Folsom, Calif., (October 21, 2014) – A new animal study published in the *Journal of Alzheimer's Disease* indicates that a diet including walnuts may have a beneficial effect in reducing the risk, delaying the onset, slowing the progression of, or preventing Alzheimer's disease.

Research led by Abha Chauhan, PhD, head of the Developmental Neuroscience Laboratory at the New York State Institute for Basic Research in Developmental Disabilities (IBR), found significant improvement in learning skills, memory, reducing anxiety, and motor development in mice fed a walnut-enriched diet.

The researchers suggest that the high antioxidant content of walnuts (3.7 mmol/ounce) may have been a contributing factor in protecting the mouse brain from the degeneration typically seen in Alzheimer's disease. Oxidative stress and inflammation are prominent features in this disease, which affects more than five million Americans.

"These findings are very promising and help lay the groundwork for future human studies on walnuts and Alzheimer's disease – a disease for which there is no known cure," said lead researcher Dr. Abha Chauhan, PhD. "Our study adds to the growing body of research that demonstrates the protective effects of walnuts on cognitive functioning."

The research group examined the effects of dietary supplementation on mice with 6 percent or 9 percent walnuts, which are equivalent to 1 ounce and 1.5 ounces per day, respectively, of walnuts in humans. This research stemmed from a previous cell culture study led by Dr. Chauhan that highlighted the protective effects of walnut extract against the oxidative damage caused by amyloid beta protein. This protein is the major component of amyloid plaques that form in the brains of those with Alzheimer's disease.
Someone in the United States develops Alzheimer's disease every 67 seconds, and the number of Americans with Alzheimer's disease and other dementias are expected to rapidly escalate in coming years as the baby boom generation ages. By 2050, the number of people age 65 and older with Alzheimer's disease may nearly triple, from five million to as many as 16 million, emphasizing the importance of determining ways to prevent, slow or stop the disease. Estimated total payments in 2014 for all individuals with Alzheimer's disease and other dementias are $214 billion.

Walnuts have other nutritional benefits as they contain numerous vitamins and minerals and are the only nut that contains a significant source of alpha-linolenic acid (ALA) (2.5 grams per ounce), an omega-3 fatty acid with heart and brain-health benefits. The researchers also suggest that ALA may have played a role in improving the behavioral symptoms seen in the study.

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An article detailing these findings, "Dietary Supplementation of Walnuts Improves Memory Deficits and Learning Skills in Transgenic Mouse Model of Alzheimer's Disease," has been published in the October issue of Journal of Alzheimer's Disease 42(4): 1397-1405 (2014) [http://iospress.metapress.com/content/n644184610325684/].

Co-authors with Dr. Chauhan are Balu Muthaiyah, PhD; Musthafa M. Essa, PhD; Moon Lee, PhD; Ved Chauhan, PhD; and Kulbir Kaur, PhD, of IBR's Department of Neurochemistry. This study was supported in part by funds from the New York State Office for People with Developmental Disabilities and the California Walnut Commission.
Cold Sore Virus Increases the Risk of Dementia

Oct 13, 2014 — Infection with herpes simplex virus increases the risk of Alzheimer’s disease. Researchers at Umeå University claim in two studies published in the journal Alzheimer’s & Dementia.

Photo: Erik Lövbom

"Our results clearly show that there is a link between infections of herpes simplex virus and the risk of developing Alzheimer's disease. This also means that we have new opportunities to develop treatment forms to stop the disease," says Hugo Lövheim, associate professor at the Department of Community Medicine and Rehabilitation, Geriatric Medicine, Umeå University, who is one of the researchers behind the study.

Alzheimer's disease is the most common among the dementia diseases. In recent years research has increasingly indicated that there is a possible connection between infection with a common herpes virus, herpes simplex virus type 1, and Alzheimer's disease. A majority of the population carries this virus. After the first infection the body carries the virus throughout your lifetime, and it can reactivate now and then and cause typical mouth ulcers. The hypothesis which links the herpes virus and Alzheimer's disease is based on a weakened immune system among the elderly that creates opportunities for the virus to spread further to the brain. This can in turn start the process which results in Alzheimer's disease.

