Could blood pressure drugs have a role in Alzheimer's disease treatment?

January 29 2016

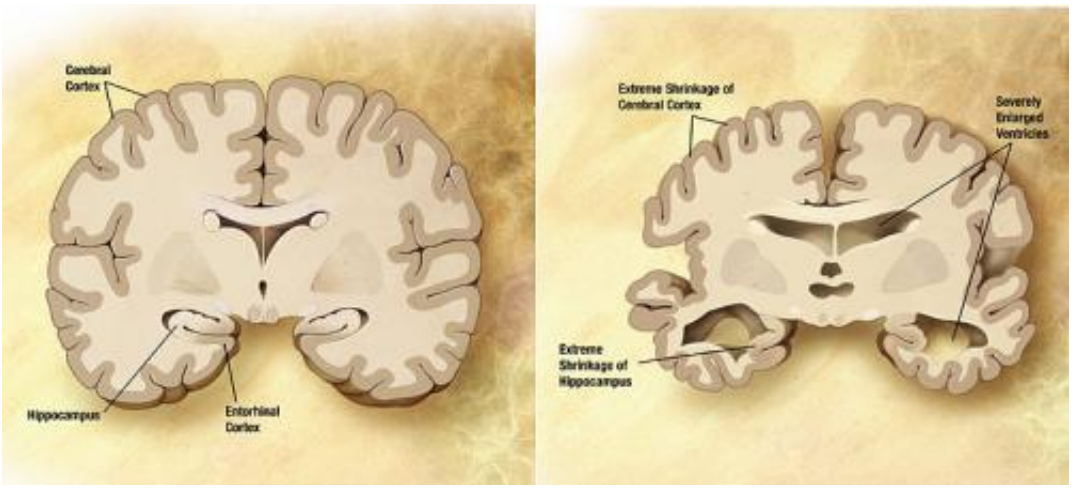

Diagram of the brain of a person with Alzheimer's Disease. Credit: Wikipedia/public domain.

In laboratory neuronal cultures, an FDA-approved drug used to treat high blood pressure reduced cell damage often linked to Alzheimer's disease, say researchers at Georgetown University Medical Center (GUMC) and the National Institutes of Health.

They say their work, published online Feb. 28 in the journal *Alzheimer's Research and Therapy*, provides information supporting the potential effect of the drug candesartan—as well as other Angiotensin receptor blockers (ARBs) for the early treatment of Alzheimer's disease.

"Our findings make sense in many ways," says the study's senior author Juan M. Saavedra, MD, from GUMC's Department of Pharmacology and Physiology. "Hypertension reduces blood flow throughout the body and brain and is a risk factor of Alzheimer's disease. Previous epidemiological studies found that Alzheimer's progression is delayed in hypertensive patients treated with ARBs."

Using neuronal cultures, the researchers explored the action of candesartan on the neurotoxic effects of exposure to excessive glutamate, a demonstrated injury factor in the early stages of Alzheimer's disease.

The scientists found that candesartan prevented glutamate-induced neuronal death. They conducted in-depth gene analyses of the laboratory results, demonstrating that candesartan prevented neuronal inflammation and many other pathological processes, including alterations in amyloid metabolism, a hallmark of Alzheimer's disease.

The study's first author, Abdel G. Elkahloun, PhD, from the Comparative Genomics and Cancer Genetics Branch of the National Human Genome Research Institute, then compared gene expression in the neuronal cultures with published gene databases of autopsy samples from Alzheimer's disease patients. "The correlations were impressive—the expression of 471 genes that were altered by excess glutamate in our cultures were also altered in brain autopsy samples from patients who suffered from Alzheimer's disease. Candesartan normalized expression of these genes in our cultures," Elkahloun says.

"We hypothesize that candesartan, or other members of the ARB group, may not only slow progression of Alzheimer's but also prevent or delay its development," Saavedra says.

The researchers say this work has immediate translational value,

supporting testing candesartan, or other ARBs, in controlled clinical studies on patients at early stages of Alzheimer's disease.

More information: Abdel G. Elkahloun et al. An integrative genome-wide transcriptome reveals that candesartan is neuroprotective and a candidate therapeutic for Alzheimer's disease, *Alzheimer's Research & Therapy* (2016). DOI: 10.1186/s13195-015-0167-5

Provided by Georgetown University Medical Center