Novel Intervention May Reverse Alzheimer's Memory Loss

Pam Harrison | October 03, 2014

A novel, comprehensive lifestyle intervention has shown promise in reversing memory loss related to Alzheimer's disease (AD), preliminary research suggests.

According to investigators, this novel intervention is aimed at "tweaking" the network of imbalances in the brain that contribute to cognitive decline.

"We've been studying the underlying mechanisms of neurodegeneration in the test tube and in transgenic mice for 25 years, and we came to the conclusion that there is an imbalance between the physiological processes that mediate plasticity in Alzheimer's disease — between synaptoblastic and synaptoclastic signaling — similar to what we see in osteoporosis, where osteoblastic signaling is chronically exceeded by osteoclastic signaling, resulting in bone loss," principal investigator Dale Bredesen, MD, professor of neurology and director, Mary S. Easton Center for Alzheimer's Disease Research, University of California, Los Angeles, told *Medscape Medical News.*

Through this lifestyle intervention, "it appears we can correct this network imbalance by tweaking it at multiple sites," Dr Bredesen added.

The study was published online September 27 in the journal *Aging.*

Sustained, Marked Improvement

A total of 10 patients with memory loss associated with either AD, mild cognitive impairment, or subjective cognitive impairment were recruited for the study.

Each participant was instructed to follow a personalized intervention program tailored to address specific metabolic deficits identified on laboratory testing as affecting the plasticity of the participant's brain, causing memory loss.

Nine of the 10 patients displayed subjective or objective improvement in cognition within 3 to 6 months of initiation of treatment. The single patient who failed to respond to the intervention had late-stage AD.

Six participants had discontinued working or were struggling with their jobs at study outset because of memory problems.

"All were able to return to work or continue working with improvement performance, and improvements have been sustained," said Dr Bredesen.

At the present time, one patient has been followed for 2.5 years from the initial presentation, and the patient continues to show "sustained and marked improvement."

Dr Bredesen noted that the level of improved function required to work effectively is an important outcome of any successful therapeutic intervention.

Optimizing Metabolic Parameters

In studies of transgenic mice, Dr Bredesen and colleagues found that beta-amyloid precursor protein (APP) signaling can be manipulated to inhibit the underlying pathophysiology that causes AD.

However, many different metabolic factors contribute to APP signaling, including hormones, inflammatory mediators, and exercise.

This suggests that the pathobiology of AD must be approached at different points of intervention and not with a single targeted agent.

"Just as for other chronic illnesses such as atherosclerotic cardiovascular disease, the goal is not simply to normalize metabolic parameters, but rather to optimize them," the investigators write.

"Based on the hypothesis that AD results from an imbalance in an extensive plasticity network, the therapy should address as many network components as possible, with the idea that a combination approach may create an effect that is more than the sum of the effects of many monotherapeutics," the researchers add.

Critical to the success of this hypothesis is the idea that there is a "threshold" at which multiple interventions will start to reverse the pathology leading to memory loss.

As Dr Bredesen points out, it has been shown by Dean Ornish, MD, founder and president of Preventive Medicine Research Institute, San Francisco, California, among others that with a large enough lifestyle change, buildup of atherosclerotic plaque and subsequent coronary artery disease can be reversed.

Similarly, in AD, if enough of the factors that contribute to the imbalance between synaptoblastic and synaptoclastic signaling in the brain can be reversed, deficits in the network that lead to memory loss can be redressed — "and you start to see improvement, which is exactly what we saw in these patients. If they follow enough of these interventions, they are able to improve," Dr Bredesen said.

Tailored Interventions

The interventions used in the 10 patients involved in the UCLA pilot project were tailored to each individual, but they shared similar elements. Typically, patients were asked to eliminate all simple carbohydrates from their diet.

They were also asked to increase consumption of fruit, vegetables, and nonfarmed fish and to follow a strict meal pattern with specifically timed interludes of fasting.

Exercise was a key component of all interventions, and participants were counseled on ways to reduce stress through practices such as yoga and meditation.

Participants also took a large variety of daily supplements, including vitamin D3, fish oil, coenzyme Q10, melatonin, and methylcobalamin.

And where appropriate, practitioners counseled their female patients to resume previously discontinued hormone replacement therapy.

"The program is not easy to follow," Dr Bredesen acknowledged. (None of the patients in this pilot project were able to fully follow the program).

"But what this program says is that we are all contributing to our own AD by the diet we chose to eat; by the way we sleep; by the stress we have in our lives; by our microbiome; and of course by our genetics.

"The important thing here is, we can alter cognitive decline by affecting each of these parameters."

Growing Evidence

Commenting on the study for *Medscape Medical News*, Heather Snyder, PhD, director, medical and scientific relations, Alzheimer's Association, Chicago, Illinois, said a number of studies have shown that lifestyle interventions can attenuate the progressive decline in cognitive function in older individuals.

Most recently, the FINGER study (Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability), which was presented earlier this year at the Alzheimer's Association International Conference 2014 and was reported by *Medscape Medical News* at that time, showed that a multipronged lifestyle intervention had a significant beneficial effect on overall cognitive performance, including memory, executive function, and psychomotor speed, in a large cohort of older participants at high risk for cognitive decline.

"The FINGER study certainly suggests that this is the kind of study we need to do in translating what Dr Bredesen did to a much larger clinical trial," Dr Snyder said.

Dr Snyder also noted that it is clear the underlying pathology driving AD is already changing well before patients manifest overt memory loss and accompanying symptoms of the disease.

"This presents us with an opportunity to identify those individuals at the earliest stage of AD, when we can intervene with a medication or some type of nonpharmacological intervention," she suggested.

Efforts to do just that are already under way with the launch of the Anti-Amyloid Treatment in Asymptomatic Alzheimer's (A4) study. The A4 study is designed to evaluate the effectiveness of an investigational drug to attenuate memory loss in patients at high risk for AD.

Dr Bredesen and Dr Snyder report no relevant financial relationships.

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