

New drug for bipolar disorder may offer fewer side effects

January 9 2013



People with bipolar disorder can experience periods of depression and mania lasting for several weeks or longer.

(Medical Xpress)—A drug for bipolar disorder that works like lithium, the most common and effective treatment for the condition, but without lithium's toxicity and problem side-effects has been identified by Oxford University researchers in a study in mice.

A drug that mimics the effect of [lithium](#) but without its [side-effects](#) would be a great improvement for patients, and has long been sought after.

While the study has been conducted in [mice](#), the newly identified drug is an existing compound called ebselen. It is known to be safe in humans and so its use for [bipolar disorder](#) can begin to be tested in clinical trials straight away.

'Lithium has been used for over 60 years and remains the most effective treatment for bipolar disorder, but suffers from [toxicity](#) and has many side effects,' says co-principal investigator Dr Grant Churchill of the Department of Pharmacology at Oxford University. 'In mice, ebselen works like lithium. Most importantly, ebselen is an [experimental drug](#) that has been tested in people for other conditions, and does not have problematic side effects like lithium does.'

He adds: 'We urgently need to test if ebselen works like lithium in people.'

The researchers report their findings in the journal *Nature Communications*. The work was funded by the UK Biotechnology and Biological Sciences Research Council.

Bipolar disorder is relatively common and can occur at any age. It is estimated to affect around one person in 100.

People with bipolar disorder can experience moods that swing from one extreme to another, having periods of depression and mania lasting for several weeks or longer. These phases of feeling high and low are often so extreme that they interfere with [everyday life](#).

60 years after its discovery, lithium remains the most effective long-term therapy for bipolar disorder – it is a mood stabiliser that has been shown to protect against both depression and mania, and reduce the risk of suicide. But it is toxic at only twice the right dose and it has unpleasant side-effects, such as weight gain and thirst, and long-term use can lead to

kidney damage.

A drug that worked like lithium without the toxicity or side-effects would be a great improvement for patients, but efforts so far to develop such a drug have proved unsuccessful.

A lithium mimic would also lessen the burden on healthcare systems. Lithium's toxicity means that getting the dose right is important, and several visits to the clinic may be required to get this right when the drug is initially prescribed. Regular check-ups are required to monitor the treatment. The side-effects also mean many people stop taking the drug and can see a return of the episodes of mania and [depression](#).

The Oxford researchers used a library of existing drugs that are considered safe but don't currently have a proven use. The US National Institutes of Health Clinical Collection includes compounds that may have been originally developed for various different diseases or conditions. These compounds have been tested in clinical trials, so their safety in humans is known.

They screened this library for any drugs that blocked an enzyme that is a prominent candidate for how lithium works in stabilising mood in bipolar disorder. In this way, they identified ebselen as a possible lithium mimic.

Ebselen is an antioxidant originally developed up to phase III clinical trials by a Japanese drug company for use in the treatment of stroke, but which never reached market and is now out of patent.

The researchers showed that ebselen has the same or similar action as lithium in the brains of mice, blocking the same enzyme.

They have also shown ebselen has the same effects as lithium in mouse

models of bipolar disorder, dampening down this behaviour in the same way.

The researchers say the next step is to test whether ebselen has the same effects as lithium in people through appropriate [clinical trials](#).

They are beginning a small study in healthy volunteers to look for effects on brain function. If that shows that ebselen continues to have similar effects to lithium in humans, the plan would be to move to a small phase II trial in people with bipolar disorder.

Should these prove successful, ebselen will be one of only a few examples of 'drug repurposing', where new uses are found for drug compounds originally developed for another condition but that may have failed for one reason or another.

Rather than these fully-developed compounds remaining unused on the shelf of a pharmaceutical company or academic laboratory, there have been recent moves to make such drug compounds more available for study by others to see if they might find other uses. So far, there have been only a few successes, but this work might add another.

'This is one of the first handful of examples of drug repurposing, where a new use has been found for an existing [drug](#),' says the other lead author, Dr Sridhar Vasudevan of the Department of Pharmacology at Oxford University.

Provided by Oxford University

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