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INDIANA ALZHEIMER DISEASE CENTER NEWSLETTER
INDIANA UNIVERSITY SCHOOL OF MEDICINE
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iADC Indiana Alzheimer Disease Center

Reflections

Studies Find Possible New Genetic Risk Factors for Alzheimer Disease

Scientists have confirmed one gene variant and have indentified several others that may be risk factors for late-onset Alzheimer disease, AD the most common form of the disorder. In the largest genome-wide association study (GWAS) ever conducted in AD research, investigators studied DNA samples from more than 56,000 study participants and analyzed shared data sets to detect gene variations that may have subtle effects on the risk for developing AD. The National Institutes of Health (NIH) funded the study appearing April 3, 2011, in the online issue of Nature Genetics.

"New technologies are allowing us to look at subtle genetic differences among large groups of study participants. By comparing people diagnosed with AD to people free of disease symptoms, researchers are now able to discern elusive genetic factors that may contribute to the risk of developing this disease", said Richard J. Hodes, MD, Director of the National Institute of Aging (NIA) at NIH. "We are entering an exciting period of discoveries in genetics that may provide new insights about novel disease pathways that can be explored for development of therapies".

Until recently, only one gene variant, Apolipoprotein E-Σ4 (APOE-Σ4), had been confirmed as a significant risk factor gene for the common form of late-onset AD, which typically occurs after age 60. In 2009 and 2010, however, researchers confirmed additional gene variants of CR1, CLU and PICALM as possible risk factors for late-onset AD. The NIA AD Genetics Consortium (ADGC) study, led by Gerard Schellenberg, PhD, of the University of Pennsylvania, confirmed that a fifth gene variant, BIN 1, affects development of late-onset AD. It also identified genetic variants significant for AD at EPHA1, MS4A, CD2AP, and CD33. The genes identified by this study may implicate pathways involved in inflammation, movement of proteins within cells, and lipid transport as being important in the disease process. The United Kingdom-based group, led by Julie Williams, PhD., Cardiff University School of Medicine, Wales, found the same genes as risk factors and identified a gene variant ABCA7 as an additional gene of interest.

Dr. Andrew Saykin, Leader of the Neuroimaging Core at the Indiana Alzheimer Disease Center and a member of the research team involved in the GWAS research said, "***It is exciting that with recent progress in genome wide studies there are now ten confirmed candidate genes for late onset AD. Genetic data from the IADC was included in one of the GWAS and genotypes from the national Alzheimer's Disease Neuroimaging Initiative (ADNI) were included in both reports. The National Cell Repository for AD (NCRAD), located at IU, processed most of the genetic data used in the ADGC GWAS. Investigators at the IADC are examining MRI scans to determine if the new candidate genes explain atrophy patterns or progression in those at risk for AD."***

Mouse Study Shows Effect of Blood Pressure Drug on Alzheimer Disease

NIH-funded study finds drug stabilizes nerve cells in the brain

A drug used decades ago to treat high blood pressure has been shown to improve learning and memory in mouse models of Alzheimer disease (AD), according to a new study by researchers at the National Institute on Aging (NIA), at the National Institutes of Health (NIH). The study found that the drug, diazoxide, acted on nerve cells in the mouse brain in ways that slowed the development of the disorder. The findings appeared in the November 2010, print edition of the *Journal of Alzheimer's Disease*.

Mark P. Mattson, PhD, Chief of NIA's Laboratory of Neurosciences in Baltimore, directed the research, in collaboration with colleagues at Konkuk University College of Veterinary Medicine, Seoul, South Korea, and the Indiana University School of Medicine, Indianapolis. Debomoy Lahiri, PhD, Professor in the Department of Psychiatry and a researcher at the IADC participated in this research.