Hugo Lövheim and Fredrik Elgh, professor at the Department of Virology, have now confirmed this link in two large epidemiological studies. In one study, which is based on the Betula project, a study on aging, memory and dementia, the researchers showed that a reactivated herpes infection doubled the risk of developing Alzheimer's disease. This study had 3,432 participants who were followed for 11.3 years on average. In another study, samples donated to the Medical Biobank at Umeå University from 360 people with Alzheimer's disease were examined and compared to matched people who had not developed dementia. The samples were taken on average 9.6 years before diagnosis. This study showed an approximate double risk of developing Alzheimer's disease if the person was a carrier of the herpes virus.

"Something which makes this hypothesis very interesting is that now a herpes infection can in principle be treated with antiviral agents. Therefore within a few years we hope to be able to start studies in which we will also try treating patients to prevent the development of Alzheimer's disease," says Hugo Lövheim.

Herpes simplex infection and the risk of Alzheimer's disease—a nested case-control study; Alzheimer's & Dementia; Published Online: October 07, 2014; doi: http://dx.doi.org/10.1016/j.jalz.2014.07.157
An innovative laboratory culture system has succeeded, for the first time, in reproducing the full course of events underlying the development of Alzheimer's disease. Using the system they developed, investigators from the Genetics and Aging Research Unit at Massachusetts General Hospital (MGH) now provide the first clear evidence supporting the hypothesis that deposition of beta-amyloid plaques in the brain is the first step in a cascade leading to the devastating neurodegenerative disease. They also identify the essential role in that process of an enzyme, inhibition of which could be a therapeutic target.

“Originally put forth in the mid-1980s, the amyloid hypothesis maintained that beta-amyloid deposits in the brain set off all subsequent events – the neurofibrillary tangles that choke the insides of neurons, neuronal cell death, and inflammation leading to a vicious cycle of massive cell death,” says Rudolph Tanzi, PhD, director of the MGH Genetics and Aging Research Unit and co-senior author of the report receiving advance online publication in Nature. “One of the biggest questions since then has been whether beta-amyloid actually triggers the formation of the tangles that kill neurons. In this new system that we call ‘Alzheimer’s-in-a-dish,’ we’ve been able to show for the first time that amyloid deposition is sufficient to lead to tangles and subsequent cell death.”

While the mouse models of Alzheimer’s disease that express the gene variants causing the inherited early-onset form of the disease do develop amyloid plaques in their brains and memory deficits, the neurofibrillary tangles that cause most of the damage do not appear. Other models succeed in producing tangles but not plaques. Cultured neurons from human patients with Alzheimer’s exhibit elevated levels of the toxic form of amyloid found in plaques and the abnormal version of the tau protein that makes up tangles, but not actual plaques and tangles.

Genetics and Aging Research Unit investigator Doo Yeon Kim, PhD, co-senior author of the Nature paper, realized that the liquid two-dimensional systems usually used to grow cultured cells poorly represent the gelatinous three-dimensional environment within the brain. Instead the MGH team used a gel-based, three-dimensional culture system to grow human neural stem cells that carried variants in two genes – the amyloid precursor protein and presenilin 1 – known to underlie early-onset familial Alzheimer’s Disease (FAD). Both of those genes were co-discovered in Tanzi’s laboratory.
After growing for six weeks, the FAD-variant cells were found to have significant increases in both the typical form of beta-amyloid and the toxic form associated with Alzheimer’s. The variant cells also contained the neurofibrillary tangles that choke the inside of nerve cells causing cell death. Blocking steps known to be essential for the formation of amyloid plaques also prevented the formation of the tangles, confirming amyloid’s role in initiating the process. The version of tau found in tangles is characterized by the presence of excess phosphate molecules, and when the team investigated possible ways of blocking tau production, they found that inhibiting the action of an enzyme called GSK3-beta – known to phosphorylate tau in human neurons – prevented the formation of tau aggregates and tangles even in the presence of abundant beta-amyloid and amyloid plaques.

“This new system – which can be adapted to other neurodegenerative disorders – should revolutionize drug discovery in terms of speed, costs and physiologic relevance to disease,” says Tanzi. “Testing drugs in mouse models that typically have brain deposits of either plaques or tangles, but not both, takes more than a year and is very costly. With our three-dimensional model that recapitulates both plaques and tangles, we now can screen hundreds of thousands of drugs in a matter of months without using animals in a system that is considerably more relevant to the events occurring in the brains of Alzheimer’s patients.”

