

Effects of blood pressure drug on Alzheimer's disease shown in mouse study

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A drug used decades ago to treat high blood pressure has been shown to improve learning and memory in mouse models of Alzheimer's disease, according to a new study by researchers at the National Institute on Aging (NIA), part of the National Institutes of Health. The study found that the drug, diazoxide, acted on nerve cells in the mouse brain in ways that slowed the development of the neurodegenerative disorder. The findings appear in the Nov. 15, 2010, print edition of the *Journal of Alzheimer's Disease*.

Mark P. Mattson, Ph.D., chief of NIA's Laboratory of Neurosciences in Baltimore, directed the research, in collaboration with colleagues at Konkuk UniversityCollege of Veterinary Medicine, Seoul, South Korea, and the Indiana UniversitySchool of Medicine, Indianapolis.

Mattson's team found that diazoxide stabilized <u>nerve cells</u> in the brain and preventeda biological cascade in the mice that can result in the destruction of thesecells. The drug also improved blood flow in the brain and prevented the harmfulaccumulation of two proteins, beta-amyloid and tau, which are hallmarks of Alzheimer's. Widely used in the 1970s and '80s to treat patients with severe hypertension, diazoxide is currently used to treat hypoglycemia, or low blood sugar.

"These intriguing findings open new avenues of basic research that may increase our understanding of how modulating the electrical activity of nerve cells may slow the damage wrought by Alzheimer's disease pathology," said NIA DirectorRichard J. Hodes, M.D. "More research



will be needed before we can determine whether this may be a potential therapy for Alzheimer's."

NIA scientists studied two groups of Alzheimer's mice, one given diazoxide indrinking water and one given a placebo. After eight months, the diazoxide group outperformed the placebo group on a standard test of learning and memory. Thebrain tissue of the treated group showed fewer deposits of amyloid and tau proteins, less damage due to oxidative stress, and better blood flow — all indications that diazoxide may have suppressed some of the harmful cellular changes associated with <u>Alzheimer's disease</u>.

"To better understand the complex biological mechanisms by which diazoxide mayexert a positive effect on nerve cells, we then studied the effects of diazoxideon cultured nerve cells," Mattson said.

The scientists found the drug activates and opens channels in the cell that enhancethe movement of potassium, which then calms the electrical activity of nervecells in parts of the brain involved in learning and memory. Diazoxide also lowered the excessive calcium often found in nerve cells in brains affected by Alzheimer's. These beneficial effects were seen with a dose of diazoxide low enough to avoid a major decrease in <u>blood pressure</u>, Mattson noted.

Provided by National Institutes of Health

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