Complement C5ar1 Antagonists for the Treatment of Autism Spectrum Disorders

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Abstract

Autism spectrum disorders (**ASD**) are characterized by troubles with social interaction and communication, and restricted and repetitive behavior.

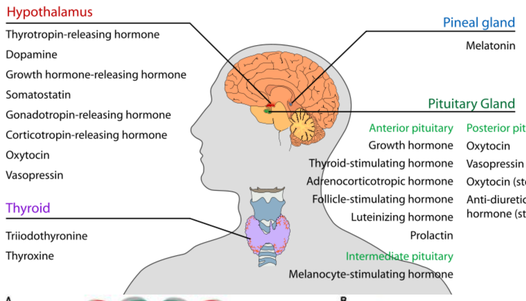
We used our ASD rat model to test whether PMX53, a complement C5ar1 antagonist, is efficient in restoring the synaptic transmission in the hypothalamic paraventricular nucleus (**PVN**) altered by the NMDA-induced ASD. The PVNs of 20 male and 20 female rats exposed to 5 experimental conditions were profiled with Agilent rat 4x44k gene expression microarrays.

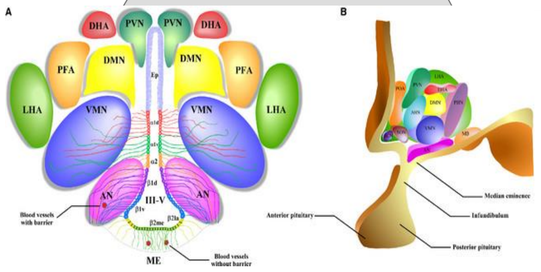
The research explained the ASD-related behavioral and pathophysiological observations by the regulation of genes involved in the glutamatergic (**GLU**), GABAergic (**GABA**), dopaminergic (**DA**), cholinergic (**ACH**) and serotonergic (**5HT**) neurotransmission.

We found that PMX53 treatment is more efficient than traditional ACTH in restoring all five types of neurotransmission altered by the NMDA-induced ASD in the rat PVN.

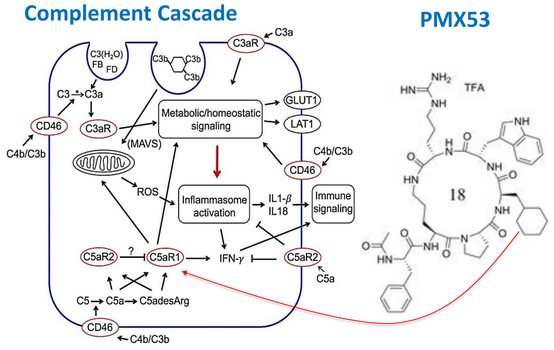
Introduction

Hypothalamic Paraventricular Nuclei (PVN)