Tanzi is the Kennedy Professor of Child Neurology and Mental Retardation, and Kim is an assistant professor of Neurology at Harvard Medical School. Se Hoon Choi, PhD, and Young Hye Kim of the MGH Genetics and Aging Research Unit are co-lead authors of the Nature paper. The study was supported by a grant from the Cure Alzheimer’s Fund and by National Institute of Health grants 5P01AG15379 and 5R37MH060009.
Physical Exercise in Old Age Can Stimulate Brain Fitness, But Effect Decreases with Advancing Age

By Dr. Marcus Neitzert
DZNE

Magdeburg/Germany, October 14th, 2014. Physical exercise in old age can improve brain perfusion as well as certain memory skills. This is the finding of Magdeburg neuroscientists who studied men and women aged between 60 and 77. In younger individuals regular training on a treadmill tended to improve cerebral blood flow and visual memory. However, trial participants who were older than 70 years of age tended to show no benefit of exercise. Thus, the study also indicates that the benefits of exercise may be limited by advancing age. Researchers of the German Center for Neurodegenerative Diseases (DZNE), the University of Magdeburg and the Leibniz Institute for Neurobiology have published these results in the current edition of the journal “Molecular Psychiatry”. Scientists at the Karolinska Institute in Stockholm and the Max Planck Institute for Human Development were also involved in the study.

The 40 test volunteers were healthy for their age, sedentary when the study commenced and divided into two groups. About half of the study participants exercised regularly on a treadmill for 3 months. The other individuals merely performed muscle relaxation sessions. In 7 out of 9 members of the exercise group who were not more than 70 years old, the training improved physical fitness and also tended to increase perfusion in the hippocampus – an area of the brain which is important for memory function. The increased perfusion was accompanied by improved visual memory: at the end of the study, these individuals found it easier to memorize abstract images than at the beginning of the training program. These effects were largely absent in older volunteers who participated in the workout as well as in the members of the control group. The study included extensive tests of the volunteers’ physical condition and memory. Furthermore, the study participants were examined by magnetic resonance imaging (MRI). This technique enables detailed insights into the interior of the brain.

Exercising against dementia
Physical exercise is known to have considerable health benefits: the effects on the body have been researched extensively, the effects on brain function less so. An increase in brain perfusion through physical exercise had previously only been demonstrated empirically in younger people. The new study shows that some aging brains also retain this ability to adapt, even though it seems to decrease with advancing age. Furthermore, the results indicate that changes in memory performance resulting from physical exercise are closely linked to changes in brain perfusion.

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“Ultimately, we aim to develop measures to purposefully counteract dementia such as Alzheimer’s disease. This is why we want to understand the effects of physical exercise on the brain and the related neurobiological mechanisms. This is essential for developing treatments that are truly effective,” is how Professor Emrah Düzel, site speaker of the DZNE in Magdeburg and director of the Institute of Cognitive Neurology and Dementia Research at the University of Magdeburg, explains the background to the study.

The goal: new brain cells
The researchers’ goal is to cause new nerve cells to grow in the brain. This is how they intend to counter the loss of neurons typical of dementia. “The human brain is able to change and evolve throughout our lives. New nerve cells can form even in adult brains,” says Düzel. “Our aim is to stimulate this so-called neurogenesis. We don't yet know whether our training methods promote the development of new brain cells. However, fundamental research shows that the formation of new brain cells often goes hand in hand with improved brain perfusion.”

Changes in the hippocampus
Indeed, it did turn out that the treadmill exercise sessions caused more blood to reach the hippocampus in younger participants. “This improves the supply of oxygen and nutrients and may also have other positive effects on the brain’s metabolism,” says the neuroscientist. “However, we have also seen that the effect of the training decreases with age. It is less effective in people aged over 70 than in people in their early 60s. It will be an important goal of our research to understand the causes for this and to find remedies.”

