INFLUENCE OF HALOPERIDOL AND CLOZAPINE ON APOPTOSIS AND AUTOPHAGY IN AN ANIMAL MODEL OF SCHIZOPHRENIA

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INTRODUCTION
Schizophrenia is a devastating neurodegenerative disease of unknown origin. One of the most recent and promising hypothesis is the theory of mitochondrial dysfunction in schizophrenia. Evidence of mitochondrial dysfunction, as well as, increased apoptosis and autophagy are frequent findings in patients with schizophrenia [1]. However it is unknown whether these changes are a consequence of the disease per se or applied antipsychotics

The aim of the present study was to assess the effects of typical (haloperidol) and atypical (clozapine) antipsychotics on the expression of apoptosis markers caspase 3 and apoptosis-inducing factor (AIF), autophagy markers Beclin 1 and p62, and density of principal neuronal cells (NeuN positive) in the cortex and hippocampus of perinatally PCP treated rats.

MATERIAL AND METHODS
Male Wistar rats were divided into six groups and subcutaneously treated on 2nd, 6th, 9th and 12th postnatal (P) day, either with PCP (10mg/kg) or NaCl. From P35 to P100, one NaCl (NaCl-H) and one PCP (PCP-H) group have received haloperidol (1mg/kg/day) and other two NaCl (NaCl-C) and PCP (PCP-C) groups have received clozapine (20mg/kg/day) dissolved in drinking water. The remaining NaCl (control) and PCP groups received drinking water. Animals were sacrificed on P100 and protein expression in the cortex and hippocampus was determined using Western blot. Density of neuronal marker NeuN positive cells was determined by immunohistochemistry. Differences among the groups were tested by one-way ANOVA following Bonferroni’s post hoc test. The threshold value for acceptance of differences was 5%.

CONCLUSION
Obtained data suggest that perinatal PCP administration and chronic administration of antipsychotics affect apoptosis and autophagy processes, as well as the density of neuronal cells. Even though we detected that both antipsychotics are capable to affect both processes, effects of clozapine treatment were more pronounced. Understanding the nature of observed changes may contribute to the elucidation of pathophysiology of schizophrenia and clarification of the molecular effects of antipsychotics.

References