

MESSAGE FROM THE CHIEF

S WE WELCOME the spectacular signs of spring and the promise of a delightful summer ahead of us, I am reminded of the saying that change is the only constant that we share. And so, with this issue of our newsletter, we are pleased to present a fresher, cleaner and more professional layout for our readers' enjoyment. We are especially excited to welcome Dr. Reisa A. Sperling as the new Director of our Education Core of our ongoing newsletter series. As many of you know, Dr. Sperling is an accomplished behavioral neurologist renowned for her expertise in neuroimaging and conducting



Dr. Hyman

clinical trials. In addition to the many 'hats' that she wears professionally here at Harvard and beyond, she is also a source of inspiration for her patients, students and colleagues.

We consider ourselves truly honored to work side by side with our study participants and patients to find effective treatments for Alzheimer's and other brain diseases. In this regard, we would like to highlight

the importance of brain autopsy (on page 7), and share with you its importance towards our common goal of finding a cure for neurological diseases (see our Guest Column on traumatic brain injury research by Dr. Ann C. McKee on page 6 and an interview with our Director of Neuropathology, Dr. Matthew P. Frosch on page 2). We invite you to join us as we pay a visit to the Greater Boston Chinese Golden Age Center's day program facility in Brighton to discover the important work that they do for the Chinese community. Last, we would welcome your ideas about how we might increase participation from minority participants so that we can all work towards eliminating the devastating effects of these diseases in diverse communities.

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INSIDE



A conversation with Matthew P. Frosch, MD, PhD, director of the MGH Neuropathology Service *Page 2*



A visit to the Greater Boston Chinese Golden Age Center *Page 4*



Guest Column on Traumatic Brain Injury Research: Ann C. McKee, MD *Page 6*

A conversation with Matthew P. Frosch, MD, PhD

Congratulations! We have just heard that you have been awarded the 2011 Donald O'Hara, PhD, Faculty Prize for Excellence in Teaching at Harvard Medical School. Tell us something about your background, and how you came to work at MGH.



Dr. Frosch

Dr. Frosch: When I graduated from medical school and graduate school, I trained in Pathology and Neuropathology. I started working on Alzheimer's disease by doing the diagnostic evaluations of brains donated through Dr. Dennis Selkoe's laboratory. This gave me a great start in the field, and encouraged me to shift the emphasis of my research away from epilepsy (which I had

studied as a graduate student) towards neurodegenerative diseases. I did my diagnostic work at MGH, BWH and CH (Children's Hospital). About a decade ago, Dr. Anne Young (MGH Chief of Neurology) and Dr. Brad Hyman recruited me to move my research lab to MGH. Since then, I have assumed the leadership of the MGH Neuropathology Division, known as the C.S. Kubik Laboratory for Neuropathology, as well as becoming director of the Massachusetts ADRC Neuropathology Core. In addition to my diagnostic work and my research lab, I also have a significant role at Harvard Medical School. I teach in the Harvard-MIT Division of Health Sciences and Technology, spending a month with second-year students teaching neuroanatomy. Within this portion of the medical school, I also chair the admissions committee. So, I follow the full triple-path of the academic physician-scientist - I do clinical work, I do research and I teach.

Do you have a 'typical' day at work?

Dr. Frosch: Nearly every day I do a combination of clinical diagnostic work with research. My clinical activities range from intra-operative consultations to the neurosurgeons working to remove brain tumors to interpreting the complex stains required to diagnose a neurodegenerative disease at autopsy. All the way along during this work, I am teaching fellows in neuropathology and residents in pathology and neurology. Because my research focuses

on neurodegenerative disease, when I am doing the clinical work I am also thinking about experiments. In particular, my lab has focused on using mouse models of human diseases – and asking important questions that can only be approached in the mouse. But I am always careful to be checking that what we are observing in the mouse makes sense in terms of what I see in the human brain on a daily basis. These two aspects of my daily activities continue to support and encourage each other. It is what makes my job so interesting and energizing each day.

Many individuals are curious to learn more about brain donation. Can you tell us more about it, and why it is so important for research?

