



MESSAGE FROM THE CHIEF

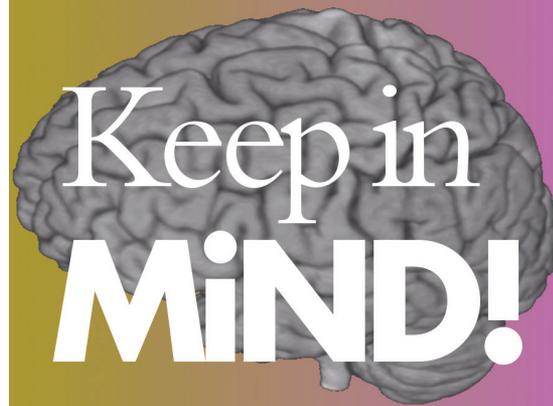
THANKS TO EVERYONE who had supported us at a diverse range of popular events in the past few months – including the Alzheimer’s Association’s 2016 Spring Research Forum; the “Still Alzheimer’s” symposium at the inaugural 2015 HUBweek festival sponsored by *The Boston Globe*, MIT, MGH and Harvard University; advocacy at the Massachusetts State House on Rare Disease Day on February 29th; outreach at the Black Lives Matter event in Roxbury, and Dr. Brad Dickerson’s successful A Night with the Arts for FTD gala event last October. We are again delighted to feature a ‘creative endeavor’ of one of our patients in this issue (*see page 7*), and highlight a patient and his spouse’s commitment to an annual event (“The Longest Day”) where groups of friends and families engage in day-long, enjoyable activities (think hiking, dance-a-thons, playing bridge) while raising funds for Alzheimer’s awareness.

We’ll also like to pique your interest in some spectacular research that our researchers are engaged in. It is known as the Human Connectome Project, where MRI (Magnetic Resonance Imaging) brain scanners will be used to map the brain’s connections by tracking the motion of water. Check out our feature on Dr. Trey Hedden’s research as part of a multi-year, nationwide project that is being funded by the National Institutes of Health (NIH), and don’t forget to go online to view some incredible Connectome images at www.humanconnectomeproject.org/gallery/ – you’ll understand why the Director of the NIH (Dr. Francis Collins) chose to blog about it in an article called ‘Symphony in your Brain’ (<http://directorsblog.nih.gov/2012/11/05/the-symphony-inside-your-brain/>). Ultimately, researchers hope that such high-resolution images of the brain’s connectivity may one day lead to improved diagnosis and better treatment of neurodegenerative diseases, brain injuries and neuropsychiatric disorders. May you, too, find beauty, symphony and even poetry in these images.

Bradley Hyman
Brad



Dr. Hyman brainstorming in the lab with Dr. Brian Bacskai (middle) and Dr. Mark Albers (right)



A NEWSLETTER FOR FRIENDS AND SUPPORTERS OF THE MASSACHUSETTS ALZHEIMER’S DISEASE RESEARCH CENTER AND THE MEMORY STUDY

www.madrc.org

INSIDE



Photo source: Alzheimer’s Association

The Longest Day *Page 2*



Photo source: Wikimedia Commons

The MIND Diet *Page 3*

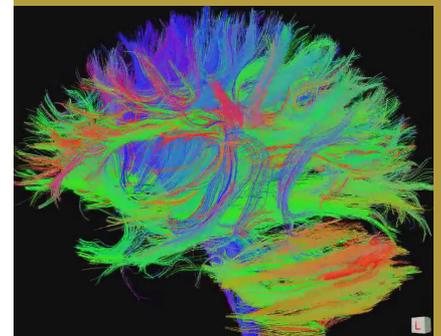
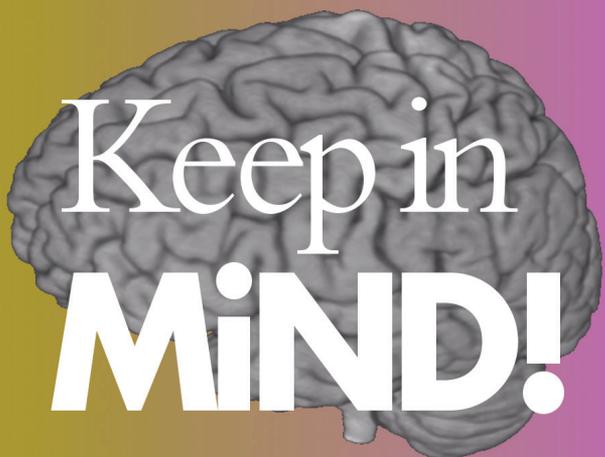


