

Personalizing bipolar disorder treatment

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Rapidly swinging from extremes of joy and energy to sadness, fatigue, and confusion, bipolar disorder (BD) patients feel desperate and largely alone in the world. And according to the National Institutes of Health, between 25-50 percent of the roughly 3% of Americans living with BD attempt suicide at least once. Lithium is among the most effective therapies for BD, and remains the first-line treatment even as other mood stabilizing drugs have become available. But about half of the patients prescribed lithium do not respond to the treatment.

A new Tel Aviv University study, published in the *Journal of Molecular Neuroscience*, may pave the way for improving the efficacy of lithium in these <u>patients</u>. The study found that the insulin-like growth factor 1 (IGF-1) hormone, known for its pivotal role in tissue growth, is also capable of increasing the lithium sensitivity of <u>blood cells</u> in bipolar disorder patients in whom lithium was originally ineffective.

The research was led by TAU postgraduate student Dr. Elena Milanesi under the guidance of Dr. David Gurwitz of the Department of Human Molecular Genetics and Biochemistry of TAU's Sackler Faculty of Medicine and Sagol School of Neuroscience and Dr. Noam Shomron of the Department of Cell and Developmental Biology at TAU's Sackler Faculty of Medicine, in collaboration with Sackler graduate student Adva Hadar and Prof. Haim Werner of TAU's Sackler Faculty of Medicine, along with researchers in Italy and Germany.

A new hope

"Lithium has been considered the cornerstone in the management of bipolar disorder for over 50 years, even though half of patients do not sufficiently respond to chronic lithium treatment," said Dr. Gurwitz. "It is often prescribed as the firstline treatment for bipolar disorder. If it works, patients take it for years. If not, they have to explore alternatives which haven't proven as effective in long-term clinical studies."

The researchers examined the in vitro effects of insulin-like growth factor 1 (IGF-1) on lithium sensitivity in blood cell lines of both lithium-responsive and non-responsive bipolar patients. They found that when IGF-1 was added to the cultured blood cells there was increased lithium sensitivity only in the blood cells of those bipolar disorder patients who did not respond to lithium therapy.

"Our study suggests that the lack of sufficient IGF-1 activity may underlie lithium resistance in the treatment of bipolar disorder, and this hormone, or drugs mimicking or promoting its action, should be considered for improved treatment of this disorder", says Dr. Milanesi.

"There are no established animal models for bipolar disorder, so it will be hard to test this idea in animals," Dr. Gurwitz added. "However, given that IGF-1 is approved for human use in people who are deficient in this hormone, a clinical trial of IGF-1 in lithium-resistant <u>bipolar disorder</u> patients is warranted."



The research on <u>lithium</u> resistance biomarkers was supported by the U.S.-Israel Binational Science Foundation (BSF).

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