Dr. Frosch: While tissue culture and mouse models have taught us a lot about neurodegenerative diseases, they remain only models – and it is essential to understand how well they model the critical aspects of human disease. Developing a treatment that cures a mouse of the disease you have

While we understand many of the aspects of neuropathology for human neurodegenerative diseases, the search for new therapies and for new targets of therapies requires continued access by researchers to brain tissues.

engineered it to get is an accomplishment, but it is actually a failure if that treatment can't be brought to people because the mouse didn't capture the essential aspects of the disease in the human brain. While we understand many of the aspects of neuropathology for human neurodegenerative diseases, the search for new therapies and for new targets of therapies requires continued access by researchers to brain tissues. In addition, it is essential that the diagnostic assessment of this tissue be done with the full resources of a committed neuropathologist interested in these diseases. Brain donation at the time of death is one of the most generous gifts a patient and family can give – it allows us to provide tissues for numerous research studies throughout the United States and internationally. Our tissue repository is funded by government grants; we do not collect fees from researchers receiving our tissue, nor do we charge families for costs incurred in obtaining the donation. In all donations, the identity of the donor remains strictly confidential. A centralized tissue resource is extremely valuable to



researchers. Standardizing the way in which laboratory studies are performed eliminates discrepancies among individual researchers, and enables them to compare their work with that of physicians, neuroscientists, biochemists, and geneticists around the world who are working on these disorders. Families, in turn, commonly find comfort in the definitive diagnosis that neuropathology can provide. Working together, the family, physician and pathologist can start to understand the connections between the physical state of the brain and the clinical or behavioral manifestations of the patient's illness.

What advice would you give to someone who wants to work in your field?

Dr. Frosch: Clinical and experimental neurosciences, which range from neuropathology to neurology to neurosurgery to psychiatry, are at an extremely exciting

time. Our ability to map diseases, understand the biology and potentially treat or prevent these diseases will change over the next few years. Admittedly I am biased but I think that neuropathology is particularly exciting because we sit at the critical point between patient care and research.

Lastly, tell us something about your personal interests that most of us do not know, and that you're willing to share!

Dr. Frosch: I enjoy what I do enormously, in large part because of the breadth of my activities – covering all the aspects of academic medicine, ranging across institutions from MGH to MIT to Harvard Medical School. When I tear myself away from the "work" portions of my life, which I must admit creep well into my non-working hours, I read a lot of history. If given the opportunity, I would go back to graduate school for another degree, this one in history (although limited by my inability in languages outside of English). ◆

GREETINGS FROM THE CLINICAL COORDINATOR

To all our Memory Study participants:

I'd like to take this opportunity to say a big THANK YOU to all of you. You are the heart and soul of our work here. Without your continued participation year after year we would not be able to meet our goals.

The Memory Study is a longitudinal, multi-center study funded by the National Institute on Aging. There are 34 other centers throughout the country doing this same study. The data from all these centers is pooled to create a powerful database of information regarding how we change as we age. We have over 800 subjects in our study here at MGH. And each and every one of you contributes valuable information to our knowledge of how our thinking and our brains change over time. What makes this information especially valuable is that it has been gathered over your many years of participation. There may be occasions when you might be wondering, "Is it really that important for me to keep coming in for study visits?" And the answer is a resounding YES. You ARE the study!

Some of you may have been asked – or will be asked – to participate in other aspects of the Memory Study or in other studies affiliated with it. Some of these involve the collection of blood samples or cerebrospinal fluid samples, which help us learn more about possible biomarkers that may turn out to be informative about the development of memory loss or to certain diseases. Some of these involve neuroimaging procedures (MRIs, functional MRIs, PET scans), which help us learn about the structure and functioning of the brain. And one of these involves brain autopsy, which puts it all together and lets us know what the brain actually looks like and how that relates to all the information we have collected over time.

Whatever you do for the study is GREATLY appreciated – whether it's a phone interview, or coming in to the office for your Memory Study appointment, or participating in any of the other studies we ask you to help us with, or agreeing to donate your brain.

If there's anything we can do to make your experience with us more pleasant or easier, please let us know. We appreciate your feedback. And we truly appreciate your being such an important part of the study team.

Jeanette Gunther Clinical Coordinator

A visit to the Greater Boston Chinese Go

The Greater Boston Chinese Golden Age Center (GAC) is the premier elder services organization dedicated to promoting the overall well-being and psychosocial needs of Chinese-speaking seniors in Massachusetts. First established as a non-profit organization in 1972 by Founder and Executive Director Ruth Moy, it has a vast network of culturally-sensitive services

been in the US from a few months to over 50 years, and speak multiple languages and dialects including Cantonese, Toisanese, Shanghainese, Mandarin and of course English. According to its director Lili Mei, close to 80 elders participate in its weekday activities between First established as a non-profit organization in 1972 by Founder and Executive Director Ruth Moy, it has a vast network of culturally-sensitive services to assist Asian elders in accessing local and federal resources and to help maintain their independence in the community.



