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

J. Oliveira[1], B. Etain[1], M. Lajnef[1], N. Hamdani[1], M. Bennabi[2], F. Bellivier[1], J.P. Kahn[3], D. Charron[2], R. Krishnamoorthy[2], M. Leboyer[1], R. Tamouza[2]

[1]Institut Mondor de Recherche Biomédicale, INSERM U955, Créteil, France ; [2]Institut Universitaire d'Hématologie, INSERM U1160, Paris, France ; [3]Centre Hospitalier Universitaire de Nancy, Service de Psychiatrie et Psychologie Clinique, Vandoeuvre Les Nancy, France

Immune dysfunction is thought to be animportant pathway underlying the association of childhood traumatic events withearly-onset of bipolar disorder (BD). The study of gene-environmentinteractions are important to better understand the genetics of resilience orsusceptibility to this severe subform of BD. We thus explored the potentialinteraction of genetic variants of *TLR2* and *TLR4*, major triggers of inflammatoryresponses in presence of pathogens, and the presence of childhood trauma on theage 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 in531 BD patients genotyped for *TLR2 rs*4696480and *rs*3804099 and *TLR4 rs*1927914 and *rs*11536891, 329 of which completed the Childhood TraumaQuestionnaire.

We report a combined effect of *TLR2 rs*3804099TT genotype and reported sexual abuse on determining an earlier age at onset ofBD 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 immuno-genetic susceptibility background. Further exploration of clinical characteristics of severity and immune phenotypes in BD may allow the development of innovative therapeutic interventions.

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