Photo source: J.G. Marcelino, Newcastle upon Tyne, UK via Wikimedia Commons

A Conversation with Trey Hedden, PhD *Page 4*



Molly’s Flowers *Page 7*



Keep in MiND!

A NEWSLETTER FOR FRIENDS AND SUPPORTERS
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www.madrc.org

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WAYS TO GIVE

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THE LONGEST DAY* ...

MY NAME IS JUDY JOHANSON, I am a Mother to two amazing children, Mother-in-Law to their wonderful spouses, Nana to three cherished grandchildren, and most importantly, I am the wife and Care Partner to my brave and grace-filled husband!

Steve was diagnosed four years ago with Younger Onset Alzheimer's Disease at age 58. Needless to say, this was an unexpected turn of events in our life, but given the circumstances, we have chosen to live our lives steered by our deep love for each other, and to strive for hope in the future, while embracing beauty in the moment!

We are blessed to be under the care of Dr Teresa Gomez Isla, and supported by multiple resources afforded us through the Alzheimer's Association. With the supportive guidance we have received, we have learned that while there may not be a cure presently, we could take an active and empowering role in the trajectory of eradicating this disease!

Post diagnosis, we enrolled in a Memory/Brain Imaging study at MGH in Charlestown. We also took part in a Fundraising Pilot event called "The Longest Day" with the Alzheimer's Association. Our Team "This Is Our Life" raised over \$12,000.00 our first year. I mentioned this fact to the technician administering Steve's MRI at a Memory Study visit, and she responded that the Alzheimer's Association was funding this study in part, and \$12,000.00 earned would cover 3 MRIs, which would ultimately contribute to the efforts of research towards a cure!

We were struck by this connection, and being put in these terms, it has helped us find more of a drive in our commitment to raising funds by our involvement with "The Longest Day."

In 4 years, our team has raised more than \$60,000.00, and in January, we were invited to take part in a Leadership Summit in Phoenix where we shared our personal journey with 700 people, and were awarded the 2015 Longest Day Volunteer Impact award. This sense of power and purpose at this time in our lives has been an invaluable gift to us!

While this disease and its relentless "taking" continues to make an impact on Steve's daily life, we are continually affirmed and encouraged by the positive gains we have realized resulting from the collaborative efforts of doctors, researchers, and those who are working so hard to end Alzheimer's!

We pray for a future where Alzheimer's is just a distant memory!!!



Steve and Judy Johanson

February 21, 2016

*summer solstice

The MIND Diet

by Miriam K. Olken, BA

DIETS ARE HARD TO FOLLOW; we have all been there, but through a study founded by the National Institute on Aging, a newly found diet known as the MIND Diet may lower the risk of developing Alzheimer’s disease and be easier to keep up than other health diets.

Developed by Rush University’s (‘Rush’) nutrition epidemiologist Martha Clare Morris, PhD, and colleagues, the MIND diet stands for the “Mediterranean-DASH Intervention for Neurodegenerative Delay” and is a combination of the “Dietary Approaches to Stop Hypertension,” also known as the DASH diet and the Mediterranean diet. The DASH diet helps to prevent and lower high blood pressure, and the Mediterranean diet helps to promote heart and brain health, prevent diabetes and control a person’s weight.