8:30 am and 4:30 pm. Health, educational and recreational programs are offered in diverse Chinese dialects. Funded by a variety of grants and contracts, the GAC has a team of about 80 full and part-time bilingual staff to care for their constituents, who enjoy activities that range from Tai Chi classes to craft lessons to field-trips to celebrations of various holiday traditions. Breakfast

is served to arriving participants at 9 am, and a delicious hot Chinese meal is provided at noon.

On the day of our visit, our 'reporter' was delightfully surprised to hear a group singing a famous Chinese song on 'a mother's love' - a tune that her own mother had hummed to her as a child. The singing was led by teacher, Philippina Loh, a long-time GAC volunteer (and a former beauty pageant winner!) who had also lived in Taiwan, Shanghai, Hong Kong and New York. When asked why she devotes her time to the GAC, Ms. Loh mentioned her desire to give back to the community, and her continued enjoyment of Chinese culture that includes traditional dance and the

martial arts. In the next activity area, a small group of women were weaving lovely paper flower baskets that would be on display at upcoming events. When interviewed, participants all cited the joys of companionship, the lack of pressure, and their desire to learn something new as to why they enjoy coming to Brighton House. On our day of visit, for example, the main topic for vivid conversation was the Royal Wedding, according to regular attendee Mme. Yong Huang Li, a native of Shanghai whose hobbies now include singing Christian songs - and who shared with our reporter how her desire to be a professional songstress was met with resistance from her tradition-bound

father during her youth.

With three day program sites in downtown Boston and Brighton and additional outreach sites in Belmont, Brookline, Cambridge, Malden, Needham and the South Shore area (including Quincy and Randolph), the GAC provides a seamless array of programs that may

to assist Asian elders in accessing local and federal resources and to help maintain their independence in the community. Since 2004, the Massachusetts ADRC has enthusiastically supported the GAC's mission by providing ongoing educational and training services to its professional staff. As we began to plan another educational series for the center targeted for Fall 2011, we decided to pay a visit to its Brighton facility to find out more about its outstanding care and friendly inhabitants.

Brighton House is located in a lovely cozy house on Cambridge Street. Since 1985, it has served as an adult day program facility for a community of elders. Participants range in age from age 55 into the 90s, have



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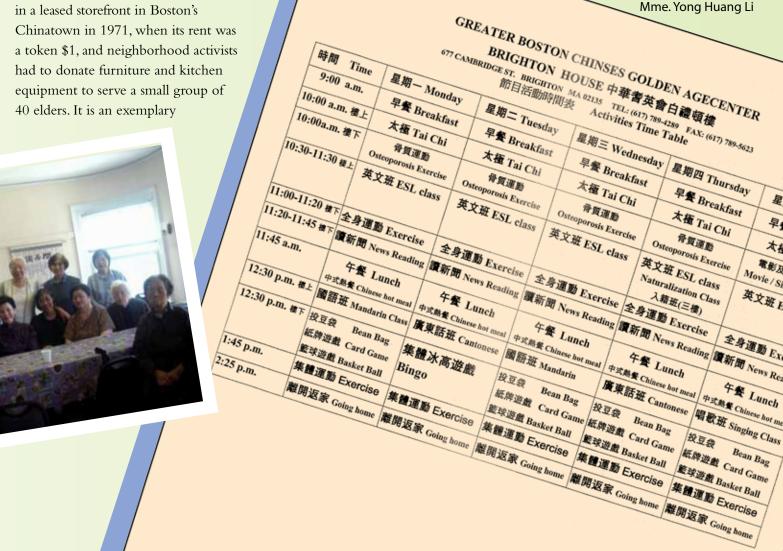
be broadly-categorized as Adult Day Health/Social Day Care; Nutrition (Including home delivery); Elder-At-Risk welfare services; Transportation; Congregate Housing (Section 8 Housing for Low-Income Elders); Social Services/Companionship/ Counseling/Letter Writing and Interpretation; Education/Recreation; Lifeline (Personal Emergency Response System); Senior Community Service Employment assistance (for low-income seniors); and SHINE program (where certified counselors provide assistance with Medicare/ Medicaid/other health plan services). Indeed, the range and depth of programs now provided by the center stand in stark contrast to its humble beginnings in a leased storefront in Boston's Chinatown in 1971, when its rent was a token \$1, and neighborhood activists had to donate furniture and kitchen equipment to serve a small group of 40 elders. It is an exemplary

model of how other minority communities can come together to celebrate their loved one's golden years. For more information about the GAC, please visit www.gbcgac.org •

The Massachusetts ADRC is honored to partner with the GAC to promote awareness of common health problems in minority communities (including dementia and other neurologic disorders like Parkinson's disease and stroke), and the importance of minority participation in research.



