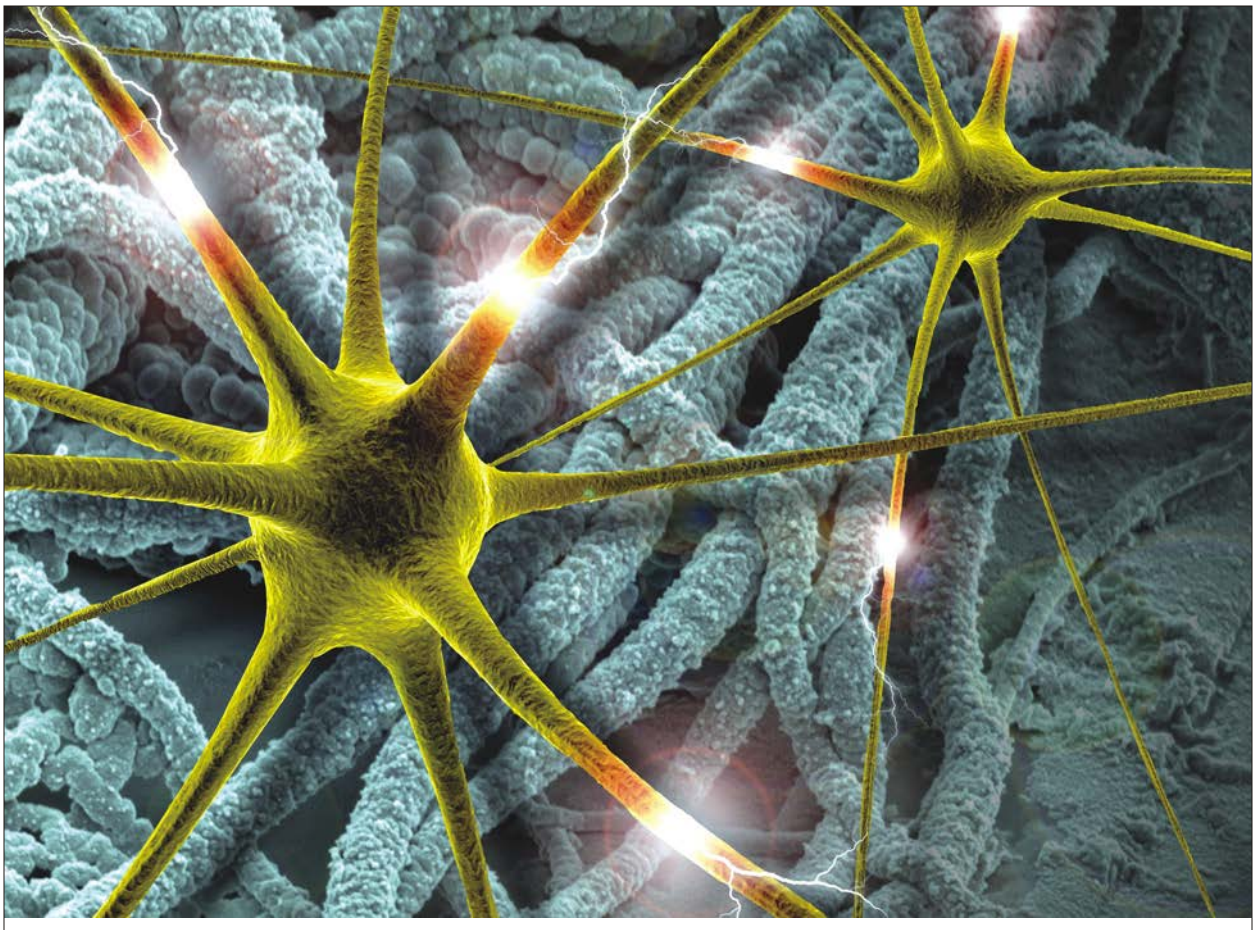

Current Research in **Neuroscience**

ISSN 1996-3408

Academic
Journals Inc.

www.academicjournals.com

Chronic High Cholesterol Diet Produces Brain Damage

Research from the Laboratory of Psychiatry and Experimental Alzheimers Research at the Medical University Innsbruck (Austria) demonstrated that chronic high fat cholesterol diet in rats exhibited pathologies similar to Alzheimer's disease.

The results were published in Molecular Cellular Neuroscience with lead author Dr. Christian Humpel. The study was co-authored by PhD students, Celine Ullrich and Michael Pirchl, from the same Laboratory.

Alzheimer's disease is a severe neurodegenerative disorder of the brain that is characterized by loss of memory and cognitive decline. The majority of Alzheimer's disease cases are sporadic (risk age >60 years), and only <2.5% have a genetic disposition. It is estimated that in 2050, approximately 80 million people will suffer from Alzheimer's disease worldwide. The major pathological hallmarks of Alzheimer's disease are extracellular aggregates (plaques) of the small peptide beta-amyloid, hyperphosphorylation of the protein tau and subsequent formation of intracellular neurofibrillary tangles, degeneration of neurons secreting the neurotransmitter acetylcholine, inflammation, and cerebrovascular dysfunction.

The causes for Alzheimer's disease are not known, but dysregulation of amyloid-precursor protein expression and beta-amyloid clearance is hypothesized (beta-amyloid cascade). Alternatively, a pathological cascade of events may trigger hyper-phosphorylation of tau, putting the tau-hypothesis into the center. A third hypothesis suggests that chronic long-lasting mild cerebrovascular damage, including inflammatory processes and oxidative stress, may cause Alzheimer's disease. It has been suggested that Alzheimer's disease starts 20-30 years before first symptoms appear and recent studies have shown, that high cholesterol levels are linked to the pathology of this disease. The aim of the study led by Humpel was to study the effects of hypercholesterolemia in adult rats. Male 6 months old Sprague Dawley rats were fed with normal food (controls) or with a special 5% cholesterol-enriched diet (hypercholesterolemia). After 5 months animals were tested for behavioral impairments and pathological markers similar to those found in the brains of patients with Alzheimer's disease. The results showed that chronic hypercholesterolemia caused memory impairment, cholinergic dysfunction, inflammation, enhanced cortical beta-amyloid and tau and induced microbleedings, all indications, which resemble an Alzheimer's disease-like pathology.

Thus the data are in line with earlier studies showing that high fat lipids, including cholesterol, may participate in the development of sporadic Alzheimer's disease. However, since Alzheimer's disease is a complex heterogenous disease, these data do not allow the conclusion that cholesterol alone is responsible for the disease. It can be speculated that chronic mild cerebrovascular damage caused and potentiated by different vascular risk factors (including cholesterol) may contribute to these pathologies. It needs to be determined in future studies how mild chronic microvascular bleedings, silent strokes and mild blood-brain barrier damage over decades may play a role in the development of this disease. Indeed several data (Ladecola, Nat.Rev.Neurosci. 5, 347-360, 2004) support the view that Alzheimer's disease can be considered as a vascular disease and that a dysfunctional clearance of beta-amyloid from brain to blood and vice versa may be a secondary important step in the cascade of initiation of the disease. This study was supported by the Austrian Science Funds (P19122-B05).