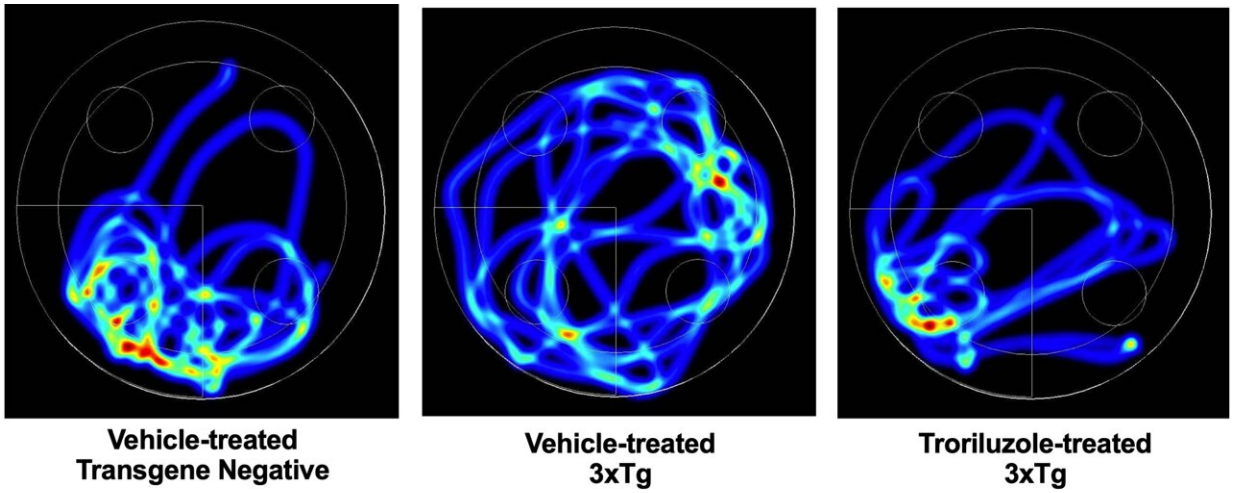
Researchers show novel drug rescues memory loss in Alzheimer's mouse model

September 4 2024



Shown are representative heatmap visualization of spatial occupancy during probe trials of the Morris water maze. The warmer the colors correlate with an increased time spent in that. Credit: Dr. Michael Gramlich & Dr. Miranda Reed

In a recent development in Alzheimer's disease research, Auburn University scientists have studied a new drug, troriluzole, that can prevent brain changes leading to memory loss and cognitive decline in a mouse model of the disease. This study, published in the *Journal of Neurochemistry*, is the first to show how troriluzole can target early-stage alterations associated with Alzheimer's, providing new hope for potential treatments.

Dr. Miranda Reed, a Professor in the department of Drug Discovery at Auburn University and Delivery and the studies main researcher, noted that "by examining how drug treatments can intervene early in the disease process, we aim to develop therapies that might prevent or even cure Alzheimer's."

"This study also highlights how scientific advancements can transform our understanding of complex diseases like Alzheimer's," said Dr. Michael Gramlich, an Assistant Professor of Biophysics and the study's other main researcher.

Breaking new ground in Alzheimer's research

Alzheimer's disease affects millions of people worldwide, causing progressive memory loss, confusion, and eventually the inability to perform basic tasks. Despite decades of research, a cure remains elusive. Alzheimer's is characterized by the accumulation of amyloid plaques and tau tangles in the brain, which disrupt neural communication.

In the early stages, excessive levels of the neurotransmitter glutamate cause damaging overactivity in synapses, the connections between nerve cells.

The study conducted by Auburn University researchers, led by Drs. Miranda Reed and Michael Gramlich, investigated how troriluzole, a novel drug, can maintain normal brain function in mice genetically modified to replicate early Alzheimer's stages.

The results are compelling: troriluzole not only reduced harmful glutamate levels but also improved memory and learning in the mice, suggesting a maintenance of healthy brain function.

"Our research demonstrates that by targeting synaptic activity early, we

may be able to prevent or slow the progression of Alzheimer's. This could revolutionize the way we approach treatment for this disease," noted both researchers.

How troriluzole works

In the Auburn study, mice treated with troriluzole showed a significant reduction in synaptic glutamate levels and decreased brain hyperactivity. These molecular changes led to tangible improvements: the treated mice performed better in memory tests, such as navigating mazes, indicating that their cognitive functions were restored.

"These findings are promising because they suggest that troriluzole can protect the brain at a fundamental level, starting with molecular changes and resulting in improved cognitive abilities," said Dr. Reed. "It's like repairing an engine before it fails completely."

This research was a collaborative effort involving Auburn University's College of Science and Mathematics, the Harrison College of Pharmacy, and the Center for Neuroscience Initiative, along with private researchers and students. The team's combined expertise in neuroscience and pharmacology was crucial to the study's success.

"This collaboration blends basic science and pharmaceutical research to tackle one of the most challenging neurological issues of our time," Dr. Gramlich emphasized. "Our work not only enhances scientific understanding of Alzheimer's disease but also offers a potential new treatment that could improve the lives of millions worldwide."

While the results in mice are encouraging, the researchers emphasize the need for further studies to determine how troriluzole works at different stages of disease progression.

More information: Jeremiah Pfitzer et al, Troriluzole rescues glutamatergic deficits, amyloid and tau pathology, and synaptic and memory impairments in 3xTg-AD mice, *Journal of Neurochemistry* (2024). DOI: 10.1111/jnc.16215