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Dietary treatment shows potential in a mouse model of Alzheimer's disease

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New research findings indicate that an early onset of dietary treatment may slow down the progression of Alzheimer's disease. The study was conducted on mice, and the results will be published in the February issue of *Journal of Nutritional Biochemistry*. Researchers from the University of Eastern Finland played a key role in the study, which was carried out as part of the LiPiDiDiet project funded by the European Union.

According to current understanding, Alzheimer's disease develops slowly and it may take up to 20 years before the first obvious symptoms occur. With the development of early diagnostics of the disease, the question of which treatments to offer to completely healthy people with an increased risk of developing Alzheimer's becomes of key importance in the field of medicine. Various dietary treatments seem a promising alternative.

Several epidemiological studies suggest that docosahexaenoic acid (DHA), an omega-3 fatty acid found in fatty fish, might reduce the risk of Alzheimer's disease. Experimental studies have also observed a positive – although modest – association between DHA and several processes behind Alzheimer's disease. This recently published study investigated whether the efficacy of DHA treatment can be enhanced by additional nutrients.

The study used transgenic female mice carrying APP and PS1 mutations linked with familial Alzheimer's disease, and wild-type mice. All the mice began the dietary intervention at 5 months and continued on the

diet until 13 months old. The fat content of the control chow was increased to better correspond to human diets. In addition to the control chow, some of the APP/PS1 mice were fed three experimental chows enriched with fish oil and having a similar fat content as the control chow: fish oil supplement only, plant sterol supplement or Fortasyn supplement, which contains uridine-monophosphate, phospholipids, B-vitamins, and antioxidants.

As expected, APP/PS1 mice performed significantly poorer than wild-type mice in the Morris swim navigation task, which measures long-term spatial memory. Among transgenic mice on the experimental diets, the mice on the Fortasyn diet performed equally well as the wild-type mice, whereas other dietary treatments showed no improvement. However, all test diets reversed the memory deficit of the APP/PS1 mice in the odour recognition task. The levels of accumulated amyloid-β protein in the brain were examined at the end of the study. A significant reduction in the amyloid-β levels was observed in the plant sterol group while other experimental diets showed no effect. However, why was a substantial reduction in brain amyloid-β levels not accompanied by a positive memory effect in the spatial task in the plant sterol group? One explanation is that the plant sterol diet increased formation of reactive oxygen species in the hippocampus, whereas the Fortasyn diet, which yielded the best results in the spatial memory task, tended to have an opposite effect.

The results indicate that even slight changes in the composition of the diet may, under a sufficiently long period of time and at an early stage of the disease process, lead to significant changes in brain metabolism and improved memory performance. On the other hand, the mere brain amyloidosis in Alzheimer's disease involves several mechanisms and it is unlikely that a single cocktail of nutrients will provide an optimal outcome. According to the researchers, the results definitely encourage further development of dietary treatments for Alzheimer's disease.

The Fortasyn supplement is found in the medical nutrition formulation Souvenaid, just introduced in Finland. In light of the present results, the product can be recommended for the treatment of mice suffering from mild cognitive impairment (pre-Alzheimer's), but will it work as efficiently in humans, too? We will probably get the answer in a year, as results from a parallel clinical study of the LiPiDiDiet project become available.

More information: "Special lipid-based diets alleviate cognitive deficits in the APPswe/PS1dE9 transgenic mouse model of Alzheimer's disease independent of brain amyloid deposition." *Journal of Nutritional Biochemistry* 2014; 25: 157–169., Hennariikka Koivisto, Marcus O. Grimm, Tatjana L. Rothhaar, Róbert Berkecz, Dieter Lütjohann, Rajsa Giniatullina, Mari Takalo, Pasi O. Miettinen, Hanna-Maija Lahtinen, Rashid Giniatullin, Botond Penke, Tamás Janáky, Laus M. Broersen, Tobias Hartmann, Heikki Tanila.

Provided by University of Eastern Finland