1B receptor gene (AVPR1b) in the patients suffering from bipolar disorder and major depressive disorder.

Methods: In the study we included 707 patients: 193 with major depressive disorder (MDD) and 514 with bipolar disorder. Consensus diagnosis by at least two psychiatrists was made, according to DSM-IV criteria, using SCID. Control group consisted of 732 healthy subjects. Genotypes for four AVPR1b gene polymorphisms (rs28632197, rs28536160, rs28373064, rs35369693) were established by TagMan SNP Genotyping Assays (Applied Biosystems) using AbiPrism 7900HT system. Linkage disequilibrium analysis was done in Haploview. Statistical analysis was performed in Statistica package v. 9.0.

Results: We have found that the promoter polymorphism rs28536160 was significantly associated with affective disorders in the whole group of patients ($p = 0.036$) as well as with type I of bipolar disorder ($p = 0.047$ for genotypes, $p = 0.032$ for alleles, $OR = 1.5$), but not with major depressive disorder. No association of the other analyzed SNPs was found with either the whole group of affective patients or stratified by diagnosis (bipolar disorder, major depressive disorder). No gender specific differences were observed for AVPR1b gene polymorphism in association with bipolar or major depressive disorder. In linkage disequilibrium analysis we have observed strong linkage disequilibrium and one haplotype block between three analyzed SNPs was created ($D' > 0.98$, $LOD > 86$; $r^2 > 0.28$). Rs28632197 was located outside the linkage disequilibrium block. None of the haplotypes was associated with the increased susceptibility to MDD or bipolar disorder.

Conclusion: The polymorphism of AVPR1b gene analyzed in this study may modify susceptibility to bipolar disorder, but does not seem to influence the development of major depressive disorder in our population.

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P.1.015 Cerebrovascular effects of mexidol in conditions of separate and combined vascular pathology of brain and heart

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The marked antioxidant, membrane-protective and neuroprotective properties of Mexidol, which was developed in Zakusov Institute of Pharmacology RAMS, are widely used in clinical practice. The present comparative study aimed to evaluate the influence of Mexidol on cerebral perfusion in conditions of ischemic brain damage, myocardial infarction and combined vascular pathology of brain and heart. Experiments were performed on narcotized (uretan; 1.3 g/kg intraperitoneally) outbred male rats (180–400g). Local cerebral blood flow was registered in the parietal region of the brain cortex of rats. For this purpose ALF-21 flowmeter ("Transonic System Inc." USA) was used. Blood pressure was measured simultaneously with the detector, connected to a plastic catheter placed in the femoral artery. All data was recorded by "BIOPAK" polygraph (USA), connected to personal computer. Global transient ischemia was caused by 10 minute occlusion of both carotid arteries and decrease of blood pressure to 40–50 mm Hg (by blood withdrawal) followed by reperfusion. Experimental myocardial infarction was caused by occlusion of left circumflex coronary artery. ECG was registered by computer electrocardiograph "Polyspecter 8/B". Substances for research: Mexidol (200 mg/kg), synthesized in the Experimental-and-Technical Department of Zakusov Institute of Pharmacology of RAMS; bicuculline (0.5 mg/kg), produced by "Serva". Substances were injected intravenously through plastic catheter, placed in the femoral vein of rats. Experiments have shown, that Mexidol (200 mg/kg iv) under conditions of global transient ischemia of brain enhances local cerebral blood flow in the brain cortex by $49.8 \pm 10.2\%$. In intact rats the same dose of Mexidol initially decreases blood flow in the brain cortex by $16.2 \pm 3.1\%$ ($n = 9$). 60 minutes after the injection local blood flow in some experiments restored to baseline level while it was slightly increased in others. After experimental myocardial infarction and in false-operated rats Mexidol didn't increase local cerebral blood flow. In conditions of combined pathology of brain and heart Mexidol substantially enhances cerebral blood flow (by $57.4 \pm 9.5\%$). Thus, Mexidol has a marked cerebrovascular activity in conditions of vascular pathology of brain and combined vascular pathology of brain and heart. Obtained data have shown, that Mexidol demonstrated selective cerebrovascular activity in conditions of ischemic brain damage, while in intact rats and after experimental myocardial infarction it was ineffective. The evaluation of the mechanism of action of Mexidol by specific $GABA_A$-receptor antagonist bicuculline allowed to establish, that cerebrovascular effects of this substance during ischemia are provided by GABAergic pathways. Our results are in line with literature data about modulating effects of Mexidol on activity of GABA-receptor complex. Observed difference in sensitivity of intact cerebral vessels and cerebral vessels during ischemia to Mexidol, as well as the role of $GABA_A$-receptors, support previous findings about specific effects of GABAergic drugs (selective influence on brain vessels in conditions of cerebrovascular disturbances) [1,2].

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P.1.016 Antiserotoninergic and cerebrovascular effects of combination of tropoxin and mexidol

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It is known, that serotoninergic and cerebrovascular mechanisms play an important role in the pathogenesis of migraine. Migraine is a common, chronic disorder with episodic attacks. It affects 10–20% of the population during the most productive periods of their working lives. According to literature data migraine is a risk