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INFLUENCE OF SURGICAL TREATMENT ON EPILEPSY SEIZURES AND COGNITIVE FUNCTIONS (CURRENT DATA)

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The review is devoted to the role of cognitive disorders in the prognosis of surgical treatment of drug-resistant epilepsy. An analysis of various aspects of surgical treatment of epilepsy is given, modern data on the prognosis of surgical intervention in relation to seizure control, cognitive functioning, mental disorders are presented.

Key words: epilepsy, drug resistance, mental disorders, cognitive disorders, surgical treatment of epilepsy.

The goal of surgical treatment of epilepsy is to achieve complete remission or reduce the frequency of seizures that impair quality of life. In 2001, the first comparative randomized controlled trial (RCT) [1, 2] of surgical and drug treatment of drug-resistant temporal lobe epilepsy was published, the results of which showed the advantages of surgical intervention in assessing seizure control: within a year after temporal lobectomy with continued drug treatment, 58% of patients were seizure-free, while in the control group this figure was 8%. Another RCT comparing surgical intervention for drug-resistant temporal lobe epilepsy with long-term drug therapy was conducted in 2012 by J. Engel et al. [3, 4]. In this study, 11 of 15 patients remained seizure-free for 2 years after temporal lobectomy, while none of the 23 patients who received drug therapy achieved complete remission. Despite the convincing results of these studies indicating the superiority of surgical intervention, it should be noted that the size of the analyzed samples was limited, as they included only patients with temporal lobe epilepsy, which does not correspond to the entire phenotypic spectrum of focal epilepsy with a drug-resistant course. D. Schmidt and K. Stavem [5, 6] conducted a meta-analysis of 20 comparative studies involving operated and non-operated patients with drug-resistant epilepsy, 19 of which were non-randomized and 17 included only patients with temporal lobe epilepsy. The results of the meta-analysis showed that 12% of patients in the drug therapy group and 44% of the

operated patients achieved complete remission. Moreover, 36% of patients in the latter group were able to completely discontinue antiepileptic therapy. A recent meta-analysis [7], which included 20 studies involving both children and adults (18 non-randomized studies, 11 evaluated only patients with temporal lobe epilepsy, 1 was devoted to the study of Lennox-Gastaut syndrome), confirmed the previous data: complete remission was achieved by 57% of operated patients and 15.3% of patients in the control group. In the main group, a reduction in anticonvulsant dosages was noted, and in 19.4% of cases, their complete discontinuation, while in the control group, no reduction in dosage was observed, and complete discontinuation of drugs was possible only in 3.9% of patients. The results of domestic studies, mainly uncontrolled, also indicate the effectiveness of surgical treatment of epilepsy. Thus, according to the data of a prospective 12-month study [8], which observed 26 patients who underwent surgical treatment of epilepsy, 69% achieved complete control over seizures, in 19% the outcome of the operation corresponded to class 2 according to Engel, in 4% - 3, in 8% - 4. Another study [9], which included operated patients with MR-negative drug-resistant epilepsy, showed similar results: complete control over seizures was achieved by 66% of patients. According to M.R. Mamatkhanov et al. [10], when performing temporal resections, the outcome of the operation corresponded to class 1 according to Engel in 75.4% of adult patients, extratemporal resections - in 58.9%. The search for real ways to increase the effectiveness of surgical treatment of epilepsy is primarily aimed at establishing predictors of effectiveness. Thus, according to the results of the analysis of a recently published systematic review [11], the independent factors of a favorable outcome of the operation in terms of seizure control include the presence of mesiotemporal sclerosis or tumor, correspondence between MRI and EEG, an indication of febrile seizures in the anamnesis, unilateral interictal epileptiform activity and completeness of resection of the epileptogenic zone. The authors indicate that the burden of the anamnesis of TBI, encephalomalacia or vascular malformations, as well as epileptiform activity determined after surgery did not have a significant effect on the outcome of surgical treatment of epilepsy. At the same time, the absence of changes on MRI, preoperative invasive EEG monitoring, the presence of focal cortical dysplasia and other malformations, as well as left-sided resection, although they can worsen the prognosis of surgical treatment, but, according to V. Vakharia et al. [12], are not a reason for refusing it.

