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Attention Deficit Disorder in Adults: Clinical and Psychophysiological Features and Treatment

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We present here the results of studies of 34 patients aged 18–30 years with attention deficit hyperactivity disorder (ADHD) (ICD-10 F90.0). The form of ADHD with predominance of inattention was more frequent in adults (50% of patients), while the form with predominance of hyperactivity (11.7%) and the combined form (38.3%) were less common. The status of adult patients with ADHD was characterized by high levels of anxiety and asthenia. The efficacy and safety of Adaptol at a dose of 1500 mg/day for eight weeks were studied in the treatment of this group of patients. Clinical, psychological, and neurophysiological data demonstrated the high efficacy (improvements in 64.7% of cases) and safety of Adaptol.

Keywords: attention deficit hyperactivity disorder (ADHD), adults, Adaptol.

The treatment of patients with attention deficit hyperactivity disorder (ADHD) is an important current problem in pediatric neurology and psychiatry. This condition occurs in 5–9% of children in the general population [1, 2, 7, 23]. Children and adolescents with ADHD are characterized by restlessness, distractibility, extreme mobility, impulsivity, low levels of success, and fatigue. In 30–50% of cases, the symptoms of ADHD, developing in childhood, continue to some extent or another into adult age [6]. The clinical manifestations of this disorder in adults have received much less attention. ADHD is found in 3–6% of the adult population [15, 17, 20].

ADHD is currently regarded as a manifestation of impaired nervous system development. It has therefore been suggested that the primary development of ADHD cannot occur in adults.

Special criteria have been development for assessing ADHD in adults [6]. According to these data, the behavior of the adult patient in childhood (retrospectively) must correspond to the DSM-IV criteria for pediatric ADHD, while in adults it must correspond to features 1 and 2 below, as well as at least two of criteria 3–7: 1. Constant movement activity. 2. Impaired attention. 3. Emotional lability. 4. Inability to complete tasks. 5. Irascibility. 6. Intolerance of stress. 7. Impulsivity.

These signs produce the features of the behavior of adult patients with ADHD in social and personal life. Despite the fact that these patients do not show cognitive impairments, their academic achievements and education do suffer. Patients with ADHD have a reduced representation in higher education and have lower work roles. These people have poor time-planning and organizational skills, change their workplaces often, and are dismissed very frequently. However, the level of unemployment among them is not significantly different from that in the control group. They have an increased frequency of being victims in road traffic collisions [10] and suffer more accidents. Worse results are obtained in psychophysiological stop signal tests, evidencing increased impulsivity [21]. Adults with ADHD have a number of difficulties in their personal life: large numbers of partners with short-lived sexual relationships, frequent separations, and lack of a systematic approach to the use of contraceptives. They also often suffer addictive disorders.

In other countries, the treatment of ADHD is mostly based on the use of psychostimulators and atomoxetine.

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

Indicator, points	Patients with ADHD		Control group
	before treatment	after treatment	
Inattention, VAS	7.2 ± 2.3##	4.54 ± 1.8*	2.6 ± 1.9
Hyperactivity, VAS	4.0 ± 1.7#	2.1 ± 1.1**	1.9 ± 1.2
Impulsivity, VAS	5.9 ± 2.6#	2.8 ± 1.3*	3.6 ± 1.5
Total asthenia, MFI-20 scale	10.3 ± 4.1##	6.6 ± 2.7*	3.4 ± 1.2
Physical asthenia, MFI-20 scale	4.0 ± 1.3	3.8 ± 1.5	2.9 ± 1.4
Mental asthenia, MFI-20 scale	10.8 ± 3.6##	4.2 ± 2.0**	2.9 ± 1.5
Decreased activity, MFI-20 scale	5.6 ± 3.5#	4.7 ± 2.6	2.4 ± 1.9
Decreased motivation, MFI-20 scale	6.3 ± 3.9##	5.2 ± 3.7	2.8 ± 1.3
Fatigue, VAS	5.3 ± 2.4#	3.6 ± 1.9*	2.2 ± 1.8
Reactive anxiety	37.4 ± 7.7##	26.3 ± 4.3**	18.5 ± 5.1
Endogenous anxiety	42.9 ± 8.6##	40.1 ± 7.8	25.3 ± 4.2
Headache intensity, VAS	6.4 ± 3.1##	3.2 ± 1.4*	0
Autonomic impairments (Vein questionnaire)	39.1 ± 10.7##	27.8 ± 9.1*	24.3 ± 5.2

Notes. #Significant difference compared with control group, $p < 0.05$; ##significant difference compared with control group, $p < 0.01$; *significant difference compared with pre-treatment value, $p < 0.05$; **significant difference compared with pre-treatment value, $p < 0.01$.

