Could Diabetes Increase the Risk of Developing Alzheimer’s?

Memory disorders such as Alzheimer’s disease (AD) are very common in older people. In fact, the likelihood of dementia in patients over 65 is about 13%, accounting for about one in eight persons over the age of 65. Diabetes, especially type II diabetes, is also a similarly common disease among the elderly and among patients with AD. According to the American Diabetes Association, over 18% of Americans over the age of 60 are affected by diabetes. Interestingly, these two conditions seem to have an impact on one another. Diabetes has been associated with changes in cognition, such as impaired learning and memory, slowed mental speed, and diminished mental flexibility. Moreover, patients with AD are more vulnerable to certain forms of diabetes.

The association between diabetes and AD appears quite strong amongst patients who carry the ApoE 4 allele, an inherited risk factor for the development of AD. The association between these two diseases is also strong in diabetic patients treated with insulin, a very common medication used to control blood sugar levels. In addition, loss of brain tissue itself, something also seen in patients with AD, seems to be more severe in elderly patients treated with insulin. There seems to be something about high levels of insulin that puts patients at risk for developing AD, as the “hyperinsulinemic state” typical of some forms of diabetes doubles the risk of AD. This is a condition that many diabetic patients experience when their own bodies produce too much insulin because their cells have become less responsive to normal levels of insulin. It has been shown that this “hyperinsulinemic state” may increase inflammation and affect the processing of molecules that lead to AD, potentially promoting memory impairment and AD. Interestingly, in addition, therapies that target this state show promise in improving cognition in patients with AD.

Other relationships between diabetes and memory loss, focusing more on demographic factors, have also been found. The Rancho Bernardo Study demonstrated a fourfold increase in cognitive decline in women with diabetes. This effect was not seen in men. In addition, improving control of blood sugar could actually ameliorate this risk in women. In the California SALSA (Sacramento Area Latino Study on Aging) study patients of both sexes with diabetes were less likely to

Research Shows that High Protein Diet May Shrink Brain

A high protein diet may help with weight loss, but according to a new study by Mount Sinai researchers, it may also increase the risk of brain shrinkage and the susceptibility to Alzheimer’s disease.

The study, published in the journal Molecular Neurodegeneration, tested the impact of several diets for their effects on Alzheimer’s disease pathology in mice. “Given the previously reported association of high-protein diet with aging-related neurotoxicity, one wonders whether particular diets, if ingested at particular ages, might increase susceptibility to incidence or progression of Alzheimer’s disease,” says lead study author Samuel E. Gandy, M.D., Ph.D., Mount Sinai Professor in Alzheimer’s Disease Research.

Dr. Gandy led an international team that included researchers from the United States and Canada.

(Continued on page 5)
Mumbai Corner

Staff from the Memory and Aging Research Center in Mumbai Visit Mount Sinai

This past June several members of the research team from the Memory and Aging Research Center at Nair Hospital in Mumbai visited the Mount Sinai ADRC. They were: Dr. Urvashi Shah, a neuropsychologist, Dr. Girish Nair, a neurologist, and psychologists Vaishali Ganwir, and Shanti Shankar, and Mr. Ajit Kadam, a senior histotechnologist. The two weeks during which our visitors were here provided an excellent learning opportunity on both sides. The visitors toured the Mount Sinai ADRC facilities, including the clinical research areas, the basic science labs, and neuropathology labs. This was followed by meetings and learning and discussion sessions. Several Mount Sinai investigators and staff met with the Mumbai team on many occasions to discuss the clinical research being developed in Mumbai and how further progress could be made through this site visit in New York. The Mumbai team attended a number of clinical conferences held at Mount Sinai which led to very important discussions of the types of illnesses and memory and other cognitive problems found in both countries. While here, Dr. Urvhashi Shah gave a wonderful presentation to Mount Sinai faculty and staff, highlighting some of the challenges that clinicians in India faced regarding testing of memory and thinking abilities. The visit was quite a success, providing a timely opportunity to the visitors to observe the excellent research establishment of the ADRC and building new relationships and strengthening the research collaboration between Mount Sinai’s ADRC and the Memory and Aging Research Center at Nair Hospital in Mumbai.