The study indicated that being on the MIND diet lowered the risk of Alzheimer’s disease (AD) by as much as 53 percent for participants who were strict with it and by about 35 percent for participants who followed it moderately. Dr. Morris and her colleagues felt that the MIND diet will motivate people more because it is an easier to adhere to meal approach.

WHAT SHOULD YOU EAT AND NOT EAT FOR A HEALTHY BRAIN

The MIND diet consists of 10 “brain healthy food groups” that include:

- Green leafy vegetables
- Other vegetables
- Nuts
- Berries
- Beans
- Whole grains
- Fish
- Poultry
- Olive oil
- Wine

And five unhealthy groups made up of:

- Red meats
- Butter, and stick margarine
- Cheese
- Pastries and sweets
- Fried or fast food

15 dietary components all together.

The MIND diet is made up of at least three servings of whole grains, a salad and one other vegetable every single day, including a glass of wine with one of the daily meals. Eating nuts and beans every other day is also encouraged, with poultry and berries at least twice a week and fish (at least) once

a week. According to Morris, the MIND diet is also easier to follow than the Mediterranean diet, which requires the daily consumption of fish, and three to four daily servings of fruits and vegetables.

Very little fruit is on the MIND diet list but the study indicated that berries help promote healthy aging and are enhancers of memory function – indeed, berries are super berries! “Blueberries are one of the more potent foods in terms of protecting the brain,” Morris said. She added that strawberries have also been shown to be an effective food on cognitive function.

Individuals are encouraged to limit their intake of the unhealthy food groups and especially butter, which has a recommended consumption amount of less than 1 tablespoon a day.

There have been many studies with research done in the past that compared different foods and nutrients to see how they affect brain health and function, but this is the first study on a combination of 2 dietary approaches and risk of developing AD. However, Morris noted that the study results will need to be confirmed in an array of populations and by other researchers through randomized study trials but for now, the MIND diet is great news for people who want to prevent the effects of AD and continue to lead a healthy life.

All the researchers on this study were from Rush except for Frank M. Sacks MD, a Professor of Cardiovascular Disease Prevention in the Department of Nutrition at the Harvard T. H. Chan School of Public Health. Dr. Sacks chaired the committee that developed the DASH diet.



Women Selling Produce, by Shiva Dayal Lal (ca. 1850, Patna).
Victoria and Albert Museum, London

A Conversation with Trey Hedden, PhD ... The Connectome Project

WHAT IS A CONNECTOME SCANNER?

It is a standard scanner, but it has been upgraded with extra-strong coils. The way that we make images of the brain is by exciting the molecules in a person's brain which we measure



Dr. Hedden and his family

as those molecules relax back into their baseline state. The stronger coils allow us to excite them more than with the standard

coil. It's specifically good for measuring white matter integrity, the connectivity of the brain through the white matter fiber tracts that connect neurons. Most people would not notice that they're in a different kind of scanner.

WHAT IS WHITE MATTER IN THE BRAIN?

Your brain is made up of two things: Gray matter, which is mostly the cell bodies of the neurons, and then there are the axons. These are the longer-range connections between neurons and they show up as white-looking material on the MRI. So we call it white matter. Basically, it's the way that neurons talk to one another.

HOW IS WHITE MATTER RELATED TO THE CONNECTOME?

A Connectome is the complete map of how a person's brain is connected. With MRI we can see the large white matter fiber bundles, which are many axons packed densely together that are running from one brain region to another, and allow those two regions to talk to one another. So what we're really studying is how do distant parts of the brain talk to one another by looking at the white matter that connects them.

HOW DID YOU GET INTERESTED IN CONNECTOMICS?