We were unable to find any studies of the diagnosis and treatment of ADHD in adults in Russia.

The aim of the present work was to describe the clinical manifestations of ADHD in adults and assess the efficacy and safety of treatment with Adaptol in its treatment.

Materials and Methods

A total of 34 patients aged 18–30 (mean 23.4 ± 4.09 years) presenting with complaints of increased movement activity and lack of attention were studied.

An obligatory condition for inclusion of patients in the study consisted of statements by the patients and/or their parents that these disorders had been present in childhood. Exclusion criteria were histories of cerebrovascular diseases, marked depression, and severe craniocerebral traumas.

Diagnoses of ADHD were made on the basis of the criteria above [6], which correspond to ICD-10 F90.0.

Neurological investigations were performed using a standard scheme. The severity of asthenic disorders and their dynamics during treatment were determined using a subjective assessment scale – the MFI-20 – with five subscales. Patients' status was also evaluated using a 10-point visual analog scale (VAS). The VAS was used for subjective assessment by the patients of their asthenia and the leading symptoms of ADHD – inattention, hyperactivity, and impulsivity.

Diagnoses of ongoing concomitant headaches were made using the classification of the International Headache Society. Headache intensity was assessed on the VAS.

Psychological investigations included the Spilberger–Hanin scale. The extent of impaired attention was assessed using the Test of Variables of Attention (TOVA), which allows the state of attention and the level of impulsivity to be evaluated in comparison with normative data.

The control group consisted of 35 essentially healthy subjects aged 18–35 (mean 22.6 ± 3.7 years).

ADHD patients were treated using courses of the non-benzodiazepine anxiolytic Adaptol.

Adaptol is known to have marked autonomic-stabilizing and moderate anxiolytic effects without producing any reduction in reaction speeds, as well as moderate nootropic effects on the background of physical and mental fatigue; it also has antihypoxic effects. Adaptol leads to increases in adaptogenic activity, has antistress and stress-protective actions; it improves mental and physical work capacity. Adaptol, in contrast to benzodiazepines, has no myorelaxant effect, does not suppress myocardial contractile activity, and produces no central side effects: low mood, lethargy, drowsiness, or emotional indifference.

Patients were prescribed Adaptol for eight weeks at a daily dose of 1500 mg, divided into three portions. Patients received no other treatment during this time or during the month before investigations.

Results

The main signs of ADHD in the study patients were inattention, hyperactivity, and impulsivity. Patients' self-

TABLE 2. Psychophysiological Indicators in Patients with ADHD, TOVA Test

Indicator		Patients with ADHD		Control group
		before treatment	after treatment	
Missed target stimuli, %	First half of test	2.6 ± 1.4##	1.2 ± 0.6**	0.3 ± 0.1
	Second half of test	3.9 ± 1.7##	1.8 ± 0.9**	0.4 ± 0.2
False alarms, %	First half of test	6.6 ± 1.3##	3.2 ± 0.9**	2.6 ± 0.3
	Second half of test	13.2 ± 4.7#	7.9 ± 3.1*	6.3 ± 2.1
Reaction time, msec	First half of test	451 ± 67	448 ± 54*	430 ± 51
	Second half of test	483 ± 75#	432 ± 59*	376 ± 62

Note. #Significant difference compared with control group ($p < 0.05$); ##significant difference compared with control group, $p < 0.01$; *significant difference compared with pre-treatment value, $p < 0.05$; **significant difference compared with pre-treatment value, $p < 0.01$.

assessment results are shown in Table 1. DSM-IV criteria identified patients with the following types of ADHD: 17 patients (50.0%) had a predominance of inattention (ADHD-I); four patients (11.7%) had a predominance of hyperactivity and impulsivity (ADHD-HI); 13 patients (38.3%) had the combined form (ADHD-C).

No focal neurological symptomatology was detected on examination of the patients. Analysis of questionnaire results using the MFI-20 scales showed that asthenic syndrome was present in 26 patients (76.5%). Quantitative assessment of the severity of asthenic syndrome showed a significant increase in values on the scales for total and especially mental asthenia (see Table 1).

Headaches were frequent in patients of the study group – present in 30 patients (88.3%). Tension headaches (THA) were seen in 22 patients (64.7%), of which 18 patients had frequent THA. Attack frequency was 3–10 per month. Diagnoses of "chronic THA" were made in four cases. Migrainous headaches were present in 13 patients (38.2%). Among these, migraine without aura was seen in 11 cases and migraine with typical aura in two cases; five patients had both migraine pain and THA. The mean intensity of headache in the study group on the VAS was 6.4 ± 3.1 points.

Signs of autonomic dysfunction (A. M. Vein criteria) were seen in 33 patients (97.1%). The complex points assessment of the severity of autonomic impairments was 39.1±10.7 points (compared with a normal score of 20–25 points).