Participating in Alzheimer’s Research – New Fact Sheet

How can we treat, prevent, or cure Alzheimer’s disease? To find the answers to these and other questions, scientists need help from all kinds of people who are willing to participate in Alzheimer’s disease research. In fact, today, at least 50,000 volunteers are urgently needed to participate in more than 175 actively enrolling Alzheimer’s clinical trials and studies in the United States.

Participating in Alzheimer’s Disease Clinical Trials and Studies, a new fact sheet from NIA’s Alzheimer’s Disease Education and Referral (ADEAR) Center offers clear, basic information on:

- how Alzheimer’s studies and trials work
- steps to finding out about and enrolling in a study or trial
- participants’ rights
- questions to consider
- resources to learn more

Available FREE: Download, read, or order at http://www.nia.nih.gov/Alzheimers
Congratulations to ADRC researcher **Michal Beeri, Ph.D.** for receiving the Faculty Council Award for Academic Excellence for Junior Faculty. The award, which honors Dr. Beeri’s dedication to the study of cognitive impairment, Alzheimer’s disease and dementia, was presented by the Mount Sinai School of Medicine at its Convocation exercises.

Dr. Beeri has concentrated much of her work on diabetes as a risk fact for dementia, making a translational contribution by bridging epidemiological and neuropathological findings. Most recently, she has received an NIA Career Development Award and a Young Investigator Award from the Alzheimer’s Association to support her groundbreaking research.

Dr. Beeri is currently researching the ways in which long-term diabetes affects cognitive decline in a population of elderly subjects in Tel Aviv, Israel. Widely published, her findings highlight a growing emphasis on the oldest-old, where she anticipates the most profound public health burden of dementia will occur.

**Samuel Gandy, M.D., Ph.D.,** was recently featured in the June 2009 issue of *GQ* Magazine, as part of the “Rock Stars of Science” campaign. Photographed with artist, Will I Am, Dr. Gandy stands amongst some of the brightest minds in Alzheimer’s disease research. From left to right stand: Ron Peterson, M.D., Ph.D. of the Mayo Clinic, Will I Am, Steven T. DeKosky, M.D. of the University of Virginia School of Medicine, and Mount Sinai’s very own Sam Gandy, M.D., Ph.D.

With its mission to accelerate science from research bench to the bedside, the “Rock Stars of Science” campaign brings together our nation’s most brilliant scientific minds with America’s most celebrated rock stars in a dedicated effort to find cures for the diseases that threaten our future as a nation.

For more information on the campaign, visit [http://www.rockstarsofscience.org](http://www.rockstarsofscience.org).

---

**memory walk 2009**

On Sunday, October 25th at New York City’s Riverside Park, thousands came out to enjoy the sunny weather and walk for the Alzheimer’s Association 21st Annual Memory Walk 2009. As part of the NY Cares team, the Alzheimer’s Disease Research Center joined forces with NYU and Columbia in efforts to raise money – and awareness – for Alzheimer’s Disease research. By the end of the day, the ADRC team was able to reach out to many Memory Walkers affected by this disease – and raised over $5000.00! The walk was a success, and if you’re still interested in donating to the Alzheimer’s Association, it’s not too late – donations are accepted year-round at 646.744.2997 or email Memorywalk@alznyc.org (Para Español, llame al 646.744.2997 y presione el #2). Thank you to all who came out to the Memory Walk 2009. We hope to see you next year!

*Article by Amanda Burden, ADRC Research Coordinator; Photos courtesy of Dara Mitchell, Family Studies Research Coordinator*
Evaluating Cognition over the Phone Works

In a recently published article in the *International Journal of Geriatric Psychiatry*, ADRC investigator, Effie M. Mitsis, Ph.D. discovered that testing elderly people’s cognitive skills by telephone is generally as effective as in-person testing. The study divided a cohort of 54 healthy women participants with an average age of 79 into two groups. The participants were given standard cognition tests, including mental status questions such as identifying the day and remembering a series of words.

