Research Article

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Structure and Dynamics of Cognitive Impairment in Neuro-Oncological Patients at the II Stage of Rehabilitation

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ABSTRACT

The analysis of the structure, degree of severity, and dynamics of disorders of higher cerebral functions in neuro-oncological pathology of the brain has been performed. Influence on the formation and regress of cognitive deficiency of a number of factors, including histological structure, tumor size and location, psychoemotional state, educational level, age of patients has been determined. The dynamics of cognitive functions in different terms after surgical treatment has been estimated.

Keywords

Brain tumor, Neurooncological pathology, Surgical treatment, Cognitive impairment, Depression, Memory, Attention, Thinking, Neuropsychological correction, Dementia, II stage of rehabilitation.

Introduction

Neurooncological pathology of the brain is a common cause of disability in developed countries. The general prevalence of tumors of the central nervous system in the population, according to WHO, is from 3.2 to 14 per 100 thousand of the population. Until now, the treatment of tumors of the central nervous system remained ineffective, and the five-year survival rate of patients did not exceed 24% [1]. The improvement of methods of surgical treatment, radiotherapy and chemotherapy is gradually leading to an increase in the life expectancy of patients of the neuro-oncological profile, making the problem of their rehabilitation urgent.

Focal damage of the brain, along with motor, sensory and speech disorders, in a number of cases is accompanied by a cognitive deficit [2,3]. According to the literature, mental disorders in patients with brain tumors occur in 25-100% of cases [4]. The incidence of cognitive impairment depends on the localization and histo-structure of the tumor [5]. Intraventricular meningiomas are accompanied by dysfunction of higher nervous activity in 29%, and gliomas of "strategic" areas – in 90% of cases [6]. The degree of severity of disorders of higher cerebral functions is variable: the easier the cognitive deficit, the higher the probability of its regression after removal of the tumor. Dementia is a consequence of volume formation with a frequency of 0-1.4% [4]. According to other researchers, tumors of the central nervous system lead to dementia more often – up to 5% of cases [7]. The development of cognitive disorders occurs gradually, as the tumor grows. In a number of cases, dysfunction of higher nervous activity in neurooncology is a side effect of chemotherapy and radiotherapy [8,9].

To date, the risk factors for the development of a deficiency in higher brain functions in neuro-oncological patients, the effect of the location and volume of the tumor, the nature of the surgical intervention, the duration of the disease, the age and sex of the patient on the rate and extent of their recovery have not been clearly determined.

Based on the foregoing, studies on the structure, severity and dynamics of cognitive impairment in patients operated on for a brain tumor are relevant.

Materials and methods

The study was based on the results of cognitive rehabilitation of

54 patients operated on for a brain tumor (33 women, 21 men, mean age 52.32 ± 15.81 years). Among them, 42 (77.78%) people underwent total tumor removal, 12 (22.22%) – partial. In 28 (51,85%) cases, the degree of malignancy of Grade I was noted, in 20 (37.04%) – Grade II, in 2 (3.70%) – Grade III, in 4 (7.41%) – Grade IV . In 21 (38,89%) cases, meningiomas were observed, in 17 (31,48%) – vestibular schwannomas, in 3 (5.56%) – astrocytomas, in 2 (3.70%) – glioblastomas, in 2 3.70%) – medulloblastoma, 1 (1.85%) - ependymomas, 4 (7.41%) – cavernomas, 2 (3.70%) – pituitary adenomas, in 1 (1.85%) – oligodendroglioma, in 1 (1.85%) – hemangioblastoma. Restorative treatment was carried out on the basis of the rehabilitation department of "Nikolaevskaya Hospital", St. Petersburg.

The localization and dimensions of the tumor were determined by the use of modern methods of neuroimaging (SCT, MRI). Also, upon admission, on all patients there was performed an electroencephalography on the 22-channel EEGC-24-01 apparatus "Telepath-106". Evaluation of the neuropsychological status was carried upon admission and upon discharge according to the scheme of A.R. Luria, in the modification of E.D. Chomskaya [4,10]. For the quantitative assessment of cognitive impairment, scaling methods were used: MMSE, FAB. In addition, all patients were tested on the Hamilton scale for assessing depression (HDRS).

