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THE NEWSLETTER OF THE
MASSACHUSETTS ALZHEIMER'S DISEASE RESEARCH CENTER

MASSACHUSETTS GENERAL HOSPITAL · HARVARD MEDICAL SCHOOL · BRIGHAM AND WOMEN'S HOSPITAL

Mild Cognitive Impairment (MCI)

A new look at early changes

MASSACHUSETTS ALZHEIMER'S DISEASE RESEARCH CENTER

Memory loss has long been viewed as an inevitable product of aging. More recently, physicians and researchers have adapted their view and now believe that a certain degree of memory loss can represent an underlying disease process occurring in the brain.

The term "dementia" has been used to characterize memory loss that exceeds what is expected during the normal aging process. People with dementia are unable to function independently at their typical level. They may no longer be able to manage their personal finances or provide for their own basic needs. It's important to know that dementia has many causes; Alzheimer's disease is the most common.

Many older individuals may complain of memory problems, but still manage to independently perform all of their day-to-day tasks. Because their memory problems do not interfere with daily activities, these people do not meet criteria for a diagnosis of dementia. This cluster of symptoms, in which a person experiences significant problems with memory, language or other functions severe enough to be noticeable to other people and show up on tests of memory, but not serious enough interfere with daily life, has been called Mild Cognitive Impairment (MCI).

Researchers now believe that MCI often represents cognitive decline that reflects a degenerative brain process beyond the scope of normal aging but precedes more severe deterioration and a diagnosis of dementia. MCI is a condition in which a person has problems with memory or thinking that are greater than those anticipated for his or her age. However, people with MCI do not have the more severe cognitive problems or functional changes that characterize Alzheimer's disease. MCI has several types. The type most associated with memory loss is called amnestic MCI.

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Until recently, physicians were not able to provide any specific information concerning the significance of MCI. However, in the last few years, there has been a substantial increase in the number of studies focusing on patients with complaints of early memory loss. Although much more work still needs to be done, doctors and researchers have made significant progress in characterizing these early memory problems and their potential outcomes.

The early stages of dementia appear as subtle changes that may only be noticeable to a trained professional or a close family member or friend. People in the early stages of MCI will often compensate for their memory problems with strategies like making lists, keeping notes, and relying more often on a calendar.

Several studies have shown that memory complaints in the elderly are associated with a higher-than-average risk of developing dementia in the future. Approximately 60% of people who meet formal criteria for MCI (i.e., memory complaint plus evidence of memory impairment on memory tests) develop Alzheimer's disease within five years. However, it is also clear that some patients with MCI will never develop dementia.

Several studies have suggested that results of certain imaging procedures like MRIs and PET scans can help to determine an individual's risk for developing dementia in the future. Researchers are now focusing their efforts on characterizing the stage of the Alzheimer's disease spectrum that precedes MCI.

Researchers at Brigham and Women's Hospital and Massachusetts General Hospital are actively seeking participants showing symptoms of MCI to participate in several studies to help them better understand the causes of MCI. There are also studies for older individuals with even milder memory changes that use brain scans to try to predict who may develop more severe problems and progress towards Alzheimer's dementia. There are also ongoing clinical trials of medications aimed at decreasing Alzheimer's pathology in the brain. With better knowledge of the earliest stages of MCI, researchers may be able to test potential treatments at earlier stages, when they may have the greatest promise for slowing down progression of this devastating disease. To learn more about how to participate in these studies, please see our study listings on the following pages.