The study found telephone and in-person assessment to be comparable, suggesting that telephone assessment may be a useful, cost-effective and time efficient alternative to in-person assessment of cognition in the elderly. Dr. Mitsis concluded, “Although telephone assessment is not a substitute for in-person assessment as conducted by neuropsychologists, many elderly patients don’t have the resources to access a neuropsychologist or ability to spend hours getting to the doctor’s office or clinic to receive an evaluation, especially one that would potentially be conducted every few months should that person decide to participate in a clinical trial.”

Dementia Risk Higher for NFL Players

A recently published study commissioned by the National Football League (NFL) indicates a possible relationship between head trauma and later memory and cognition problems. In this study, researchers contacted 1,063 retired NFL players who had played for 3 or more seasons to survey their health and well-being over the phone. It was found that 6.1% of former players aged 50 and over received a dementia-related diagnosis, five times higher than the national average of 1.2%. For retired players aged 30-49, dementia-related diagnoses were 19 times higher than the national average of 1%. According to Daniel P. Perl, M.D., neuropathology director at Mount Sinai School of Medicine, “I think this complements what others have found – there appears to be a problem with cognition in a group of NFL football players at a relatively young age”. This study will continue to be reviewed by the research community and the NFL. It is hoped that the findings will contribute towards greater understanding of the role that head-related injuries plays in dementia-related diseases.

Goodbye Erica & Katya!

Our clinical research coordinators and dear friends, Erica Mirigliani and Katya Gaynor, have recently left the ADRC. Erica will be starting medical school this upcoming year at Ross University. Katya will leaving to Costa Rica to work at Casa Ames, with the Costa Rica Internship Institute.

We would like to take this opportunity to thank Erica and Katya for all their hard work at the ADRC. We wish them both the best in all their future endeavors!
Could Diabetes Increase the Risk of Alzheimer’s?
Corbett Schimming, M.D. (continued from page 1)

develop cognitive and physical decline symptoms if they were taking diabetes medications. Despite the work that has been done so far, this area of research is still in its early stages.

The presence of memory loss and other cognitive impairments can interfere with almost every area of elderly patients’ medical care. This is especially so for individuals with diabetes, as patients with this condition must monitor their blood sugar levels, understand complex medication regimens, and adapt to complicated dietary changes and lifestyle modifications. In addition, patients’ rapidly changing treatment plans, many of them carrying the potential for dangerous adverse effects, further complicate the treatment management of patients with diabetes and concurrent cognitive deficits. Although researchers have begun clarifying the links between diabetes and AD, much is still not understood about how they may affect one another. Given the apparent associations between the two diseases, it is of particular interest to understand the molecular mechanisms underlying these interactions, as well as ways of preventing or ameliorating the effect of diabetes on memory. With an increasing percentage of America’s elderly population being affected by both diabetes and AD, better understanding of the possible relationship between these illnesses may have significant implications for the prevention and treatment of AD.

Research Shows that High Protein Diet May Shrink Brain (continued from page 1)

The researchers tested four different diets on mice that had been genetically altered to be susceptible to Alzheimer’s disease. The mice were fed either the standard commercial diet that all mice in the facility receive; a custom-made high-fat, low-carbohydrate diet; a high protein, low carbohydrate diet; or a diet high in carbohydrates, but low in fat. The mice consumed these diets beginning at age four weeks until they were 18 weeks old. The researchers then looked at the brains and body weights of the mice, as well as plaque build-up and differences in the structure of the hippocampus, a brain region involved in memory.

They found that mice fed a high-protein, low-carbohydrate diet had brains 5 percent lighter than all the other mice, and regions of their hippocampus were less developed. Surprisingly, mice on a high-fat diet had raised levels of plaque proteins, but no loss of brain mass. This dovetails well with the knowledge that some fats, such as cholesterol, raise plaque levels, while other fats, such as those found in fish oil, protect from plaque.

One theory, says Dr. Gandy, is that a high-protein diet may leave neurons more vulnerable to Alzheimer’s disease plaque, but more research must be done to weed out the neurological impact of consuming different diets.

“At the end of the day, these are mouse experiments,” says Dr. Gandy. “Next, we want to see whether this is important for humans. There is enormous interest in identifying high-risk dietary components, but studying diets as though they were drugs is very challenging and, as with drugs, randomized double-blind clinical trials will be required if we are ever to be able to prescribe a diet that lowers the risk for Alzheimer’s.”

