

# MBP-hydrolyzing abzymes as a peripheral markers associated with impaired myelination in schizophrenia

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## INTRODUCTION

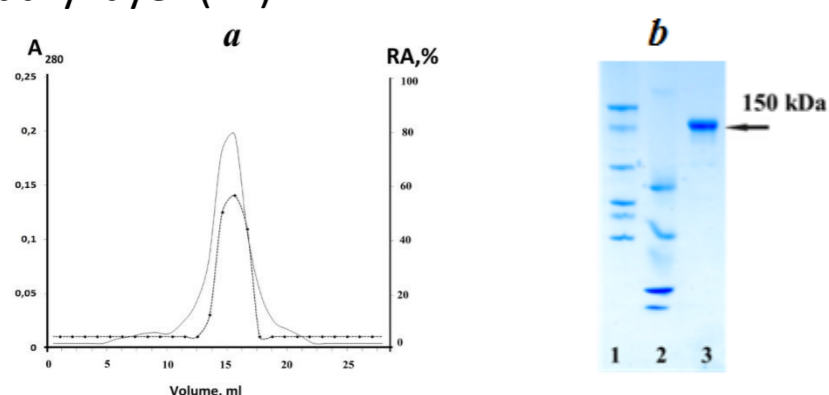
It is well-known that the pathology of myelin and oligodendrocytes is involved in the pathogenesis of schizophrenia. Anomalies in oligodendrocytes and myelin can be a source of neuronal disruption. The discovery of catalytic antibodies (abzymes) allows us to investigate their pathological role in various conditions. One of the possible ways of inducing proteolytic antibodies is the appearance in the peripheral blood of a substrate in the form of damaged protein fragments. In our previous study, it was shown that the IgG of schizophrenia patients can hydrolyze the myelin basic protein - one of the main components of the central nervous system myelin. The study of IgG proteases in accessible biomaterial (serum) and their association with myelination disturbance in schizophrenia may be potential criteria for monitoring the severity of mental disorders.

## OBJECTIVE

This study focuses on investigation the level of activity of MBP-hydrolyzing antibodies and myelin density in patients with schizophrenia.

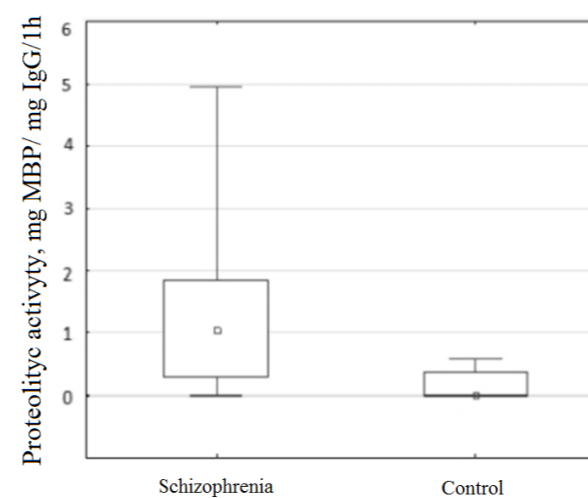
## METHODS

In this work, 15 patients with paranoid schizophrenia and 14 healthy donors of match age were recruited to study. Polyclonal IgGs were purified by affinity chromatography on protein G-Sepharose. Strict criteria were testing to assign detected catalytic activity to the antibodies: electrophoretic homogeneity of Abs, gelfiltration in acid conditions (pH shock analysis). Images were acquired by using a 1.5-T imager (Magnetom Essenza; Siemens, Germany) with implication of fast three-dimensional whole-brain MPF mapping protocol. These classes correspond to pure white matter (WM), pure gray matter (GM), mixed voxels that contained partial volumes from WM and GM (PVWGM), and mixed voxels that contained a partial volume from cerebrospinal fluid - boundary layer (BL).