According to Dr. Lahiri, "***recent failures of AD drugs, especially drugs which alter amyloid precursor protein (APP) processing to generate fewer amounts of amyloid β (Aβ) peptides in clinical trials, have propelled AD researchers to find alternative strategies in the area of drug development for AD. In this context, the present article carries enormous importance as diazoxide, a KATP channel activator, was found to ameliorate the pathologies of AD in APP-transgenic mice. One of the most important findings of this study was identifying diazoxide's beneficial roles in several pathological cascades involved in AD. Effective roles of a single drug in several molecular pathways in AD could have potential therapeutic values in clinical settings."***

Mattson's team found that diazoxide stabilized nerve cells in the brain and prevented a biological flow in the mice that can result in the destruction of these cells. The drug also improved blood flow in the brain and prevented the harmful accumulation of two proteins, beta-amyloid and tau, which are hallmarks of AD. Widely used in the 1970s and 1980s to treat patients with severe hypertension, diazoxide is currently used to treat hypoglycemia--low blood sugar.

"These intriguing findings open new avenues of basic research that may increase our understanding of how modulating the electrical activity of nerve cells may slow the damage wrought by Alzheimer disease pathology," said NIA Director Richard J. Hodes, MD. "*More research will be needed before we can determine whether this may be a potential therapy for AD,"* he said.

NIA scientists studied two groups of mice with AD, one given diazoxide in drinking water and one given a placebo. After eight months, the diazoxide group outperformed the placebo group on a standard test of learning and memory. The brain tissue of the treated group showed fewer deposits of amyloid and tau proteins, less damage due to oxidative stress, and better blood flow—all indications that diazoxide may have suppressed some of the harmful cellular changes associated with AD.

"*To better understand the complex biological mechanisms by which diazoxide may exert a positive effect on nerve cells, we then studied the effects of diazoxide on cultured nerve cells*", Matson said. He found the drug activated and opened channels in the cells that enhanced the movement of potassium, which then calmed the electrical activity of the nerve cells in part of the brain involved in learning and memory. Diazoxide also lowered the excessive calcium often found in nerve cells in brains affected by AD. "*These beneficial effects were seen with a dose of diazoxide low enough to avoid a major decrease in blood pressure*," Mattson noted.

Adapted from a recent NIA news release

Continued on page 7

Empowering and Strengthening Your Brain

As we get older, our minds seem less like a steel trap and more like sieves. However recent research suggests that here is some good news for your 100 billion neurons: Just as the brain can get weaker, it can also grow stronger. Scientists are finding more things you can do to invigorate your brain, here are some of the latest findings:

1. **Volunteering stimulates the prefrontal cortex,** which analyzes, plans, and problem solves. A John Hopkins study found that older women who tutored kids for six months developed sharper cognitive skills. The social and mental activity required for teaching sends blood rushing to this part of the brain.
2. **Working out stimulates the hippocampus, which forms memories.** Arthur Kramer, PhD, a researcher at the University of Illinois, used MRI's to show that exercise actually makes your hippocampus bigger. Physical activity may increase the number of capillaries in the hippocampus, which in turn helps new cells grow. Dr. Kramer prescribes one-hour sweat sessions three times a week.
3. **Learning a new physical skill as this stimulates the intraparietal sulcus**, which directs hand-eye coordination. At Oxford University, researchers taught 24 people to juggle and found that after six weeks this area of the brain had an increased density of white matter (the fibers that let neurons communicate). Any novel activity that is practiced intensely, such as tennis or guitar playing, will likely have this effect, says the study author, Heidi Johansen-Berg.
4. **Exercising to keep the weight off as extra pounds can actually shrink the brain**. In a 2009 study, brain scans of older adults revealed that over-weight individuals had an average of 4 percent less brain tissue than normal-weight people. Also, obese people have a loss of tissue that is so significant that their brains appeared 16 years older than those of thinner people of the same age.
5. **Wiggling your eyes can help memory.** Can't remember where you stashed your glasses? Try looking from side to side. Rapid horizontal eye movements cause the brain's two hemispheres to interact with each other more efficiently, explains memory researcher Andrew Parker, PhD. In moments of temporary amnesia, that action may help you pull up information.
6. **Taking a snooze.** In a University of California Berkeley study, participants improved their scores on a memory test by 10 percent when they repeated the test after taking a nap. Non-nappers saw a 10 percent decline in their scores the second time they took the quiz. Here's why: New facts enter your brain like e-mails arriving in your in-box. Just as your in-box can overflow over the course of a day, so can your brain. During sleep, your brain shuffles recently received data into storage, creating space for fresh information.
7. **Eating brain foods rich in B12, antioxidants, or essential fatty acid** such as:
    - Bananas
    - Kale
    - Tomatoes
    - Blueberries
    - Swiss cheese
    - Chocolate
    - Salmon
    - Brussels sprouts
    - Apples
    - Olive oil
    - Coffee beans
    - Oranges
    - Nuts

