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Hypomethylation of Line-1 is Associated with Lifetime Experience of Traumatic Events in Firstepisode Schizophrenia Patients

B. Misiak<sup>1</sup>, E. Szmida<sup>2</sup>, P. Karpinski<sup>2</sup>, A. Kiejna<sup>3</sup>, D. Frydecka<sup>3</sup>

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

<sup>2</sup>Department of Genetics, Wroclaw Medical University, Wroclaw, Poland ; <sup>3</sup>Department of Psychiatry,

Wroclaw Medical University, Wroclaw, Poland

Introduction: Accumulating evidence indicates concordant epigenetic dysregulation in the brain and peripheral blood leukocytes in schizophrenia. It has also been found that stressful and traumatic events may alter DNA methylation; however, such studies have not been performed in schizophrenia patients.

Objectives: This study aimed at comparing LINE-1 methylation in first-episode schizophrenia (FES) patients and healthy control (HC) subjects with respect to the history of trauma.

Methods: We recruited 40 FES patients and 49 HC subjects matched for age, gender and body mass index (BMI). The early trauma self-report – short form (ETISR-SF) was administered to assess traumatic events. In addition to assessment of LINE-1 methylation, serum levels of homocysteine, folate and vitamin B12 were measured in all subjects.

Results: There was no significant difference in LINE-1 methylation between FES patients and HC subjects. However, LINE-1 methylation was significantly lower in FES patients with positive history of trauma when compared with FES patients and HC subjects with negative history of trauma ( $58.08\pm3.27\%$  vs.  $61.28\pm4.12\%$ , p = 0.022 and  $58.08\pm3.27\%$  vs.  $61.12\pm4.73\%$ , p = 0.038, respectively). There was no significant difference in LINE-1 methylation between FES patients and HC subjects with negative history of trauma. There was a negative correlation between total trauma score and LINE-1 methylation (r = -0.390, p = 0.012). After controlling for confounding variables (age, gender, treatment duration, pack-year index, metabolic parameters), LINE-1 methylation was associated with total trauma score (p = 0.011).

Conclusions: Traumatic events might be associated with lower global DNA methylation in FES patients.