dramatically, the HYS level changed rather mildly. Time delay in the effects of Thp and Rac observed in KM rats led us to suggest that the neurotransmitter abnormalities found might be associated with genetic peculiarities of these animals.

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**P5.036** Role of lipid peroxidation and metabotropic glutamate receptors during experimental audiogenic seizures

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The insufficient efficacy of modern anticonvulsive drugs used in clinical practice as well as the wide global distribution of epilepsy make very actual the design of novel compounds and study of its mechanisms of action. Recent data concerning this problem added proof to the hypothesis on a crucial role of free radicals in the pathogenesis of epilepsy. In our previous work we showed that the agonist of glutamate ionotropic receptors blocks seizures as well as the increase of lipid peroxidation (LPO) products induced by NMDA injection. The situation in relation to metabotropic receptors and LPO is less clear. A goal of the current study was to determine a possible involvement of LPO process in the pathophysiology of audiogenic convulsions and to elucidate whether antagonists of metabotropic glutamate (mGlu) receptors are neuroprotective via a mechanism involving the regulation of LPO. Experiments were carried out on 3 strains of animals with audiogenic seizures: genetically epilepsy prone (GEP) rats (n=19), Krushinskii–Molodkina (KM) rats (n=16) and DBA/2 mice (n=24). Wistar rats (n=16) were considered as a control group. The sound stimulation (120 and 109 dB for rats and mice, respectively) were presented for 60 s or until the onset of clonic–tonic seizures. Determination of LPO processes in brain tissue was performed by measuring thiobarbituric acid reactive substances (TBARS). A nearly 2-fold elevation of TBARS content was found during tonic–clonic seizures induced by sound stimulation in cortex of GEP and KM rats as well as in whole brain of DBA/2 mice in comparison to that of animals with no sound stimulation. A mGlu receptors antagonist, (RS)-1-aminoindan-1,5-dicarboxylic acid (AIDA), 1 μmol, i.c.v., injected before sound stimulation suppressed sound-induced clonic–tonic seizures in DBA/2 mice and prevented the increase of TBARS level produced by sound stimulation. The mGluR1/mGluR5 agonist, 3,5-dihydroxyphenylglycine, DHPG, 1 μmol, i.c.v., was proconvulsant in DBA/2 mice and produced a dramatic increase in TBARS content. Thus, the mGluR1 antagonist AIDA proved to be highly effective in reducing LPO intensity, and might be considered as potent anticonvulsant drug. In conclusion, our findings demonstrate that following sound-induced seizures TBARS levels were increased in the cortex of animals with audiogenic epilepsy and substances with antioxidant properties might be used in the therapy of convulsive disorders.

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**P5.037** Clinical pharmaco-EEG characteristic of the novel nootropic drug noopept

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Electroencephalography is one of the informative methods used for the evaluation of psychopharmacological effects. Noopept (N-phenylacetyl-L-prolylglycine ethyl ester), a novel nootropic drug developed at the Institute of Pharmacology RAMS, is on clinical trials now. EEG recording in patients with cognitive disorders of different origin treated with noopept was performed. 36 patients with cognitive disorders caused by vascular pathology (18 elderly patients, group 1) and posttraumatic brain disturbances (18 middle-aged patients, group 2) have been surveyed. Changes in EEG spectral characteristics (absolute spectra) and interhemispheric coherence in a frequency range of 1–30 Hz after a single test dose of noopept (15 mg) and 28 days of course therapy (30 mg daily) were investigated. It was shown that a test dose of noopept caused significant changes in frequencies of alpha rhythm (increase) and beta 1, beta 2 rhythms (increase) widespread in all brain areas. These changes have been more pronounced in group 1 than in group 2. In group 2 significant decrease of delta rhythm was registered, while in group 1 changes of delta rhythm were in the opposite direction (increase). The EEG changes revealed after a test dose of noopept were the same at the end of course treatment, but their statistical significance in some cases reduced. In both groups changes of EEG spectral characteristics in the right hemisphere have been expressed more than in the left. Different changes in interhemispheric coherence of occipital and frontal brain areas were established. For EEG
Noopept (N-phenylacetyl-L-prolylglycine ethyl ester), a novel original peptide drug with nootropic and neuroprotective activity, was developed at Zakusov Institute of Pharmacology Russian Academy of Medical Sciences, Baltiyskaya str. 8, 125315 Moscow, Russia.