The basic method of cognitive rehabilitation was neuropsychological correction using classical techniques based on theories of the development of cognitive functions of L.S. Vygotsky and dynamic localization of cognitive functions of A.R. Luria. In the absence of contraindications, a course of 10 procedures of transcranial electromagnetic stimulation was included in the complex of restorative treatment. In addition, computer support scientific brain training PRO was used: rehabilitation [11-13].

The comparative effectiveness of cognitive rehabilitation was reflected in the form of the index of dynamics (the increase in scores) in the tests used. Statistical processing of the results was performed using Statistica for Windows, version 10. Nonparametric methods of statistical analysis were used.

Results

The testing of patients operated on for brain tumors, according to the MMSE scale, led to the following results: in 15 (27.78%) observations, the use of this test did not reveal any cognitive impairment (the result was from 28 to 30 points); in 21 (38.89%) observations, pre-dementia impairments were detected (24-27 points); in 11 (20.37%) cases, mild dementia (20-23 points) occurred; finally, in 7 (12.96%) cases, moderate dementia was observed (11-19 points). The average MMSE score was 24.68±4.12 points.

Testing using the battery of frontal dysfunction (FAB) revealed that in 23 (42.59%) cases the result varied from 16 to 18 points, which corresponded to the norm; in 16 (26.63%) cases – from 12 to 15 points, which corresponded to moderate frontal dysfunction; in 15 (27.78%) cases the result was less than 12 points, which corresponded to pronounced frontal dysfunction. The average score of the FAB was 11.0±4.20 points.

The greatest difficulty was caused by the test for the memorization of 9 words (4 (7.41%) patients succeeded), the delayed reproduction of 9 words (completely fulfilled by 2 (3.70%) subjects), the visual memory test of A. Benton (none of the subjects succeeded), as well as a test for learning 10 words (completely fulfilled by 2 (3.70%) patients). Thus, the observed subjects were the worst at coping with tasks aimed at checking memory parameters. Nevertheless, with the introduction of a common semantic attribute, 20 (37.04%) of the subjects coped with the memorization task, which indicates a preserved ability to use compensation strategies. The best results were obtained in the test with the drawing of geometric figures (completely fulfilled by 26 (48.15%) observed subjects), with the solution of arithmetic problems (36 (66.67%) patients succeeded), as well as with the tasks for updating the information reinforced in the past (completely fulfilled by 24 (44.44%) of the observed subjects). Figure 1 presents the results of an evaluation of the structure of cognitive impairment in neuro-oncological patients.

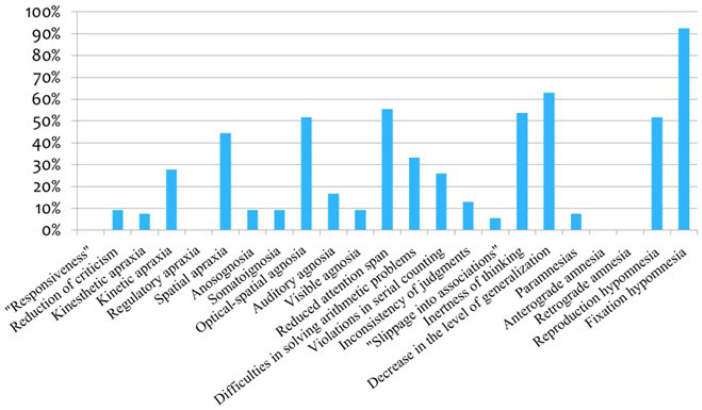

Figure 1: Structure of cognitive impairment in patients with brain tumors.

