Insulin’s Relationship to Alzheimer’s Disease

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Insulin is critical for normal brain function, and several observations including an increased risk of developing Alzheimer’s Disease (AD) for diabetic patients, and reduced insulin levels in the brain tissue of AD patients, have suggested a link between the two diseases.

The Rotterdam Study in the Netherlands was one of the first epidemiological surveys to provide convincing evidence for a relationship between diabetes mellitus and AD by demonstrating that diabetes mellitus doubled the risk for AD, particularly in individuals who required insulin.

It has been hypothesized that raising brain levels of insulin to normal might help patients suffering from Mild Cognitive Impairment or AD to maintain cognitive ability, and last year a phase II clinical trial of inhaled insulin demonstrated that participants who took 20 IUs of insulin a day showed some improved memory functioning.

Now, two back-to-back research articles recently published in the Journal of Clinical Investigation – led by Konrad Talbot colleagues at the University of Pennsylvania and by Fernanda De Felice and colleagues at the University of Rio de Janeiro – address the connection between insulin resistance and AD on a molecular level. The University of Pennsylvania team examined insulin signaling and found that the activation of many insulin signaling molecules were highly related to memory and cognitive function, and were directly affected by beta-amyloid. They further confirmed that insulin resistance is a common and early feature of AD.

The Rio de Janeiro group further observed impaired insulin signaling in a mouse model of AD as well as from tissue from human patients. They went on to show in the mouse model of AD that treatment with a new anti-diabetic drug, Exendin-4, normalized insulin signaling and improved cognitive function. The drug was discovered as a protein in 1992, as a naturally secreted substance in the saliva and concentrated in the tail of the Gila monster. In 2005, the FDA approved the synthetic version called Exenatide for patients whose diabetes was not controlled by oral medications.
The cumulative results of these two studies should be put into context: Beta-amyloid that has been formed in the brain, but yet to deposit into plaques, is thought to be the main cause of memory loss and brain cell injury in AD. It appears that insulin may activate a defense mechanism that protects brain cells from damage caused by beta-amyloid. And the protective action of insulin requires signals that are transmitted inside of brain cells and block beta-amyloid from binding to neurons. However, beta-amyloid disrupts this very mechanism and leads to further brain cell injury.

Undoubtedly, follow up research is needed to confirm these findings and extend them towards developing anti-diabetes drugs that could potentially treat the symptoms of AD.

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**The Pioneers: Alzheimer’s Disease and Solomon Carter Fuller, MD**

Solomon Carter Fuller, born in 1872, was a neurologist and the United States’s first African-American psychiatrist. He played a key role in the development of psychiatry in the 1900s and is well known for his research on dementia. Dr. Fuller is credited with helping make the United States the leader in psychiatry that it is today.

Dr. Fuller’s grandfather had been a slave in Virginia who purchased his freedom and moved his family to Liberia. At the age of seventeen, Fuller left Liberia to attend Livingstone College in North Carolina. He studied medicine at Long Island College Hospital and Boston University School of Medicine where he received his MD in 1897. Dr. Fuller then went to the University of Munich where he studied under Emil Kraepelin, the founder of modern psychiatric genetics, and Alois Alzheimer.

Upon graduation, Dr. Fuller became a pathologist at Westborough State Hospital in Massachusetts where he worked for twenty-two years. Dr. Fuller also joined the medical faculty at Boston University School of Medicine and taught for thirty-four years, eventually becoming emeritus professor of neurology.

Fuller became known for his work on AD and on the biological causes of disorders such as schizophrenia and manic depressive psychosis (bipolar disorder). He published the first comprehensive clinical review of all Alzheimer’s cases known at the time and was also the first person to translate much of Alois Alzheimer’s work on AD from German to English.

Today, in recognition of Dr. Fuller’s achievements, the mental health facility at Boston University is now officially known as the Dr. Solomon Carter Fuller Mental Health Center. And in 1972, the American Psychiatric Association and the Black Psychiatrists of America established the Solomon Carter Fuller Institute.

*Excerpted from the U.S. Department of Health & Human Services, Office of Minority Health*

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**Caregiver Compendium**

**Highlights of the Caregiver Sections of the Draft National AD Plan**

The National Alzheimer’s Project Act of 2011 (NAPA) mandates that the US Department of Health and Human Services (HHS) develop a National Plan for Alzheimers Disease and Related Disorders (National Plan). With input from the public-private Advisory Council on Alzheimer’s Research, Care and Services (Advisory Council), one important component of the draft National Plan deals with some of the challenges faced by families and caregivers in Alzheimer’s Disease (AD).

