Medical Xpress

Reducing the toxicity of lithium

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Lithium is the most effective treatment for bipolar disorder.

However, its use is limited because of neurological side effects and a risk for overdose-induced toxicity. Many of the beneficial effects of lithium are mediated by its inhibition of GSK-3 proteins, but whether this is the mechanism underlying its negative effects has not been determined.

However, Raquel Gómez-Sintes and José Lucas, at CSIC/UAM, Spain, have now delineated a molecular pathway by which chronic administration of therapeutic doses of lithium has negative effects in mice. Specifically, they found that gait abnormalities and nerve cell death in several regions of the brain were a result of GSK-3 protein inhibition, which led to increased nuclear localization of NFATc3/4 proteins and increased levels of the death-inducing molecule Fas ligand.

The authors hope that these data might provide new ideas for combination therapies that diminish the toxicities of lithium, which has been proposed as a treatment for Alzheimer disease.

More information: www.jci.org/articles/view/3787 … 6336b61bbbea56ebf13c

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