In a detailed analysis of the structure of cognitive deficits, it was found that the most common in patients operated on for neurooncological pathology of the brain was fixative hyponasia, manifested in a decrease in the ability to memorize new information (50 (92.59%) observations). Reproduction hyponasia – difficulties in reproducing certain specific events – was recorded in 28 (51.85%) observations. In addition, in 4 (7.41%) of the observed subjects, paramnesia, "false memories", pathognomonic for brain tumors were noted.

Among the impairments of thinking, the reduction in the volume of generalization was noted most often (in 34 (62.96%) observations). Pathological inertia was noted in 29 (53.70%) patients. In 3 (5.55%) observations, "slippage into associations" was noted, and in 7 (12.96%) – the inconsistency of judgments. Violations of serial counting were recorded in 14 (25.93%) of the observed subjects, and difficulties with solving arithmetic problems – in 18 (33.33%).

A decrease in the amount of attention was noted in 30 (55.56%) observations, but this symptom was not significant, and the average score of Schulte was 79.48 points.

Optical agnosia was detected in only 5 (9.26%), and auditory agnosia was detected in 9 (16.67%) observations. Violations of optic-spatial gnosis were recorded more often – in 28 (51.85%) cases. Kinetic apraxia was described in 15 (27.78%) patients, kinesthetic – in 4 (7.41%), spatial – in 24 (44.44%) of the observed subjects.

An analysis of the psychoemotional status of patients revealed that in 30 (55,56%) cases there was an easy depressive episode (8-13 points according to HDRS), and in 5 (9.26%) – moderate depressive symptoms (14-18 points by HDRS, respectively). Euphoria, anosognosia were noted in 5 (9.26%) observations. Table 1 describes the cognitive status of neuro-oncological patients, depending on the severity of depression.

Scales M (25%, 75%)	Severity of depression (HDRS)		
	No depression (0-7 points) (n = 19)	Easy depressive episode (8-13 points) (n = 30)	Moderate depressive episode (14-18 points) (n = 5)
MMSE	27.0 (25.0; 28.0)	26.5 (23.25; 27.75)	25.0 (22.0; 25.0)
FAB	16.0 (14.0; 17.0)	15.0 (13.25; 17.0)	12.0 (11.0; 16.0)

Table 1: Cognitive status of patients operated on for a brain tumor, upon admission, depending on the severity of depression.

Table 1 clearly reflects the tendency to aggravation of cognitive impairment with an increase in the severity of depression. Differences in the cognitive status of patients who did not have depressive symptoms and patients with a mild depressive episode were considered statistically significant ($U = 8$, $p < 0.05$).

The effect of age on the state of higher cerebral functions in patients with a neuro-oncological profile has not been investigated to date. Table 2 presents data of a comparative assessment of the cognitive status of patients of different ages who underwent surgery for a brain tumor.

Scales M (25%, 75%)	Age group (WHO)			
	Young age (18-44 years) (n = 16)	Middle age (45-59 years) (n = 17)	Elderly age (60-74 years) (n = 19)	Old age (75-90 years) (n = 2)
MMSE	26.0 (24.5; 27.5)	25.0 (23.0; 27.5)	27.0 (22.0; 28.0)	27.0 (26.5; 27.5)
FAB	16.0 (14.5; 17.0)	14.0 (11.0; 16.5)	14.5 (7.0; 16.25)	15.5 (14.75; 16.25)

Table 2: Cognitive status of patients of different ages, operated on for a brain tumor, upon admission.

A comprehensive analysis of the cognitive status of patients of different ages, operated on for a brain tumor, revealed no patterns: in all age groups, the results of the evaluation of the state of higher cerebral functions by scale methods were comparable ($p > 0.05$). Integral methods in this case are not entirely correct, since the peaks of incidence of tumors of different histo-structure are at different ages. For objectivization, observations with meningiomas and schwannomas, as most frequently encountered in this study, were analyzed separately. It was revealed that in patients operated on for meningioma, the degree of cognitive deficiency increased with age; the difference in testing between young and elderly patients was considered statistically significant (for MMSE $U = 4$, $p < 0.05$). Similar conclusions can be drawn about patients admitted to the rehabilitation department after removal of the vestibular schwannoma: young patients were characterized by mild cognitive impairments, significantly less pronounced than those in the elderly people (MMSE $U = 0.5$, $p < 0.01$).