Need a Memory Evaluation?
The ADRC’s Memory & Aging Center (MAC) provides comprehensive evaluation for those who have memory complaints.

Experts: Our team includes experts in geriatrics, geriatric psychiatry and neuropsychology, neurology, and radiology.

Quick: The evaluation can be completed in one visit, including evaluation by a geriatric memory specialist, neuropsychological testing, and neuroimaging.

To make an appointment, please call us at (212) 241-1844.

ADRC Upcoming Events

Participants’ Appreciation Day
Thursday, April 22, 2009
Save the date!

Our third annual Participants’ Appreciation Day is right around the corner. Join us for a morning full of activities, information, food, and a raffle. Stay posted for more information; invitations will follow.
Dimebon—The Mystery Cure for Alzheimer’s?

Samuel Gandy, M.D., Ph.D. was recently featured in a Newsweek Web Exclusive article, entitled, “Are We Taking the Wrong Approach to Curing Alzheimer’s?” The article sheds light on the recent discovery of Russian antihistamine, dimebon, that not only stopped the cognitive decline of Alzheimer’s but also reversed it, with benefits lasting up to at least a year. However, in studies unveiled at the International Conference on Alzheimer’s Disease in Vienna just a few months ago, dimebon was found to actually increase the amount of beta amyloid in the brain, the very molecule that was believed to be responsible for the disease.

For Newsweek, Dr. Gandy stated, "I would say that conventional wisdom in the field . . . is that an amyloid benefit would mean amyloid-lowering. Certainly, up until now, no one has been looking to treat Alzheimer’s by raising amyloid levels. [So] it was startling to observe that a compound with an apparently beneficial clinical effect on cognition caused acute elevation of amyloid beta levels in 3 out of 3 systems, in 2 labs." One of the most obvious implications of this finding is that pharmaceutical companies that are hoping to discover amyloid-busting compounds may be taking the wrong approach. Although the data is still “not enough to make an educated guess,” the role of Dimebon in the world of Alzheimer’s research may continue to be an important research effort for the treatment of this disease.

“I Remember Better when I Paint”

In the Spring of 2010, the ADRC will host a screening of I Remember Better When I Paint, a 2009 international documentary film about the positive effects of art therapy on those with memory disorders. The film is narrated by Olivia de Havilland and features Yasmin Aga Khan, President of Alzheimer’s Disease International and daughter of Rita Hayworth, who had Alzheimer's disease. The feature-length film includes interviews with our own Dr. Sam Gandy as well as Dr. Robert Butler, the founder of the Mount Sinai Department of Geriatrics and founding director of the National Institute for Aging. Those of you who attended our Participant’s Day in 2009 may remember the wonderful lecture by our colleagues at the Museum of Modern Art (MoMA), and this film ties in nicely with the ADRC’s collaborative work with MoMA’s art programs for those with memory disorders.

Mild Memory Loss Support Group

The Memory Support group at Mount Sinai has a few openings for people with early stage memory problems. Founded over 18 years ago the support group is a valuable resource for people dealing with a diagnosis of Alzheimer’s disease or other memory problems. If you know someone who could benefit from talking about the day to day realities of dealing with the challenges of memory loss please consider referring them.

Each week, we come together to share our thoughts, feeling, fears, as we support each other. The group is lead by Elizabeth Fine, LCSW, however, much of the direction of the group comes from its members, and they take an ownership interest in the value of the group. The group is currently looking for new members. “I feel badly that there are people who need this group who don’t know about it. I want to help people with memory problems to join a group. Support groups take away a lot of the fear” says one member of the group.

At a recent session members expressed themselves in poetry about what the group has meant to them. Here is their collective voice:

If you or someone you know is interested in joining our group please contact Elizabeth Fine, LCSW at 212-659-9230

Margaret
ADRC Studies Currently Enrolling

Nerve Growth Factor (NGF) Study
CERE-110 is a research drug being used in gene therapy research for Alzheimer’s disease (AD). In this study, genes are transferred to brain cells via neurosurgery so that the body can make NGF, a naturally occurring protein that might increase the survival of neurons that die in AD. The purpose of this phase 2 clinical trial is to find out if this type of gene therapy technique, neurosurgically injecting CERE-110, is safe, well-tolerated, and of benefit when given to people with AD. For more information, please contact Judy Creighton, M.A., at (212) 659-8885 or via email at Judy.Creighton@mssm.edu. MSSM #09-0367; Principal Investigator: Judy Neugroschl, M.D. MSSM approved through 4/23/10.

