MEDICAL FOOD, NUTRITIONAL SUPPLEMENTS, & ALZHEIMER’S DISEASE: DO THEY WORK AND ARE THEY SAFE?

GREETING FROM THE PRINCIPAL INVESTIGATOR PAGE 2

THE AMYLOID THEORY- STILL VIABLE?

RESEARCH ROUND-UP

PAGE 6

WWW.ADCS.ORG
Dear HBA Participants,

It’s hard to believe that summer is here. Wasn’t it New Year’s just yesterday? Remember all those New Year’s resolutions and promises to improve or change some aspect of your life? Well, it’s much like the HBA trial. Resolutions require follow up in order to make them stick; just like recruitment into a research trial (like HBA) requires more than enrolling willing volunteers into a study. After enrollment comes follow up, constant and consistent follow up. In other words, staying the course of the whole study.

I am sure you have heard how costly it is both in time and money to conduct research. Yes it is expensive, but it is money and time well spent for the good of finding out if theories work and improving health. The initial expense of conducting a study is the recruitment phase, when we were looking for you and asking you to participate in this study. As a study progresses people sometimes want to quit and if they do all the data we have collected on those people will be for naught and the time and money everyone invested (including the study volunteers) will be lost. In short, we can’t do this trial without you continuing to the very end. We know it is a long study and we know it can be burdensome at times, and we know there may be other things you would like to do, but we implore you to stay with us. We would not ask if it wasn’t important. I assure you it is that important. We’re in this together.

Finally, I would like to encourage you to send us any ideas you may have about HBA. For example in the last issue we inserted a pre-paid postcard asking you what you liked and/or disliked about this newsletter. Based on your responses we made the articles “meatier” with more information on research. We listened and are featuring several exciting articles in this issue and will continue to do so in the future. Our next newsletter will report to you on how we are doing with follow-up in this study. We will let you know how many of you successfully completed each of the visits and we will tell you how we will use the data to improve our methods of assessing memory and thinking in your home. If you have any other ideas please email us at Brainlink@ucsd.edu. We want to hear from you.

Thank you for staying with us. We cannot express enough how grateful we are.

Mary Sano, Ph.D
HBA Principal Investigator
Director, Mount Sinai Alzheimer’s Disease Research Center
Much ink has been spilled as to whether the amyloid hypothesis is the correct path for Alzheimer’s disease (AD) research. The amyloid hypothesis is supported by a huge body of evidence, but to my thinking the most convincing support is based on genetically determined AD.

Mutations of three different genes can cause familial autosomal dominant (FAD) AD in affected families. In such families, the mutated gene is causative, that is, each child who inherits the mutated gene will definitely develop the disease, often within a narrow age range (e.g., between ages 38 and 41). Children of an affected parent have a 50% chance of inheriting the mutated gene.

A gene codes a single protein. When a gene causes a disease, it means that the protein coded by that gene causes the disease. We know that AD can be caused by three distinct proteins coded by the mutated genes. These proteins must be sufficient to cause familial AD.

And what are these proteins? Amyloid precursor protein (APP), presenilin (PS) 1 and PS2. What do these mutated proteins have in common? The proteins are each directly involved in generating beta-amyloid, a hallmark of AD. The mutations of APP alter how APP is processed in the brain, resulting in excess generation of beta-amyloid. PS1 and PS2 mutations increase the generation of the most toxic form of beta-amyloid. So each of the mutations does the same thing: increases generation of toxic beta-amyloid. The only reasonable conclusion is that beta-amyloid causes FAD.

Moreover, the gene for APP is located on chromosome 21, and people with an extra copy of this chromosome (those with Down Syndrome) almost universally exhibit AD by age 40. Almost all cases of AD are sporadic, that is, not caused by the inherited genetic mutations associated with FAD; FAD is rare. However, FAD only differs from sporadic AD in terms of age of onset and inheritance. This very strongly indicates that sporadic AD is also triggered by beta-amyloid.

Why is excess beta-amyloid produced in sporadic AD, that is, in the absence of the mutations that cause FAD? Multiple factors are likely to contribute to excess production of beta-amyloid. These include genetic (e.g., the form of apolipoprotein E inherited from one’s parents), biological (e.g., aging) and environmental (e.g., head trauma, lifestyle) factors. These factors together determine one’s susceptibility to sporadic AD.

For now, we believe the best path to finding an effective treatment for AD lies in further research on beta-amyloid and determining best how to not only treat the disease when it manifests but to prevent it from occurring in the first place.
Many people with memory problems look beyond medications to dietary supplements or so-called medical foods for additional help. Is this wise? Recent surveys have shown that approximately 50% of elders take at least one dietary supplement. Though the label might claim that this pill or drink can “improve memory” or “treat Alzheimer’s,” it is important to have a full understanding about these products before making a decision to take one.

