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Diagnosis and Treatment of Cognitive Impairments in Attention Deficit Syndrome in Adults

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Objectives. To clarify cognitive impairments in adults with attention deficit hyperactivity syndrome (ADHD) and to assess the efficacy of the formulation Memoplant in the treatment of this pathology. **Materials and Methods.** The results of clinical, psychological, and electroencephalographic studies of 40 patients aged 18–45 years with ADHD are presented. From recruitment into the study, all patients received Memoplant at a daily dose of 240 mg for eight weeks. **Results and conclusions.** Adult patients with ADHD had both subjective and objective impairments to memory and attention. EEG results suggested that patients showed dysfunction of the frontothalamic regulatory system and deficit of nonspecific activation by the reticular formation. Courses of Memoplant were followed by clinical improvements in 24 patients (60.0%). Repeat psychological and neurophysiological studies demonstrated decreases in attention deficit and improvements in memory measures.

Keywords: attention deficit hyperactivity disorder, Memoplant.

Attention deficit hyperactivity disorder (ADHD) is encountered in 2–6% of adults [1–4]. Thus, there is interest in Russian data obtained from studies of the prevalence of ADHD among 580 students at Pomorskii University, Kirov (mean age 19 ± 0.5 years) [5]. The prevalence obtained in this study was 8.8% (8.9% of males and 8.7% of females).

ADHD in adults is regarded as a consequence of impairments development of the nervous system. Genetic factors constitute one of the leading causes of ADHD, as do low body weight at birth, intrauterine hypoxia, and other perinatal factors [6–8]. The operation of the dopaminergic and noradrenergic neurotransmitter systems of the brain play an important role in the pathogenesis of ADHD. In this regard, the dopamine D4 receptor gene (DRD4) and the dopamine transporter gene (DAT1) are of great importance [9–11].

Adult patients with ADHD have impaired attention, impulsivity, emotional lability, and low stress resistance. Several authors [12, 13] have noted memory impairments. Patients with ADHD are known to receive higher education more rarely, and then to work at lower professional levels [14].

The aims of the present work were to clarify impairments in adults with ADHD and to assess the efficacy of the use of Memoplant in the treatment of this pathology.

Materials and Methods. The study group included 40 patients aged 18–45 years, presenting complaints of increased motor activity and lack of attention. An obligatory condition for inclusion into the study was the presence of signs of ADHD in childhood.

The group of patients was dominated by females (n = 30). Mean age was 24.5 ± 6.3 years. all patients had received higher education or were studying in higher educational institutions.

Diagnoses of ADHD were made using the Wender criteria. The ASRS-V1.1 questionnaire was also employed; this is widely used for the diagnosis of ADHD in adults [15]. Diagnoses were consistent with ICD-10 F90.0.

Exclusion criteria were the presence of cerebrovascular diseases, marked signs of depression, and histories of severe craniocerebral trauma.

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TABLE 1. Dynamics of Clinical Psychological Measures in Patients with ADHD Before and After Courses of Treatment

Measure	Patients with ADHD (before treatment)	Patients with ADHD (after treatment courses)	Control group
ADHD on ASRS-V1.1	49.2 ± 13.7**	21.2 ± 12.3	9.4 ± 5.3
Subjective complaints, (CFQ)	64.8 ± 19.5**	33.6 ± 17.1	20.7 ± 9.6
Short-term memory loss, volume of memory (number of words)	5.8 ± 1.9*	6.7 ± 1.3	7.8 ± 2.1
Long-term auditory memory, fixation of memory traces (number of words reproduced)	5.4 ± 1.8*	6.8 ± 2.1#	7.5 ± 1.7
Short-term visual memory (volume of memory)	6.3 ± 2.8*	7.6 ± 2.1#	8.3 ± 1.5

Here and Table 2: $*p < 0.05$ – significant differences compared with control group; $**p < 0.01$ – significant differences compared with control group; $^{\#}p < 0.05$ – significant differences compared with pre-treatment value.

TABLE 2. TOVA Psychophysiological Test Results in the Study Groups

Measure	Patients with ADHD (before treatment)	Patients with ADHD (after treatment courses)	Control group
Target stimuli missed, %			
first half of test	2.5 ± 1.2**	1.3 ± 0.5#	0.5 ± 0.2
second half of test	4.2 ± 1.9**	3.5 ± 1.8	0.7 ± 0.3
False alarms, %			
first half of test	6.3 ± 1.9**	2.3 ± 1.4##	2.2 ± 0.7
second half of test	10.3 ± 5.4*	8.9 ± 4.6	5.5 ± 2.8
Reaction time, msec			
first half of test	464 ± 98*	323 ± 65#	367 ± 63
second half of test	521 ± 82**	412 ± 53**	376 ± 62

$^{\#\#}p < 0.01$ – significance of differences compared with pre-treatment values.