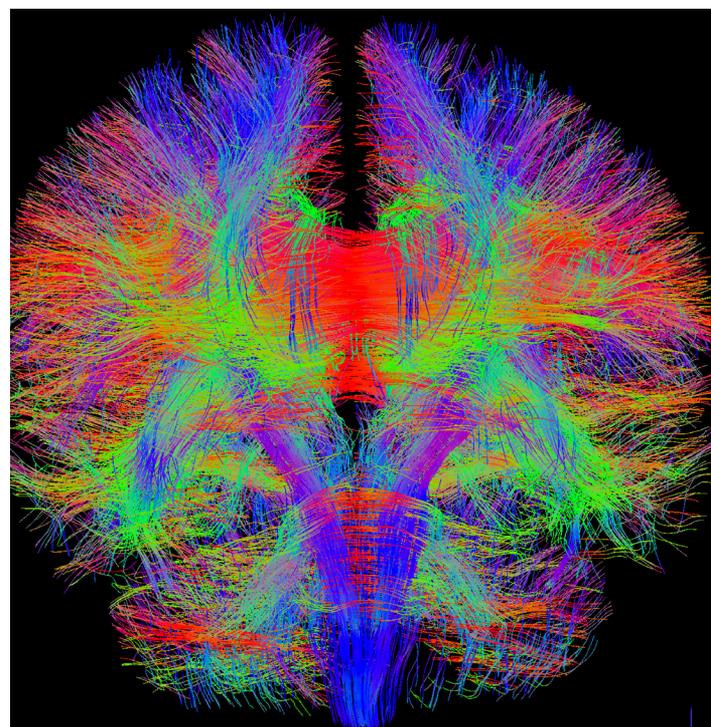
It really came through an interest in brain networks. I investigate how the brain changes with aging and preclinical Alzheimer's disease, not just in one particular region, but in multiple regions at once. We look for regions that fluctuate in synchrony with one another, which we think form a functional network. A couple of these networks seem to be particularly impacted by Alzheimer's disease. So we thought, "We're looking at the functional side of this, but now let's look at the structural side of how those different regions in a network talk to one another. What are

the white matter pathways that enable them to hook up with one another and communicate?" The Connectome scanner lets you measure both of these. When you put those together – the functional ways in which these regions are talking with the structural pathways by which they're connected – that gives you a comprehensive view of how the network is operating, and which parts might be affected by disease.

HOW ARE THESE FUNCTIONAL NETWORKS RELATED TO THE STRUCTURAL NETWORKS YOU'RE MEASURING WITH THE CONNECTOME SCANNER?

If you think of it like a tree, the tree might have branches that shake together – that's the functional network. The arborization of the tree that leads from one branch to another – that's the structural network. The structural network will stay constant,

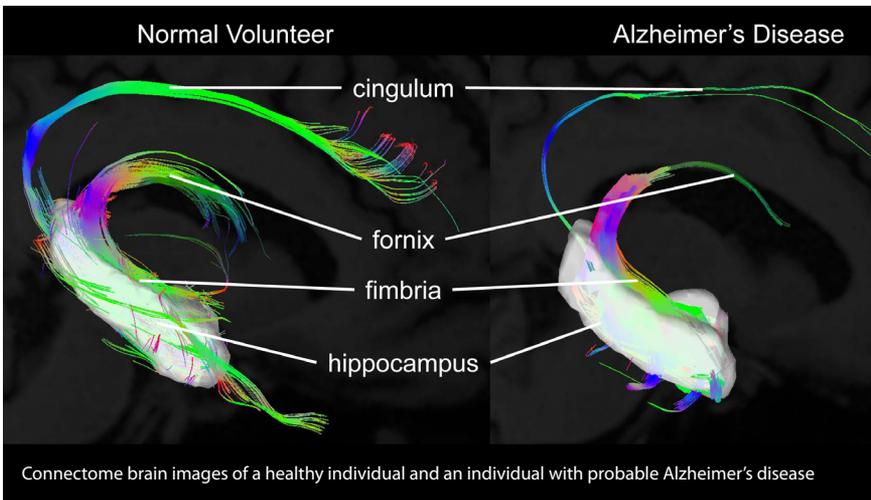
A Connectome is the complete map of how a person's brain is connected



A spectacular Connectome image



The ADRC Connectome Team (L - R): Dr. Hedden, Dr. Jenny Rabin, Dr. Rodrigo Perea and Emily Shaw



Connectome brain images of a healthy individual and an individual with probable Alzheimer's disease

whereas what branches are shaking in time together will fluctuate and change. One brain region might be part of one functional network at one moment and it might interact with another network at another time. I wouldn't say there's a one-to-one correspondence between structural and functional networks, but they're definitely related. The leaves on branches that are shaking together can't be connected unless they have a pathway that's running between them.