**Expanded Support for Caregivers and Families**

Family members and other informal caregivers, who take on the responsibility of caring for a loved one with AD, need support. The majority of people with AD live in the community, where their families provide most of their care. The constant need to provide care can take a toll - with about one-third of caregivers reporting symptoms of depression. In addition, stigmas and misconceptions associated with AD are widespread and profoundly impact the care provided.

In April, the Advisory Council will begin to draft the final National Plan. The following text outlines certain substantive issues, policies, and resources related to families and caregiving within the draft National Plan.
Caregiver Compendium continued:

The Draft National Plan recognizes that people with AD and their families need support that goes beyond the care provided in formal settings. To address these issues, the Draft Plan sets forth the following:

**Issue:** Ensure receipt of education, training, and support materials

Caregivers report that they feel unprepared for some of the challenges of caring for a person with Alzheimer’s disease—such as caring for a loved one with sleep disturbances, behavioral changes, or in need of physical assistance. There are many opportunities for informatics to support caregiver needs including cognitive support to help with reminders; messaging between caregivers, patients, and providers; in-house monitoring tools; pharmacy error checking; and enhanced decision support for self-care.

**Issue:** Identify unmet service needs to enable family caregivers to provide care while maintaining their own health and well-being

While they are providing care, support for families and caregivers can help lessen feelings of depression and stress and help delay nursing home placement.

HHS will analyze surveys and datasets, such as the Caregiver Supplement to the National Health and Aging Trends Study, to identify the service needs of caregivers of people with AD. HHS will work with its partners at the state and local levels to identify unmet service and respite needs.

**Issue:** Review the state of the art of evidence-based interventions that can be delivered by community-based organizations

HHS will partner with private organizations to convene a meeting, with leading AD scientists, physicians and researchers, to focus on interventions that have been effective in improving the health and well-being of persons with Alzheimer’s disease and their caregivers.

**Issue:** Develop and disseminate evidence-based interventions for people with Alzheimer’s disease and their caregivers

HHS will expand its support for research and conduct trials and demonstration projects for evidence-based interventions to support individuals with Alzheimer’s disease and their caregivers.

**Issue:** Provide effective caregiver interventions through AD-capable systems

The US Administration on Aging (AoA) will expand efforts to develop more AD-capable long-term services and supports systems designed to meet the needs of AD caregivers. Caregivers will be connected to supportive services such as respite care. Caregivers will be linked to interventions shown to decrease burden and depression among caregivers and enhance the care received by people with AD.

**Issue:** Examine awareness of long-term care needs and barriers to planning for these needs

HHS is working to better understand why middle-aged adults do or do not plan for long-term care needs. HHS will conduct a national survey to examine attitudes toward long-term care. It will also identify barriers to long-term care planning. HHS will incorporate information about AD into its materials for the public “Long-Term Care Awareness Campaign.”

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**NIH Expands Site and Resources on NIHSeniorhealth.gov**

NIHSeniorHealth.gov has a fresh look and enhanced features including 60 health topics relevant to older Americans, more than 150 health videos, plenty of frequently asked questions (FAQs) and more. The revamped web site is a great resource for anyone seeking fast, reliable, up-to-date information about older adults and health. You will also find extensive, streamlined, current information relating to Alzheimer’s Disease and a Alzheimer’s caregiving. [http://nihseniorhealth.gov/category/memoryandmentalhealth.html](http://nihseniorhealth.gov/category/memoryandmentalhealth.html)
ADCS Trials Enrolling...

Nerve Growth Factor Study (NGF)

The NGF is a Phase II clinical study of Ceregene’s CERE-110, a gene therapy product designed to deliver nerve growth factor (NGF) to the brain for the treatment of Alzheimer’s disease (AD) is currently underway. This study is a randomized, double-blind, placebo-controlled trial and employs gene therapy to deliver nerve growth factor (NGF) directly into the brain.

http://adcs.org/Studies/NGF.aspx

ADNI II Study

The goal of the Alzheimer’s Disease Neuroimaging Initiative Study is to learn how to stop the progression of mild cognitive impairment (MCI) and Alzheimer’s disease in future generations. Information from the study might, in the future, lead to new treatments.

http://adcs.org/Studies/ImagineADNI2.aspx

Next Month in the Newsletter:

Resveratrol for Alzheimer’s – the clinical trial begins

Resveratrol for Alzheimer’s Disease