Conclusion: 1. Nasal chemoreceptors appear to be a portal of entry for substances affecting feeling states. 2. The rapid and temporary effect in GAD suggests that ADOL may be useful in rapid-onset and short-lived psychiatric conditions. FDA approved clinical trials of ADOL in social anxiety disorder are currently in progress.

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P-20-004 The influence of an a5GABAA selective agonist XLi356 on rats' performance in morris water maze

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Objective: The impairing effects of diazepam in Morris water maze (MWM) could be partially antagonized with co-administration of an α5 subunit selective antagonist XLi093 (Savić et al., 2009). In order to further assess the role of the α5GABAA receptors population in mediating amnesic effects in rats, the present study examined effects of an α5GABAA selective agonist XLi356 on the MWM performance.

Methods: Male Wistar rats were given vehicle or 5, 10 and 20 mg/kg of XLI356 intraperitoneally 20 minutes before the testing. A single-day water maze task had three swimming blocks, each consisting of 4 trials, lasting a maximum time of 60 s each. Afterwards, a probe trial was given and a number of standard parameters was calculated. Additionally, rats were tested in spontaneous locomotor activity (SLA) and elevated plus maze (EPM) tests, where the sedative and anxiolytic effects were assessed.

Results: Results were analyzed using one-way ANOVA with post hoc Student-Newman-Keuls test where applicable. XLi356 significantly increased latency to platform ($F(3,444) = 3.1287$, $p = 0.026$); post hoc test revealed that the dose of 20 mg/kg was significantly different from vehicle. The same dose of XLi356 significantly increased cumulative distance from the platform zone ($p = 0.028$) and the time spent in the periphery ring ($p = 0.009$), while the path efficiency was on the control level. On the other hand, XLi356 did not show behavioral activity in SLA and EPM tests at either of three doses tested.

Conclusion: The present results suggest that ligands with appreciable agonist activity at GABAA receptors containing α5 subunits may impair memory acquisition in Morris water maze task, without discernible effects on general behavior. Thus the activity of the benzodiazepine type drugs at α5GABAA receptors should be decreased if the amnesic effects are to avoid.

P-20-005 The investigation of 2-mercaptobenzimidazole derivatives interaction with sigma-1 receptors in mice

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Objective: At present sigma-1 (σ1) receptor is considered to be prospective target for neuroprotective and anxiolytic drugs. In ''Zakusov Institute of Pharmacology'' RAMS neuroprotector and anxiolytic afobazole (5-ethoxy-2-[2-(morpholino)-ethylthio] benzimidazole dihydrochloride) was developed. In vitro afobazol revealed ligand properties towards MT1, MT3, σ1 receptors and MAOA with $IC50 = 2.7 \times 10^{-5}$ M, 9.9×10^{-7} M, 7.1×10^{-6} M, 6.2×10^{-6} M correspondingly (Seredenin et al., 2009). The main metabolite of afobazole (2-[2-(3-oxomorpholine-4-yl)-ethylthio]-5-ethoxy benzimidazole hydrochloride) interacted only with MT3 receptors with $Ki = 9.7 \times 10^{-7}$ M. The aim of the research is to study the interaction of afobazole and its main metabolite with σ1 receptors versus prototype σ1 ligands of different pharmacological groups on mice ex vivo.

Methods: Binding experiments were carried out in P2 fraction obtained from brain of male CD-1 mice according Entrena et al. with slight modifications (Entrena et al., 2006).The radioligand used in the assays was [Ring-1,3–3H]-(+)-Pentazocine in final concentration of 1 nM. The cold ligands of different pharmacological groups were used with a concentration range of 10^{-3}–10^{-12} M.

Results: In ex vivo experiments the displacement curves of [Ring-1,3–3H]-(+)-Pentazocine by afobazole versus ligands of different pharmacological groups were obtained. IC50 obtained for afobazole was $2{,}67*10^{-5}$ M. The value is close to compounds, considered as endogenous ligands DHEA and progesterone. IC50 for afobazol main metabolite was in the millimolar range. The results of research on male CD-1 mice confirmed the previously established ligand properties of afobazole and its main metabolite in regard to σ1 receptors in vitro experiments.

Conclusion: Binding experiment with afobazole versus prototype σ1 ligands on CD-1 mice was carried out. Due to the results obtained from the binding experiments afobazol can be regarded as a novel σ1 ligand.

P-20-006 Non-selective and a_5 subunit-selective negative modulators of $GABA_A$ receptors in a single-day morris water maze task in rats

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Objective: It is well known that benzodiazepine binding site ligands influence learning and memory and that the α_5 subunit is significantly involved in cognition enhancement mediated by the negative modulation of $GABA_A$ receptor function. PWZ-029, a moderately selective α_5GABA_A receptor inverse agonist, improved learning in passive but not in active avoidance test, without effects on anxiety or muscle tone. The aim of this study was to investigate effects of PWZ-029 and DMCM, a non-selective inverse agonist, on learning ability and short-term memory in Morris water-maze (MWM) test.

Methods: MWM test was conducted 20 minutes after intraperitoneal administration of treatments (solvent, 5, 15 or 30 mg/kg PWZ-029 or 2 mg/kg DMCM) to male Wistar rats. The single-day MWM task consisted of 3 consecutive blocks of 4 trials lasting maximally 60 s each and a probe trial. During spatial learning the platform was hidden in the middle of the NE quadrant.

Results: Two-way ANOVA with one repeated measure (block) and animals nested in treatment has shown that latency to find the platform, path efficiency and total distance travelled were on the control level for DMCM and all doses of PWZ-029. Factors block and treatment were significant only for latency to first entry to the NE quadrant [block effect: $F(2,386) = 10.50$, $p < 0.001$, treatment effect: $F(4,31) = 3.10$, $p < 0.05$]. Tukey's post-hoc test revealed that animals treated with DMCM and 5 mg/kg of PWZ-029 had longer latency to first entry to the target quadrant than those treated with solvent ($p = 0.001$, $p < 0.001$, respectively). Probe trial performance did not differ significantly between treatments.

Conclusion: These results suggest that neither non-selective nor β_5 subunit-selective negative modulation of $GABA_A$ receptors is sufficient to enhance learning and short-term memory in the single-day MWM spatial task.

P-20-007 Riluzole produces distinct anxiolytic-like effects in rat innate anxiety models

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Objective: Growing evidence suggests that sodium channel blockers, such as riluzole and lamotrigine, are effective as non-benzodiazepine treatments of anxiety disorders. In the present study, we first investigated the anxiolytic-like effect of riluzole using innate anxiety models in rats.

Methods: Male Wistar rats were used for experiments. We used three different innate anxiety models, such as the elevated plus-maze, the light/dark and the open-field tests. A benzodiazepine, diazepam, was used as a positive control anxiolytic drug. To clarify the involvement of sodium channels in the anxiolytic-like effects of riluzole, we examined the effect of co-administration of the sodium channel activator, veratrine.

Results: In the elevated plus-maze test, riluzole (3 mg/kg) significantly increased the time spent in, and entries into, the open arm after 60 min administration. This finding was supported by results obtained from the light/dark and the open-field tests. The magnitude of