Neuroscience and Behavioral Physiology, Vol. 43, No. 2, February, 2013

Efficacy of Cortexin in the Treatment of Memory Disorders in Children

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Translated from Zhurnal Nevrologii i Psikhiatrii imeni S. S. Korsakova, Vol. 111, No. 9, Iss. 2, V Pomoshch Prakticheskomu Vrachu, pp. 37–40, September, 2011.

Children aged 7–12 years with memory disorders were treated with Cortexin (30 patients) or Encephabol (30 patients). A comparative study of the efficacy and safety of each of these agents was conducted. Cortexin was found to have greater efficacy (improvements in 86.7% of cases) than Encephabol (improvements in 63.3% of cases), supported by neuropsychological and neurophysiological results.

Keywords: Cortexin, treatment, memory disorders, children.

Memory disorders represent a widespread cause of school maladaptation. As there is a close relationship between memory and the development of speech, children with these disorders are also characterized by difficulties in speech development and poor vocabulary. Lack of memory also has adverse influences on the development of writing skills.

The most common impairments are in short-term auditory verbal and visual memory. Lack of short-term visual memory is characterized by poor perception of the configurations of words and slow acquisition of reading skills. Impairments to short-term auditory verbal memory produce the following signs: reductions in the volume of material remembered; inability to retain a sequence of words (permutations of words); the introduction of adventitious (i.e., non-presented, new) words or words close in meaning or sound to the stimuli; poor fixation of memory traces (in delayed recall).

Memory disorders not associated with trauma or infectious disease in children have in recent decades been categorized using the concept of developmental dysmnesia [4, 10].

Mnestic disorders are traditionally treated using nootropic agents. These include the peptide neuroprotector Cortexin, which is a complex of polypeptides of up to 10 kDal extracted with acetic acid from the cerebral cortex of calves aged no more than 12 months. Cortexin improves memory and learning parameters in animals, evidencing its nootropic activity [3, 6]. The pharmacological effects of Cortexin are believed to be based on normalization of metabolism in neurons, with a regulatory influence on the activity of the cerebral cortex, including neurotransmitter levels in cortical structures.

In humans, Cortexin has positive actions not only on attention and memory, but also on emotional state [2]. Use of Cortexin increases work capacity and decreases fatigue and daytime drowsiness [8]. Cortexin is highly effective in the treatment of craniocerebral trauma, impairments to cerebral circulation, neuroinfections, and asthenic states [1, 6]. In pediatric practice, Cortexin is used in rehabilitation in various types of infantile cerebral palsy, the sequelae of craniocerebral trauma, delayed psychomotor development, and attention deficit syndrome [5, 6, 9].

The aim of the present open controlled study was to evaluate the efficacy of Cortexin in comparison with Encephabol in children with memory disorders.

Materials and Methods

A total of 60 children aged 7–12 (mean 9.2 ± 2.8) years attending normal schools were studied. The parents of all the children felt that they were suffering from decreased memory.

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0097-0549/13/4302-0237

TABLE 1. Dynamics of Neuropsychological Study Results after Courses of Treatment

Parameter	Before treatment		After treatment with Encephabol		After treatment with Cortexin	
	7–9 years	10–12 years	7–9 years	10–12 years	7–9 years	10–12 years
Short-term auditory memory: volume of memory (number of words)	2.9 ± 0.5	5.5 ± 0.7	3.6 ± 0.6	7.2 ± 0.8*	4.7 ± 0.5*#	8.3 ± 0.7**#
Short-term auditory memory: volume of memory (order of words)	Did not follow order of words	Order not considered	Transposition of words	Order not considered	Order unaltered	Order not considered
Short-term auditory memory: fixation of memory traces (number of words reproduced)	1.8 ± 0.3	3.3 ± 0.5	2.7 ± 0.8	5.7 ± 0.6*	3.3 ± 0.9*	6.8 ± 0.7**#
Short-term visual memory: volume of memory	3.1 ± 0.8	6.5 ± 0.9	5.4 ± 1.6*	8.2 ± 2.6*	6.3 ± 1.2**	9.4 ± 2.1**#

Note. *$p < 0.05$ for differences compared with the corresponding pre-treatment values; **$p < 0.01$, #significant differences compared with corresponding values in the reference group.

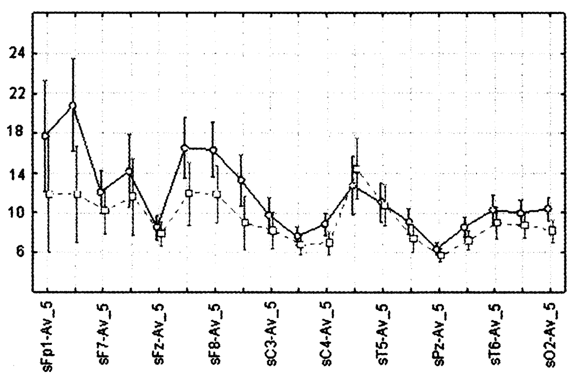

Fig. 1. Changes in the power spectrum of θ activity on the EEG in group of children receiving Cortexin. ○) Before treatment; □) after treatment. Here and in Fig. 2: the continuous line shows pre-treatment values and the dotted line shows post-treatment values. The abscissa shows electrode locations as per the 10–20 system; the ordinate shows relative power, %; $p = 0.0015$.