CONCERT: A Phase 3 Study Evaluating Dimebon in Alzheimer’s Patients on Donepezil
Mount Sinai researchers will be participating in a phase 3 study being conducted nationwide to evaluate how well and how safely a study medication, Dimebon, is in combination with donepezil (Aricept®) in patients diagnosed with mild-to-moderate Alzheimer’s disease (AD). This research study will work to evaluate whether Dimebon may improve both the function and outgrowth of brain cells, which is often compromised in a number of neurodegenerative diseases such as AD. Further, the study will evaluate whether Dimebon could provide improvements in cognition and activities of daily living when given in combination with donepezil. Study participants will receive active study drug or placebo (inactive pill) for 12 months for the duration of the study, while continuing to take the prescribed donepezil. All participants will be carefully monitored at the research clinic throughout the study, and will be compensated for transportation to and from the clinic. Participants are eligible to participate if they meet the following criteria: are 50 years of age or older and have mild-to-moderate AD; have a Mini-Mental State Examination (MMSE) score of 12-24, inclusive; have a brain computed tomography (CT) or magnetic resonance imaging (MRI) scan consistent with a diagnosis of probable AD within 12 months prior; have been taking donepezil for at least six months, with stable dosing at 10 mg/day for at least the past four months; have a caregiver who is able to attend all study visits. For more information, please contact Andrew Vigario at (212) 241-5692, or via email at Andrew.Vigario@mssm.edu. MSSM #09-0279; Principal Investigator: Hillel Grossman, M.D. MSSM approved through 3/16/10.

The Gammaglobulin Alzheimer’s Partnership Study
The Gammaglobulin Alzheimer’s Partnership (GAP) Study is designed to evaluate the safety, efficacy, and tolerability of the investigational drug Immune Globulin Intravenous (IGIV) for the treatment of mild-to-moderate Alzheimer’s disease (AD). IGIV is a biologic agent with anti-inflammatory and immunomodulating properties; this study is being conducted to determine if IGIV can help slow the progression of AD and its symptoms. The Gammaglobulin Alzheimer’s Partnership (GAP) Study is seeking volunteers who: 1. Are aged 50-89, and who have probable mild-to-moderate AD. 2. Have a Mini-Mental Status Exam (MMSE) score of 16-26. 3. Have not suffered from serious or unstable diseases within the past 3 months. 4. Have a study partner who can actively participate in the study with the volunteer. For more information, please contact George Marzloff at (212) 241-1514, or email at George.Marzloff@mssm.edu. MSSM #08-1326; Principal Investigator: Hillel Grossman, M.D. MSSM approved through 3/16/10.

Investigational Clinical Amyloid Research in Alzheimer’s
We’re looking for volunteers to participate in a clinical study to evaluate the safety and effectiveness of an investigational drug to help control the progression of Alzheimer’s disease. Study participants will be randomized to the investigational product or placebo (a treatment with no active ingredient). There is a 60% chance of receiving the investigational drug and a 40% chance of receiving a placebo. Study participants will be asked to attend 15 study visits during an 83-week period, receive six infusions of the investigational drug every 13 weeks for 65 weeks, and have blood tests and study-related physical and clinical exams. Study participants may be eligible if they are between 50-85 years of age, have a diagnosis of probably AD, and have a caregiver who is willing to be involved in the study. For more information, please call George Marzloff at (212) 241-1514, or email at George.Marzloff@mssm.edu. MSSM #08-0241, 08-0242; Principal Investigator: Hillel Grossman, M.D. MSSM approved through 3/16/10.

