Genetically predicted bipolar disorder is causally associated with increased risk of breast cancer: a Mendelian randomization analysis

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Background

Epidemiologic findings suggested that bipolar disorder (BD) may be associated with increased risk of breast cancer. However, there are few studies that comprehensively evaluate their correlation and the causal effect remains unknown. With a Mendelian randomization (MR) approach, we were able to investigate the causal relationship between genetically predicted BD and breast cancer risk.

Methods

Utilizing 6 BD-related single nucleotide polymorphisms as instrumental variables identified by the latest genome-wide association studies, we investigated the correlation between genetically predicted BD and breast cancer risk using summary statistics from the Breast Cancer Association Consortium, with a total of 122, 977 cases and 105, 974 controls. Study-specific estimates were summarized using inverse-variance-weighted (IVW) method. To further evaluate the pleiotropy, the weighted median and the MR-Egger regression method were implemented. Subgroup analyses according to different immunohistochemical type of breast cancer were also conducted.

Results

MR analyses demonstrated that genetically predicted BD was causally associated with an increased risk of breast cancer (OR = 1.058; 95% CI 1.023-1.093, $p < 0.001$). When results were examined by immunohistochemical type, a strong association was observed between genetically predicted BD and estrogen receptor (ER) -positive breast cancer (OR = 1.048, 95%CI 1.008-1.090 p = 0.0177) rather than ER-negative breast cancer (OR = 1.026, 95%CI 0.975-1.081 p = 0.3231). Additionally, the results demonstrated the absence of the horizontal pleiotropy.

Conclusions

Our findings provide evidence for a causal relationship between genetically predicted BD and increased breast cancer risk, overall and among specific immunohistochemical type. Further studies are warranted to investigate the underlying mechanism.