Mme. Yong Huang Li



BU Center Uses Brain Tissue to Understand the Impact of Head Trauma in Athletes and Veterans

In September 2008, a group at Boston University (BU) began a study of the long-term effects of repetitive brain trauma in athletes. This condition, which doctors call Chronic Traumatic Encephalopathy (or occasionally dementia pugilistica or punch drunk), is a progressive disease that eventually leads to dementia. Although originally observed in boxers, in recent years the condition has been



Dr. McKee

shown to affect other athletes, including football players, and to occur in veterans exposed to repetitive blast injury. The work of this innovative BU center really demonstrates the ways in which the study of brain tissue after death can contribute to understanding the causes and prevention of brain disease.

This initiative is a joint effort between researchers at BU, the Department of Veterans Affairs (VA), and the non-profit Sports Legacy Institute, and its

co-directors are Drs. Robert Stern, Robert Cantu, Christopher Nowinski, and Ann McKee. The initial goals of the center were:

- (1) To create a brain donation registry for living athletes (active and retired) who wished to donate brain tissue after death and participate in annual telephone interviews throughout their life;
- (2) To collect preliminary clinical, genetic and neuroimaging data on the disease;
- (3) To create a brain bank (at the Bedford VA Medical Center) of tissues from donors in the registry; and
- (4) To compare the clinical and brain trauma histories of athletes with brain autopsy results.

In the year and a half since its establishment, the center has obtained grant funding from the National Institute on Aging and from the National Operating Committee on Standards for Athletic Equipment, as well as an unrestricted gift of 1 million dollars from the National Football League. There are now more than 360 current or retired professional and amateur athletes who have enrolled in the brain donation registry, and BU staff have been conducting

interviews with these individuals. Researchers at Brigham and Women's Hospital have begun to collect initial neuroimaging data from former athletes as well. The center has also expanded its focus to include research on the long-term effects of repetitive brain trauma and exposure to blast injury in military service members and veterans. The center's Brain Bank currently has over 70 brains, the majority from deceased football players, but a growing number from veterans as well.

To date, Chronic Traumatic Encephalopathy has been found in the brains of 14 of 15 deceased professional football players examined by Dr. McKee. The condition was also found in the first two NHL hockey players examined by the center, and has also been found in other athletes, including those without any professional experience, and in individuals as young as 18 years.

Findings from the BU center have played a major role in significant changes to the rules of the National Football League. Both the NFL and the NFL Players Association have publicly supported the research, and have encouraged active and retired players to participate in center studies. The center's research has also played a role in major changes to other sports at all levels of play, including youth sports, and is expected to have an impact on treatment and rehabilitation of



Some thoughts from our participants

My wife Kathy passed away on August 5, 2009 at age 57. We had received a diagnosis of MCI, which developed into Alzheimer's' Disease 38 months before she had passed away. Along the way, Kathy and I signed on with the Memory Study through Doctor John Growdon. In January of 2009 we were asked if we would, upon our death; consent to donate our brains for research. Initially, I was



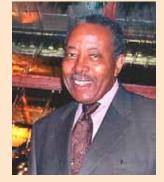
somewhat reluctant to sign the release, for what I now know to be a lot of meaningless reasons. After a brief period of reflection and discussion with my four children, we decided to go for it, and we are glad that we did.

At the time of Kathy's passing, I had to make just one phone call to the program coordinator at MGH, and she then took care of the rest. She contacted the Funeral Home and took care of the transport, and two days later we had a wake with an open casket that was flawless. A few short weeks later, we received the results of Kathy's brain autopsy, with the results very conclusive that Kathy had died from complications of Stage Seven Alzheimer's Disease. From these results we were completely satisfied that all of our efforts with Kathy had been focused in the right area. Additionally, we are very pleased that the research that will be performed on Kathy's brain may bring the researchers one step closer to finding a cure for this horrible disease. We can be confident that Kathy's life was not given in vain.

Thank you, Robert E. Heffernan May 11, 2011

Thanks for this opportunity to share a few octogenarian thoughts with your organization.

