Objectives: A single nucleotide polymorphism within the CACNA1C gene (rs1006737) has been found to confer increased risk of Bipolar Disorder (BD) and has been linked to altered neuronal gating and emotional behaviour. As current models of BD suggest abnormal integration within frontolimbic networks, our aim was to explore the effect of the CACNA1C genotype on prefrontal and limbic activation.

Methods: We genotyped 90 participants from the Vulnerability to Bipolar Disorder Study comprising of 41 euthymic BD patients and 49 healthy controls. Functional magnetic resonance imaging data were obtained while participants performed a fearful versus neutral facial affect processing task.

Results: We found a significant diagnosis by genotype interaction with BD patients homozygous for the risk allele having reduced prefrontal activation compared to the other groups.

Conclusions: The present findings support the hypothesis that the rs1006737 polymorphism in the CACNA1C gene confers increased risk of BD by modulating amygdala and PFC activation during emotional processing.