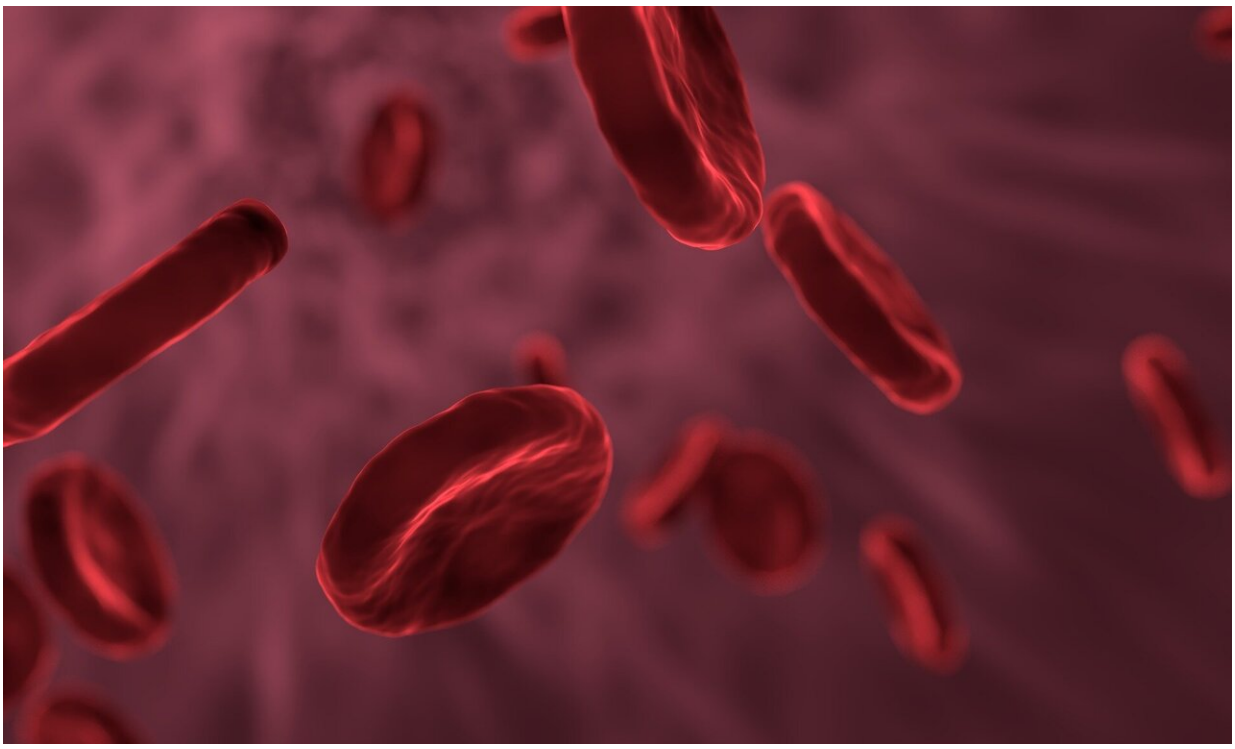
Whole blood exchange could offer disease-modifying therapy for Alzheimer's disease, study finds

July 14 2022



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A novel, disease-modifying therapy for Alzheimer's disease may involve the whole exchange of blood, which effectively decreased the formation of amyloid plaque in the brains of mice, according to a new study from

UTHealth Houston.

A research team led by senior author Claudio Soto, Ph.D., professor in the Department of Neurology with McGovern Medical School at UTHealth Houston, in collaboration with first author Akihiko Urayama, Ph.D., associate professor in the department, performed a series of whole blood exchange treatments to partially replace blood from mice exhibiting Alzheimer's disease-causing amyloid precursor proteins with complete blood from healthy mice of the same genetic background. The results of the study were published today in *Molecular Psychiatry*.

"This article provides a proof-of-concept for the utilization of technologies commonly used in medical practice, such as plasmapheresis or blood dialysis, to 'clean' blood from Alzheimer's patients, reducing the buildup of toxic substances in the brain," said Soto, director of the George and Cynthia Mitchell Center for Alzheimer's Disease and Related Brain Disorders and the Huffington Foundation Distinguished Chair in Neurology at McGovern Medical School. "This approach has the advantage that the disease can be treated in the circulation instead of in the brain."

Previous studies by Soto and other UTHealth Houston researchers have shown that the misfolding, aggregation, and buildup of amyloid beta proteins in the brain plays a central role in Alzheimer's disease. Therefore, preventing and removing misfolded protein aggregates is considered a promising treatment for the disease.

However, the treatment of Alzheimer's disease has long been complicated, due to the difficulty in delivering therapeutic agents across the blood-brain barrier. Through their latest research, Urayama, Soto, and others discovered that manipulating circulating components in Alzheimer's disease could be the key to solving this issue.

"Blood vessels in the brain are classically considered the most impermeable barrier in the body," Urayama said. "We have been aware that the barrier is at the same time a very specialized interface between the brain and the systemic circulation."

After multiple blood transfusions, the researchers found that the development of cerebral amyloid plaques in a transgenic mice model of Alzheimer's disease was reduced by 40% to 80%. This reduction also resulted in improved spatial memory performance in aged mice with the amyloid pathology, and lowered the rates of plaque growth over time.

While the exact mechanism by which this blood exchange reduces amyloid pathology and improves memory is currently unknown, there are multiple possibilities. One possible explanation is that lowering amyloid beta proteins in the bloodstream may help facilitate the redistribution of the peptide from the brain to the periphery. Another theory is that blood exchange somehow prevents amyloid beta influx, or inhibits the re-uptake of cleared amyloid beta, among other potential explanations.

However, regardless of the mechanisms of action associated with the blood exchange treatment, the study shows that a target for Alzheimer's disease therapy may lie in the periphery.

More information: Preventive and therapeutic reduction of amyloid deposition and behavioral impairments in a mice model of Alzheimer's disease by whole blood exchange, *Molecular Psychiatry* (2022). DOI: 10.1038/s41380-022-01679-4

Provided by University of Texas Health Science Center at Houston