Neurological investigations were standard. Subjective complaints of memory and attention disorders were evaluated using the CFQ (Cognitive Failures Questionnaire) [16]. Memory impairments were evaluated using the Luriya method. The extent of impairments to attention was assessed using the Test of Variables of Attention (TOVA), which provides for assessment of the state of attention and the level of impulsivity as compared with normative data.

Apart from psychological investigations, all patients underwent electroencephalographic (EEG) studies. EEG recordings were made using 19 electrodes positioned on the surface of the head in accordance with the international 10–20 scheme in the resting state with the eyes closed and open (3 min each). Eye movements were monitored using the electrooculogram. Routine analysis of traces consisted of assessing the overall functional state of the brain, regional EEG changes and the locations of pathological changes, and the presence/absence of epileptiform changes.

Before calculation of EEG spectra, traces were subjected to preliminary processing in WinEEG to remove artifacts. Curve segments deviating from the isoline by more than 150 μV in the period of 200 msec before/after and slow waves of frequency 0–1 osc/sec and amplitude greater than 50 μV were not analyzed. EEG spectra were computed as follows. The whole period of the EEG trace was divided into segments of equal length. The segment length corresponding to the duration of the analysis epoch was 4 sec. Segments overlapped by 50% and each sequential epoch (starting from the second) was an EEG trace segment shifted by half its length relative to the previous segment. After division of EEG traces into segments (analysis epochs), computations for each channel were run separately.

As data before and after treatment were obtained in the same patients, treatment efficacy hypotheses as clinical psychological indicators evolved were tested using the paired Wilcoxon test (tests for paired observations).

From inclusion into the study, all patients received daily doses of Memoplant 240 mg (one tablet twice daily) for eight weeks.

The active component of Memoplant is EGb 761 – a relict *Gingko biloba* leaf extract standardized in relation to the active ingredients – flavonoid glycosides, ginkgolides, and

TABLE 3. Comparison of EEG Spectra in the θ and α Ranges Before and After Treatment of ADHD Patients and the Healthy Group

EEG lead	Patients with ADHD (before treatment)		Patients with ADHD (after treatment)		Control group	
	θ range, %	α range, %	θ range, %	α range, %	θ range, %	α range, %
F3	18.69	25.07	14.85*	19.17	11.5	15.07
F4	16.82	20.58	15.35*	18.58	13.75	20.03
Fz	21.88	20.20	19.14*	19.53	15.15	21.31
C3	14.42	39.25	17.91	28.77*	10.39	23.52
C4	15.02	33.87	15.56	28.06*	11.70	25.01
Cz	20.35	23.30	22.98	19.53	14.82	16.86
P3	14.16	34.52	14.14	31.07*	11.01	20.84
P4	14.72	34.13	12.94	30.60*	12.50	23.87
Pz	15.10	28.64	15.73	25.70*	13.85	26.36

*Statistically significant results after treatment.

bilobalides, which normalize vascular tone in the microcirculatory bed, particularly affecting impaired arterioles without inducing a steal effect. Other active substances in EGb 761 include ginkgolides, which act on blood cells, decreasing platelet and erythrocyte aggregation. The formulation has neuroprotective and neuromodulatory effects [17, 18].

Patients received no other treatment. Monitoring studies for analysis of treatment efficacy were run after completion of treatment courses.

The control group consisted of 30 essentially healthy people aged 18–45 years.

Results. Patients displayed no focal neurological symptomatology. The main signs of ADHD were inattention and impulsivity. Complaints of memory impairments were presented by 27 ADHD patients (67.5%).

Patients with ADHD were characterized by significantly higher levels of complaints of impairments to memory and attention than the control group.

Psychological assessments identified impairments to both auditory and visual memory in ADHD patients (Table 1). The psychophysiological TOVA evaluation showed that patients with ADHD gave significantly greater measures of inattention, impulsivity, and reaction times as compared with the control group (Table 2). Attention is drawn to a significant increase in the number of errors in the second half of the test.

Visual analysis of the EEG with the eyes open showed that 27 patients (67.5%) displayed a tendency for the α rhythm to spread to the anterior areas of the cerebral cortex, while 10 patients (25%) showed brief periods of synchronization of rhythms in the α range and 29 patients (72.5%) showed groups of diffuse θ waves in the frontal-temporal leads of both hemispheres, with amplitude slightly greater than background. Signs of epileptiform activity were not seen in any patient.

