MedicalXpress

Findings point toward one of first therapies for Lou Gehrig's disease

June 12 2014

Researchers have determined that a copper compound known for decades may form the basis for a therapy for amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease.

In a new study just published in the *Journal of Neuroscience*, scientists from Australia, the United States (Oregon), and the United Kingdom showed in laboratory animal tests that oral intake of this compound significantly extended the lifespan and improved the locomotor function of transgenic mice that are genetically engineered to develop this debilitating and terminal disease.

In humans, no therapy for ALS has ever been discovered that could extend lifespan more than a few additional months. Researchers in the Linus Pauling Institute at Oregon State University say this approach has the potential to change that, and may have value against Parkinson's disease as well.

"We believe that with further improvements, and following necessary human clinical trials for safety and efficacy, this could provide a valuable new therapy for ALS and perhaps Parkinson's disease," said Joseph Beckman, a distinguished professor of biochemistry and biophysics in the OSU College of Science.

"I'm very optimistic," said Beckman, who received the 2012 Discovery Award from the OHSU Medical Research Foundation as the leading medical researcher in Oregon.

ALS was first identified as a progressive and fatal neurodegenerative disease in the late 1800s and gained international recognition in 1939 when it was diagnosed in American baseball legend Lou Gehrig. It's known to be caused by motor neurons in the spinal cord deteriorating and dying, and has been traced to mutations in copper, zinc superoxide dismutase, or SOD1. Ordinarily, superoxide dismutase is an antioxidant whose proper function is essential to life.

When SOD1 is lacking its metal co-factors, it "unfolds" and becomes toxic, leading to the death of motor neurons. The metals copper and zinc are important in stabilizing this protein, and can help it remain folded more than 200 years.

"The damage from ALS is happening primarily in the spinal cord and that's also one of the most difficult places in the body to absorb copper," Beckman said. "Copper itself is necessary but can be toxic, so its levels are tightly controlled in the body. The therapy we're working toward delivers copper selectively into the cells in the spinal cord that actually need it. Otherwise, the compound keeps copper inert."

"This is a safe way to deliver a micronutrient like copper exactly where it is needed," Beckman said.

By restoring a proper balance of copper into the brain and spinal cord, scientists believe they are stabilizing the superoxide dismutase in its mature form, while improving the function of mitochondria. This has already extended the lifespan of affected mice by 26 percent, and with continued research the scientists hope to achieve even more extension.

The compound that does this is called copper (ATSM), has been studied for use in some cancer treatments, and is relatively inexpensive to produce.

"In this case, the result was just the opposite of what one might have expected," said Blaine Roberts, lead author on the study and a research fellow at the University of Melbourne, who received his doctorate at OSU working with Beckman.

"The treatment increased the amount of mutant SOD, and by accepted dogma this means the animals should get worse," he said. "But in this case, they got a lot better. This is because we're making a targeted delivery of copper just to the cells that need it.

"This study opens up a previously neglected avenue for new disease therapies, for ALS and other neurodegenerative disease," Roberts said.

Provided by Oregon State University