Table 3 shows the results of testing patients who entered the rehabilitation department at different times after surgical treatment.

Scales M (25%, 75%)	Early postoperative period (5 days – 3 weeks) (n = 20)	Nearest postoperative period (3 weeks – 3 months) (n = 29)	Remote postoperative period (more than 3 months) (n = 5)
MMSE	23.5 (20.5; 25.75)	27.5 (25.5; 28.0)	27.0 (25.5; 27.0)
FAB	13.5 (7.5; 15.0)	16.0 (13.5; 17.0)	16.0 (14.5; 17.0)

Table 3: Cognitive status of patients with a neuro-oncological profile with different prescription period of surgical treatment upon admission.

Comparative analysis of the state of higher cerebral functions of patients with different prescription degrees of surgical treatment revealed that the cognitive deficiency was most pronounced in the observations of the early postoperative period, and in the observations of the nearest postoperative period there were significantly higher scores of scoring scales (for MMSE $U = 45$, $p < 0.01$). The results of testing patients who entered within the remote postoperative period were comparable to those in patients of the nearest postoperative period ($p > 0.05$).

When comparing the cognitive status of patients with different educational levels, it was found that neuro-oncological patients with secondary special education had more pronounced cognitive impairment upon admission than the observed subjects with higher education ($U = 83$, $p < 0.05$).

The nature and severity of cognitive deficits in neurooncological patients is largely determined by the histological structure of the tumor. In the present study, the most pronounced cognitive impairment, reaching a degree of dementia, was noted in observations with formations of a high degree of malignancy (glioblastomas, medulloblastomas, hemangioblastomas). It should be noted that cognitive impairment of patients operated on for meningiomas and vestibular schwannomas was comparable in severity ($p > 0.05$). Meanwhile, in the works devoted to the quality of life after the removal of the vestibular schwannoma, disorders of higher cerebral functions have not been given attention so far [14].

In order to determine the relationship between the structure of

cognitive deficits and the localization of the pathological process, all tumors were divided into supratentorial (28 observations) and subtentorial (26 observations). Fixation hypomnesia with volume formations of supratentorial and subtentorial localization was registered equally often ($p>0.05$), and reproductive hypomnesia was significantly more often observed in observations with subtentorial tumors ($U = 242$, $p<0.05$). Thinking disorders, violations in counting were recorded at the same frequency, regardless of the location of the tumor ($p>0.05$). Reduction of the amount of attention was significantly more often observed with subtentorial formations ($U = 214$, $p<0.01$). Disturbances of gnosis and praxis occurred mainly in observations with tumors of supratentorial localization, which corresponds to data on their cortical representation [10,14]. Nevertheless, single cases of visual, auditory agnosia, kinetic and kinesthetic apraxia were recorded even in subtentorial formations. A possible explanation for this fact is the dissociation of cortical-subcortical tracts by a growing tumor.

For the observations with the vestibular schwannoma, the relationship between the size of the tumor and the degree of cognitive deficits was separately analyzed (Table 4).

Scales M (25%, 75%)	Tumor size (Nikitin I.A, 1989)			
	<2 cm (n=2)	2-3 cm (n=3)	3-4 cm (n=8)	>4 cm (n=4)
MMSE	28.5 (28.25; 28.75)	27.0 (27.0; 27.5)	24.0 (21.0; 26.25)	21.5 (20.75; 22.25)
FAB	18.0 (16.0; 18.0)	17.0 (16.5; 17.5)	14.5 (10.75; 16.25)	9.5 (7.25; 11.75)

Table 4: Cognitive status of patients with different sizes of the vestibular schwannoma upon admission.

