EXPRESSION OF EGR1, EGR2 AND EGR3 PROTEINS IN POSTMORTEM HUMAN BRAIN OF SCHIZOPHRENIC SUBJECTS

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INTRODUCTION

Early growth response proteins (EGR) are a family of four transcription regulatory factors implicated in neuronal activation and synaptic plasticity.

Several lines of evidence suggest that the EGR family of transcription factors is associated with the neuronal dysfunction seen in schizophrenia: two genes associated with schizophrenia risk, neuregulin-1 and calcineurin, modulate the expression of the EGR gene family; hallucinogenic serotonin 5-HT_{2A} receptor agonists affect the expression of EGR1, EGR2 and EGR3 transcripts in mouse cerebral cortex; and lower expression level of EGR1, EGR2 and EGR3 mRNAs has been found in postmortem human brain of antipsychotic-treated schizophrenic subjects.

OBJECTIVES

1) To compare the expression level of EGR1, EGR2 and EGR3 proteins in prefrontal cortex of schizophrenic subjects and controls individually matched by gender, age and postmortem delay.
2) To study the effect of antipsychotic treatment on the expression level of these three immediately early proteins

MATERIAL & METHODS

SUBJECTS

Postmortem cortical samples (Brodmann s area 9) were obtained at autopsies from the Basque Institute of Legal Medicine (Bilbao, Spain) and immediately stored at -70ºC until assay. Based on toxicological data about the absence or presence of antipsychotic drugs in blood, the schizophrenic subjects were grouped as "antipsychotic-free" (AP-free, n=18) and "antipsychotic-treated" (AP-treated, n=9) subjects.

The study was developed in accordance with policies of research and ethical review boards for postmortem brain studies.

METHODS

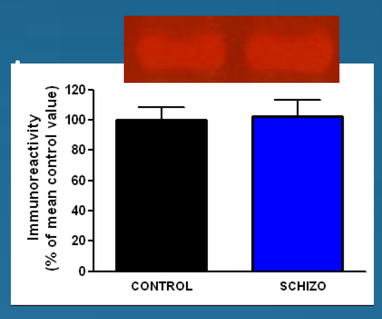
Immunodetection of EGR proteins was made in total homogenates by western blot experiments following standard protocols, and using commercially available primary antibodies. Beta-actin signal was used as loading control.

The statistical comparison between means was made by Student's t-test with a significance level of $p<0.05$.

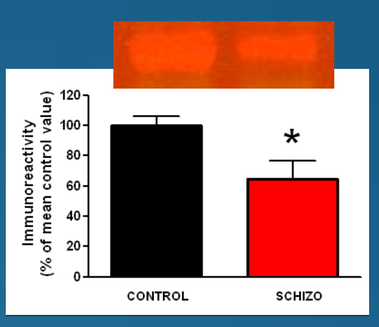
RESULTS

EGR1

AP-free



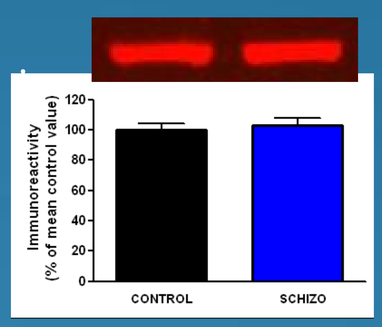
AP-treated



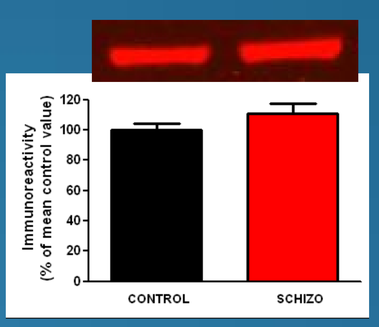
Immunoreactivity of EGR1 in AP-free schizophrenic subjects did not differ from that of respective matched control subjects, but it was significantly decreased in AP-treated schizophrenic subjects (65 12% vs matched controls; $p<0.05$)

EGR2

AP-free



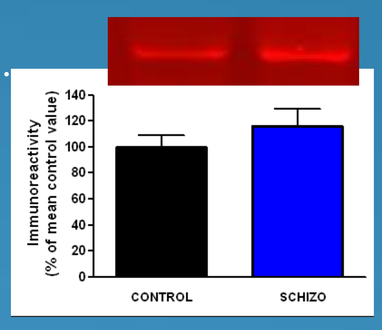
AP-treated



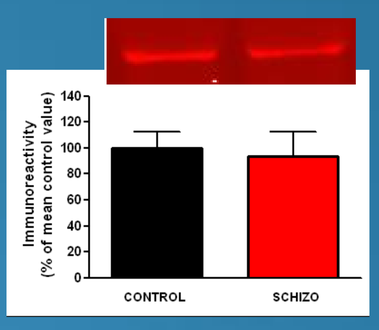
Immunoreactivity of EGR2 was not different in schizophrenic subjects with respect to their matched controls.

EGR3 (band at 51 kDa)

AP-free

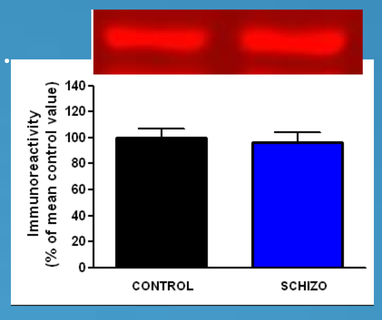


AP-treated

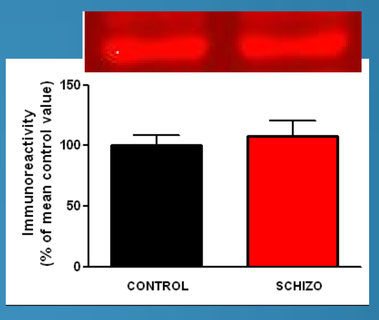


EGR3 (band at 41 kDa)

AP-free



AP-treated



Immunoreactivity of EGR3 (41 and 51 bands) was not different in schizophrenic subjects with respect to their matched controls.

CONCLUSION

These results provide the first evidence of specific modulation of EGR1 protein expression by antipsychotics in postmortem human brain of schizophrenic subjects. Our data further support the role of the transcription factor EGR1 in the molecular mechanisms underlying schizophrenia and psychosis.

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