MedicalXpress

Low-dose lithium prevents Parkinson's symptoms in aged mice with a human mutation for the disease

December 18 2014

Low-dose lithium prevented symptoms of Parkinson's disease in aged mice genetically engineered to develop the incurable, degenerative motor disease that is diagnosed in about 60,000 Americans each year. The research, led by Buck Institute faculty Julie Andersen, PhD, showed that lithium prevented the motor impairment and dopaminergic loss that are hallmarks of the disease. The study is now online in the journal *Brain Research.*

Lithium is a naturally occurring element, not a 'developed' molecule like most medications. It was approved by the FDA for the treatment of bipolar disorder in 1970 and has shown to be effective for treating mood disorders and suicidal thoughts. Previous studies suggest that at low doses lithium has a protective effect in neurodegenerative diseases such as Parkinson's, Alzheimer's and Huntington's.

In this study, Andersen and her team dosed the genetically-engineered mice with an amount of lithium equivalent to about a quarter of what humans receive for the treatment of psychiatric diseases. Treatment began when the mice reached late middle-age, the human equivalent of about 60, which is the average age of onset of Parkinson's in humans. "We clearly saw a prevention of the motor difficulties we would expect to see in the animals," said Andersen. "The treatment also protected the area of the brain that is normally damaged by Parkinson's."

Andersen says the mechanistic action of lithium is not entirely clear. In the treated animals researchers saw a reduction of inflammation in astrocytes and microglia, cells that play "housekeeping" roles in the brain. "Our findings suggest that low dose lithium could be an anti-inflammatory," said Andersen. "This gives us another avenue to study its effects in humans."

There is currently no cure for Parkinson's, which is characterized by tremor, slowness of spontaneous movement, rigidity and postural instability. As the disease progresses, patients often suffer from cognitive decline. Existing treatments can help ease symptoms, but over time the drugs themselves can cause debilitating side effects. "Developing new treatments for Parkinson's requires extensive preclinical testing and expensive human trials," said Andersen. "In lithium we have a medication that provides neuroprotection and is already approved for clinical use. It is an ideal candidate for therapy."

"While it would be premature for PD patients to take lithium supplements based on these data, this study is sufficiently promising to warrant further study," said David K. Simon, MD, PhD, Associate Professor of Neurology at Harvard Medical School in Boston. Simon chairs the Scientific Review Committee for the Parkinson's Study Group, a not-for-profit network of Parkinson's Centers. "While questions remain about optimal doses for human studies and we still need sufficient safety and efficacy data in PD patients, I do agree that Dr. Andersen's work along with other data, make a strong argument for further studies, potentially even early phase clinical studies of low-dose lithium as a disease modifying agent in PD."

More information: Christopher A. Lieu, Colleen M. Dewey, Shankar J. Chinta, Anand Rane, Subramanian Rajagopalan, Sean Batir, Yong-Hwan Kim, Julie K. Andersen, "Lithium prevents parkinsonian behavioral and striatal phenotypes in an aged parkin mutant transgenic

mouse model," *Brain Research*, Volume 1591, 3 December 2014, Pages 111-117, ISSN 0006-8993, dx.doi.org/10.1016/j.brainres.2014.10.032.