References and Resources:

1. National Institute on Aging, Alzheimer's Information website link: http://www.nia.nih.gov/Alzheimers/AlzheimersInformation/GeneralInfo/
2. Alzheimer's Disease Cooperative Study website link: http://www.adcs.org/studies/ImagineADNI.aspx
3. Alzheimer's Association website link: http://www.alz.org and choose "TrialMatch" for helpful information about participating in research studies

November is National Alzheimer's Disease Awareness Month and National Family Caregivers Month

According to the Alzheimer's Association *2010 Alzheimer's Disease Facts and Figures* report, there are more than 5 million Americans living with Alzheimer's and as many as 10 million family caregivers. This November, during National Alzheimer's Disease Awareness Month and National Family Caregivers Month, the Alzheimer's Association is providing insight and support to those caring for someone with Alzheimer's with two new resources: *Alzheimer's Association Caregiver Notebook* and Alzheimer's Association Comfort Zone™. For more information on these resources, contact the Alzheimer's Association at http://www.alz.org or 1-800-272-3900.

The Center for Alzheimer Research and Treatment (CART)
At Brigham and Women's Hospital

Reisa Sperling, MD, MMSc.

Associate Professor of Neurology, Harvard Medical School
Director, Center for Alzheimer Research and Treatment (CART)
Brigham and Women's Hospital and Massachusetts General Hospital

The Center for Alzheimer Research and Treatment (CART) was launched in April 2009. The mission of the CART is to provide state-of-the-art clinical research opportunities to improve the early diagnosis and treatment of Alzheimer's disease. At CART, we conduct two major types of clinical research studies: Observational or natural history studies and Interventional or therapeutic clinical trials. In observational studies, participants undergo memory and thinking tests as well as brain imaging scans. Researchers at CART are working on developing more sensitive cognitive tests, biomarkers and neuroimaging techniques like MRI and PET scans to detect early brain changes related to Alzheimer's disease, and to differentiate these changes from "normal aging". In the therapeutic clinical trials, participants receive an experimental drug or a placebo to test new potential therapies to treat Alzheimer's disease. The CART is currently enrolling participants in multiple studies, including studies for older individuals with normal cognition, subjects with mild cognitive impairment (MCI), and patients who have been diagnosed with mild Alzheimer's disease dementia. Some of these studies are described on the following pages.

For more information about participating research studies at CART, please call Meghan Frey at 617-732-8085

CART is located at 221 Longwood Avenue, at Brigham and Women's Hospital, and is closely affiliated with the Massachusetts Alzheimer's Disease Research Center.

CART 617-732-8085 *CART@partners.org.*

Massachusetts Alzheimer's Disease Research Center researchers need *older people with and without memory trouble* to participate in clinical research studies to help us find better treatments for Alzheimer's Disease.

You may be eligible to participate if you (or someone you care for or know) has:

- Normal memory and no concerns
- Some memory problems or concerns
- A diagnosis of Mild Cognitive Impairment
- A diagnosis of Alzheimer's Disease

If you are interested in participating in a research study, please call either the specific person listed for each study, or contact Meghan Frey at 617-732-8085 (mfrey1@partners.org) for help deciding which study you or the person you are calling for may be eligible to participate in. Following are some of our studies.

Research Opportunities, continued

1. ALZHEIMER'S DISEASE NEUROIMAGING PROTOCOL GRAND OPPORUNITY (ADNI-GO)

We are seeking **healthy adults, 55 to 90 years of age** to participate in a research study. The goal of the study is to determine whether imaging of the brain (through MRI, PET and amyloid imaging scans) can help predict and monitor the onset and progression of Alzheimer's disease. In addition to neuroimaging, the study will collect and test blood and cerebral spinal fluid to determine if biomarkers can predict and monitor the disease. Testing cerebral spinal fluid is the only way to obtain important brain information. Participants will be asked questions about their memory and thinking and must have a friend or relative who can answer 30 minutes of questions about your day-to-day activities and accompany you to all clinic visits. If you qualify, you will be asked to have 6 brain scans over the course of 18 months, follow-up memory and thinking testing as well as blood draws every 6 months after the initial visit for a period of 18 months. You will also be asked to have a lumbar puncture (spinal tap).

Contact Meghan Frey at 617-732-8085 or mfrey1@partners.org.

