

Brain-Derived Neurotrophic Factor and It's Precursor ProBDNF Serum Levels in Adolescents with Mood Disorders: 2-Year Follow-Up Study

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Abstract : Introduction: Neurotrophic factors have been implicated in neuropsychiatric disorders. Brain-Derived Neurotrophic Factor (BDNF) influences neuron differentiation in development as well as synaptic plasticity and neuron survival in adulthood. BDNF is widely studied in mood disorders and has been proposed as a biomarker for depression. BDNF is synthesized as precursor protein - proBDNF. Both forms are biologically active and exert opposite effects on neurons. Aim: The aim of the study was to examine the serum levels of BDNF and proBDNF in unipolar and bipolar young patients below 24 years old during hypo/manic, depressive episodes and in remission compared to healthy control group. Methods: In a prospective 2 years follow-up study, we investigated alterations in levels of BDNF and proBDNF in 79 patients (23 males, mean age 19.08, SD 3.3 and 56 females, mean age 18.39, SD 3.28) diagnosed with mood disorders: unipolar and bipolar disorder compared with 35 healthy control subjects (7 males, mean age 20.43, SD 4.23 and 28 females, mean age 21.25, SD 2.11). Clinical characteristics including mood, comorbidity, family history, and treatment, were evaluated during control visits and clinical symptoms were rated using the Hamilton Depression Rating Scale and Young Mania Rating Scale. Serum BDNF and proBDNF concentrations were determined by Enzyme-Linked Immunosorbent Assays (ELISA) method. Serum BDNF and proBDNF levels were analysed with covariates: sex, age, age > 18 and < 18 years old, family history of affective disorders, drug-free vs. medicated status. Normality of the data was tested using Shapiro-Wilk test. Levene's test was used to calculate homogeneity of variance. Non-parametric Tests: Mann-Whitney U test, Kruskal-Wallis ANOVA, Friedman's ANOVA, Wilcoxon signed rank test, Spearman correlation coefficient were applied in analyses The statistical significance level was set at $p < 0.05$. Results: BDNF and proBDNF serum levels did not differ between patients at baseline and controls as well as comparing patients in acute episode of depression/hypo/mania at baseline and euthymia (at month 3 or 6). Comparing BDNF and proBDNF levels between patients in euthymia and control group no differences have been found. Increased BDNF level in women compared to men at baseline ($p=0.01$) have been observed. BDNF level at baseline was negatively correlated with depression and mania occurrence at 24 month ($p=0.04$). BDNF level at 12 month was negatively correlated with depression and mania occurrence at 12 month ($p=0.01$). Correlation of BDNF level with sex have been detected ($p=0.01$). proBDNF levels at month 3, 6 and 12 negatively correlated with disease status ($p=0.02$, $p=0.008$, $p=0.009$, respectively). No other correlations of BDNF and proBDNF levels with clinical and demographical variables have been detected. Discussion: Our results did not show any differences in BDNF and proBDNF levels between depression, mania, euthymia, and controls. Imbalance in BDNF/proBDNF signalling may be involved in pathogenesis of mood disorders. Further studies on larger groups are recommended. Grant was founded by National Science Center in Poland no 2011/03/D/NZ5/06146.

Keywords : bipolar disorder, Brain-Derived Neurotrophic Factor (BDNF), proBDNF, unipolar depression

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