Medical Xpress

Gene-based tests may improve treatment for people with bipolar disorder

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Responsiveness to lithium – the gold standard of bipolar treatment – runs in families. Credit: Francisco Gonzalez/unsplash

Bipolar affective disorder (BPAD) affects around 2% of the world's population, leaving them with bouts of severe depression and episodes of

what is commonly referred to as "mania".

A range of drug treatments are available, but choosing the right medication, or range of medications, can be a struggle – sometimes spanning many years.

But new research aims to shorten this process by matching drug treatments to individual patients, based on their genetic profile.

What is bipolar disorder?

When depressed, people with bipolar have a low mood, poor energy levels, and lose interest in pleasurable activities over the course of many weeks. They also notice ongoing negative thoughts about themselves and their environment.

In the most severe cases, people lose their appetite, are unable to sleep, and have thoughts that circle around death and suicide.

During manic episodes, patients become increasingly unpredictable and engage in activities that are often "out of character". They might sleep less than usual, spend unreasonable amounts of money (unlike their usual spending patterns), engage in superficial relationships, and start new projects without being really interested in completing them.

As mania progresses, patients can become irritable, impatient, and aggressive towards others. Often they find themselves in conflict with their family or people at work.

In episodes of severe mania, people can develop beliefs that are not in keeping with reality. They might believe they have special powers, or that they are being targeted or threatened by others.

During manic episodes, sufferers typically lose the ability to recognise the changes in their behaviour and thinking, and blame others for their difficulties. They usually also see no reason to seek medical assistance, and can react strongly if others recommend doing so.

Depressive and manic episodes can occur within short periods of time, or after long periods of normal mental health.

Usually, these episodes lead to severe disruptions of a person's life, and patients are unable to carry out their duties at work and at home. Admissions to psychiatric inpatient units for treatment may be required, sometimes against the patient's will.

Towards tailored treatments

Most patients with bipolar disorder are prescribed "mood-stabilising" medication for treatment during episodes and to prevent relapse. This usually consists of one, or a combination, of three types of medicine:

lithium saltsanti-epileptic medicines such as sodium valproate, andsome "antipsychotics" such as risperidone, quetiapine, or olanzapine.

It's hard to predict which drug will work best for each person, so these treatments are generally selected by trial and error.

It can take years until the optimal medication is determined. During this time, patients often experience ongoing mood symptoms, relapses, medication side effects, and reduced functioning.

Psychiatric research labs are now developing tests for personalised drug selection for people with bipolar. The hope is that genetic and blood test information could help determine which drug may work best for a patient, and what should be avoided.

A focus of these research efforts is the mood stabiliser lithium. Lithium is an elementary metal that naturally occurs as a salt, and is seen as the "gold standard" treatment for bipolar. It is useful in treating acute mania, protects against further illness episodes, enhances antidepressant treatments, and can prevent suicidal thoughts and actions.

But only 30% of bipolar patients experience the full range of lithium benefits. For some others, additional medicines have to be added to control the illness. And about 30% of bipolar patients get no benefit at all from lithium, and need to use other types of mood stabilisers.

Responsiveness to lithium can run in families. A patient is more likely to do well on the drug if their parent or sibling (if they also suffer from bipolar disorder) also shows a good response. This suggests a genetic, or heritable, component to the medication response.

Research from our group and others has now begun to untangle the underpinnings of these genetic effects. We found, for example, that bipolar patients who carry many "risk" genes for certain other medical and psychiatric disorders, such as schizophrenia, are less likely to have a good outcome with lithium.

Further, a large-scale genetic study we were involved in found a small number of genes that specifically determine lithium response.

Other studies are starting to uncover the biological effects of these genetic variations. There is increasing evidence, for instance, that people who do well on lithium have specific disturbances in molecular pathways that regulate energy within nerve cells.

These studies suggest people with bipolar illness have a "biological signature" that can predict how they will response to different mood stabilising medicines.

But much work needs to be done, over several years, before these findings can be translated into tests that can be run routinely in psychiatric clinics.

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