2. BMS-708163 (GAMMA SECRETASE INHIBITOR)

The purpose of this clinical trial is to evaluate the efficacy, safety and tolerability of BMS-798163, a drug that has the potential to treat Alzheimer's disease. We are looking for participants who have been diagnosed with **mild cognitive impairment / prodromal (early stage) Alzheimer's disease**; are **between the age of 45 and 90**; have a reliable caregiver or family member who is able to accompany them to study visits; are in stable medical condition; are willing to undergo a lumbar puncture (spinal tap). People taking approved Alzheimer's medications (donepezil/Aricept, galantamine/Razadyne, rivastigmine/Exelon) except for memantine/Namenda are eligible to participate in this study and can continue taking these medications during the study. This study does include placebos (pills that do not contain active drug). 50% (half) of the participants will receive the study drug and the other 50% (half) will receive placebo. ***For more information, contact: Martha Vander Vliet (mvandervliet@partners.org); 617-732-8085.***

3. CONCERT STUDY (DIMEBON)

The CONCERT Study is a Phase III, safety and efficacy study of Dimebon for the treatment of Alzheimer's disease (AD). Dimebon is an orally available investigational product with a novel mechanism of action. This study drug appears to work in several different ways including stabilization of mitochondrial depolarization. The study participants will be randomly assigned to receive one of the two doses of the study drug (Dimebon 5mg or Dimebon 20mg) or the placebo. The study drug should be taken three times a day. Participants in CONCERT Study must have **mild to moderate AD**; be **50 years of age or older**; have been **taking Aricept (Donepezil) for at least six months**; have a caregiver who assists(or directly supervises) the patient at least five days per week for at least three hours a day; living in the community and may be living in a assisted care facility if living independently.

Contact: Martha Vander Vliet (mvandervliet@partners.org); 617-732-8085.

Research Opportunities, continued

4. RESEARCH STUDY IDENTIFYING EARLY MARKERS OF ALZHEIMER'S DISEASE

We are seeking healthy volunteers and individuals with **Mild Cognitive Impairment or Mild Alzheimer's Disease, ages 55 to 90** who are interested in taking part in a clinical research study to find out if functional MRI images of the brain can be used to diagnose and monitor the course and treatment of Mild Cognitive Impairment (MCI) and Alzheimer's disease (AD). Subjects must have a study partner and be willing to come to 6 to 8 clinic visits over the course of 2 to 3 years. At each of these visits, subjects will be asked to have blood drawn, undergo tests of memory and have an MRI scan of the brain. Each visit will last between 4 to 5 hours. Study participants will be reimbursed $50.00 for the completion of each clinic visit and $50 for each MRI scan, for a total of $650.00 (AD subjects) or $750.00 for (MCI and healthy volunteer subjects). Subjects who participate in the PET sub-study will be reimbursed $100.00 for each PET scan and testing for a total of $200.00. A parking voucher will be given at each visit. ***For more information, please call us at 617-732-8085 or email our study coordinator Meghan Frey at mfrey1@partners.org.***

5. HARVARD AGING BRAIN STUDY

We are seeking **healthy adults, 65 to 90 years of age**. The purpose of the research study is to understand changes in memory and thinking with aging. You will undergo testing of your memory and thinking, blood draws for genetic and biomarker studies and 8 brain scans. You may also take part in an optional lumbar puncture study. All evaluations will be free of cost and reimbursement for time and transportation is $1600 for all procedures. ***For more information, contact: Lauren Wadsworth, Massachusetts General Hospital, 617-643-0143***

6. MEMORY STUDY

We are seeking healthy individuals with **high blood pressure or taking blood pressure medications**, **age 60 and older**, of diverse ethnic backgrounds, **with memory problems** for a multi-year research study. Participants will be interviewed each year. Imaging tests will be given at study entry and at 2 years. Each participant must have a study partner who can provide information about the participant. Eligible participants and their study partners will each be paid $40 for clinic visits, and subjects will be paid $50 for scan visits. ***If interested, please call the Gerontology Research Unit at Mass General Hospital 617-726-6205.***

