

# MIT research offers new hope for Alzheimer's patients

April 27 2006

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MIT brain researchers have developed a "cocktail" of dietary supplements, now in human clinical trials, that holds promise for the treatment of Alzheimer's disease

For years, doctors have encouraged people to consume foods such as fish that are rich in omega-3 fatty acids because they appear to improve memory and other brain functions.

The MIT research suggests that a cocktail treatment of omega-3 fatty acids and two other compounds normally present in the blood, could delay the cognitive decline seen in Alzheimer's disease, which afflicts an estimated 4 million to 5 million Americans.

"It's been enormously frustrating to have so little to offer people that have (Alzheimer's) disease," said Richard Wurtman, the Cecil H. Green Distinguished Professor of Neuropharmacology at MIT, who led the research team. The study appears in the May 9 issue of *Brain Research*.

Wurtman will present the research at the International Academy of Nutrition and Aging 2006 Symposium on Nutrition and Alzheimer's Disease/Cognitive Decline in Chicago on Tuesday, May 2.

The three compounds in the treatment cocktail -- omega-3 fatty acids, uridine and choline -- are all needed by brain neurons to make phospholipids, the primary component of cell membranes.

After adding those supplements to the diets of gerbils, the researchers observed a dramatic increase in the amount of membranes that form brain cell synapses, where messages between cells are relayed. Damage in brain synapses is believed to cause the dementia that characterizes Alzheimer's disease.

If the successful results obtained in gerbils can be duplicated in the ongoing human trials, the new treatment could offer perhaps not a cure but a long-term Alzheimer's treatment similar to what L-dopa, a dopamine precursor, does for Parkinson's patients, said Wurtman, a professor in the Department of Brain and Cognitive Sciences.

"It doesn't cure Parkinson's, but what it does do is to help replace something that's missing. It's not permanent, but it has had an enormous impact on people who have Parkinson's," he said.

The new potential treatment offers a different approach from the traditional tactic of targeting the amyloid plaques and tangles that develop in the brains of Alzheimer's patients. Until recently, most researchers believed these plaques and tangles caused the cognitive decline. But the failure of this hypothesis to lead to an effective treatment for Alzheimer's disease has caused some scientists to theorize that, though the plaques and tangles are always associated with the disease, they may not be the main cause of the dementia, nor the best target for treating it.

Instead, the new research focuses on brain synapses, where neurotransmitters such as dopamine, acetylcholine, serotonin and glutamate carry messages from presynaptic neurons to receptors in the membranes of postsynaptic neurons. In Alzheimer's patients, synapses in the cortex and hippocampus, which are involved in learning and memory, are damaged.

After the dietary supplements were given, the researchers detected a large increase in the levels of specific brain proteins known to be concentrated within synapses, indicating that more synaptic membranes had formed, Wurtman said. Synaptic membrane protein levels rose if the gerbils were given either omega-3 fatty acids or uridine plus choline. However, the most dramatic upsurge was observed in gerbils fed all three compounds.

"To my knowledge, this is the first concrete explanation for the behavioral effects of taking omega-3 fatty acids," said Wurtman.

Choline can be found in meats, nuts and eggs, and omega-3 fatty acids are found in a variety of sources, including fish, eggs, flaxseed and meat from grass-fed animals. Uridine, which is found in RNA and produced by the liver and kidney, is not obtained from the diet. However, uridine is found in human breast milk, which is a good indication that supplementary uridine is safe for humans to consume, Wurtman said.

Recent studies by the researchers at MIT, and by scientists at Cambridge University in England, showed that either uridine or omega-3 fatty acids can promote the growth of neurites, which are small outgrowths of neuronal cell membranes. That further supports the hypothesis that omega-3 fatty acids increase synaptic membrane formation, said Wurtman.

Alzheimer's patients in the clinical trials, which will involve multiple medical centers, are being given a drink that contains the compounds under study, or a taste-matched placebo.

"If it works as well on the brains of people with Alzheimer's disease as it does in laboratory animals, I think there will be a lot of interest," Wurtman said.

Other authors on the paper are Ismail Ulus, Mehmet Cansev, Carol Watkins, Lei Wang and George Marzloff of MIT's Department of Brain and Cognitive Sciences. Ulus and Cansev also work at the Uludag University School of Medicine in Turkey.

Source: MIT

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