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IBMC institute of biomedical chemistry

Quantitative differences in the proteomic composition of the blood serum of patients with simple and paranoid schizophrenia

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INTRODACTION

The study of mental disorders becomes more relevant in the 21st century. Schizophrenia refers to socially significant diseases, since it is a chorionic disease that begins at a young age. Its etiology and pathogenesis, response to treatment and its consequences are not yet completely understood. As a rule, only anamnestic and clinical psychopathological data are used for diagnostics. Patients, entering a psychiatric clinic for the first time, have particular difficulties in making a diagnosis. At present, the search for peripheral biomarkers, which can be used for differential diagnosis and prognosis of therapy (theranostic), becomes particularly important. Work on proteomic analysis in schizophrenic patients was carried out mainly on post-mortem material. However, so far, the search for markers of mental disorders has not been successful. The identification of peripheral biomarkers is an important step towards personalized medicine.

METHODS

The protein spectrum of the blood serum was analyzed in following groups: 20 patients with acute paranoid schizophrenia (F20.0); 15 patients with simple schizophrenia (F20.6) and 10 healthy people, Blood serum samples were obtained from most patients in acute state before the start of the study. The serum was purified by affinity chromatography from six major proteins (albumin, immunoglobulin G, immunoglobulin A, antitrypsin, transferrin and haptoglobin). In the next step the purified proteins were separated by vertical electrophoresis in a 12% polyacrylamide gel according to the Lemmli method. Then, after trypsinolysis and peptide extraction from the gel, the proteins were identified by HPLC / mass spectrometry on Q-exactive HF mass spectrometer (Thermo Scientific). Mass spectrometry was performed in Centre of Collective Usage “Human proteome» of IBMC, Moscow.

The mass spectrometric data were analyzed with the MaxQuant software (version 1.6.3.4). Only proteins quantified with at least two peptides were considered for quantitation. Quantitative LC-MS-SRM analysis was performed on QQQ TSQ Vantage (Thermo Scientific) equipped with a nano-electrospray ion source. Each sample was analyzed for five times using Dionex UltiMate 3000 RSLCnano System Series (Thermo Scientific).

Statistical analysis was performed using STATISTICA version 10.0 (StatSoft, Tulsa, OK, USA).

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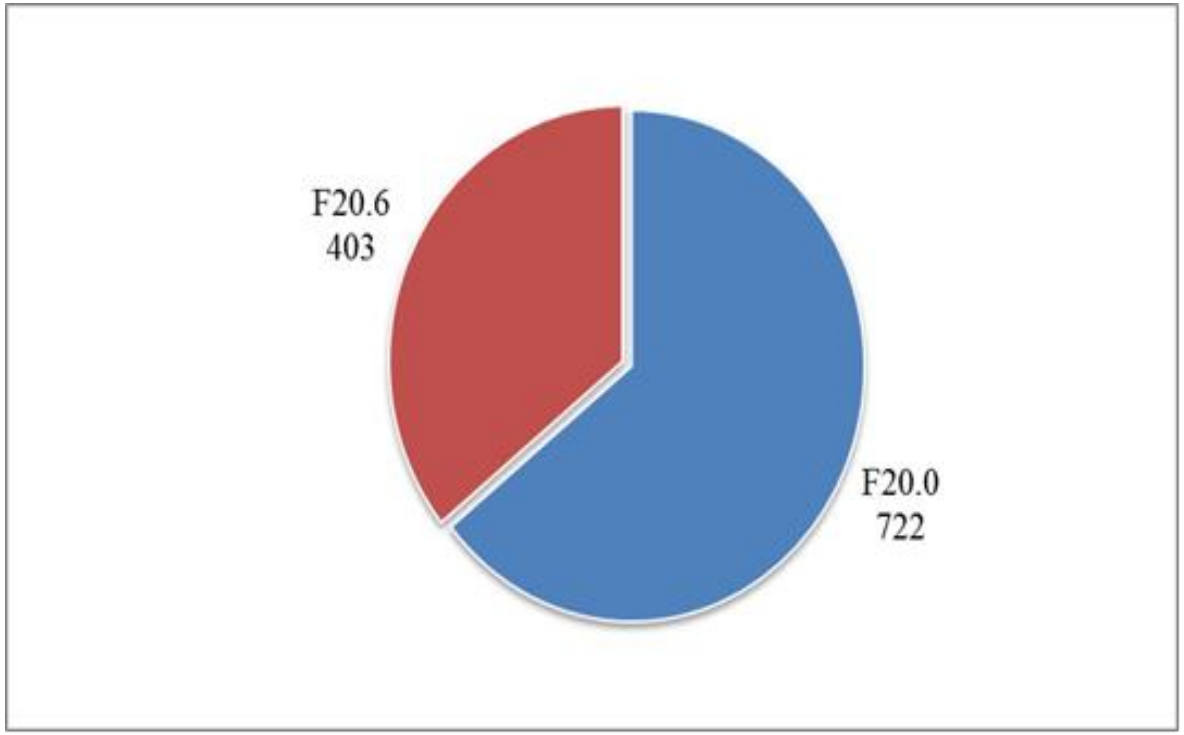
RESULTS