Continued on page 4...

Empowering and Strengthening Your Brain

8. **Chronic stress can rob your body**. Prolonged exposure to the fight or flight hormone cortisol and other brain chemicals can actually kill neurons by exciting them to death. You can help minimize this problem by staying connected to family and friends. A six year Harvard University study of 16,638 people found that those with the largest social network had the slowest rate of memory decline. Family and friends can lessen the intensity of stress and the brain's chemical response.
9. **Sleep apnea, another thief, can lower the oxygen levels in your blood**. This disorder is marked by loud snoring and exhaustion upon waking. Your airway spontaneously closes or becomes blocked for several seconds at a time. This causes a dip in the oxygen level in your blood, which cause brain cells to starve. Studies show that losing 10 percent of your body weight is enough to improve symptoms. Your doctor may recommend using a CPAP machine (continuous positive airway pressure) while you sleep. It fits over your nose and mouth and generates a steady flow of air to keep the airway open.
10. **Hypothyroidism can also affect one's memory.** An underactive thyroid slows metabolism, which leads to fatigue, which leads to a foggy brain. One of the symptoms of this disorder, affecting about 17 percent of women over is the difficulty committing new information to long-term memory. A common cause of the problem is insufficient levels of iodine, which the body needs in order to produce thyroid hormones, so seek out lots of iodine-rich foods, such as seafood and dairy products.
11. **Heavy smoking in midlife more than doubles your odds of developing AD**. The long-term consequences of heavy smoking can significantly increase chances of developing AD and vascular dementia. People who smoke have increased inflammation and inflammation appears to play a part in AD. This is another good reason to quit smoking. There are many cessation clinics or programs available, at no or low cost; check with your physician.

Adapted from a NIH article Fall 2010

Caregiver Related Web Sites

There are many websites available to caregivers and older adults that can help make finding information about aging and/or caring for an aging relative much easier. Here are some helpful websites to check out. It is also a good idea to look for and gather information when there is no immediate crisis, this way you are better prepared to deal with an issue should it arise.

AARP: www.aarp.org

Alzheimer's Association: www.alz.org

Alzheimers Disease Education and Referral: www.nia.nih.gov/alzheimers

Association for Frototemporal Degeneration: www.theftd.org

Bureau of Aging and In Home Services: www.in.gov/fssa

National Alliance for Caregiving: www.caregiving.org

National Council on Aging: www.benefitscheckup.org

National Institute on Aging: www.nia.nih.gov

Please note that the websites listed here are not owned or managed by the IADC and the IADC cannot be not responsible for their content.

The IADC is providing these resources for information and convenience and all websites should be used with discretion .