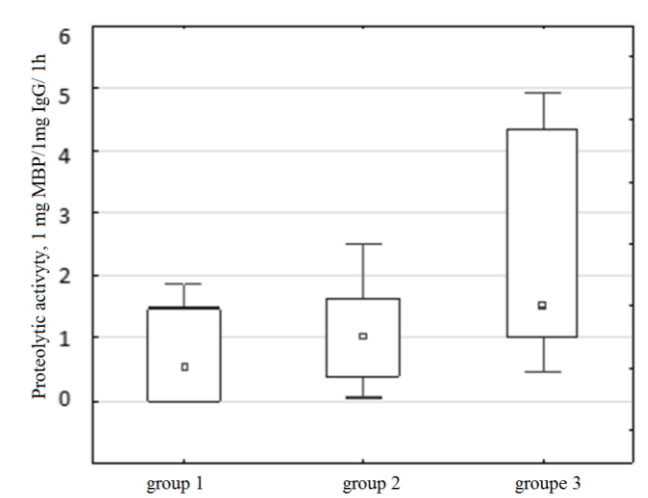


**Figure 1.** **a** - Gel filtration of IgG on a Superdex 200 column in an acidic buffer (pH 2.6) after preincubation of the Abs in the same buffer: (—) absorbance at 280 nm (A280), which reflects the content of IgG; (■). **b** - Electrophoretic SDS-PAGE analysis of homogeneity of proteins corresponding to the IgG (lane 3) from the sera of schizophrenia patients in 4–16% gradient SDS-Page gel followed by Coomassie staining. Arrows (lane 1,2) indicate the positions of high and low molecular mass markers

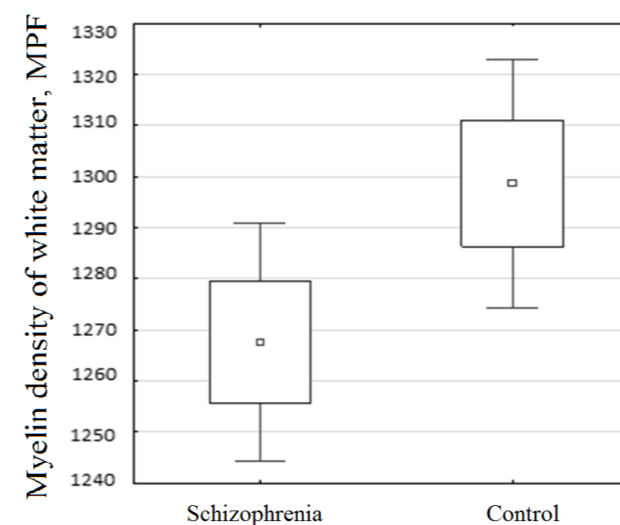
## RESULTS



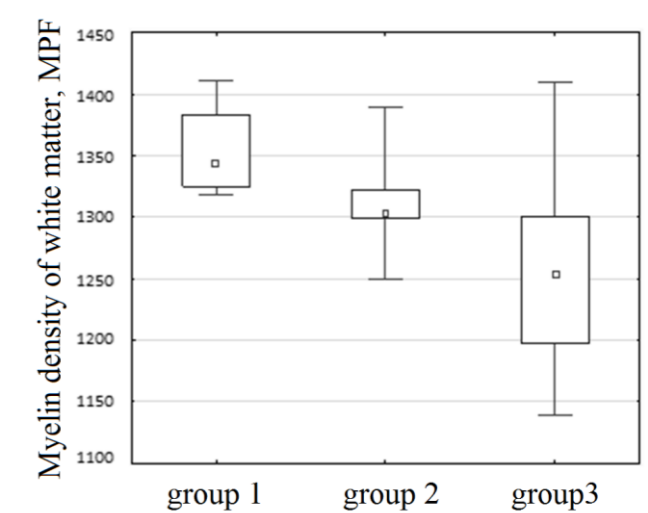
**Figure 2.** IgG-induced hydrolysis of MBP in serum of patients with schizophrenia and healthy individuals



**Figure 3.** IgG-induced hydrolysis of MBP in and schizophrenic patients with different duration of the disease



**Figure 4.** Comparative characteristics of the molecular proton fraction of healthy individuals and persons with schizophrenia



**Figure 5.** Comparative characteristics of the MPF in white matter of schizophrenia patients with different duration of the disease

Table 1 Correlation between the level of specific activity of MBP-hydrolyzing IgG and density of MPF in patients with schizophrenia

Tissue	Density MPF, Me [Q <sub>25</sub> ; Q <sub>75</sub> ] mpf	R*	p
Global gray matter	751,702±49,623	-0,321	0,243
Weight matter	1268,974±75,694	-0,593	0,019*
Cortical gray matter	895,159±53,790	-0,311	0,260
Boundary layer	618,109±39,832	-0,314	0,254
Global gray matter	355,901±37,454	0,064	0,820

## CONCLUSION

The proteolytic activity levels of IgG and MPF density in same group of patients with schizophrenia showed similar changes. Correlation analysis revealed a reliable negative correlation of average strength ( $r = -0.593$ ;  $p = 0.019$ ) between the level of specific activity of MBP-hydrolyzing IgG and decrease in myelin density (MPF) in the white matter of the brain.

The presented results show that catalytic antibodies with MBP-hydrolyzing activity can be used as peripheral markers which reflect a decrease in the density of myelin in the the brain.