

B. Misiak<sup>1</sup>, D. Frydecka<sup>1</sup>, R. Slezak<sup>2</sup>, P. Piotrowski<sup>1</sup>, A. Kiejna<sup>2</sup>

<sup>1</sup>Department of Psychiatry, Wrocław Medical University, Wrocław, Poland ; <sup>2</sup>Department of Genetics, Wrocław Medical University, Wrocław, Poland

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**Introduction.** Inconsistent results indicate that plasma levels of homocysteine (Hcy), folic acid (FA) and vitamin B12 are altered in first-episode schizophrenia (FES) patients.

**Objectives.** The aim of this study was to assess the association between alterations in plasma Hcy, FA, vitamin B12 and lipid profile and schizophrenia.

**Methods.** We recruited 45 FES patients and 23 healthy age-matched controls (HC). Diagnosis of schizophrenia was based on ICD-10 and DSM-IV criteria, and confirmed using Operational Criteria for Psychotic Illness (OPCRIT). We excluded patients with drug and/or alcohol abuse within one year of onset of psychotic symptoms.

**Results.** There was no difference in mean plasma biochemical parameters between FES patients and HC with exception of high density lipoproteins (HDL) level (FES:  $52.69 \pm 17.07$  vs. HC:  $68.35 \pm 16.99$  mg/dl,  $p = 0.001$ ). However, there were significant differences between FES patients with and without positive history of life-time cannabis abuse/dependence in Hcy ( $16.11 \pm 7.62$  vs.  $10.56 \pm 3.61$   $\mu\text{mol/l}$ , respectively,  $p < 0.001$ ), FA ( $4.82 \pm 1.81$  vs.  $7.22 \pm 3.29$  ng/ml, respectively,  $p = 0.006$ ) and HDL ( $45.87 \pm 20.24$  vs.  $57.85 \pm 13.27$  mg/dl, respectively,  $p = 0.004$ ). These differences were independent of age, gender, BMI and cigarette smoking. In addition, Hcy level was significantly higher and HDL was significantly lower in patients with positive family history of schizophrenia ( $p = 0.002$ ).

**Conclusions.** Our results indicate that cannabis abuse or dependence and family history of schizophrenia may account for metabolic disturbances in FES.