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神经退行性疾病与遗传病专栏

# Neuroprotective action of lithium in disorders of the central nervous system

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摘要：

ObjectiveMethodsResultsConclusionSubstantial in vitro and in vivo evidence of neurotrophic and neuroprotective effects of lithium suggests that it may also have considerable potential for the treatment of neurodegenerative conditions. Lithium’s main mechanisms of action appear to stem from its ability to inhibit glycogen synthase kinase-3 activity and also to induce signaling mediated by brain-derived neurotrophic factor. This in turn alters a wide variety of downstream effectors, with the ultimate effect of enhancing pathways to cell survival. In addition, lithium contributes to calcium homeostasis. By inhibiting N-methyl-D-aspartate receptor-mediated calcium influx, for instance, it suppresses the calcium-dependent activation of pro-apoptotic signaling pathways. By inhibiting the activity of phosphoinositol phosphatases, it decreases levels of inositol 1,4,5-trisphosphate, a process recently identified as a novel mechanism for inducing autophagy. These mechanisms allow therapeutic doses of lithium to protect neuronal cells from diverse insults that would otherwise lead to massive cell death. Lithium, moreover, has been shown to improve behavioral and cognitive deficits in animal models of neurodegenerative diseases, including stroke, amyotrophic lateral sclerosis, fragile X syndrome, and Huntington’s, Alzheimer’s, and Parkinson’s diseases. Since lithium is already FDA-approved for the treatment of bipolar disorder, our conclusions support the notion that its clinical relevance can be expanded to include the treatment of several neurological and neurodegenerative-related diseases.

关键词：

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