Antioxidant may disrupt Alzheimer's disease process

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Alzheimer's disease (AD) is now the sixth leading cause of death among Americans, affecting nearly 1 in 8 people over the age of 65. There is currently no treatment that alters the course of this disease. However, an increasing amount of evidence suggests that changes in the way the body handles iron and other metals like copper and zinc may start years before the onset of AD symptoms. A new study shows that reducing iron levels in blood plasma may protect the brain from changes related to AD.

In the current study a group of investigators from led by Dr. Othman Ghribi, PhD, Associate Professor, Department of Pharmacology, Physiology, and Therapeutics, University of North Dakota School of Medicine and Health Sciences, rabbits were fed a high-cholesterol diet which caused them to accumulate plaques of a small protein called beta-amyloid (Aβ). These plaques are toxic to neurons and central to the development of Alzheimer's disease. The rabbits also developed changes in tau protein, which is part of the skeleton of neurons. When this protein becomes heavily phosphorylated, the ability of neurons to conduct electrical signals is disrupted. Following treatment with a drug called deferiprone (an iron chelator), the iron level in the rabbits' blood plasma was reduced and the levels of both beta-amyloid and phosphorylated tau in the brain were returned to normal levels.

Another degenerative process in AD involves the production of reactive oxygen species (ROS) that can damage neurons in the brain. Deferiprone is also thought to suppress this reactive oxygen damage caused by free iron in the bloodstream, however in this study there was no difference in

reactive oxygen species in the treated group. It appears that iron in the AD brain is located in the wrong places – in particular it accumulates to very high levels in the cores of beta-amyloid plaques and is very reactive in this setting.

According to Dr. Ghribi, "Our data show that treatment with the iron chelator deferiprone opposes several pathological events induced by a cholesterol-enriched diet…Deferiprone reduced the generation of Aβ and lowered levels of tau phosphorylation." While there was no effect on ROS levels, he comments that "It is possible that a higher dose of deferiprone, or combination therapy of deferiprone together with an antioxidant to prevent ROS generation would more-fully protect against the deleterious effects of cholesterol-enriched diet that are relevant to AD pathology."

Noted expert on metals metabolism research on AD Ashley Bush, MD, PhD, Mental Health Research Institute, Melbourne, Australia, adds that "this research highlights the role of metal ions as key modulators for the toxic interactions of risk factors for Alzheimer's disease, in this case cholesterol. Drugs targeting these metal interactions hold promise as disease-modifying agents."

More information: Deferiprone Reduces Amyloid-β and Tau Phosphorylation Levels but not Reactive Oxygen Species Generation in Hippocampus of Rabbits Fed a Cholesterol-Enriched Diet. Jaya R.P. Prasanthi, Matthew Schrag, Bhanu Dasari, Gurdeep Marwarha, Wolff M. Kirsch and Othman Ghribi. *Journal of Alzheimer's Disease* 30(1) May 2012, DOI: 10.3233/JAD-2012-111346

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