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Dietary Supplement May Prevent Cognitive Decline

Liam Davenport | June 09, 2016

A dietary supplement containing ingredients commonly found in health food stores appears to prevent the decline in brain structure and function typically seen in Alzheimer's disease, the results of an animal study indicate.

In a mouse model of accelerated aging and severe cognitive decline, a combination of vitamins and minerals, as well as nutraceuticals, such as beta carotene, bioflavonoids, cod liver oil, flax seed, garlic, and green tea extract, not only maintained brain cell numbers and mass and cognitive function but also appeared to prevent deterioration of sight and smell.

The study was led by Jennifer Lemon, PhD, research associate in the Department of Medical Physics and Applied Radiation Sciences, McMaster University, Hamilton, Ontario, Canada.

She said that she was "shocked, along with everybody else" that a nutraceutical combination "that's considered by most practitioners in the medical field to be either ineffective or benign can actually have such a profound effect on function."

Dr Lemon told *Medscape Medical News* that she is nevertheless "optimistic" that the effects of the supplement will translate into humans. One of the main reasons is that "the supplement works on fundamental mechanisms that are pretty much ubiquitous across any organism that breathes air, essentially."

These mechanisms, which include oxidative stress, inflammation, and mitochondrial dysfunction, "happen in a multitude of species as they get older" and are not "something that is specifically a human phenomenon that has been attempted to be recreated in a mouse model," she noted.

The study was published online May 20 in *Environmental and Molecular Mutagenesis*.

Cognitive Function Restored

Previous research by the team showed that the supplement extended longevity and reduced cognitive and age-related physical deterioration in both normal mice and transgenic growth hormone mice (TGM). TGM are characterized by accelerated aging accompanied by severe cognitive decline, as well long-term oxidative stress, insulin resistance, and other traits.

For the current study, the team mated heterozygous TGM and normal mice to create equal numbers of TGM and normal mice with a similar genetic background. The mice were then randomly assigned at weaning either to receive a liquid form of the supplement every day, with the doses of the ingredients adjusted to correspond to the amounts recommended for humans, or to be left untreated.

The mice then underwent a series of somatosensory tests to determine the severity of age-related losses in motor coordination and overall mobility. Their brains were examined for histologic changes, and the degree of apoptosis and changes in cell counts were assessed. Single-photon emission computed tomography and positron-emission tomography scanning was also performed.

The team found that compared with normal mice, untreated TGM displayed brain cell losses, deterioration of sensory function, and reductions in cerebral metabolic rate and blood perfusion that were equivalent to those seen in patients with Alzheimer's disease.

Specifically, the mice had greater than a 50% loss at a cellular level, a 36% reduction in brain mass, and at least twofold reductions in brain metabolism and blood flow at 12 months. Furthermore, in the untreated TGM, motor and cognitive functions were severely compromised.

Although the supplement did not have significant effects on brain cell numbers, brain weight, or brain metabolism or perfusion in normal mice, it had striking effects in TGM.

With the supplement, brain mass and brain cell density were maintained at levels seen in young mice. Brain metabolic activity

was comparable to that in control mice, with no significant difference between the groups. Moreover, the supplement was associated with a twofold increase in brain perfusion in TGM.

The results also showed that the supplement restored cognitive function in TGM and led to significant improvements in motor coordination. It also appeared to reduce anxiety, allowing TGM to explore "unsafe/novel" environments.

The team found that the supplement appeared to offset deterioration of visual acuity in TGM. It was associated with increases in the thickness of the retinal outer nuclear layer and outer segment of 26% and 29%, respectively, in TGM compared with untreated mice.

TGM that received the supplement also showed improvements in olfactory sensitivity and greater numbers of mitral cells in the olfactory bulb in comparison with untreated mice. Inasmuch as olfactory loss is associated with an increased risk of developing severe neurodegenerative conditions, the researchers say these findings suggest that the supplement may be offsetting neurodegeneration throughout the brain.

Striking a Balance

For Dr Lemon, the findings support the notion that nutraceuticals are more likely to be effective when taken in combination with other supplements rather than when taken alone as a single supplement.

"Our criteria for including things in the supplement were mainly that there was scientific evidence to show that they worked on a particular mechanism. It didn't have to be that it had a great whole-body effect, because most individual supplements don't," she said.

"That is typically because our cells are working in such a complex way that we have many mechanisms that are occurring simultaneously, and when something's going wrong, it's usually knocking everything out of balance."

Dr Lemon explained that when the level of one particular component is increased in the cells, "you tend to also knock everything out of whack.

"There are a lot of studies that show that high doses of single things, like vitamin E, for instance, can create disease or can make disease worse. A lot of that has to do with the fact that the cell works optimally when it's balanced, and when you put one thing in, particularly something that is used as an antioxidant, you can turn it into a pro-oxidant, exacerbating free radical production within the cells," she said.

One aspect of the supplement that sets it apart from a novel pharmaceutical agent is that it is not subject to the same degree of intellectual property protection, owing to the fact that it is composed of nutraceuticals that are available in health food stores.

Acknowledging that this "will always be a problem here," Dr Lemon said that although a company has licensed the formulation from McMaster University to commercialize it, it is likely that, should the supplement be shown to have similar effects in humans, "people would try to make versions of it."

There are, however, "some very specific things that we've done to try to make that a little bit more difficult," Dr Lemon added.

Specifically, she noted that mice do not have diurnal rhythms such as those seen in humans. The team has therefore worked on formulating the supplement as two pills, one to be taken in the morning, and the other in the evening, "depending on what functions you're trying to protect."

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