Statistical analysis of EEG power spectra with the eyes open showed that in the θ range, patients with ADHD displayed greater power levels in almost all leads than the control group ($p < 0.005$) (Table 3). In the α range, healthy subjects and patients with ADHD showed statistically significant differences ($p < 0.05$) in the parietal-central leads of both hemispheres. The greater values were obtained in ADHD patients (Table 3).

After treatment with Memoplant, clinical improvements were seen in 24 patients (60.6%). Patients reported that they became more attentive to tasks and coped better with productive activities. After courses of treatment, patients showed marked reductions in complaints of impairments to memory and attention. In addition, there were marked improvements in measures on the ASRS-V1.1 scale (see Table 1). There were marked improvements in measures of auditory and visual memory (see Table 1).

Repeat psychophysiological investigations after courses of Memoplant identified statistically significant decreases in measures of inattention and marked reductions in reaction time (see Table 2). There were no significant changes in impulsivity.

After treatment, visual analysis with the eyes open showed that 21 patients (52.5%) experienced reductions in episodes of rhythm synchronization in the α range. After treatment, the frontal-temporal leads in 23 patients (63%) showed decreases and 11 (27.5%) showed the absence of grouped elements in the θ range. Statistical analysis of the quantitative EEG yielded the following results: the α range showed a statistically significant ($p < 0.05$) decrease in power in the central-parietal leads. The θ range also sowed a reduction in power, which was most marked in the frontal leads from both hemispheres ($p < 0.05$) (see Table 3 and Fig. 1).

No undesirable side effects or complications were seen.