Trial of a Nutritional Supplement in Alzheimer’s Disease
We are seeking patients with Alzheimer’s disease to participate in a research study on an antioxidant formula containing resveratrol. Some study participants will receive the formula and some will receive a placebo (sugar pill). Participation in the study includes memory testing, neurological exams and blood tests. Resveratrol may reduce brain cell damage caused by harmful chemical byproducts. This study is investigating if resveratrol can help the cognition of Alzheimer’s disease patients. The study will be conducted over 12 months and is funded by the Alzheimer’s Association. For more information, please contact Devin Bove at (212) 241-8885, or email at Devin.Bove@mssm.edu. MSSM #05-1394(0001); Principal Investigator: Mary Sano, Ph.D. MSSM approved through 4/30/10.

Functional Deficits of ACC in MCI
A new study is being conducted to examine the effects of aging on memory and attention. Volunteers will be trained for a simple computer task and will perform this task in an MRI scanner. All participants will be compensated for time and travel. Participants are eligible to participate if they meet the following criteria: 1. are between 55 - 90 years of age, 2. are either free of memory problems or are experiencing some memory problems, 3. have a Mini-Mental Status Exam (MMSE) score higher than 24 (if not known, this can be determined through evaluation), 4. have no metal in their body, 5. do not have any current psychiatric disorders, 6. are not claustrophobic. For more information, please contact Yunsoo Park, Clinical Research Coordinator at the Mount Sinai Lab of Neuroimaging by phone at (212) 241-1613, or via email at yunsoo.park@mssm.edu. MSSM GCO #08-00443 IRB approved through 6/19/10.
Mount Sinai Researchers to Test First Gene Therapy to Improve Brain Function In Alzheimer’s Patients

Judy Creighton, M.A.

AD is a degenerative and ultimately fatal disorder affecting as many as five million Americans; that number is expected to soar to more than 11 million by 2040. Scientists are actively looking at new and more innovative ways to treat the disease. Now, for the first time in AD research, scientists are about to test the efficacy of a gene therapy called CERE-110. Mount Sinai School of Medicine is one of 12 sites in the nation selected to participate in a multicenter clinical trial to examine the safety, efficacy, and benefits of a neurosurgical gene therapy technique for Alzheimer’s disease (AD). Judy Neugroshch, M.D., an expert in dementia and Ron Alterman, M.D., an experienced neurosurgeon, will join efforts for this aggressive new approach to treat AD. Although neurosurgical techniques are used to treat other neurological disorders, there is no FDA approved surgical treatment for AD. In fact, relatively few studies have utilized this approach in AD research.

The experimental treatment utilizes a viral-based gene transfer system, CERE-110, that makes Nerve Growth Factor (NGF). NGF is a naturally occurring protein that helps maintain nerve cell survival in the brain. In animal studies, NGF has been shown to support the survival and function of the neurons that deteriorate in Alzheimer’s patients. These neurons produce the chemical acetylcholine, which is important in memory and cognitive function. The hope is that improvement of this system’s function may lead to better memory performance in Alzheimer’s patients.

CERE-110 is an experimental treatment that will be injected into a specific region of the brain that is affected by AD, the nucleus basalis of Meynert (NBM). CERE-110 has been studied in animals and humans. In aged monkeys and rats, CERE-110 reversed brain degeneration. Thus, these studies demonstrated that CERE-110 can safely induce long-term production of Nerve Growth Factor (NGF) by brain cells. A Phase 1 study conducted with humans was performed at Rush University in Chicago and the University of California San Diego, where the treatment was found to be generally safe and well tolerated. The 10 subjects underwent cognitive testing, measures of activities of daily living, and MRI and PET (positron emission tomography) scans. Researchers observed increases in brain metabolism in several cortical regions of the brain at six months and 12 months in some of the participants, as compared to other severity-matched individuals with AD. This suggests a potential reversal of patterns typically observed in AD. With follow up ranging from six months to more than four years post-treatment, there have been no side effects thought to be caused by CERE-110.

The Phase 2 trial will be conducted at 12 U.S. sites, including Mount Sinai School of Medicine’s Alzheimer Disease Research Center. The local study will involve approximately four to six volunteers between the ages of 50 and 80 with mild to moderate Alzheimer’s symptoms.

For more information about this study, please contact Judy Creighton, M.A., at 212-659-8886.

Information can also be found on the ADCS website: http://www.adcs.org/Studies/NGF.aspx, or you can call the NIA’s Alzheimer’s Disease Education and Referral (ADEAR) Center at 1-800-438-4380.