New approach to fighting Alzheimer's shows potential in clinical trial

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(PhysOrg.com) -- In the early stages of Alzheimer's disease, patients typically suffer a major loss of the brain connections necessary for memory and information processing. Now, a combination of nutrients that was developed at MIT has shown the potential to improve memory in Alzheimer's patients by stimulating growth of new brain connections.

In a clinical trial of 225 Alzheimer's patients, researchers found that a cocktail of three naturally occurring nutrients believed to promote growth of those connections, known as synapses, plus other ingredients (B vitamins, phosopholipids and antioxidants), improved verbal memory in patients with mild Alzheimer's.

"If you can increase the number of synapses by enhancing their production, you might to some extent avoid that loss of cognitive ability," says Richard Wurtman, the Cecil H. Green Distinguished Professor of Brain and Cognitive Sciences, who did the basic research that led to the new experimental treatment. He is an author of a paper describing the new results in the journal *Alzheimer's and* Dementia.

There is currently no cure for Alzheimer's disease, though some medications can slow the progression of the disease. In particular, many U.S. patients take cholinesterase inhibitors, which increase levels of acetylcholine, a neurotransmitter important for learning and memory.

While those treatments target the symptoms of Alzheimer's, Wurtman hopes to attack what he believes is the root cause of the disease: loss of

synapses. The three nutrients in his dietary cocktail — uridine, choline and the omega-3 fatty acid DHA (all normally present in breast milk) — are precursors to the fatty molecules that make up brain cell membranes, which form synapses.

In animal studies, Wurtman has shown that these nutrients boost the number of dendritic spines (small outcroppings of neural membranes). When those spines contact another neuron, a synapse is formed.

Three additional clinical studies in Alzheimer's patients are now underway, one in the United States and two in Europe. Results are expected to be available between 2011 and 2013.

The first clinical study was sponsored by the French company Danone, known in the United States as Dannon; the study was conducted primarily in Europe and was led by Philip Scheltens, director of the Alzheimer Center at Vrije Universiteit Medical Center in Amsterdam. Wurtman and MIT have patented the mixture of nutrients used in the study, and Nutricia Advanced Medical Nutrition, a unit of Danone, holds the exclusive license on the patent.

Patients with mild Alzheimer's drank the cocktail (made in the form of a nutrient drink called Souvenaid, with the collaboration of Danone) or a control beverage daily for 12 weeks. Patients who received the nutrients showed a statistically significant level of improvement compared to control subjects: 40 percent of the treated patients improved performance in a test of verbal memory (memory for words, as opposed to memory of locations or experiences) known as the Wechsler Memory Scale, while 24 percent of patients who received the control drink improved their performance. Among those who received the cocktail, patients with the mildest cases of Alzheimer's showed the most improvement.

The drink appeared to have no effect on patients' performance in another commonly used evaluation for Alzheimer's patients, the ADAS-cog test. Wurtman believes that is because ADAS-cog is a more general assessment that tests for orientation and movement/spatial memory as well as cognition. So in subjects with early Alzheimer's who show principally cognitive changes, more than the 225 subjects in the first study will probably be required to yield significant ADAS-cog changes after Souvenaid. The 500 subjects in the ongoing study in the United States may be sufficient.

John Growdon, a neurologist at Massachusetts General Hospital, says that trying to regrow synapses is an innovative strategy and offers a complementary approach to two other lines of attack in treating Alzheimer's: targeting the amyloid plaques that accumulate in patients' brains, and minimizing the damage done by toxic metabolites that build up in Alzheimer's-affected brains.

"I don't think any one approach has a monopoly, and that's good," Growdon says. "You need to have a lot of different approaches because no one knows what's going to work."

Wurtman believes his approach to Alzheimer's may eventually prove beneficial in treating other diseases. If these nutrients prove to be successful in Alzheimer's patients, "then you can think about other diseases in which there are too few synapses," such as Parkinson's disease, he says. "There are a lot of diseases associated with synapse deficiency."

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