Psychological evaluations showed increased (sometimes significantly) levels of both reactive and endogenous anxiety in 29 ADHD patients (85.3%).

Psychophysiological assessments using the TOVA scale showed that patients with ADHD had significant increases in measures of inattention, impulsivity, and reaction times as compared with the control group (Table 2).

After treatment with Adaptol, improvements in status were noted in 22 patients (64.7%). Patients showed significant improvements in self-assessments of attention, hyperactivity, and impulsivity (see Table 1). Patients reported that they became more diligent during tasks and reached production targets more quickly. In addition, there were improvements in interactions with close persons and colleagues in situations in which conflicts had previously frequently arisen.

Quantitative assessments of the severity of asthenic syndrome decreased significantly after treatment on the total and particularly the mental asthenia scales (see Table 1). Assessment of pain on the VAS showed a mean intensity of headache after treatment of 3.2 ± 1.4 points. The greatest decreases in headache intensity were seen in patients with THA.

Treatment with Adaptol was also followed by significant reductions in the signs of autonomic dysfunction. The complex points assessment of the severity of autonomic impairments was 27.8 ± 9.1 after treatment ($p < 0.05$).

Psychological study results after treatment showed significant decreases in anxiety (see Table 1).

No side effects or complications were seen, providing evidence of the safety of Adaptol.

Discussion

ADHD, a disorder traditionally studied by pediatric psychiatrists and neurologists, also poses a major social problem in relation to adult patients, as it has negative impact on general adaptation processes. It was noted above that adult patients with ADHD have low levels of education and problems with employment [11, 13]. Among the causes of ADHD, the main are genetic and perinatal factors: Trzhesoglava [5] notes that the possibility that several factors may be operating must always be considered.

We have previously [8] presented data on the clinical heterogeneity of ADHD in children. These observations showed that ADHD in adults was significantly more often the form with predominance of inattention and more rarely the combined form or the form with a predominance of hyperactivity.

Many authors [22] have noted high levels of anxiety in children with ADHD. The present studies found high levels of anxiety combined with marked asthenia.

In addition, frequent concomitants of ADHD in both children and adults were autonomic dysfunctions, sleep disorders, and headaches. However, migrainous headaches were significantly less common in children. Psychophysical investigations using the TOVA test showed that patients with ADHD had significant increases in inattention and impulsivity compared with the control group (see Table 2).

Our previous studies demonstrated the efficacy of Adaptol in the treatment of ADHD in children. Treatment decreased hyperactivity and impulsivity, leading to improvements in behavior at school and at home [9]. Adaptol is known to show antagonist activity in relation to the excitatory adrenergic and glutamatergic systems, increasing the functioning of the inhibitory serotoninergic and GABAergic mechanisms of the brain. In addition, Adaptol has dopamine-positive influences, which are apparent clinically in the activatory component of its action [3]. This latter component is very important, given the role of impairments to dopamine metabolism in the pathogenesis of ADHD [18, 24]. Thus, the gene for the dopamine D4 receptor (*DRD4*) is very important, as is the "dopamine transporter gene" (*DAT1*). The dopamine receptor *D4* gene has been shown to play a role; the dopamine receptor *D4* is known to suppress the function of the prefrontal cortex and the 7-repeat allele of the *D4* gene is known to moderate the interaction between ADHD and cognitive disorders. These changes determine decreases in the functioning of the dopaminergic neurotransmitter system of the brain [12, 14, 16, 19].

Our results show that use of Adaptol leads to significant decreases in the severity of ADHD in almost 65% of adult patients. Thus, there were marked decreases in inattention and impulsivity. Furthermore, there was a marked reduction in the level of anxiety, with a decrease in the intensity of concomitant headache, and normalization of autonomic balance, which can be explained by the anxiolytic and autonomic-stabilizing effects of the agent.

Zhivolipov et al. [4] showed that use of Adaptol produced a statistically significant increase in the concentration of brain-derived neurotrophic factor (BDNF) in serum, this being a marker for neuroplasticity. This is evidence that the positive action of Adaptol is based on modulation of neuroplasticity due to increased BDNF expression.

It should be noted that use of Adaptol does not restrict work and social activities associated with increased concentration of attention, nor does it produce habituation or the development of a withdrawal syndrome.

Thus, Adaptol is a highly effective and safe substance for the treatment of the clinical signs of ADHD in both children and adults.

