A new type of MRI imaging has enabled University of Iowa researchers to discover previously unrecognised differences in the brains of patients with bipolar disorder. In particular, the researchers found differences in the white matter of patients' brains and in the cerebellum, an area of the brain not previously linked with the disorder.

Using an MRI technique known as quantitative high-resolution T1 rho mapping, the researchers also observed that the cerebellar differences were not present in patients taking lithium, the most commonly used treatment for bipolar disorder. This imaging technique is sensitive to certain byproducts of cell metabolism, including levels of glucose and acidity in the brain.

Scientists do not have a good understanding of what causes bipolar disorder, which is characterised by sudden mood shifts from normal to depressed or to an abnormally elevated or "manic" mood state. This psychiatric condition affects about one percent of the population.

The study, published in the journal *Molecular Psychiatry*, examined 15 patients with bipolar disorder and 25 control subjects matched for age and gender. The bipolar patients were all in normal (euthymic) mood state during the study.

Compared to the brains of people without bipolar disorder, the UI team found that the MRI signal was elevated in the cerebral white matter and the cerebellar region of patients affected by bipolar disorder. The elevated signal may be due to either a reduction in pH or a reduction in glucose concentration, both factors influenced by cell metabolism, said the researchers.

Based on previous research, abnormal cell metabolism may play a role in bipolar disorder. However, investigating metabolic abnormalities in the brain has been hindered by a lack of good imaging tools. Available methods are slow, low-resolution, and require researchers to identify the region of interest at the onset of the study. In contrast, the new MRI imaging technique can rapidly obtain a high-resolution image of the whole brain.

The UI study is the first time the novel MRI technique has been used to investigate a psychiatric disease. "This imaging technique appears to be sensitive to things that just have not been imaged effectively before. So it's really providing a new picture and new insight into the composition and function of the brain [in bipolar disease]," said the study's senior author John Wemmie, MD, PhD, UI professor of psychiatry.

One reason researchers did not know that the cerebellum might be important in bipolar disorder, is because no one chose to look there, noted co-author Casey Johnson, PhD, UI postdoctoral researcher. "Our study was..."
essentially exploratory. We didn't know what we would find. The majority of bipolar disorder research has found differences in the frontal region of the brain. We found focal differences in the cerebellum, which is a region that hasn't really been highlighted in the bipolar literature before."

The finding motivated Johnson and Wemmie to do an extensive search of the scientific literature on bipolar disorder. They began to collect pieces of evidence that suggested that the cerebellum may function abnormally in bipolar disorder and that lithium might potentially target the cerebellum and alter glucose levels in this brain region.

The new insights provided by the T1 rho imaging could help to broaden understanding of the abnormalities that underlie bipolar disease and lead to better ways to diagnose and treat this problem.

Lithium may be an effective mood stabiliser for people with bipolar disorder, but it causes numerous unpleasant side effects for patients. As Dr. Wemmie noted: "If lithium's effect on the cerebellum is the key to its effectiveness as a mood stabiliser, then a more targeted treatment that causes the same change in the cerebellum without affecting other systems might be a better treatment for patients with bipolar disorder."

Source: University of Iowa Health Care
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