

**ASSOCIATION STUDY BETWEEN TOLL-LIKE RECEPTORS 2 AND 4 SINGLE NUCLEOTIDE POLYMORPHISMS AND BIPOLAR DISORDER**

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**Introduction:** Immune dysfunction is thought to play a critical role in the pathophysiology of bipolar disorder (BD). Better insight into the genetic control of innate immune responses is of importance due to possible interactions with environmental risk factors such as infectious agents, particularly early in life.

**Objectives:** Given the importance of Toll-like receptors (TLRs) in innate immunity, we analysed the association of selected genetic variants of TLR-2 and TLR-4, both major sensors of pathogenic infectious and non-infectious structures, with BD.

**Aims:** Explore possible implications of the innate arm of the immune response in BD.

**Methods:** Genomic DNAs from 572 BD patients and 202 controls were analyzed for the distribution of polymorphisms on the TLR-2 and TLR-4 loci using TaqMan<sup>®</sup>. Associations were examined using Chi-square test.

**Results:** We found that TLR-4 *rs1927914* AA and *rs11536891* TT genotypes were more frequent in BD patients than in controls (corrected *p*; *p*<sub>c</sub> = .02 and .02 respectively) particularly in early-onset BD (EOBD) patients (*p*<sub>c</sub> = .004 and .006) born during the summer season (*p*<sub>c</sub> = .02 and .002 respectively). We also found that TLR-2 *rs3804099* TT and *rs4696480* TT genotypes were significantly more prevalent in EOBD group as compared to the late-onset BD (LOBD) subset, the latter only after excluding patients with positive family history of psychiatric disorders (*p*<sub>c</sub>=0.024 and 0.002 respectively).

**Conclusions**

We report an association between BD and TLR-2 and TLR-4 genetic variants suggesting an important role for pathogens in disease development.