychometrician Elana Cook

Funded by the National Institute on Aging, the *Health Outreach Program for the Elderly* (HOPE) study evaluates memory and thinking abilities of older adults throughout their lives. The HOPE study serves as the Boston University Alzheimer's Disease Center (BU ADC) research registry and includes approximately 500 participants, all of whom agree to be contacted for recruitment into other BU ADC-approved studies. On June 5th, 2009, the HOPE study held its participant appreciation event, the HOPE Brunch, at the Marriot hotel in Newton, MA, with over 200 people in attendance.

The purpose of the brunch was to recognize participants for their valued involvement in the HOPE study and to provide the latest updates on Alzheimer's disease (AD) research. According to Eric Steinberg, HOPE study project manager, "It's very heartening for volunteers who are committed to the fight against AD to come together for an educational experience."

The event began with introductions from Mr. Steinberg, BU ADC Director Dr. Neil Kowall, and Mr. Michael Kincade, who serves as Safety Services and Community Programs Manager for the Massachusetts/New Hampshire Chapter of the Alzheimer's Association. The program continued with short presentations from a panel of BU ADC researchers that focused on the latest research on AD prevention and treatment methods, the results of the HOPE satisfaction survey, and scientific advances that have resulted directly from the participation and dedication of HOPE participants. Dr. Ann McKee, BU ADC Neuropathology Core Director, elaborated on the purpose of brain donation in AD research. HOPE participant Ms. Phyllis Eliasberg then read a touching letter that she had written to her sons about her decision to participate in the BU ADC brain donation program.

Throughout the brunch, raffles were held with prizes, and certificates of distinction were awarded to individuals for participation in the HOPE study for six years or longer. The BU ADC would like to extend a sincere thank you to everyone who attended the brunch.

Honorary and Memorial Contributions

The Boston University Alzheimer's Disease Center (BU ADC) is involved in a variety of clinical, research, and educational activities. These activities are funded by grants awarded from the National Institutes of Health and nonprofit organizations. Often, research study participants, families, or community leaders wish to contribute to the fight against Alzheimer's disease (AD), and these private donations are equally important to advancing the BU ADC's mission. The BU ADC welcomes honorary and memorial donations, as these gifts are an excellent way to pay tribute to a family member or friend while making a contribution to the advancement of research in the field of AD. Please call Harriet Kornfeld at 617-638-5676 or visit us online at www.bu.edu/alzresearch if you would like to make a donation.

The BU ADC would like to recognize the following private donors for their greatly appreciated contributions:

In memory of
Philip Balducci
Dominic and Rosalie Cardone

In memory of
Ben Chinitz
Ron Jacobs

In memory of
Eileen Consolmango
Julie Holland
Renee Metterville
Rich and Ka Nelson
Joseph H. & Judith A. Porto
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In memory of
Robert J. Therrien
William and Rita MacLeod
Cynthia and Saul Bauman
Mr. and Mrs. Henry Therrien
Paul Paslaski

In memory of
Frank Sirois
Denise Hamel
Mr. and Mrs. Philip Sirois

In memory of
Morris Phipps
Brent and Laurie Brooks

Alzheimer's Disease Center Leadership

The Boston University Alzheimer's Disease Center (BU ADC) is primarily supported through a grant from the National Institute on Aging. The BU ADC supports cutting-edge research and provides education and clinical care to families affected by Alzheimer's disease. Its leadership is listed below, alphabetically by Center Core.

Neil Kowall, MD, *Center Director and Administrative Core Director*

Andrew Budson, MD, *Center Associate Director of Research*

Richard Fine, PhD, *Pilot Grant Program Director*

Robert Green, MD, MPH, *Clinical Core Director and Center Associate Director*

Robert Stern, PhD, *Clinical Core Associate Director*

Christine Chaisson, MPH, *Data Management & Statistics Core Director*

Angela Jefferson, PhD, *Education & Information Transfer Core Director*

Ann McKee, MD, *Neuropathology Core Director*

Alpaslan Dedeoglu, MD, PhD, *Translational Animal Core Associate Director*

Lee Goldstein, MD, PhD, *Translational Animal Core Director*

The *BU ADC Bulletin* is published twice annually (**Dr. Angela Jefferson,** *Editor*; **Dr. Kathy Horvath,** *Co-Editor*; **Nicole Cantwell,** *Editorial Assistant*).

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