P-699 - SELECTIVE DNA METHYLATION OF BDNF PROMOTER IN BIPOLAR DISORDER: DIFFERENCES AMONG PATIENTS VS CONTROLS AND POTENTIAL INFLUENCE OF PHARMACOLOGICAL TREATMENTS

B.Dell'Osso[1], C.D'Addario[2], M.Palazzo[1], B.Benatti[1], L.Lietti[1], E.Cattaneo[1], D.Galimberti[3], C.Fenoglio[3], F.Cortini[3], C.Dobrea[1], E.Scarpini[3], B.Arosio[4], M.Di Benedetto[5], P.Romualdi[6], S.Candeletti[5], D.Mari[4], M.Mari[4], M.Maccarrone[2,7], A.C.Altamura[1]

[1]Department of Mental Health, Università degli Studi di Milano, Milan, [2]Department of Biomedical Sciences, University of Teramo, Teramo, [3]Department of Neuroscience, Università degli Studi di Milano, [4]Geriatric Unit, Fondazione IRCCS Ca' Granda Ospedale Policlinico, Milan, [5]Department of Pharmacology, University of Bologna, Bologna, [6]Department of Pharmacology, University of Bologna, Milan, [7]European Center for Brain Research (CERC), Santa Lucia Foundation, Rome, Italy

Introduction: The etiology of bipolar disorder (BD) is poorly understood, involving genetic, epigenetic mechanisms and environmental contributions.
Aim: Among the candidate genes associated with major psychoses, the present study investigated the degree of DNA methylation at brain-derived neurotrophic factor (BDNF) gene promoter in peripheral blood mononuclear cells (PBMCs) isolated from bipolar patients.
Methods: DNA was isolated from the blood of 94 BD patients (49 BD I and 45 BD II) and 52 controls and converted with sodium bisulfite. Real Time Methylation Specific PCR was performed to quantify promoter methylation.
Results: A significant BDNF gene expression down-regulation was observed in BD II 0.53 ± 0.11%; p< 0.05), but not in BD I (1.13 ± 0.19%) patients compared with controls (CONT: 1±0.2%). Consistently, an hypermethylation of the BDNF promoter region was specifically found in BD II patients (CONT: 24.0±2.1%; BDI: 20.4±1.7%; BDII: 33.3±3.5%, p< 0.05). Of note, higher levels of DNA methylation were observed in BD subjects on pharmacological treatment with mood stabilizers plus antidepressants (34.6 ±4.2 %, predominantly BD II) compared with those exclusively on mood stabilizing agents (21.7±1.8%; p< 0.01, predominantly BD I). Moreover, among the different pharmacological therapies, lithium (20.1 ±3.8%, p< 0.05) and valproate (23.6±2.9 %, p < 0.05) were associated with a significant reduction of DNA methylation compared to other drugs (35.6±4.6%).
Conclusions: Present findings suggest selective changes in DNA methylation of BDNF promoter in subjects with BD type II and highlight the importance of epigenetic factors in mediating the patophysiology an treatment response of BD.

https://doi.org/10.1016/S0924-9338(12)74866-6 Published online by Cambridge University Press