7. WHAT ARE THE EARLIEST SIGNS OF ALZHEIMER'S DISEASE IN THE EYE?

The purpose of this research study at the Massachusetts Eye and Ear Infirmary is to find out how much nerve cell loss there is in the retina and how much of a decrease in retinal blood supply there is in people with early Alzheimer's Disease and in people with Mild Cognitive Impairment. Participants must be **between 55 & 90 years old** with **either: no memory or cognitive concerns**; **mild memory impairment ("Mild Cognitive Impairment") or mild Alzheimer's Disease**. The retina, located in the back of the eye, is an extension of the brain. The degeneration of nerve cells that takes place in the brain from Alzheimer's Disease also takes place in the retina. Noninvasive optical techniques can be used to measure the loss of nerve cells and the decrease in blood supply that accompanies the nerve cell loss. Participants receive a detailed eye exam at no cost and are compensated for their time and travel expenses. ***Contact: Gilbert T. Feke, PhD: (617) 912-7413 feke@schepens.com***

Massachusetts Alzheimer's Disease Research Center

Massachusetts General Hospital | Harvard Medical School | Brigham and Women's Hospital

Bradley T. Hyman, M.D., Ph.D.
John B. Penney, Jr. Professor of Neurology
Program Director

John H. Growdon, M.D.
Professor of Neurology
Founding Director

Massachusetts General Hospital WACC 720 15 Parkman Street Boston, MA 02114
Gerontology Research Unit MGH East, Charlestown Navy Yard 149-2691 13th Street, Suite 2690 Charlestown, MA 02129-2000

The Massachusetts Alzheimer's Disease Research Center (ADRC) was established in 1984 with funding from the National Institute on Aging. Now in its 27th year of operation, the ADRC is a consortium of Harvard affiliated facilities, including the Massachusetts General Hospital; the Brigham & Women's Hospital; the Harvard Division on Aging and the Institute for Aging Research at Hebrew SeniorLife. The staff and programs of the **Massachusetts Alzheimer's Disease Research Center** and **Massachusetts General Hospital Memory Disorders Unit** are dedicated to research on Alzheimer's disease, and improving the well-being and quality of life of our patients and their families.

A major activity of our center is recruiting and following a **Longitudinal Cohort** of individuals with normal cognition, Mild Cognitive Impairment (MCI) and milder degrees of memory loss, and Alzheimer's disease and other dementia who can contribute to our understanding of memory changes over time and participate in our other studies. We have 859 subjects enrolled in this Cohort, of which 37% are cognitively normal, 35% have MCI or other mild impairments, and 28% have dementia. Almost three-fourths have completed at least two study visits, and almost half have completed three or more visits. We are grateful to all these participants, and look forward to seeing them each year. **Please call Jeanette Gunther at 617-726-5571 if you have any questions regarding your participation in the Longitudinal Cohort.**

The Alzheimer's Association, Massachusetts/New Hampshire Chapter

Providing education, care and support

The Alzheimer's Association, Massachusetts and New Hampshire Chapter provides programs and services for families, patients and caregivers coping with Alzheimer's Disease and related dementias.

Helpline: The Helpline is available to families and professionals 24 hours a day, seven days a week. You can always reach a trained counselor by calling the toll free Helpline at **800-272-3900**

Support Groups: Support groups provide a forum for family members and caregivers of people with Alzheimer's disease to share feelings, concerns and information, and to support each other in coping with the effects of the disease or a related disorder. 150 support groups throughout Massachusetts.

311 Arsenal Street, Watertown, MA 02472 * 617.868.6718 * www.alzmass.org
Offices in Watertown, Raynham, Springfield and Worcester, MA and Bedford, NH.

INTRODUCING: TRIALMATCH

Alzheimer's Association Clinical Studies Matching Service

Trialmatch uses information about your diagnosis, location and preferences to match you with current Alzheimer's clinical trials.

Www.Alz.org/trialmatch 800-272-3900