Combined Effect of TLR2 Gene Polymorphism and Early Life Stress On the Age at Onset of Bipolar Disorders

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Immune dysfunction is thought to be an important pathway underlying the association of childhood traumatic events with early-onset of bipolar disorder (BD). The study of gene-environment interactions are important to better understand the genetics of resilience or susceptibility to this severe subform of BD. We thus explored the potential interaction of genetic variants of TLR2 and TLR4, major triggers of inflammatory responses in presence of pathogens, and the presence of childhood trauma on the age at onset of BD.

TLR2 and TLR4 risk genotype carrier state and history of childhood emotional, physical and sexual abuses were analyzed in relation to age at onset of BD in 531 BD patients genotyped for TLR2 rs4696480 and rs3804099 and TLR4 rs1927914 and rs11536891, 329 of which completed the Childhood Trauma Questionnaire.

We report a combined effect of TLR2 rs3804099TT genotype and reported sexual abuse on determining an earlier age at onset of BD by means of a Kaplan-Meier survival curve (p = 0.02). Regression analysis was non-significant for the TLR2-CTQ sexual abuse interaction term.

The pathological effect of childhood adversity may be of greater importance in patients with an immunogenetic susceptibility background. Further exploration of clinical characteristics of severity and immune phenotypes in BD may allow the development of innovative therapeutic interventions.