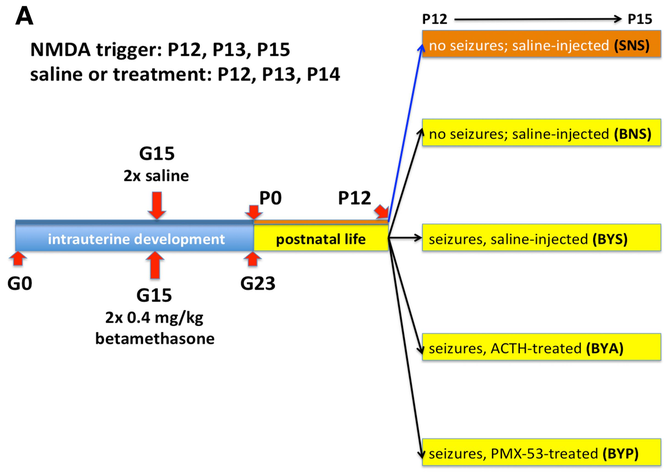


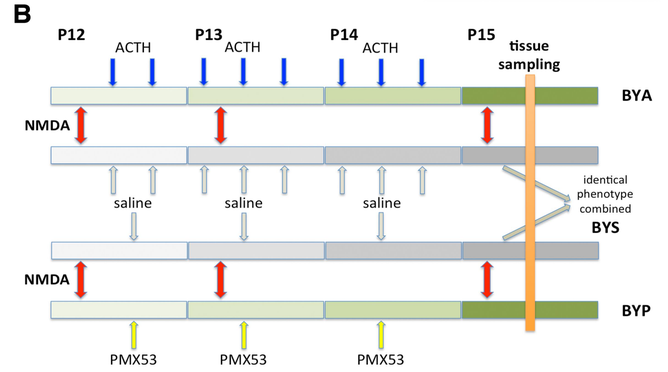
Complement Cascade



PMX53

Methods

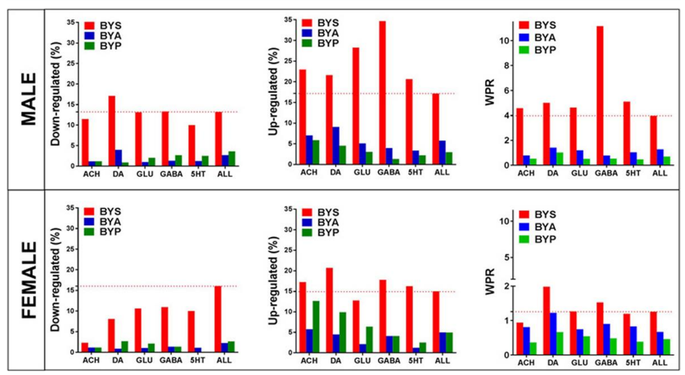




A. Groups of four rats used in this experiment.

B. Treatment scheme of rats with triggered spasms (BYS).

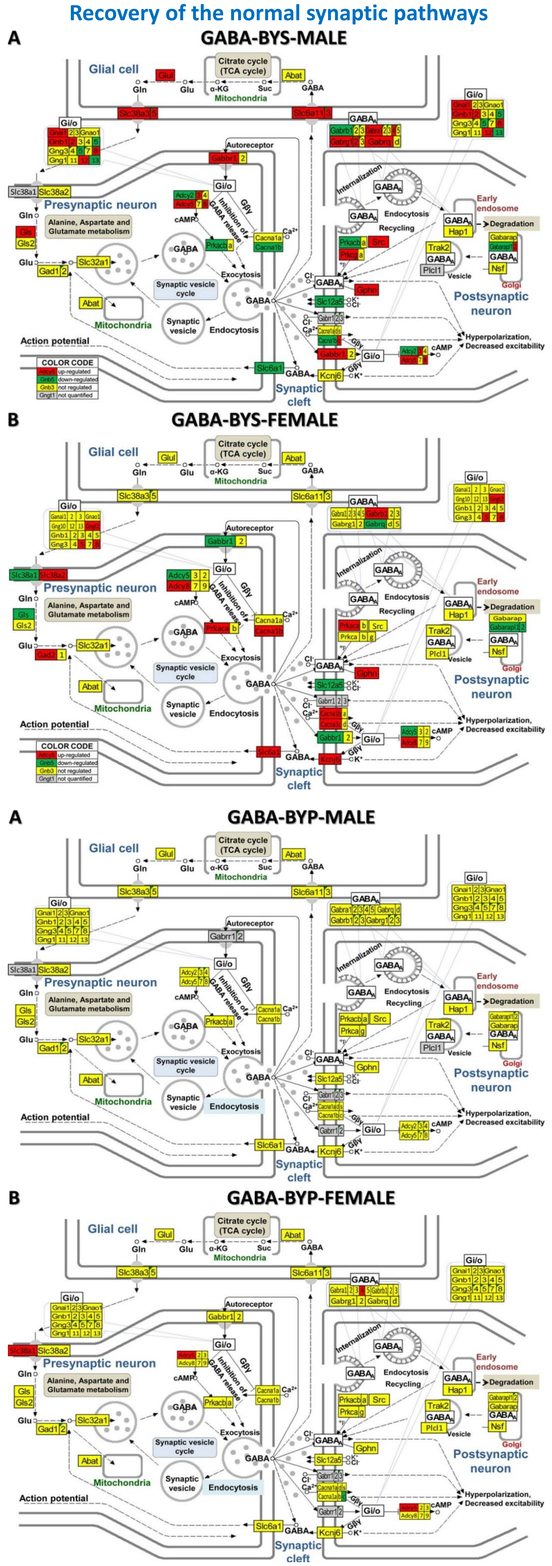
Results

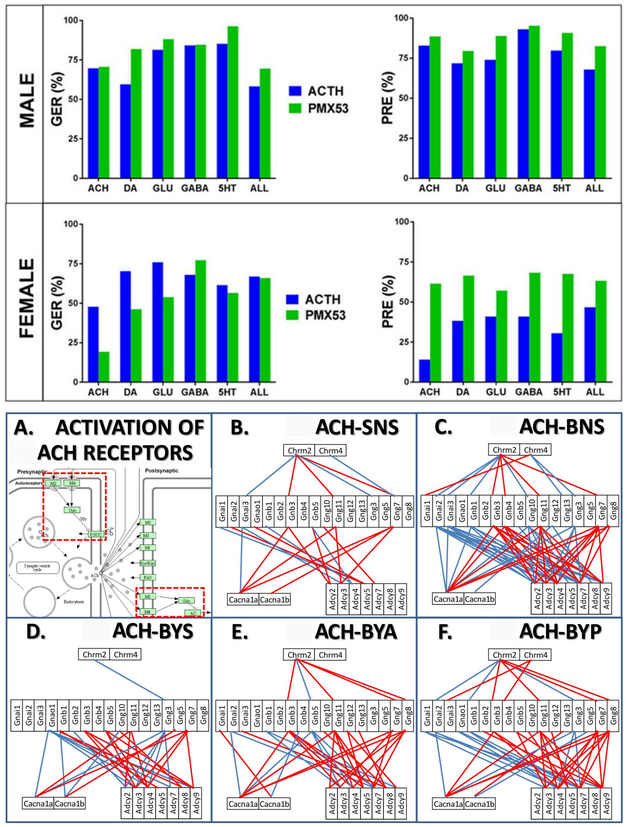


Transcriptomic alterations in response to NMDA-induced spasms in rats treated with ACTH (BYA), PMX53 (BYP) or just saline (BYS) compared to rats without ASD (BNS). GLU is the most abundant excitatory and **GABA** the most abundant inhibitory neurotransmission associated with major mental functions. **ACH** facilitates learning, memory and attention, **DA** controls learning, memory, motivation and reward, and **5HT** is involved in learning and memory, emotion, and abnormal mood and cognition.

Results

Recovery of the normal synaptic pathways





Conclusion:
PMX53 is Effective for ASD treatment

References

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- 5 genomic experimental series in NCBI GEO

Acknowledgments

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