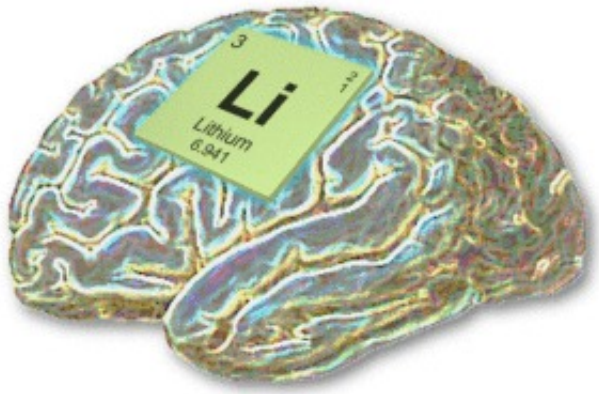
How can lithium prevent stroke – Is the inner cell layer of our vessels the key?

Since decades, lithium is one of the most effective drugs for psychiatric diseases such as bipolar disorders; but lithium has a narrow therapeutic window. This means that lithium concentration in patients' blood should be kept in a very small concentration range (for example 0.4 to 1.0 millimole per liter). Interestingly, lithium was recently reported to prevent stroke in bipolar disorder patients. Moreover, a study by Bosche and co-workers (Bosche et al. BBRC, 2013) found that lithium protects the inner cell layer of blood vessels – the so called vessel endothelium, which is important for the opening (=relaxation) of blood vessels. However, the mechanisms of this potential protective effect are not fully understood, yet.



In the recent study of Bosche and co-workers, they hypothesize that at different lithium concentrations, the effects on endothelium reverses even within the narrow therapeutic (concentration) window, i.e. lithium improves but also impairs endothelium–dependent opening or widening of blood vessels. Therefore, vessels pieces taken from mice aortas and from swine brains were preconditioned using nutrient media supplemented with lithium. The opening (or relaxation) capacity of preconditioned vessels was assessed by measuring the positive or negative vessel muscle force (negative for opening and positive for constricting of the vessels). The ability to open vessels is one of the major strategies of our vessel system to avoid vessel occlusions such as stroke. At the concentration of 0.4 millimole per liter lithium, the vessel opening (negative force) was increased, however, diminished in vessels preconditioned with lithium at slightly higher concentrations (0.8 millimole per liter). Moreover, they found that only the endothelium–dependent vessel opening was lithium sensitive, i.e. showed these opposing effects of the same drug at different concentrations including a protective effect for the dynamic vessel function at the lower lithium concentration. Lithium elicits opposing effects on endothelial functions representing a differential impact on the endothelium within the narrow therapeutic window. The differentially modified vessel opening response represents a new mechanism contributing to therapeutic effects

of lithium and (more important) can therefore explain, why lithium protect against stroke in patients, who take lithium for a totally different reason aiming to treat a psychiatric disorder.

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