Current Studies on AD and Related Disorders Research Enrolling Participants

Who is needed?	For which study?	Length of study?	Please contact…
To participate, volunteers must have a diagnosis of one of the following: • Probable Alzheimer Disease • Mild Cognitive Impairment • Lewy Body Disease • Frontal Temporal Dementia • Mixed Dementia • Vascular Dementia • Parkinson's Dementia	• This Registry/database is used to capture data for self-referred volunteers and established clinic patients that have interest in participating in various clinical research studies includes drug studies now and in the future.	• Information regarding research projects will be disclosed prior to enrollment in specific research studies. • Length varies by individual study.	Julie Dickson, RN 317-278-4333 or 866-257-0195
• Qualifying families with 2 or more living siblings diagnosed with probable AD • Plus a 3rd family member who is either >60 yrs and not affected or >50 yrs with memory problems	• The Genetics of Late Onset Alzheimer's Disease (LOAD) Study	• Longitudinal; over a lifetime or as long as person is willing • Visits include: neurological exam, cognitive evaluation, informant interview and provide a blood sample for DNA at first visit .	NCRAD 1-800-526-2839 alz@iupui.e
• Healthy Older adults • With mild to moderate memory difficulties • 60 years of age + • Right-Handed • Completed at least 10th grade of education	• Study of memory in health older adults • Study includes a brain scan, blood draw, eye exam and cognitive testing	• 3-year study with 3 assessments 18 months apart • Each visit is 7-8 hours and can be scheduled over 2 days • Compensation for time and effort provided	Tamiko MaGee, MS 317-278-3121 tmagee@iupui.edu

The Shriver Report: A Woman's Nation Takes on Alzheimer's Disease

A Study by Maria Shriver and the Alzheimer's Association

This report was written because the impact of Alzheimer disease (AD) on women in America is both significant and under-examined. Ten million American women are either suffering from AD or caring for someone who has AD. Family members suffer alongside those diagnosed with AD and often stretch emotional and financial resources to their limits. In most families it is highly likely that a woman is providing the majority of care. By 2050, the number of women diagnosed with or caring for someone with AD is expected to triple. Ms. Shriver partnered with the Rockefeller Foundation, *Time Magazine*, NBC News and others to begin an ongoing conversation across the political divide, from the White House and Congress to neighborhoods, conference rooms and kitchen tables across the nation.

This ground breaking study examines the fundamental transformation in the way America works, lives and how all too often public policy remains out of step with the needs of modern American families. The *Shriver Report* underscores the stress, strain and sacrifice American workers endure—and the stark gaps in our societal support structures that, if filled, could help relieve some of these hardships. Ms. Shriver writes about the powerful economic engine women have become in the USA and yet many obstacles still exist that keep women from realizing their full potential to contribute to the strength of the American economy.

One finding of the report shares that women's role in the house is as busy as ever. Millions of women play dual roles as both breadwinner and caretaker, putting in 40 or more hours of work per week outside the home while still providing the vast majority of child and family care. Men are increasingly stepping up to the plate, but women are still juggling the majority of responsibilities of this dual role in a society whose institutions have yet to catch up with modern family life.

The Shriver Report also acknowledges that the bulk of eldercare, helping parents and elderly friends cope with the slow onset of aging and its associate conditions rests with unpaid caregivers. For instance, over 11.2 million Americans provide billions of hours of unpaid care to people with AD or other dementia, and the majority of the caregivers are women. The parent suffering from AD or any other illnesses that accelerate and complicate aging—comes at a huge emotional, financial and spiritual toll to oneself and one's family.

As America's 78 million baby boomers begin turning 65 this year, families will confront age-related diseases with increasing frequency. ***The Shriver Report: A Woman's Nation Takes on Alzheimer's*** looks through the lens of this wasting disease and at working women who provide the majority of care to aging friends and family. There are 7 chapters with tips and stories by Dr. Oz, Barbara Streisand, Former First Lady Laura W. Bush, professional caregivers like Doris T. and Terrell Owens. To obtain a copy of the book visit the Alzheimer's Association website, www.alz.org or call 1-800-272-3900. It is a book that will motivate you, make you cry, enlighten and empower you.

In Memory….

