Summary

The interest in the role of NMDA receptor dysfunction in the pathophysiology of schizophrenia is supported by the psychotomimetic action of the NMDA receptor antagonists phencyclidine and ketamine and also the results of adjuvant treatment trials with the NMDA receptor modulators D-cycloserine, D-serine and glycine. Excitatory amino acids D-serine and glycine act as endogenous selective full co-agonists at the glycine site of the NMDA receptor and modulate glutamatergic neurotransmission and long-term potentiation (LTP). Significantly decreased D-serine and glycine levels in blood serum and cerebrospinal fluid were reported in patients with schizophrenia in comparison to healthy control subjects. Positive clinical effect of peripherally administered D-serine and glycine was demonstrated. Augmentation by D-serine and glycine improved negative, positive, cognitive and depressive symptoms in patients treated with first and second generation antipsychotics. However, the systematic review and meta-analysis of clinical effects of the NMDA receptor agonists did not confirm the results: D-serine and glycine improved only negative symptoms. We hypothesized that D-serine and glycine serum levels might be associated with specific characteristics of psychopathology in schizophrenia. The main objective of our study was to test the hypothesis of the association between D-serine and glycine serum levels and negative symptoms in patients with schizophrenia. Secondary objective was to examine the assumption of D-serine and glycine serum levels differences between a population of mostly chronic patients with schizophrenia and healthy controls.

50 outpatients with schizophrenia diagnosed in agreement with the ICD-10 (Diagnostic Criteria for Research) and 50 age and gender matched healthy control subjects were recruited into the study. D-serine and glycine serum levels were measured by high-performance liquid chromatography (HPLC) in all subjects. The Positive and Negative Syndrome Scale (PANSS) and the Scale for the Assessment of Negative Symptoms (SANS) were used to assess the symptoms of schizophrenia in the patients. We confirmed the hypothesized association between glycine serum level and intensity of negative symptoms assessed by the SANS or the PANSS negative symptoms subscale in patients with schizophrenia. Mean glycine serum level was signficantly lower in patients as compared to healthy controls. We did not find a significant association between serum level of D-serine and negative symptoms. We also did not confirm the association of schizophrenia with decreased D-serine serum levels in the sample of patients. On the contrary, the total serine serum levels in our patients were lower and D-serine/total serine ratio higher than in healthy controls. We found lower total serine serum levels associated with the higher intensity of negative symptoms assessed by the PANSS and the SANS. These findings had not been reported previously and may be related to the effects of the NMDA receptor agonists on negative symptoms in clinical studies.

It is difficult to account for the differences in findings of D-serine, serine and glycine serum levels in patients with schizophrenia. Although, its practical significance appear to be considerable for the targeted treatment with the NMDA receptor agonists. We assumed that various biochemical and clinical profiles can help to identify the specific subtypes of schizophrenia. Serum assays of endogenous D-serine and glycine may become future tests that detect biomarkers of specific treatment indications related to NMDA receptor dysfunction in schizophrenia.