

# Causal Association of Bipolar Disorder and Post-traumatic Stress Disorder

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## Abstract

*Background:* Epidemiological and clinical studies have suggested comorbidity between bipolar disorder and post-traumatic stress disorder (PTSD). However, the direction and magnitude of the causal relationships between bipolar disorder and PTSD have not been established for the possible presence of recall bias and confounders in observational studies. *Methods:* Linkage Disequilibrium Score Regression and two-sample Mendelian randomization (MR) were used to test for genetic correlation ( $rg$ ) and bidirectional causal effects using European ancestry genome-wide association studies of bipolar disorder (41,917 cases and 371,549 controls) and PTSD (1103 cases and 198110 controls). The data for bipolar disorder was obtained from Psychiatric Genomics Consortium, and the data for PTSD was obtained from FinnGen database. *Results:* The Mendelian randomization analysis revealed that genetic liabilities to bipolar disorder [odds ratio (OR) = 1.550; 95% confidence interval (CI), 1.168-2.058;  $P = 0.002$ ] was associated with an increased risk of developing PTSD later in life. However, no evidence supported that genetic liability to PTSD could elevate the risk of bipolar disorder. *Conclusion:* The findings of this study supported that bipolar disorder may increase the risk of PTSD, but not vice versa, supporting the need for early and effective treatment of bipolar disorder. Our findings emphasize the importance of bipolar disorder in the prevention and treatment of PTSD.

## Keywords

Bipolar Disorder, Post Traumatic Stress Disorder, Mendelian Randomization, Comorbidities