The Indiana Alzheimer Disease Center Fund gratefully thanks and acknowledges the following individuals for their generous contributions from January 1, 2011 to present

In memory of Pamela J Bienvenu
Claude & Sandra Barnhart
Ken Frisard
Huey & Bonnie Herbert
Hollie Hemple
John Lamb
Robert Nester
Gordon & Krista Reina

In memory of Marianne Combs
Anonymous
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In memory of James Gorman
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Ira & Karen Schaeffer

In memory of A. Elease McQueen
Dan & Donna Moore

In memory of Dean B. Needham
Jane Needham

In memory of Brenda Thurston
Jimmie Thurston

Donors
Rafik & Patricia Bishara
Deborah Cox
Jimmie Thurston

Caregiver Support Group Available

Are you caring for a family member or friend with AD, dementia or related disorder? Do you have questions or concerns about providing care, about AD or other dementia? Our support group meeting may be your answer. The IADC together with the Healthy Aging Brain Center and the Alzheimer's Association, facilitates a monthly support for caregivers. All family members are welcome.

The meeting is held on **the 4th Friday of each month from 1:00 – 3:00 pm at the Indianapolis Senior Center at 801 East Michigan Street**. We meet in the community room.

Feel free to join for education and social support. For more information please contact the Education Core at 317.274.4939 or email rcludy@iupui.edu.

Mouse Study

(Continued from page 2)

Dr. Martin Farlow, Core Leader of the Clinical Core at the Indiana Alzheimer Disease Center said, ***"New approaches to drug therapy in AD are badly needed. The mechanism being investigated here is lowering potentially toxic levels of calcium in nerve cells with the drug diazoxide. Previous studies with drugs having similar effects on intracellular calcium levels have not proved beneficial in human trials. Nonetheless, all potential leads need to be developed and it will be interesting to see if diazoxide proves helpful for treating AD patients in the future".***

IADC's 5th Annual Spring Symposia Huge Success

On March 18th and 19th 2011 the Indiana ADC hosted its annual spring symposia. The scientific program, held on March 18th, provided participants with an overview of the many areas of research currently underway at the IADC. On March 19th, the 5th Annual Martin Family AD Caregiver Symposium, entitled, *Caring for the Person with Dementia in the Home* provided participants with useful, practical tips for providing care in the home. We are particularly thankful to our sponsors and exhibitors whose generous support helped to make this year's symposia a huge success.

Our appreciation goes out to the following sponsors and exhibitors:

- IUPUI Conference Fund
- IU Department of Psychiatry Wesley P Martin Professorship for AD Education
- **Presenting Sponsor—** CICOA Aging & In-Home Solutions
- Our parking sponsor— Home Instead Senior Care, To us, it's personal.
- Our coffee break sponsor— Joy's House, Care and Community for Adults

Exhibitors

- IU Center for Alzheimer Disease and Related Disorders National Cell Repository Clinical Drug Trials, Basic and Social Behavioral Research — Indiana University School of Medicine
- The Alzheimer's Association of Greater Indiana — alzheimer's association, the compassion to care, the leadership to conquer
- Community Hospital's — Touchpoint, Healthy Life Transition

We look forward to seeing everyone at the 6th annual symposia in 2012.

Save the Dates...Save the Dates...Save

Memory University 2011

Riley Outpatient Center Auditorium
702 Barnhill Drive
Indianapolis, IN 46202

Four Consecutive Thursdays:
May 26th, June 2nd, 9th, and 16th

For more information or to register for these programs call 317.274.4939 or email: rcludy@iupui.edu

Is Alzheimer Disease in your family photo?

If there are two or more living members of your family suffering from serious memory loss, our researchers may be interested in your family.

Please contact the National Cell Repository for Alzheimer Disease, (NCRAD) to learn more about this research opportunity.

E-mail NCRAD at alzstudy@iupui.edu

or call

317- 274-7360

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