The cognitive “turn” in brain science has become a powerful factor in terms of interdisciplinary research into cognitive functions in epilepsy and the impact of various

treatment methods, including surgery, on them. Epilepsy is known to be a factor that negatively affects cognitive functions. Even in adult patients, memory, psychomotor speed, and executive functions deteriorate within a year of illness [13]. In patients with drug-resistant epilepsy, cognitive impairment most often affects the areas of attention and information processing, as well as visual and verbal memory [14, 15]. Despite the interest of researchers in studying the consequences of surgical intervention for epilepsy in the area of cognitive functioning, the results obtained are quite contradictory. E. Sherman et al. [16] assessed the neuropsychological outcome of surgical treatment of epilepsy based on the ratio of deterioration and improvement in cognitive functions based on a systematic review. The authors found that this ratio for left-hemisphere operations for verbal memory was 44 and 7%, visual - 21 and 15%, nominative speech function - 34 and 4%, speech fluency - 10 and 27% and attention - 6 and 10%, and for right-hemisphere operations it was 20 and 14% for verbal memory, 23 and 10% for visual, nominative speech function - 0 and 4%, speech fluency - 21 and 16% and attention - 2 and 15%. According to subjective assessment data, regardless of the side of the operation, 9% of patients noted a deterioration in cognition, and 18% indicated its improvement. The authors noted a discrepancy between objective and subjective assessments of the dynamics of cognitive functions, in which subjective improvement was determined by patients in cases where objective methods revealed a decrease (for example, verbal memory and speech function). The results of another meta-analysis conducted by employees of the Department of Neurosurgery [17] indicate that patients who underwent surgical treatment of epilepsy subjectively assessed their cognitive functions better than those who were on drug therapy. C. Helmstaedter et al. [18] in a long-term study studied the cognitive functions of patients with epilepsy, comparing adult patients with drug-resistant epilepsy who underwent temporal lobectomy with patients in the control group who received drug therapy. In both groups, a decrease in memory was noted, but in patients in remission, achieved mainly with the help of surgical intervention, memory was more likely to be restored within 1 year. Unsuccessful surgical intervention, especially in the case of left-sided resections, on the contrary, accelerated memory decline. According to the authors, the predictors of a favorable effect on cognitive impairment in the postoperative period were achieving complete control over epileptic seizures and an initially higher level of cognitive functioning. A number of comparative studies [19, 20, 21] devoted to the analysis of the effect of surgical and non-surgical treatment of epilepsy on cognitive indices provide opposite data indicating a deterioration after surgery in immediate semantic memory, delayed recall, memory productivity, and verbal recall. The results of domestic studies

assessing cognitive functions before and after surgical treatment of epilepsy indicate that the developed postoperative cognitive disorders, represented mainly by aphasia and decreased auditory-verbal memory during interventions on the left temporal lobe or visual dysmnesia during right-sided operations, are compensated for within 12 months. It is worth noting that, according to V.R. Kasumov et al. [22, 23, 24], diffuse neuropsychological symptoms determined in the preoperative period are a predictor of insufficient effectiveness of surgical treatment of epilepsy, while unilateral neuropsychological disorders, on the contrary, improve the prognosis of the operation. M. Perry and M. Duchowny [25, 26, 27] adhere to the same point of view, noting that in cases of achieving complete remission after surgery, the restoration of cognitive functioning may take years. At the same time, the discontinuation of pharmacotherapy is an additional factor contributing to the restoration of cognition. However, as the authors point out, in case of failure of surgical treatment of epilepsy, already existing cognitive disorders may worsen or new ones may arise. Thus, most authors noted a close connection between the success of surgical intervention in terms of controlling epileptic seizures and the subsequent level of cognitive functioning of patients.

Factors that have a negative impact on cognitive functions after surgery include additional damage to brain tissue, postoperative complications, the functional significance of resected areas, the placement of deep electrodes in non-resected areas of the brain, the absence of changes on MRI, bilateral brain damage (for example, sclerosis of both hippocampi), as well as severe cognitive impairment detected during pre-surgical preparation [28, 29, 30].

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