Drug that slows progression of ALS may provide the same benefit for people with Alzheimer's disease

July 28 2021

Credit: Unsplash/CC0 Public Domain

Riluzole, a drug that has been used for more than 20 years to slow the progression of ALS, commonly known as Lou Gehrig's disease, was

shown in a pilot phase 2 study to slow brain metabolic decline and have a positive effect on cognitive performance versus placebo in people with mild Alzheimer's disease. The study was pre-published in a recent online issue of the journal *Brain*. The Alzheimer's Drug Discovery Foundation (ADDF) provided funding and expertise to study investigators, helping to bring this research into phase 2 clinical testing.

"Using two types of brain scans as biomarkers, this study was able to measure improvements in brain metabolism among treated patients and correlate those improvements with cognitive changes and disease progression," said study co-author Howard Fillit, M.D., ADDF's Founding Executive Director and Chief Science Officer. "Riluzole represents many of the ADDF's research priorities. It is a repurposed drug, which helps speed the research process. It targets an important and understudied biological mechanism that goes awry with aging, and the rigorous design of this trial measured both biomarker and clinical outcomes."

The trial randomly assigned 50 patients aged 50 to 90 years to receive either the active drug (n=26) or placebo (n=24) twice daily for six months. Riluzole works by modulating a neurotransmitter in the brain called glutamate, which plays an essential role in the ability of nerve cells to send signals to one another. Glutamate dysregulation is thought to begin a cycle of toxicity that underlies the development of Alzheimer's disease.

The study met its main primary outcome, confirming a difference in brain metabolic changes between patients on active treatment and placebo. The changes were measured and analyzed using a specialized PET scan that measures glucose metabolism called FDG PET. Changes in FDG PET scans correlated with cognitive decline and predicted Alzheimer's disease progression. In this trial, FDG PET progression scores also correlated with changes in patients' cognitive functions,

including memory, attention, language, and visual-spatial skills.

Secondary outcomes were also met, including significant changes in glutamate levels measured through magnetic resonance spectroscopy, correlations between cognitive measures assessed through neuropsychological testing and neuroimaging biomarkers. Another primary endpoint, change in N-acetylaspartate, a marker of neuron health, was not met. Finally, several regions of the brain showed preserved glucose metabolism, but most prominently a region called the posterior cingulate which is a hub network for Alzheimer's disease.

The study found no difference in adverse events between the treatment and placebo groups. Using repurposed drugs like riluzole comes with the benefit of having, in this case, two decades of experience showing the drug's safety. This helps to speed and streamline costs of the drug testing process.

Lead investigator Dr. Ana Pereira, Assistant Professor of Neurology and Neuroscience at the Icahn School of Medicine at Mount Sinai in New York, NY, said the promising results support moving the drug into a phase 3 trial with larger numbers of patients followed for a longer time for further testing of safety and efficacy.

"We are deeply appreciative to the ADDF not just for their investment in our work, but for their commitment to novel scientific approaches to Alzheimer's research," said Dr. Pereira.

Thanks to its deep connections throughout the Alzheimer's research community, the ADDF was able to connect Dr. Pereira with another of its funded investigators, Dawn Matthews, Chief Executive Officer at ADM Diagnostics, an ADDF-funded company. The two worked together on designing the trial to take advantage of new technology from ADM that allowed for a more robust analysis of the PET scan data.

More information: Dawn C Matthews et al, Riluzole, a glutamate modulator, slows cerebral glucose metabolism decline in patients with Alzheimer's disease, *Brain* (2021). DOI: 10.1093/brain/awab222

Provided by Alzheimer's Drug Discovery Foundation