patients with superficial, neurotic mental pathology. In this case specific features of drug actions can predetermine the result of therapy. Afobazole (5-etoxy-2-[2-(morpholino)-ethylthio]benzimidazole dihydrochloride), which was developed on the basis of the pharmacogenetic concept of anxioselective effect, shows anxiolytic action in stress-sensitive animals and (in contrast to benzodiazepines) has no sedative effect in stress-resistant ones. The aim of the study was to investigate clinical and pharmacological features of afobazole in patients with anxious disorders and various (sthenic and asthenic) personality traits. The patients had "simple" structure of anxious and anxious-asthenic disorders classified by ICD-10 as "Generalized anxiety disorder" (F.41.1) and "Neurasthenia" (F.48.0). The drug action was estimated by symptomatic scales, scales for anxiety by Hamilton, Zung, Spielberger; self-estimation test, scale of Clinical General Impression (CGI). For estimation of personality traits of the patients the MMPI test was used. It was found that, in patients with asthenic and sthenic types, therapeutic action of afobazole was determined by its anxiolytic or stimulatory effects or by their combination. In patients of asthenic type the anxiolytic component of afobazole action was prevalent. In patients of sthenic type, the stimulatory effect dominated. These individual differences in afabazol action suggest that the stimulatory component of its psychotropic effect is probably similar to specific effect of psychostimulators, which are also more effective in sthenic persons. Dependence of psychotropic action of afobazole on typological traits of patients with polar premorbide personality traits is in accord with experimental studies, which have shown anxiolytic and stimulatory effect of the drug in animals with a "passive" phenotype of emotional reaction to stress. Probably, the anxiolytic effect of afobazole in patients with both asthenic and sthenic features may be explained by a common mechanism of anxiogenesis in anxious disorders, that does not depend on the structure of a premorbid person. It may also be explained by transformation of adaptive systems in initially stress-resistant individuals by stress and deficiency in mechanisms of emotional reactions to stress that leads to neurotic states.

P.3.039 Phase-I investigation of selective anxiolytic afobazole

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Objective: Novel anxiolytic afobazole was designed on the basis of an innovative concept of anxioselective effect.

Purpose: The aim of present study was to examine the effects of afobazole when compared to a typical benzodiazepine tranquilizer in healthy volunteers. This placebo-controlled research was performed in the framework of a phase-I clinical trail.

Methods: Participants were 30 healthy young males. They were randomized to a double-blind treatment with either 10 mg Mobazol, 0.5 mg benzodiazepine tranquilizer phenazepam or placebo in parallel group design. A battery of standard psychological and psychophysiological methods, modelling the operatory performance at rest and under emotional stress, was used. The volunteers were divided into two groups: stress-resistant and stress-unresistant according to the psychological testing.

Results: The combination of anxiolytic and mild activating effects of afobazole was established. Neither sedative and myorelaxant nor undesirable side effects were observed. Afobazole exerted a positive influence on some cognitive functions. Mobazol was more effective in stress-unresistant individuals and it exerted no negative influence on stress-resistant participants. In contrast, the benzodiazepine tranquilizer phenazepam caused a decrease in operatory performance due to sedative and myorelaxant effects. Some disturbances in cognitive-mnestic functions and sensorimotor reactions were observed, especially in the group including the stress-resistant participants.

Conclusion: Data obtained permit the conclusion about the anxioselective properties of Mobazol in contrast to the benzodiazepine tranquilizer phenazepam.

P.3.040 A comparison of clinical efficacy and safety of proproten and diazepam for the treatment of anxiety disorders

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Current drug therapies for anxiety disorder have limitations. At present, pharmacological research is focusing to find anxiolytic drugs as efficacious as benzodiazepines but without side-effects. Proproten, ultra-low doses of antibodies to S-100 protein for oral use, since 1999, is produced, marketed, and widely used in medical practice in Russia as a treatment for alcohol withdrawal. Animal studies revealed that proproten possesses a marked anxiolytic profile in basic models of anxiety (Vogel conflict test, elevated plus-maze, open-field etc; Voronina et al., 2003).

