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SELECTIVE DNA METHYLATION OF BDNF PROMOTER AND NOCICEPTIN GENE IN BIPOLAR DISORDER

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Introduction: The etiology of bipolar disorder (BD) is still poorly understood and it has been proposed that altered expression of multiple mRNAs, affecting neurotransmission, in psychotic subjects may be due to epigenetic mechanisms (e.g., DNA methylation or histone modification).
Aims: The present collaborative study was aimed to investigate, in subjects with BD, dysregulation of DNA methylation, in the brain-derived neurotrophic factor (BDNF), previously associated with psychosis and linked to epigenetic changes at promoter regions, and in the nociceptin gene (N/OFQ), a new proposed target in psychiatric disorders.
Methods: DNA was isolated from blood of patients diagnosed with BD (either type I [n = 19] or II [n = 20]) according to DSM-IV criteria, and from healthy controls (n = 20) and, thereafter, bisulfite conversion was performed. Real-Time Methylation Specific PCR (MSP) was used for the quantification of the methylated promoters in all samples.
Results: A hypermethylation of BDNF promoter region was observed in BD II patients (but not in BD I) compared to controls (CONT: 19.0 ± 3.2 %; BD I: 27.2 ± 4.0 %; BD II: 36.3 ± 6.2 % * P = 0.0167; ANOVA F = 3.464; P = 0.0384; Bonferroni´s post hoc test). No significant differences were found for DNA methylation of N/OFQ promoter.
Conclusions: Present preliminary findings suggest selective changes in DNA methylation of BDNF promoter in type II bipolar patients and highlight the importance of epigenetic factors in mediating the onset and/or susceptibility to BD, providing new insight into the mechanisms of gene expression.

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