Noopept (N-phenylacetyl-L-prolylglycine ethyl ester), a novel original peptide drug with nootropic and neuroprotective activity, was developed at Zakusov Institute of Pharmacology. A standard clinical pharmacological study of noopept (with previous placebo control, using psychological, psychophysiological methods and EEG) was carried out on 40 patients with psychoorganic syndrome. All patients had organic asthenic disorders (emotional lability) of vascular and posttraumatic genesis (F06.60, F06.61). The test dose of noopept was 5 and 10mg, and during the course treatment – 15 and 30mg per day. Clinical trials lasted 28 days. It was shown that noopept doses of 15 and 30mg per day relieved the main symptoms of organic disease: cerebroasthenic, hyperesthetic and sleep disturbances, vegetative dysfunctions as well as cognitive and dismnestic problems (attention, memory, efficacy of activity). Therapeutic effects of noopept were connected with mild stimulatory, anxiolytic, nootropic effects and vegetostabilization. The stimulatory effect differed from that of psychostimulators: it was not accompanied by anxiety, aggressiveness, sleep and vegetative disturbances. The medicine did not demonstrate real hypnotic effect, but clear positive normalizing influence on nocturnal sleep was revealed. The specific nootropic effect of noopept developed after a latent period, starting from the 3–4th week of therapy, which agrees with traditional dynamic characteristic of medicines with nootropic action. A positive effect in cognitive disorders was also observed (improvement of memory, attention, minimization of mistakes with interference, improvement of short memory). The most marked improvement was in attention (distribution, stability and volume), increase of complex sensomotor reactions, volume of short visual memory. The analysis of EEG showed general improvement in alpha-rhythm frequencies, decrease in delta-rhythm frequencies and increase in beta-rhythm in frontal and central parts of the brain.

It was established that noopept is an effective drug for the treatment of psychoorganic disorders with cerebroasthenic and cognitive disturbances. Equal therapeutic response was observed in patients of young and medium age with the course of 30mg daily. With the course of 15mg daily younger patients with psychoorganic syndrome of posttraumatic origin showed better results. The present study of noopept demonstrated that during therapy of asthenic disorders of organic nature the effect of the medicine is characterized by non-specific "fast" antiasthenic and anxiolytic effect, as well as by specific nootropic effect. The results obtained suggest that noopept could be employed in clinical practice as effective nootropic drug.

Clinical pharmacological study of the novel peptide nootropic drug noopept

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Noopept (N-phenylacetyl-L-prolylglycine ethyl ester), a novel original peptide drug with nootropic and neuroprotective activity, was developed at Zakusov Institute of Pharmacology. A standard clinical pharmacological study of noopept (with previous placebo control, using psychological, psychophysiological methods and EEG) was carried out on 40 patients with psychoorganic syndrome. All patients had organic asthenic disorders (emotional lability) of vascular and posttraumatic genesis (F06.60, F06.61). The test dose of noopept was 5 and 10mg, and during the course treatment – 15 and 30mg per day. Clinical trials lasted 28 days. It was shown that noopept doses of 15 and 30mg per day relieved the main symptoms of organic disease: cerebroasthenic, hyperesthetic and sleep disturbances, vegetative dysfunctions as well as cognitive and dismnestic problems (attention, memory, efficacy of activity). Therapeutic effects of noopept were connected with mild stimulatory, anxiolytic, nootropic effects and vegetostabilization. The stimulatory effect differed from that of psychostimulators: it was not accompanied by anxiety, aggressiveness, sleep and vegetative disturbances. The medicine did not demonstrate real hypnotic effect, but clear positive normalizing influence on nocturnal sleep was revealed. The specific nootropic effect of noopept developed after a latent period, starting from the 3–4th week of therapy, which agrees with traditional dynamic characteristic of medicines with nootropic action. A positive effect in cognitive disorders was also observed (improvement of memory, attention, minimization of mistakes with interference, improvement of short memory). The most marked improvement was in attention (distribution, stability and volume), increase of complex sensomotor reactions, volume of short visual memory. The analysis of EEG showed general improvement in alpha-rhythm frequencies, decrease in delta-rhythm frequencies and increase in beta-rhythm in frontal and central parts of the brain.

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Experimental and clinical pharmacokinetics of noopept

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The present study was conducted with the purpose to examine experimental and clinical pharmacokinetics of a new dipeptide drug noopept (N-phenylacetyl-L-prolylglycine ethyl ester) possessing nootropic, anxiolytic and neuroprotective activities [1]. The experiments have been performed using high performance liquid chromatography technique. The results obtained from experimental pharmacokinetic studies showed noopept to be more resistant to the action of metabolizing enzyme systems as compared to naturally occurring neuropeptides. Noopept was determined in rat blood plasma independently of the route of administration for 25 min. Noopept was subjected to an intense biotransformation thus demonstrating rather low bioavailability. Pharmacokinetic investigation was carried out with two formulations for peroral usage: tablets (Technological Department of Zakusov State Institute of Pharmacology RAMS) and capsules (DVD Pharma Inc.,