Experimental drug shows promise for genetic form of ALS

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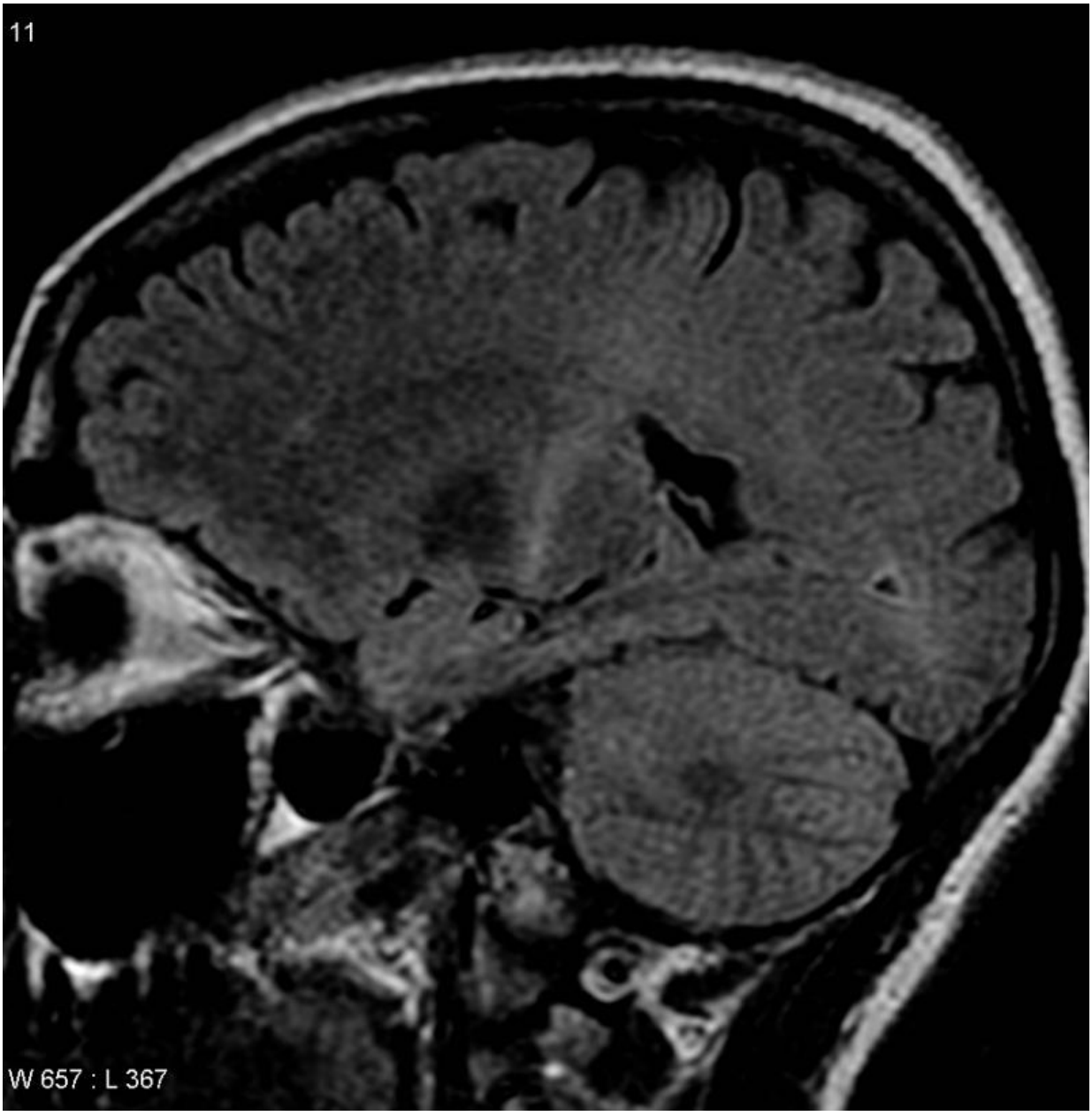

An MRI with increased signal in the posterior part of the internal capsule which can be tracked to the motor cortex consistent with the diagnosis of ALS. Credit: Frank Gaillard/Wikipedia

An early stage trial of an investigational therapy for amyotrophic lateral sclerosis (ALS) suggests that people could tolerate the experimental drug and, in exploratory results, the experimental drug was linked to possible slower progression in people with a genetic form of the disease caused by mutations in a gene called superoxide dismutase 1 (SOD1). The preliminary study released today will be presented at the American Academy of Neurology's 71st Annual Meeting in Philadelphia, May 4 to 10, 2019.

ALS is a progressive neurodegenerative disease that affects nerve cells in the brain and the spinal cord. People with ALS lose the ability to initiate and control muscle movement, which often leads to total paralysis and death. The average life span after diagnosis is two to five years. Approximately 10 percent of all ALS cases are genetic and about a fifth of those are caused by SOD1 gene mutations.

"The treatment that we researched in this study, an antisense oligonucleotide called tofersen (BIIB067), works by targeting and reducing protein created by the mutated gene," said study author Timothy M. Miller, MD, Ph.D., of Washington University School of Medicine in St. Louis, Mo., and a member of the American Academy of Neurology. "That mutated protein is toxic and leads to ALS by damaging the nerve cells that control movement. Our research aimed to decrease the production of that protein."

This component of the study involved 50 people with ALS who had an

SOD1 genetic mutation. Participants received five doses of either 20, 40, 60 or 100 milligrams (mg) of the experimental drug, or placebo, through a lumbar puncture, or spinal tap, over approximately 3 months. Researchers examined the safety, dosage and exploratory efficacy of the experimental drug.

Researchers found that the 10 people who were given 100 mg of the experimental drug had a 37 percent reduction of the SOD1 protein in spinal fluid when compared to 12 people who received the placebo.

Miller, who received the 2018 Sheila Essey Award for ALS Research from the American Academy of Neurology, the ALS Association and the American Brain Foundation said, "Lower concentrations of the protein in the spinal fluid suggest that there were also lower concentrations in the brain and spinal cord. Such reductions could lead to preservation of motor neurons and slow progression of the disease, but more study is needed to examine this further."

Researchers also found that those on the 100 mg dose scored better on tests that measure breathing capacity, muscle strength, and how well people functioned on activities, when compared to people who were given a placebo. On the scale that measures how well people functioned on activities, with 48 points being the highest possible score, patients who received the 100 mg dose experienced an average 1.1 point decline compared to people who were given a placebo who experienced an average 5.3 point decline. Given the short duration of treatment, the observed difference between 100 mg and placebo-treated patients was more apparent in patients with rapidly progressing SOD1 ALS.

The most common side effects were mild to moderate and included headache, pain due to the procedure and post lumbar puncture syndrome.

Limitations of the study include its small number of participants and short time frame. More studies are needed to see if the experimental drug works in larger groups of people and over longer periods of time.

Provided by American Academy of Neurology