HOW WILL THE CONNECTOME HELP DISEASE TREATMENTS FOR ALZHEIMER'S?

What I think we're coming to realize is that there is a white matter component of the disease that is not only impacted by the plaques and tangles but also has a vascular component that is likely related to the disease as well. Although we don't have any current treatments for the plaques and tangles, we do have ways to treat vascular risk. You can take care of your heart, decrease your blood pressure, and lower your cholesterol with statins and so on. That might actually help keep the integrity of

the white matter intact, and might allow a person to function for longer than they would otherwise as they progress through the disease.

DO CHANGES IN YOUR CONNECTOME ALWAYS INDICATE DAMAGE?

Technically no – it depends on where you are in your lifespan. There are many white matter pathways that don't fully develop until you're in your early 20s. As you age, people start to become more at risk for neurodegenerative disorders, where you can see declining changes. So it depends on which way you're going: You'll see changes on the way up and changes on the way down.

WHAT'S ON THE HORIZON FOR THE CONNECTOME SCANNER AND YOUR STUDIES?

I think of it as personalized medicine, that you're trying to identify risks for individuals before they actually experience problems so you can take steps to prevent those things. You can always expand this technology out and say, "What's different about different disorders? What does that enable us to learn about how the brain is connected? What early treatments could we

use?" What's interesting about the connectome technology is that it has informed the next generation of scanners. Eventually, you might very well be able to go to your doctor and get something similar to a connectome scan.

ARE YOU CURRENTLY RECRUITING FOR ANY OF YOUR STUDIES?

We are actively looking for individuals with mild cognitive impairment and subjective cognitive concerns who might be interested. Several of my colleagues have studies that need Parkinson's disease and Alzheimer's disease patients. The other category we're trying to draw more folks in for is frontotemporal lobe dementia.

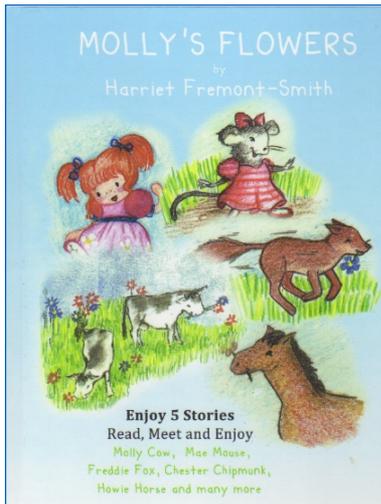
Dr. Hedden is an Assistant Professor of Radiology at Massachusetts General Hospital/Harvard Medical School.

This interview was conducted by Jonathan D. Jackson, PhD

WE'RE CURRENTLY RECRUITING!