The objective of this study was to assess clinical efficacy and safety of proproten in anxiety disorders in comparison with diazepam.

A multicenter randomized open-label comparative trial was conducted in four clinical centers in Russia. A total of 247 male and female outpatients (mean age – 38.8±0.7; baseline HAM-A – 28.0±0.4) who met IDC-10 criteria for general anxiety disorder, mixed anxiety and depressive disorder, mixed anxiety and depressive reaction, and neurasthenia were randomly assigned to receive proproten (127 pts, 6–12 tablets/day) or diazepam (120 pts, 15 mg/day) in a 4-week study. Symptoms of the anxiety disorders were evaluated at baseline, day 7, day 14 and day 28. Primary endpoints were Hamilton Anxiety scale (HAM-A) total score, response (≥50% reduction in HAM-A score) and remission rates (HAM-A ≤7). State-Trait Anxiety Inventory scale (STAI) was the secondary endpoint.

The study demonstrated good clinical efficacy and safety of proproten (6–12 tablets/day) in anxiety disorders in comparison to diazepam (15 mg/day). The mean baseline-to-endpoint decreases in total HAM-A score in the patients given proproten (–15.3±0.6) was comparable to the decrease in those given diazepam (–17.6±0.6). Effect of proproten rose gradually: as early as week 1, proproten did not significantly reduce the total HAM-A score compared with diazepam and almost equaled diazepam at week 4. The number of responders to proproten and diazepam were 69.3% and 78.3% respectively. The complete remission rate for both preparations was rather low (diazepam – 20.8%; proproten – 12.6%), as a four-week period is a short one to reach remission. Diazepam caused adverse reactions in 40.0% of patients (proproten – 5.5%). The most frequent adverse events reported for diazepam were somnolence, dizziness and headache. There were no serious adverse events reported by patients given proproten, and no withdrawal syndrome was associated with proproten treatment.

These results indicate that proproten is an effective and safe treatment for anxiety disorders. In this treatment schedule, proproten does not appear to cause adverse reactions and the withdrawal symptoms often associated with the benzodiazepines.

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P.3.041 Clinical and neurophysiological efficacy of neurofeedback in the combined therapy of anxiety disorders resistant to psychopharmacotherapy

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Objectives: To determine if there exists a connection between clinical and neurophysiological changes under neurofeedback (NFB) through alpha-rhythm training in the combined therapy of anxiety disorders resistant to psychopharmacotherapy.

Materials and methods: 60 patients (43 women and 17 men) aged between 17 and 48 years (the mean age was 27±9.3) were included. Inclusion criteria: the intensity of anxiety over 20 points on Hamilton Anxiety Rating Scale, resistance to administered standard psychopharmacotherapy. By resistance we mean the absence of the expected outcome at least under two courses of adequate psychopharmacotherapy (in recommended therapeutic dosages for no less than 4 weeks each) by drugs of different chemical classes (benzodiazepines, SSRI, clomipramine). The study sample included the following subgroups (according to ICD-10): obsessive-compulsive disorder (OCD) (16 patients), social phobia (16 patients), panic disorder (PD) (with or without agoraphobia) (14 patients), depressive episode of moderate severity and disthymic disorder with anxiety (14 patients). Patients were randomly divided into 3 treatment groups of 20 persons each: the first group received psychopharmacotherapy and NFB; patients in the second group received only NFB, patients in the third group received psychopharmacotherapy and NFB-placebo.

The course of neurofeedback lasted 4 weeks and consisted of 20 training sessions. Psychopharmacotherapy was continued, it was not changed during the whole training course. As clinical responders we regarded the patients with 40% reduction by Hamilton anxiety scale. Patients with over 20% increase in the alpha-rhythm power in occipital sinister (OS) for the course of therapy were considered neurophysiological responders. Contingency tables analysis and chi-square criterion was applied to reveal the significance of the results.

Summary of results: In the first therapeutic group 16 (80%) patients were regarded as clinical responders. In the second therapeutic group 11 (55%) patients were considered clinically successful. In the third group only 9 (45%) patients achieved clinically significant improvement. Pearson Chi-square test showed significant difference between the first and the third group ($p = 0.022$).