REFERENCES

1. L. O. Badalyan, N. N. Zavadenko, and T. Yu. Uspenskaya, "Attention deficit disorder in children: A review," *Obozr. Psikh. Med. Psikhol. V. M. Bekhtereva*, No. 3, 74–90 (1993).
2. I. P. Bryazgunov and E. V. Kasatikova, *The Restless Child, or All About Hyperactive Children*, Institute of Psychotherapy Press, Moscow (2001).
3. L. A. Gromov and E. T. Dudko, "'Typical' and 'atypical' tranquillizers," *Vestn. Farmakol. Farmatsii,* No. 10, 11–17 (2003).
4. S. A. Zhivolupov, I. N. Samartsev, A. A. Marchenko, and O. V. Pulyatkina, "Prognostic significance of blood levels of brain-derived neurotrophic factor (BDNF) in the treatment of various functional and organic diseases of the nervous system using Adaptol," *Zh. Nevrol. Psikhiat,* **112**, No. 4, 37–41 (2012).
5. Z. Trzhesoglava, *Mild Cerebral Dysfunction in Children*, Meditsina, Moscow (1986).
6. P. Wender and R. Sheider, "Attention deficit hyperactivity disorder," in *Psychiatry* [Russian translation], R. Sheider (ed.), Moscow (1998), pp. 222–236.
7. L. S. Chutko, A. B. Pal'chik, and Yu. D. Kropotov, *Attention Deficit Hyperactivity Disorder*, MAPO Press, St. Petersburg (2004).
8. L. S. Chutko, *Attention Deficit Hyperactivity Disorder and Concomitant Disorders*, Khoka, St. Petersburg (2007).
9. L. S. Chutko and S. Yu. Surushkina, "Clinical heterogeneity of attention deficit disorder," *Zh. Nevrol. Psikhiat.*, No. 8, 123–131 (2008).
10. R. A. Barkley, *Attention Deficit Disorder with Hyperactivity: A Handbook for Diagnosis and Treatment*, New York (1988).
11. R. A. Barkley, "Adolescents with attention-deficit/hyperactivity disorder: an overview of empirically based treatments," *J. Psych. Practice*, No. 10, 39–56, (2004).
12. M. A. Bellgrove, Z. Hawi, M. Gill, and T. H. Robertson, "The cognitive genetics of attention deficit hyperactivity disorder (ADHD): sustained attention as a candidate phenotype," *Cortex*, **42**, No. 6, 838–845 (2006).
13. J. Biderman and S. Faraone, "Attention deficit hyperactivity disorder," *Lancet*, **366**, 237–248 (2005).
14. U. Ettinger, R. Joober, R. De Guzman, et al., "Schizotypy, attention deficit hyperactivity disorder, and dopamine genes," *Psychiatry Clin. Neurosci.*, **60**, No. 6, 764–767 (2006).
15. S. Faraone, "What is the prevalence of adult ADHD? Results of a population screen of 966 adults," *Atten. Disord.*, **9**, No. 2, 384–391 (2005).
16. S. V. Faraone and S. A. Khan, "Candidate gene studies of attention-deficit/hyperactivity disorder," *J. Clin. Psych.*, **67**, Supplement 8, 13–20 (2006).
17. J. Fayyad, R. De Graaf, R. Kessler, et al., "Crossnational prevalence and correlates of adult attention-deficit hyperactivity disorder," *Brit. J. Psychiat.*, **190**, 402 (2007).
18. M. Gill and G. Daly, "Confirmation of association between attention deficit hyperactivity disorder and a dopamine transporter polymorphism," *Mol. Psychiatry*, **2**, No. 4, 464–468 (1997).
19. C. H. Kim, M. K. Hahn, Y. Joung, et al., "A polymorphism in the norepinephrine transporter gene alters promoter activity and is associated with attention-deficit hyperactivity disorder," *Proc. Natl. Acad. Sci. USA*, **103**, No. 50, 19164–19169 (2006).
20. G. Polanczyk, M. S. de Lima, B. H. Horta, et al., "The worldwide prevalence of ADHD: a systematic review and metaregression analysis," *Am. J. Psychiat.*, **164**, 942 (2007).
21. J. Sergeant, "The cognitive-energetic model: An empirical approach to attention-deficit hyperactivity disorder," *Neurosci. Biobehav. Rev.*, **24**, 7–12 (2000).
22. D. B. Schatz and A. L. Rostain, "ADHD with comorbid anxiety: A review of the current literature," *J. Atten. Disord.*, **10**, No. 2, 141–149 (2006).
23. M. L. Wolraich, "Addressing behavior problems among school-aged children: traditional and controversial approaches," *Pediatr. Rev.*, **18**, No. 8, 266–270 (1997).
24. A. J. Zametkin and J. L. Rapoport, "Noradrenergic hypothesis of attention deficit disorder with hyperactivity: A critical review," in: *Psychopharmacology: The Third Generation of Progress* H. V. Metsler (ed.), Raven, New York (1987), pp. 837–846.