Düzel adds: “It is encouraging to see that visual memory improved as brain perfusion increased. However, effective treatments would also have to affect other brain functions. In our study, the effect was limited to visual short-term memory.”

A combined training for body and mind
Other experiments are now under way in Magdeburg in which test participants are sent on an unusual kind of scavenger hunt: they are assigned the task of finding objects concealed in a computer-generated landscape which is pictured on a large screen. Movement control in this virtual world is done with the help of a treadmill. “This complex situation makes high demands on motor skills and sense of orientation,” explains Düzel. “It challenges both the brain as well as the muscles.”

In the long term, the scientists aim to include people in the early stages of Alzheimer’s disease in their study program. “We are looking for ways of delaying or even stopping the progression of the disease. And we are also researching methods of prevention,” emphasizes Düzel. “Connecting physical activity and mental exercise may have a broad impact, and combined training might become a therapeutic approach. However, this has yet to be shown. In fact, our current results suggest that we may need pharmacological treatments to make exercise more effective.”

Vascular hippocampal plasticity after aerobic exercise in older adults
Anne Maass, Sandra Düzel, Monique Goerke, Andreas Becke, Uwe Sobieray, Katja Neumann, Martin Lövdén, Ulman Lindenberger, Lars Bäckman, Rüdiger Braun-Dullaeus, Dörte Ahrens, Hans-Jochen Heinz, Notger G. Müller, Emrah Düzel.
Molecular Psychiatry, 2014, doi:10.1038/mp.2014.114
By Barbara Overholser, University of Pennsylvania

What’s it like to live with Mild Cognitive Impairment? What’s a typical day for an Alzheimer’s patient? How does a painter express what the mind is? How does a singer tell the story of her mother’s dementia?

These are some of the stories you can read about, listen to, and watch on the new website [makingsenseofalzheimers.org](http://makingsenseofalzheimers.org). It was produced by the Penn Neurodegenerative Disease Ethics and Policy program and the Outreach, Recruitment, and Education Core of the Alzheimer’s Disease Center at the University of Pennsylvania and made possible by a startup grant from MetLife Foundation. The website launched in September 2014.

Making Sense of Alzheimer’s is an evolving forum for conversation about the disease. Its collection of ideas captures the many dimensions of Alzheimer’s, through the perspective of caregivers, patients, artists, researchers and clinicians. Utilizing multi-media formats such as slideshows, video, and audio clips, along with written stories, the site explores the changing understanding of what Alzheimer’s is and how it affects our ethics and ideas of personhood.

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Making Sense cont’d……

Jason Karlawish, M.D., director of Penn’s Neurodegenerative Disease Ethics and Policy program and director of the Outreach, Recruitment and Education Core at Penn’s ADC, explains, “Making Sense of Alzheimer’s is a space where we can think about the language of Alzheimer’s disease, including terms like “biomarkers,” “preclinical Alzheimer’s disease,” “amyloid imaging,” and “mild cognitive impairment due to Alzheimer’s disease,” so that people can understand and critique the changing dynamics involved in the diagnosis and treatment Alzheimer’s disease.”

The site is organized into four categories.

“History of Alzheimer’s” features pieces about the history and possible futures of the disease and interviews with researchers and clinicians. A detailed, interactive timeline walks visitors through important dates in Alzheimer’s research history.

“Making Sense of It” explores the perspective of patients, caregivers, family members and others affected by the disease. Here, a poem reflects on issues around personhood and anatomy; a video interview with singer Jonatha Brooke looks at her musical play, My Mother Has 4 Noses; and a writer caring for her mother with dementia finds solace in meditation.

Because Alzheimer’s is more than a disease of the brain — it’s also a disease of the mind — “Art of the Mind” features a rotating slate of artists exhibiting their reflection of what the mind means to them.

The fourth category – “What’s Coming Up?” offers previews of stories in development.

“Makingsenseofalzheimers.org springs from the ideas and stories of our community,” says website editor Barbara Overholser. “Contributors can email ideas and comments to comments@makingsenseofAD.org.”
Would-be parents from families carrying devastating genetic mutations face a formidable decision: Should they have children and risk passing on the disease? It is even more complicated when the at-risk parent doesn’t know his or her genetic status, and wants to keep it that way. There is a procedure that enables them to circumvent these concerns. At the 139th annual meeting of the American Neurological Association, held October 12-14 in Baltimore, Murali Doraiswamy of Duke University, Durham, North Carolina, described the first such case from a family carrying a presenilin 1 (PS1) mutation. The woman, who chose to remain anonymous, now has 2-year old twins who have almost zero chance of carrying a familial AD mutation.