There are two broad categories for these non-drug products: nutritional supplements and medical foods. Nutritional supplements include vitamins, minerals, herbs, meal supplements or sports nutrition products. These supplements usually come in a pill or drink form and are promoted to healthy adults to maintain good health or to help with a specific function such as energy or memory. Medical foods on the other hand are particular foods or diets that target people with a specific disease and may require a doctor’s prescription. A specifically formulated low protein diet for patients with kidney failure is an example of a medical food. These products are regulated as foods, meaning that Food and Drug Administration (FDA) inspectors are entitled to information about the manufacture of these foods in terms of cleanliness, consistency and quality control. Unlike drugs, however, medical foods do not need FDA review or approval to determine that they actually help patients. They are subject to the rules related to the safety of foods only. A drug must typically have been tested on hundreds or thousands of people starting with healthy volunteers and then moving to people with the actual disease. In contrast, nutritional supplements and medical foods do not need to be tested for efficacy – they are foods and food does not have to be useful or even healthy (e.g. the ingredients of a custard doughnut may be FDA-approved but certainly are not healthy or recommended regularly).

Let’s look at Axona™, an increasingly popular medical food targeted for Alzheimer’s patients. According to the company’s website, Axona™ (trade name for the AC-1202-containing drink) “is a specially formulated medical food intended for the clinical dietary management of the metabolic processes associated with mild to moderate AD.”

If you try to unpack the claim above, you will see the product is called a medical food (so outside the purview of FDA drug regulations), and it is targeted for Alzheimer’s patients but does not make claims to improve memory. Rather it is for the “management of metabolic processes.” This is a broad statement that doesn’t mean much. There are no ‘metabolic processes’ in Alzheimer’s that we understand sufficiently to recommend any specific intervention. This statement is the equivalent of saying, “patients with Alzheimer’s should exercise and follow a healthy diet.” It is true for all adults and has no proven specific benefit for Alzheimer’s. There are no claims made that this food product will help memory or function, the primary concerns of Alzheimer patients.

Are supplements and medical foods safe? “They are natural so they must be.”

Medical foods and food supplements are usually made from natural ingredients categorized as GRAS or generally regarded as safe. There is an assumption of safety, but the GRAS categorization does not mean,
Results from a randomized, double-blind, placebo-controlled, multicenter study of Souvenaid, a proprietary nutritional drink, in people with mild Alzheimer’s disease were recently published. The objective of the trial, printed in the latest issue of Alzheimer’s and Dementia, was to restore neuronal synapses by providing “rate-limiting precursors for membrane phosphatide synthesis, such as...uridine, omega-3 polyunsaturated fatty acids, and choline,” which Souvenaid contains.

Citing animal-model studies, the authors claimed, “These nutrients synergistically increase brain levels of phosphatide molecules that comprise the bulk of synaptic membranes, and brain levels of specific synaptic proteins, suggesting that they also increase synapse formation.” The researchers hypothesized that a similar effect in patients with Alzheimer’s disease might have clinical benefits. To test the idea, they enrolled 225 patients with mild disease, defined as a score of between 20 and 26 on the Mini-Mental State Examination.

The patients were randomly assigned to take 125-milliliters of the cocktail once a day, at breakfast, or a similarly packaged drink without the active ingredients (placebo). Although some results on memory performance were encouraging, the major outcome measures showed no effect at any time point.

Two additional trials with Souvenaid are underway: a European study, a 24-week study in drug-naive mild AD patients and a US based study (S-Connect), which will be a 24-week long study in mild-to-moderate AD patients already using AD medication.

- Michael Rafii, M.D.
Mediterranean Diet, Exercise and Risk of Developing Alzheimer’s Disease

Nikolas Scarmeas, M.D., associate professor of clinical neurology in the Department of Neurology, in the Sergievsky Center and in the Taub Institute for Research on Alzheimer’s Disease and the Aging Brain at Columbia University Medical Center, examined the association between physical activity and risk of AD and also the effect of physical activity and adherence to a Mediterranean-type diet on AD risk. This population-based study in a multi-ethnic community living in Northern Manhattan, observed 1880 elderly subjects, with an average age of 77. The participants were interviewed about their level of physical activity and dietary habits, and their responses were then summarized into two single scores. The study subjects were then followed to observe which subjects went on to develop Alzheimer’s over the course of approximately five and a half years.

To learn about their physical exercise routine, participants were queried about their activity during a two week period prior to the interview. The subjects were asked to quantify how many times they engaged in physical activity and for how long. Participants were queried regarding three categories of activities: vigorous activity (i.e., jogging etc), moderate activity (i.e., hiking, bicycling, etc), and light activity (i.e., golfing, gardening, etc).

