

## Body clocks may hold key for treatment of bipolar disorder

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Scientists have gained insight into why lithium salts are effective at treating bipolar disorder in what could lead to more targeted therapies with fewer side-effects.

Bipolar disorder is characterised by alternating states of elevated mood, or mania, and <u>depression</u>. It affects between 1% and 3% of the general population.

The extreme 'mood swings' in bipolar disorder have been strongly associated with disruptions in <u>circadian rhythms</u> – the 24-hourly rhythms controlled by our body clocks that govern our day and night activity.

For the last 60 years, <u>lithium</u> salt (lithium chloride) has been the mainstay treatment for bipolar disorder but little research has been carried out to find out whether and how lithium impacts on the brain and peripheral body clockwork.

"Our study has shown a new and potent effect of lithium in increasing the amplitude, or strength, of the clock rhythms, revealing a novel link between the classic mood-stabiliser, bipolar disorder and body clocks," said lead researcher Dr Qing-Jun Meng, in the University's Faculty of Life Sciences.

"By tracking the dynamics of a key clock protein, we discovered that lithium increased the strength of the clockwork in cells up to three-fold by blocking the actions of an enzyme called glycogen synthase kinase or



GSK3.

"Our findings are important for two reasons: firstly, they offer a novel explanation as to how lithium may be able to stabilise mood swings in bipolar patients; secondly, they open up opportunities to develop new drugs for bipolar disorder that mimic and even enhance the effect lithium has on GSK3 without the side-effects lithium salts can cause."

These side-effects include nausea, acne, thirstiness, muscle weakness, tremor, sedation and/or confusion. Promisingly, GSK3 inhibiting drugs are already in development, as they have been shown to be important in other diseases, including diabetes and Alzheimer's disease.

Dr Meng added: "Lithium salt has a wide spectrum of targets within cells, in addition to GSK3; drugs which only block the actions of GSK3 would therefore have the major advantage of reduced 'off-target' effects of lithium.

"Our study has identified the robust rhythm-enhancing effect of GSK3 inhibition, which has potential to be developed as a new pharmacological approach to regulate <u>body clocks</u>. The implications of our study are that there may also be beneficial effects leading to new treatments for <u>bipolar disorder</u>, and this now needs to be tested."

The research, funded by the Medical Research Council and the Biotechnology and Biological Sciences Research Council (BBSRC), is published in the journal *PLoS One*.

**More information:** 'Lithium Impacts on the Amplitude and Period of the Molecular Circadian Clockwork,' *PLoS One*.



## Provided by University of Manchester

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