For the past two decades, doctors have used a combination of in vitro fertilization and preimplantation genetic diagnosis (PGD) to implant only embryos they know to have escaped the particular family mutation. Doctors can perform the procedure without revealing whether the parent carries the harmful gene. However, even after 20 years, PGD remains relatively unknown, especially among families carrying alleles for familial Alzheimer’s disease (FAD). Not even a dozen couples from such families have used the procedure to conceive, in part because few know about it.

While this 30-year-old woman wanted to spare her children the prospect of early onset Alzheimer’s, she did not want to know if she carried the mutant PS1 herself. To conceal her status, a team headed by Svetlana Rechitsky of Reproductive Genetics Institute, Northbrook, Illinois, performed what’s called indirect linkage analysis on cells from nine embryos conceived by in vitro fertilization. This was to ensure the woman passed on a normal copy of the PS1 gene, inherited from her father, rather than a mutant copy, which would have come from her mother, who had a confirmed diagnosis of AD. Rechitsky and colleagues conducted genetic testing on the couple and their parents to identify genetic markers that lay near PS1. Then they screened the embryos to identify those that contained the unaffected grandfather’s copy of the gene, then implanted only those embryos. The point of this process is that the researchers never looked for the mutant PS1 allele itself. If a chromosome had markers around PS1 from the woman’s affected mother, that embryo was considered “at risk” of containing the mutated PS1 allele, and was not implanted.

PGD is not widely recognized as a potential solution for families who carry early onset AD mutations. Some of the few couples who have undergone PGD for FAD know about it from their own professional experience as doctors, geneticists, or neuroscientists, or they found out about it while seeking in vitro fertilization for other reasons, Doraiswamy told Alzforum. Some who learned about it in later years say they would have considered it before having children, but only a trickle of FAD cases comes through the door, said Doraiswamy. “Doctors and patients need to be educated,” he said.

Another problem is that few insurance companies in the United States, and only some in other countries, cover in vitro fertilization for fertile couples, while PGD is not covered for any conditions in the United States, according to Doraiswamy. The expense for combined PGD and in vitro fertilizations, which can run to $30,000 or more, deters couples, he said. On the other hand, a young woman from a different family who is similarly at risk of FAD but was not connected to this case told Alzforum, on condition of anonymity, that even if her insurance did cover PGD, she would not trust that her information would be kept confidential.

So long as cost and genetic privacy remain obstacles, PGD may well remain a high-tech option for the affluent few.—Gwyneth Dickey Zakaib
ADCS Clinical Trials Enrolling...

For information on the following studies please visit:

http://www.adcs.org/Studies/clinalResearchStudy.aspx

A4 – Anti Amyloid in Asymptomatic Alzheimer’s Disease

NOBLE
A New Study for People with Mild to Moderate Alzheimer’s Disease

On a temporary enrollment hold:
SNIFF – the Study of Nasal Insulin to Fight Forgetfulness
The Dominantly Inherited Alzheimer Network (DIAN). DIAN is an international research partnership of leading scientists determined to understand a rare form of Alzheimer’s disease that is caused by a gene mutation. Understanding of this form of Alzheimer's disease may provide clues to decoding other dementias and developing dementia treatments.

Funded by a multiple-year research grant from the National Institute on Aging, DIAN currently involves thirteen outstanding research institutions in the United States, United Kingdom, Germany and Australia. John C. Morris, M.D., Friedman Distinguished Professor of Neurology at Washington University School of Medicine in St. Louis, is the project’s principal investigator.

DIAN is currently enrolling study participants who are biological adult children of a parent with a mutated gene known to cause dominantly inherited Alzheimer’s disease. Such individuals may or may not carry the gene themselves and may or may not have disease symptoms (click here for information about genetic testing).

To register for DIAN drug trials or DIAN, visit www.DIANExpandedRegistry.org.