STUDY TITLE	WE'RE LOOKING FOR	BRIEF STUDY DESCRIPTION
Dominantly-Inherited Alzheimer Network (DIAN)	Adults (age 18 +) with a biological parent who has Dominantly-Inherited Alzheimer's Disease (DIAD)	The purpose of the study is to try to understand the changes that occur in patients with genetic mutations causing DIAD over time. The DIAN research volunteers are members of families in which AD is dominantly-inherited, meaning that about 50% of the individuals in each generation of a family develop AD, generally before age 60. Over time, participants will have MRIs, PET scans, Lumbar Punctures, and memory testing.
Evolution of Memory-Related fMRI Activation Over the Course of MCI and AD	Healthy adults, age 65-90, and adults with MCI and mild AD dementia, age 55-90	The purpose of this research study is 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 AD (Mild Alzheimer's Disease). Subjects must have a study partner and be willing to come for six to eight clinic and imaging visits over the course of two to three years.
Connectome Imaging in Aging and Dementia	Adults with AD, FTD, MCI or cognitive complaints, age 50-90	The purpose of this research study is to look at brain connectivity in a variety of people with memory problems, including people with complaints about their memory and people diagnosed with a neurodegenerative disease. The study involves one 3-hour visit to the Charlestown Navy Yard where participants watch a movie during a one-hour brain scan (MRI) and complete some questionnaires.
A Placebo-Controlled, Double-Blind, Parallel-Group, Bayesian Adaptive Randomization Design and Dose Regimen-Finding Study to Evaluate Safety, Tolerability, and Effectiveness of BAN2401 in Subjects with Early Alzheimer's Disease (BAN2401-G000-201)	Adults with AD, age 50 - 90	79 week clinical trial to evaluate the effectiveness and safety of BAN2401 in reducing abnormally high levels of a protein called amyloid that is found in Alzheimer's Disease (AD). We are looking for participants between the age of 50 and 90 in stable medical condition and with a reliable study partner able to accompany them to visits. Must have been diagnosed with Mild Cognitive Impairment (MCI) or mild AD and are willing to undergo MRI and PET scans. Compensation is provided for participation.
Anti-Amyloid Treatment in Asymptomatic Alzheimer's Study ('A4')	Adults with normal thinking and memory function, ages 65-85	The purpose of the study is to investigate a new drug intervention that may reduce the impact of a protein known as 'beta amyloid'-forming plaques in the brain. It may take 3 years to complete the study. During the study, you may be given the test drug or a placebo (substance without active ingredients), be asked to have 4 MRI scans, at least 2 PET scans, routine blood tests, memory tests and physical exams. You may also participate in an optional sub-study for lumbar puncture.
Disentangling the Contribution of Tau to Aging, Dementia, and Neurodegeneration	Healthy Adults and adults with AD, MCI, CTE, and FTD, ages 20-90	The purpose of this study is to determine the presence of the protein Tau in the brain in a variety of populations, ranging from healthy adults to those diagnosed with a neurodegenerative disease. It will take up to 6 visits to complete this study. Over the course of these visits, you will be asked to have 1 MRI scan, 1 T807 PET scan, 1 PIB PET scan, 1 fasting blood draw, and 2 cognitive testing sessions. You may also participate in an optional sub-study for lumbar puncture.

For information on these or additional studies, contact our Outreach & Recruitment Coordinator, Sehily Jaimes, at 617-643-5200



I'M HARRIET FREMONT-SMITH.

I know who I am, but there is a shadow that follows me, that won't leave my side. That shadow is Dementia.

When I was diagnosed with Dementia I felt angry and afraid. Dr. Gomez-Isla's, (my neurologist) gentle and compassionate manner has helped turn my anger into acceptance. I've been overcoming my fear with her support,

my trust in SpringHouse (my caring assisted living residence), and the love of my family; but at times, the silhouette I see does not resemble the Harriet I know.

While moving into Springhouse, my children rediscovered Molly the Cow, a story I wrote in the 1970's. Molly was my children's bedtime companion, their nightly guardian watching over their hearts and dreams.

At the urging of my children to share their beloved Molly with the world, I published Molly's Flowers in 2014. Molly is a reflection of my true self and through her, I'm able to live on in the minds and hearts of children. Molly has allowed my mind to stay focused, keeping my shadow companion at bay. I've just begun a new series so Molly can continue to comfort and brighten the lives of children around the world.

There are some things in my life I wish I could forget, like how I feel about Dementia, but there are many wonderful things I hope I never forget! I want to always remember the love I have had – and continue to experience – and the millions of hugs and kisses from my children and grandchildren.

I know dementia will always be with me. I also know my guardians – Molly, Dr. Gomez-Isla, Springhouse, and my loving family – will always be with me too, brightening my way as I navigate my new world.