In the work, a qualitative and quantitative analysis of the proteomes of the blood serum between patients with two different forms of schizophrenia (simple and paranoid) and healthy individuals was carried out. In patients with a paranoid form of schizophrenia, 1440 proteins were identified. Of these, 722 proteins showed significant differences with the proteins of healthy individuals. Patients with a simple form of schizophrenia identified 720 proteins, of which 403 proteins showed significant differences with control. Significant differences in 317 proteins were obtained between patients with simple and paranoid forms of schizophrenia. Most of them from set of proteins in schizophrenia were typically associated with processes, which are responsible for protein synthesis and the processes of transduction and translation; immune response, oxidative stress, apoptosis and cell communication.



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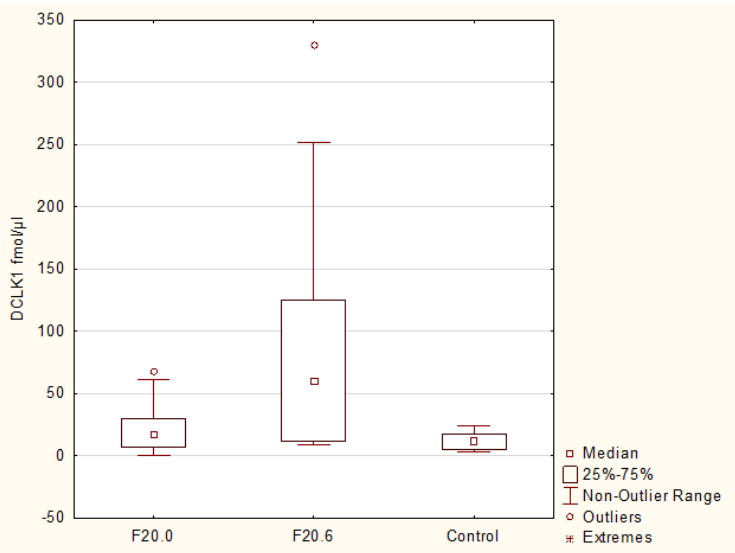
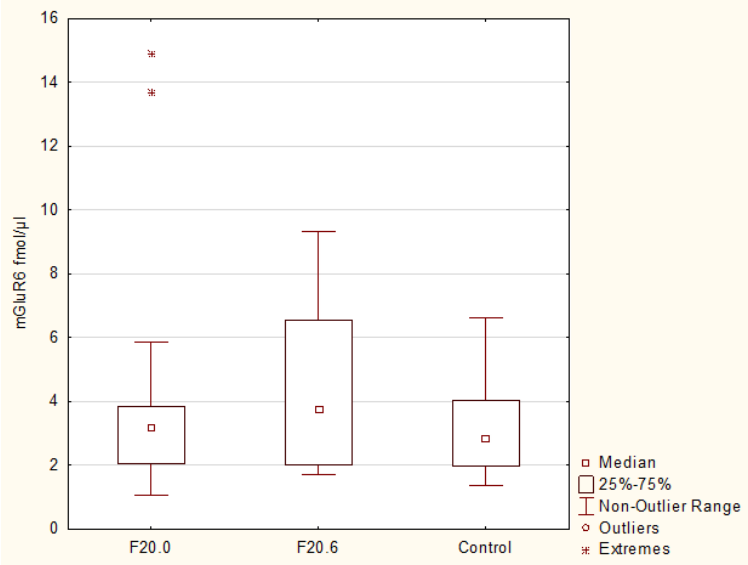
RESULTS

For further research by the method of quantitative mass spectrometry using labeled peptide standards, several proteins involved in neurogenesis and proteins of neuronal receptors were selected: NMDAZ1, RIPK1, mGluR6, DCLK1. Kruskal-Wallis test ANOVA by Ranks showed significant differences between three studied groups for protein DCLK1 (p =,0118) and, accordingly, significant pairwise differences between all the studied groups.

The results of quantitative determination of DCLK1



The results of quantitative determination of mGluR6



In the blood serum of patients in the general group of schizophrenia, a significant increase in the number of RIPK1, mGluR6 receptors was revealed in comparison with healthy people. In addition, the amount of mGluR6 was significantly higher in patients with a simple form of schizophrenia than in patients with a paranoid form (p=0.021). In the general group of patients with schizophrenia, divided accordingly by the prevailing symptoms, a more than twofold increase in the number of RIPK1 was revealed in patients with leading negative symptoms. Thus, most of the specific proteins were significantly increased depending on the severity of the disease (a simple form of schizophrenia, leading negative symptoms).