Membership in AARP, coupled with family experiences, stimulated my concern for my long term physical and mental well being. Your advertisement in Fifty Plus brought me to the MGH research

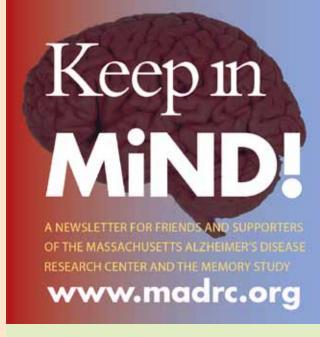


program. I have participated in other physical and mental research programs, related to aging, but this is the only program in which I am actively engaged.

The cordial and competent staff at MGH have enhanced my development of an "early warning and preventative" health care strategy. Participation in your program has made family conversations around proxies, wills and religion less stressful. This was an unexpected benefit. The questions and activities are interesting, challenging and non-intrusive. Learning something new about my physical and mental well being at each visit is pleasing.

My participation is built upon a personal creed of "help myself to help others." A weekly round of golf, exercise and outdoor barbecues for pleasure. The theater and music for entertainment. Non-fictional reading, television documentaries and historical presentations as avocations.

Clifton E. Reed April 25, 2011



Spring/Summer 2011 Vol. 2 Issue 1

DIRECTOR, MASSACHUSETTS ADRC

Bradley T. Hyman, MD, PhD

LEADER, MADRC EDUCATION CORE

Reisa A. Sperling, MD, MMSc

CONTRIBUTING WRITERS

Matthew P. Frosch, MD, PhD Jeanette M. Gunther, MS Rebecca K. Rudel, BA Liang Yap, PhD

GUEST WRITER

Ann C. McKee, MD

DESIGN AND PRODUCTION

Arch MacInnes

FOR MORE INFORMATION

If you want further information about the Memory Study or to be added to or removed from the mailing list, please contact:

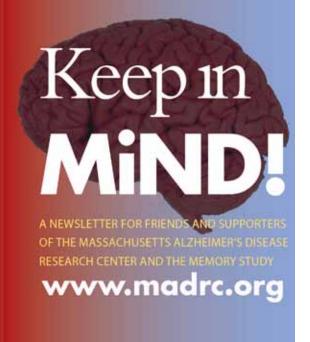
Jeanette M. Gunther, MS Gerontology Research Unit Massachusetts General Hospital Building 149, Suite 2691 149 13th Street Charlestown, MA 02129

Tel: 617.726.5571

Or visit our website at www.madrc.org

WAYS TO GIVE

For information about ways to support the clinical care, research, teaching and community health activities of the Massachusetts ADRC, please contact Liang Yap at 617.726.3987/lyap@partners.org



Some Facts to Keep in Mind

The Memory Study has enrolled 1,070 subjects. Of these, we are actively following 803. Although most of our subjects are over 65, you are a diverse group in other respects. Here are some "fun facts" about how the older population in the US is gaining in numbers and strength, and about how our study participants compare to the city of Boston, the Commonwealth of Massachusetts, and the US overall.

- Older women outnumber older men at 23 million older women to 17 million older men.
- Over one in every eight, or 13 percent, of the population is over the age of 65.
- The population 65 and over will increase 36 percent from 2010 to 2020.
- The 85+ population is projected to increase
 15 percent from 2010 to 2020.
- Minority elders are projected to increase from 8.0 million in 2010 (20 percent of the elderly) to 13 million in 2020 (24 percent of the elderly).
- Since 1900, the percentage of Americans 65+ has more than tripled.
- There were 64,024 persons aged 100 or more in 2009.
 This is a 72 percent increase from the 1990 figure of 37,306.
- By 2030, there will be about 72.1 million older persons, almost twice the number in 2008.

SOURCES:

 $http://www.aoa.gov/aoaroot/aging_statistics/Profile/2010/docs/2010profile.pdf$

http://quickfacts.census.gov/qfd/states/25000.html

http://boston.areaconnect.com/statistics.htm





RESEARCH STUDIES

Interested in participating in research? Check these studies out at our website **www.madrc.org** or call 617-726-5571 for more information.

Memory and Hypertension (Brain imaging markers in mildly impaired cognition)

Cerebral Amyloid Angiopathy (CAA) Study

Alzheimer's Disease Neuroimaging Initiative

Harvard Aging Brain Study

Bapineuzumab Clinical Trial

Neuroimaging Initiative in Frontotemporal Degeneration

Affective Reactivity in Frontotemporal Dementia