

Abnormal brain changes found to develop over time with bipolar disorder

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Bipolar disorder is characterized by transitions between depression and mania.
Credit: Wikipedia

Bipolar disorder (BD) is a debilitating psychiatric disorder characterized

by fluctuating periods of depression and mania. Researchers have long suspected that BD may be accompanied by abnormal structural and functional changes in the brain. Small cross-sectional brain imaging studies of people with BD have shown hints at those changes, but the ability to interpret data collected at a single timepoint is limited. Now, a multi-center longitudinal study shows aberrant changes over time in the brains of people with BD. Some changes were specifically associated with more episodes of mania.

The report appears in *Biological Psychiatry*. The study involved a large international multi-center team of more than 70 researchers from the ENIGMA Bipolar Disorder Working Group.

"The ENIGMA Bipolar Disorder Working Group report illustrates the power of large-scale multi-center collaboration," said John Krystal, MD, Editor of *Biological Psychiatry*. "Longitudinal neuroimaging studies are extremely challenging to conduct. Here, by combining data from 14 sites, we get one of the clearest pictures we have of the neurotoxic impact of bipolar disorder, particularly manic episodes."

The researchers gathered magnetic resonance imaging (MRI) and detailed clinical data from 307 people with BD and from 925 healthy controls (HC) from 14 clinical sites worldwide. Participants were assessed at two timepoints, ranging from six months to nine years apart.

The most striking finding was that the cortex, the brain's outermost layer, thinned over time to a greater extent in people who experienced more manic episodes. Those who did not have mania showed no cortical thinning or even cortical thickening. The changes were most evident in the prefrontal cortex (PFC), an area associated with executive control and emotion regulation.

"The fact that cortical thinning in patients related to manic episodes

stresses the importance of treatment to prevent mood episodes and is important information for psychiatrists," said senior author Mikael Landén, MD, Ph.D., Professor and Chief Physician at the Institute of Neuroscience and Physiology, University of Gothenburg, Sweden. "Researchers should focus on better understanding the progressive mechanisms at play in bipolar disorder to ultimately improve treatment options."

Compared to HC, people with BD showed a faster enlargement in the brain's ventricles, cavities within the brain that contain cerebrospinal fluid. In cortical areas outside the PFC, BD participants actually showed slower thinning than HC participants.

Lead author Christoph Abé, Ph.D., Assistant Professor, Karolinska Institutet, Sweden, said: "The abnormal ventricle enlargements and importantly the associations between cortical thinning and manic symptoms indicate that [bipolar disorder](#) may in fact be a neuroprogressive disorder, which could explain the worsening of bipolar symptoms in some patients."

One possibility to explain why BD patients may have slower thinning of the cortex compared to HC is that lithium, a medication used to treat BD, is known to have neuroprotective effects and could bolster cortical thickness. Regardless, the study provides new clues about the structural effects of BD on the brain over time.

More information: Christoph Abé et al, Longitudinal structural brain changes in bipolar disorder: A multicenter neuroimaging study of 1,232 individuals by the ENIGMA Bipolar Disorder Working Group, *Biological Psychiatry* (2021). [DOI: 10.1016/j.biopsych.2021.09.008](https://doi.org/10.1016/j.biopsych.2021.09.008)

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