January 31, 2016

"How beautiful this flower is," thought Howie ... I wonder if this flower had a hard time growing from a seed into a bud, and then opening into such a healthy flower ... It must be very hard to be a seed, and you must want to be a beautiful flower very much to go to such trouble to pop out of the earth one spring morning."

"Little Flower, if you, so small and weak, could grow up and wave your hand so proudly in the wind, I guess a big, strong, horse, like me, can try again." Howie galloped off toward the race track and would always remember his beautiful flower – the one that Molly Cow had given to make him smile.

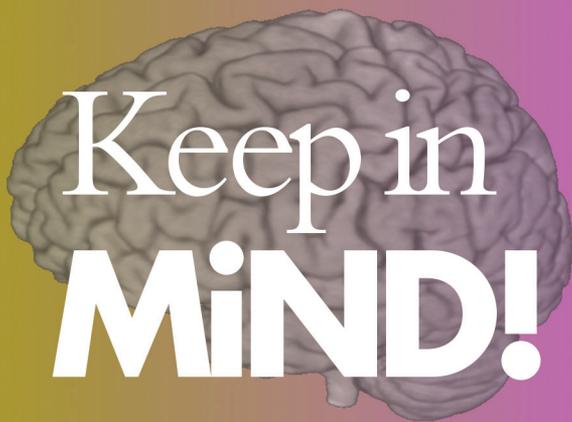
To all our research participants~

Punxsutawney Phil did not see his shadow this Groundhog Day! And he was proven correct! We've had an early spring ... AND a very mild winter! This means we've been plowing full steam ahead, working very hard in all our various research endeavors. No snow days for us this year! We've been busy beavers!

When you've come for your research visits, you've probably been asked many questions, performed a wide variety of tests, and been seen by different doctors and research assistants. (In fact, even before you come in, we often ask you to fill out forms!) I know we ask a lot of you! But all of the information you give us is so very valuable. Without your help, we'd be a shadow of ourselves.

Much time, effort, and money go into our research. But the most important ingredient is YOU! You inform us and from there we can hopefully translate that into a better understanding of the brain and how it changes in normal aging and in various neurodegenerative diseases. So "THANK YOU" from all of us to all of you!

**Jeanette Gunther, MS
Clinical Coordinator
Gerontology Research Unit**



Keep in MiND!

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Some thoughts from the Harvard Aging Brain Study ...

by Rebecca E. Amariglio, PhD

Recent work on the Harvard Aging Brain Study (HABS) has shown people's own memory complaints may indicate some of the earliest changes due to Alzheimer's disease, even if they perform normally on pencil and paper tests. While many people notice a slide in their memory as they age, some people experience memory decline that might indicate the very beginning of changes in the brain. While it is common for patients with dementia to show a lack of awareness of their memory deficits, recent research suggest that very early in the disease process, many years before the onset of dementia, individuals may start to notice memory changes before anyone else, such as a family member or a doctor. In HABS, participants were asked questions about their memory and also had brain scans that allowed researchers to see how much amyloid they had in their brain. Amyloid is a protein that is associated with risk for developing Alzheimer's disease. Even though participants were not considered to have memory impairment on standardized cognitive tests, findings revealed that individuals with a greater amount of self-reported memory complaints were also more likely to have amyloid than those with fewer memory complaints.

While these findings may be useful in identifying individuals who may be at risk for Alzheimer's disease for future studies, it is important to remember that noticing a change in memory is quite common in older age and often not reason for concern. Common complaints in normal aging include, forgetting the name of an acquaintance or a movie title. Another common complaint is walking into a room and forgetting what you were doing. Occasionally misplacing belongings may also happen as people get older. However, individuals that become concerned about recent forgetfulness in multiple arenas of everyday life that appears worse than others their age may wish to consult with their doctor.

More information about the HABS study may be found at <http://www.madrc.org/harvard-aging-brain-study>



The Elderly Couple Jo and Uba, Spirits of the Pine Tree, with Rake for Collecting Pine Needles, by Chosui Yabu (ca. 1860, Edo Period). Brooklyn Museum collection