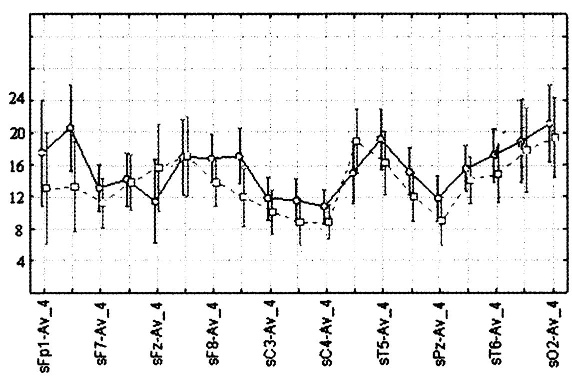

Fig. 2. Changes in the power spectrum of θ activity on the EEG in group of children receiving Encephabol. ○) Before treatment; □) after treatment.

Subjects were divided into two age groups: 7–9 years (33 children) and 10–12 years (27 children).

At recruitment, the following criteria were applied: age 7–12 years; parents complaining that their children had memory impairments; correspondence with the clinical criteria of mild cognitive impairment (ICD-10, F.06.7) or organic asthenic disorder (ICD-10, F.06.6); parental consent to take part in the study.

Exclusion criteria were: age less than seven or greater than 12 years; significant focal neurological symptomatology; memory impairment after craniocerebral trauma or neuroinfection; attention deficit hyperactivity disorder; severe somatic pathology; epileptic seizures; mental retardation; use of medications affecting the CNS.

During the study, clinical histories were taken and standard neurological examination was performed [7].

Short-term auditory verbal memory was assessed using the following methods: in children aged 7–9 years by memorization of two groups of three words and five words; in children aged 10–12 years by memorization of two groups of five and 10 words. Visual memory was tested by memorization of five figures and six letters.

Electroencephalography was also performed. EEG recordings were made using 19 electrodes positioned according to the international 10–20 system in the state of rest with the eyes open (for 3 min). Eye movements were monitored by recording electrooculograms (EOG). Absolute EEG power was calculated and comparisons between groups of subjects were made in the θ (4–7 Hz), α_1 (8–13 Hz), β_1 (14–25 Hz), and β_2 (25–35 Hz) ranges.

Patients were divided into two groups:

1) The study group (30 children), who received Cortexin (Gerofarm, St. Petersburg) as i.m. injections at a dose of 10 mg; this is provided as a sterile lyophilized powder in 10-mg vials. Courses consisted of 10 injections given daily or every other day for 20 days.

2) The reference group (30 children) had memory disorders and clinical-neurophysiological characteristics analogous to those in the study group. Children of this group received 100-mg Encephabol tablets at a dose of one tablet twice a day for 30 days (0.5 tablet twice daily for the first five days). Treatment results were evaluated on day 30.

Patients of the study and reference groups received no other treatment.

Results

After courses of treatment, improvements were obtained in 26 children (86.7%) in the study group, in whom improvements were generally seen after 6–7 injections. The parents in all cases reported improvements in memory. The noted that their children coped with homework more quickly and made more progress at school. Three cases (10%) showed minor hyperarousal, which passed after the end of treatment courses. There were no other side effects or complications.

Psychological investigations after courses of Cortexin demonstrated improvements in auditory and auditory verbal memory (see Table 1). The children required less repetition of material in performing standard tests.

In the reference group, improvements were obtained in 19 children (63.3%), whose parents also noted improvements in memory. In addition, 11 children (36.7%) noted hyperarousal and sleep disorders, which passed after completion of courses of Encephabol. There were no other side effects or complications. The results of psychological investigations demonstrated improvements in measures of auditory and visual memory (see Table 1).

The data presented in Table 1 provide evidence that courses of Cortexin led to more marked improvements in measures of memory than courses of Encephabol. In addition, the smaller number of side effects recorded during treatment with Cortexin should be noted.

Comparison of EEG spectral power with the eyes open in the θ range before and after treatment with Cortexin showed a statistically significant decrease in the power spectrum after treatment in the frontal and central leads of both hemispheres: $F(18,1278) = 2.7052$, $p = 0.00015$ (Fig. 1).

Similar results in the projections of the frontal and central areas of the cerebral cortex were obtained using Encephabol. After treatment with Encephabol, there was a statistically significant decrease in the power spectrum of θ waves in leads *F7*, *F3*, *Fz*, *F4*, *F8*, *C3*, *Cz*, and *C4* ($F(18,1350) = 1.8624$, $p = 0.01531$) (Fig. 2).

Comparison of results in the two groups showed more marked decreases in the power spectrum of θ waves after treatment with Cortexin than Encephabol. This provides grounds for suggesting that Cortexin has a more marked activatory influence than Encephabol.

Thus, use of Russia-produced peptide neuroprotector Cortexin was characterized by high efficacy in the treatment of memory disorders in children. Treatment was followed by significant increases in the number of words remembered and the degree of fixation of memory traces on testing auditory verbal memory; there were increases in the numbers of figures and letters remembered on testing visual memory.

The dynamics of the results of neurophysiological investigations provided evidence of activation of the frontothalamic system after courses of treatment, with increases in nonspecific activatory influences and decreases in signs of functional immaturity of the brain. These data are consistent with our previous results from quantitative electroencephalographic studies in children with attention deficit syndrome, where courses of Cortexin were followed by significant decreases in the ratio of the θ rhythm to the β rhythm and significant increases in the power of the α rhythm in the occipital areas in all age groups [9]. Cortexin also produced increases in α activity.

These changes indicate the efficacy of this treatment. Results obtained from using Cortexin were significantly better than those with Encephabol.

The safety of Cortexin and the absence of side effects allow Cortexin to be recommended for the treatment of developmental dysmnesia.

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