For the dietary portion of the study, subjects were asked regarding their food consumption over the course of the previous year. Their responses were then grouped into nine food categories, the sum of which represented the Mediterranean-type diet score. A Mediterranean-type diet is typically characterized by high intake of fish, vegetables, legumes, fruits, cereals and monounsaturated fatty acids; relatively low intake of dairy products, meats and saturated fats; and moderate alcohol consumption.

Standardized neurological and neuropsychological measures were administered approximately every 1.5 years from 1992 through 2006. The participants received measurements of their adherence to a Mediterranean-type diet (scale of 0-9; categorized as low, middle, or high) and their physical activity (sum of weekly participation in various physical activities, weighted by the type of physical activity [light, moderate, vigorous]; categorized into no physical activity, some, or much, also low or high), separately and combined. A higher score for diet was obtained with higher consumption of fruits, vegetables, legumes, cereals, and fish; lower consumption of meat and dairy products; a higher ratio of monounsaturated fats to saturated fats; and mild to moderate alcohol consumption.

Individuals were followed up for an average of 5.4 years, during which a total of 282 developed AD. In considering only physical activity, the researchers found that more physical activity was associated with lower risk for developing AD. Compared with physically inactive individuals, report of some physical activity was associated with a 29 percent to 41 percent lower risk of developing AD, while report of much physical activity was associated with a 37 percent to 50 percent lower risk.

Further research will be needed to better understand the significance of this correlation.
New Form of Prion Disease that Damages Brain Arteries Study in Mice May Offer Clues for Treating Alzheimer’s Disease

Scientists investigating how prion diseases destroy the brain have observed a new form of the disease in mice that does not cause the sponge-like brain deterioration typically seen in prion diseases. Instead, it resembles a form of human Alzheimer’s disease, cerebral amyloid angiopathy, that damages brain arteries.

The study results, reported by scientists at the National Institute of Allergy and Infectious Diseases (NIAID), are similar to findings from two newly reported human cases of the prion disease Gerstmann-Straussler-Scheinker syndrome (GSS). This finding represents a new mechanism of prion disease brain damage, according to study author Bruce Chesebro, M.D., chief of the Laboratory of Persistent Viral Diseases at NIAID’s Rocky Mountain Laboratories.

Prion diseases, also known as transmissible spongiform encephalopathies, primarily damage the brain. Prion diseases include mad cow disease or bovine spongiform encephalopathy in cattle; scrapie in sheep; sporadic Creutzfeldt-Jakob disease (CJD), variant CJD and GSS in humans; and chronic wasting disease in deer, elk and moose.

The role of a specific cell anchor for prion protein is at the crux of the study. Normal prion protein uses a specific molecule, glycoposphoinositol (GPI), to fasten to host cells in the brain and other organs. In their study, the scientists genetically removed the GPI anchor from study mice, preventing the prion protein from fastening to cells and thereby enabling it to diffuse freely in the fluid outside the cells.

The scientists then exposed those mice to infectious scrapie and observed them for up to 500 days to see if they became sick. The researchers documented signs typical of prion disease including weight loss, lack of grooming, gait abnormalities and inactivity. But when they examined the brain tissue, they did not observe the sponge-like holes in and around nerve cells typical of prion disease. Instead, the brains contained large accumulations of prion protein plaques trapped outside blood vessels in a disease process known as cerebral amyloid angiopathy, which damages arteries, veins and capillaries in the brain. In addition, the normal pathway by which fluid drains from the brain appeared to be blocked.

Their study indicates that prion diseases can be divided into two groups: those with plaques that destroy brain blood vessels and those without plaques that lead to the sponge-like damage to nerve cells. The presence or absence of the prion protein anchor appears to determine which form of disease develops.

The new mouse model used in the study and the two new human GSS cases, which also lack the usual prion protein cell anchor, are the first to show that in prion diseases, the plaque-associated damage to blood vessels can occur without the sponge-like damage to the brain. If scientists can find an inhibitor for the new form of prion disease, they might be able to use the same inhibitor to treat similar types of damage in Alzheimer’s disease.

Do you have a friend or family member who is interested in participating in an AD research study? If so, information on research studies can be found at http://adcs.org/studies/clinicalresearchstudy.aspx.
BRAIN EXERCISE

Mind Games are a really fun way to exercise the mind. Check out the mind games on the BrainBashers website — http://www.brainbashers.com — good for people who want to stay sharp.

What is represented by this BrainBat?

***

A
D
M
E
U

Triangle

What is represented by this BrainBat?

****

D D D D D D D D D D D D D D D D

West Indies

Which of these is correct?

Six and six IS eleven or six and six ARE eleven

The answer is twelve!

What is represented by this BrainBat?

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D D D D D D D D D D D D

Bermuda

(WEST in "D"s)