Brain receptor cell could be new target for Alzheimer's

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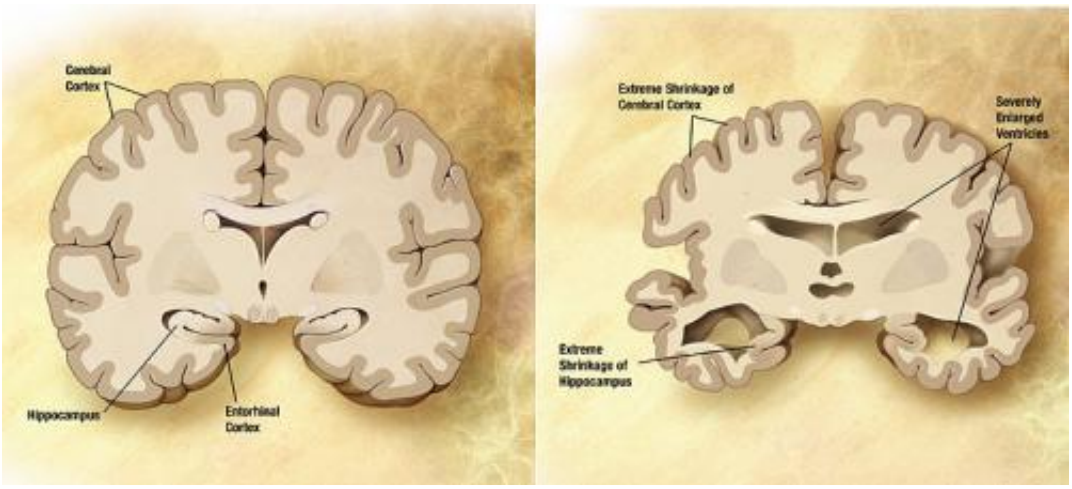

Diagram of the brain of a person with Alzheimer's Disease. Credit: Wikipedia/public domain.

Blocking a key receptor in brain cells that is used by oxygen free radicals could play a major role in neutralizing the biological consequences of Alzheimer's disease, according to researchers at Temple University.

The researchers' findings, "Modulation of AD Neuropathology and Memory Impairments by the Isoprostane F2α Is Mediated by the Thromboxane Receptor," were published Oct. 13 by the journal *Neurobiology of Aging*.

The human body's use of oxygen to produce energy often results in the

formation of highly reactive molecules called oxygen free radicals. Oxidative stress occurs when the production of these free radicals is greater than the body's ability to detoxify them.

"Besides the two major signature brain pathologies associated with Alzheimer's disease, amyloid beta plaques and the tangles which are formed from the phosphorylation of the tau protein, researchers have also known for a while that there is a signature from oxidation stress," said Domenico Praticò, professor of pharmacology and microbiology and immunology in Temple's School of Medicine, who led the study. "But it has always been believed that oxidative stress was just a bystander and did not have an active function in the development of the disease."

In their study, Praticò and his colleagues discovered that the free radicals produced from oxidative stress actually bind to a protein receptor in the brain called the thromboxane receptor, or TP, and transmit signals to the neuronal cells to increase the production of amyloid beta or phosphorylated tau, the two major Alzheimer's pathologies.

"Basically, it sends the wrong message inside the neuronal cells, and with time, this definitely will result in all the clinical manifestations of the disease, such as cognitive impairment, loss of memory and brain cell death," he said.

The researchers introduced free radicals into the brain of a mouse model for Alzheimer's and witnessed a worsening of the animal's memory and learning capabilities, as well as an increase in amyloid beta and tangles.

However, they also treated a subset of the mice with a compound known to block the TP receptor in the brain. In this group, said Praticò, there was no manifestation of the cognitive impairment experienced by the non-treated mice.

"This indirectly confirmed for us that the free radicals worked through this receptor," he said. "Using this compound, we were able to completely neutralize the biological consequences of the free radicals in terms of the amyloid beta production (plaques) and tau phosphorylation (tangles)."

Praticò said that the findings implicating oxidative stress and the TP receptor open an important chapter for Alzheimer's treatment.

"For the first time we have identified this receptor as the culprit responsible for the bad things that happen with the disease when high levels of oxygen free radicals are produced."

Praticò said that the TP receptor can now be considered a new target for therapies, and his group is working on developing additional compounds that even more efficiently block the receptor, making it unavailable to free radicals.

Provided by Temple University