Stress hormone could trigger mechanism for the onset of Alzheimer's

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(Medical Xpress)—A chemical hormone released in the body as a reaction to stress could be a key trigger of the mechanism for the late onset of Alzheimer's disease, according to a study by researchers at Temple University.

Previous studies have shown that the chemical hormone corticosteroid, which is released into the body's blood as a stress response, is found at levels two to three times higher in Alzheimer's patients than non-Alzheimer's patients.

"Stress is an environmental factor that looks like it may play a very important role in the onset of Alzheimer's disease," said Domenico Praticò, professor of pharmacology and microbiology and immunology in Temple's School of Medicine, who led the study. "When the levels of corticosteroid are too high for too long, they can damage or cause the death of neuronal cells, which are very important for learning and memory."

In their study, "Knockout of 5-lipoxygenase prevents dexamethasone -induced tau pathology in 3xTg mice," published in the journal *Aging Cell*, the Temple researchers set up a series of experiments to examine the mechanisms by which stress can be responsible for the Alzheimer's pathology in the brain.

Using triple transgenic mice, which develop amyloid beta and the tau protein, two major brain lesion signatures for Alzheimer's, the Temple

researchers injected one group with high levels of corticosteroid each day for a week in order to mimic stress

While they found no significant difference in the mice's memory ability at the end of the week, they did find that the tau protein was significantly increased in the group that received the corticosteroid. In addition, they found that the synapses, which allow neuronal cells to communicate and play a key role in learning and memory, were either damaged or destroyed.

"This was surprising because we didn't see any significant memory impairment, but the pathology for memory and learning impairment was definitely visible," said Pratico. "So we believe we have identified the earliest type of damage that precedes memory deficit in Alzheimer's patients."

Pratico said another surprising outcome was that a third group of mice that were genetically altered to be devoid of the brain enzyme 5-lipoxygenase appeared to be immune and showed no neuronal damage from the corticosteroid.

In previous studies, Pratico and his team have shown that elevated levels of 5-lipoxygenase cause an increase in tau protein levels in regions of the brain controlling memory and cognition, disrupting neuronal communications and contributing to Alzheimer's disease. It also increases the levels of amyloid beta, which is thought to be the cause for neuronal death and forms plaques in the brain.

Pratico said the corticosteroid causes the 5-lipoxygenase to over-express and increase its levels, which in turn increases the levels of the tau protein and amyloid beta.

"The question has always been what up-regulates or increases

5-lipoxygenase, and now we have evidence that it is the stress hormone," he said. "We have identified a mechanism by which the risk factor—having high levels of corticosteroid—could put you at risk for the disease.

"Corticosteroid uses the 5-lipoxygenase as a mechanism to damage the synapse, which results in memory and learning impairment, both key symptoms for Alzheimer's," said Pratico. "So that is strong support for the hypothesis that if you block 5-lipoxygenase, you can probably block the negative effects of corticosteroid in the brain."

More information: onlinelibrary.wiley.com/doi/10 … /acel.12096/abstract

Provided by Temple University