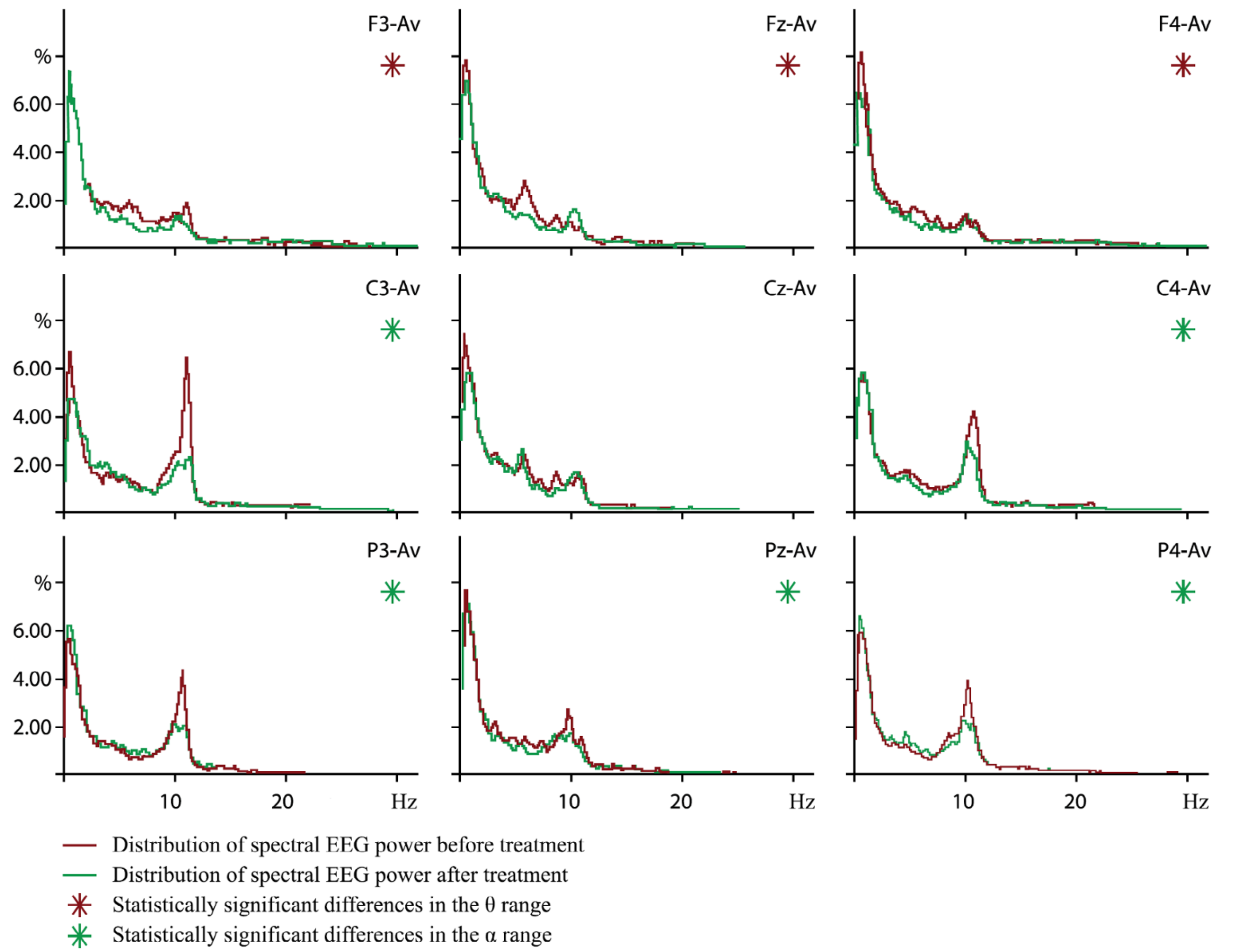

Fig. 1 Absolute EEG spectral data from patients with ADHD before and after treatment with Memoplant.

Discussion. The cognitive features of adult patients with ADHD have the result that they suffer in terms of academic achievement and education. Analysis of the academic success of students showed that those with ADHD had lower mean scores and a higher frequency of experiencing difficulty with studies than their peers without signs of ADHD.

Our results support the view that adult patients with ADHD are characterized by both subjective and objective impairments to memory and attention [19–21].

The psychophysiological investigation TOVA showed that patients with ADHD display significant increases in measures of inattention and impulsivity than the control group (see Table 2). Increases in the numbers of errors in the second half of the test provide evidence of marked fatigue. Overall, these data can be regarded as one of the signs of executive dysfunction. Executive functions are higher-level cognitive processes such as planning, cognitive flexibility, and control, and impairments to them are a component of neurocognitive deficit. Barkley and Fischer [22] and Grane et al. [23] reported impairments to cognitive control in adult patients with ADHD.

EEG results suggest that patients with ADHD show dysfunction to the frontal-thalamic regulatory system (increases in the power of the θ range in the frontal leads of both hemispheres as compared with the healthy level) and deficit of nonspecific activation by the reticular formation (presence of synchronization in the α range in the central-parietal areas of the cerebral cortex). In turn, insufficient activation of particular cortical zones affects the formation of different components of attention, its low stability, deficit in motivation, and impairments to the processes of involvement in actions on execution of cognitive tasks. The frontal cortex and inferior parietal areas of the cerebral cortex are also known to have a role in organizing complex forms of behavior and perception processes, and constitute components of the system regulating complex automated motor acts.

It can be suggested that with the eyes open, the patients do not receive the level of activation from the reticular formation of the brainstem required for processing sensory information.

The presence of cognitive impairments in patients with ADHD provides grounds for using neuroprotective agents in their treatment. Regular use of EGb 761 has been shown to strengthen dopaminergic and noradrenergic transmission in the frontal cortex, i.e., to accelerate neurotransmitter synthesis in brain areas responsible for intellect and the concentration of attention [24]. Considering the role of changes to the dopaminergic and noradrenergic neurotransmitter systems in the pathogenesis of ADHD, these observations are of great importance.

The results of this study showed that the use of Memoplant produces significant reductions in the severity of clinical psychological signs in almost 60% of adult patients with ADHD. Marked reductions in inattention were noted, along with major improvements in memory measures. The results of repeat psychophysiological studies after courses of Memoplant confirmed the clinical data and provided evidence of decreased asthenia and neurocognitive deficit.

After treatment, there was a reduction in the proportion of α waves in the parietal-central leads of both hemispheres, along with a significant reduction in episodes of rhythm synchronization in the α range. Analysis of these changes suggests that the reticular formation of the brain had a normalizing influence on the cerebral cortex, i.e., the level of activation of the cerebral cortex required for processing sensory information with the eyes open was achieved.

In addition, treatment was followed by a decrease in the absolute power of the θ range, more marked in the frontal-central leads of both hemispheres, which is evidence of a reduction in the predominance of synchronizing influences from thalamic structures. These changes suggest normalization of the operation of the frontal-thalamic regulatory system and achievement of the optimum level of activation of neocortical structures in the state of calm waking.

Boiko et al. [25] demonstrated the efficacy of Memoplant in the treatment of moderate cognitive impairments. Particularly marked improvements were seen in relation to attention, memory, visuospatial functions, and signs of anxiety and depression. Litvinenko et al. [26] obtained evidence of the efficacy and good tolerance of this medication for correcting mental disorders in patients with cognitive impairments with cerebral ischemia.

We have previously shown that the use of Memoplant in the treatment of asthenic disorders on the background of emotional burnout syndrome is highly effective. After treatment, there were significant reductions in measures of fatigue, asthenia, and overall indicators characterizing emotional burnout syndrome [27].

Thus, Memoplant is an effective substance for the treatment of cognitive impairments in adult patients with ADHD.

The authors have no conflicts of interests.

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