It is noteworthy that the majority of patients (70.59%) were transferred to the II stage of rehabilitation after removal of the large or giant size vestibular schwannoma. In this case, patients who underwent surgery for small (less than 2 cm) formations had a significantly lower cognitive deficit compared to patients with a tumor size of 3-4 cm (for MMSE $U = 0$, $p<0.01$) and more than 4 cm (for MMSE $U = 0$, $p<0.01$).

In assessing the effectiveness of cognitive rehabilitation activities, the following results were obtained. In patients operated on for neurooncological pathology of the brain, the average MMSE score on the 30th day of stay in the rehabilitation department was 29.0 (27.0, 30.0) points, the dynamics index was 2.5 (1.0, 5.0) points. When testing the FAB on the day of discharge, the average score was 18.0 (17.0, 18.0) points, the dynamics indicator was 2.0 (1.0, 3.0) points.

Discussion

As a result of a detailed analysis of cognitive disorders in neuro-oncological pathology of the brain, a number of regularities were determined. Available literature sources do not fully cover the problem of depression after surgical treatment of volumetric brain formations. So, according to research, depressed mood accompanies 33.1% of patients operated on for the vestibular schwannoma, 20% of patients operated on for meningiomas of different locations [9,11,15]. In this study, patients with moderate-degree depression had significantly higher cognitive deficits than patients without emotional disorders ($p<0,05$).

The presence of higher education in patients with neuro-oncological pathology was statistically significantly associated with a lower severity of cognitive deficits ($p<0,05$). A low level of education, according to research, correlates with an unfavorable prognosis in terms of recovery of higher cerebral functions in focal brain damage [16].

Physiological aging of the nervous system, accumulation of changes at the biochemical and ultrastructural level, and a decrease in the potential of neuroplasticity may worsen the rehabilitation prognosis of neuro-oncological elderly patients [5,14]. According to the literature, the course of the neurooncological disease in elderly patients has a number of distinctive features. Due to atrophic changes in the brain, the effects of edema are not very pronounced, and the clinical manifestations of the tumor process debut with focal neurological symptoms. In addition, background vascular pathology often leads to stroke-like course of the disease and prevents reorganization of brain tissue after surgical intervention [16]. In this study, however, the fact of the increase in the severity of cognitive impairment with age has been proved only for vestibular schwannomas and meningiomas ($p<0,05$); in observations with volumetric formations of another histological structure, age did not significantly affect cognitive status. Thus, the effect of aging on the recovery of cognitive functions after focal brain damage is not so unambiguous.

According to the literature, the frequency of intraoperative and postoperative complications depends on the size of the formation; a correlation between the size of schwannoma and the quality of life of patients after surgical treatment has been revealed [15]. Nevertheless, there is no evidence of the influence of the size of the vestibular schwannoma on the degree of severity and the reversibility of cognitive impairment in modern literature. Analysis of the cognitive status of the patients studied revealed that the size of the tumor statistically significantly affects cognitive deficits, which is quite natural: large and gigantic neoplasms compress the brain stem, breaking the liquor dynamics and causing hypertensive-hydrocephalic syndrome.

In the observations with neurooncological pathology of the brain, there was a tendency for spontaneous regression of disorders of higher cerebral functions ($p<0,05$). According to the literature, the restoration of cognitive functions in neurooncological patients is most effective in the early postoperative period, especially in case of total removal of the tumor. A year later, the cognitive status remains at the same level for the majority of patients, and some worsen due to the growth of vascular and atrophic changes recorded by methods of neuroimaging [6].

The most common symptoms in most patients were fixated

hypomnesia (noted in 92.59% of observations), pathological inertia of thinking (described in 53.70% of cases) and decreased attention (recorded in 55.56% of patients). The obtained data fit into the concept of A.R. Luria on the three functional blocks and characterize the imbalance of the first of them, uniting subcortical formations and providing a sufficient level of wakefulness, concentration, motivation [4,10,14]. Decreased memory is often found in stem-diencephalic neoplasms, as well as tumors of the temporomandibular divisions [3]. In addition, it is necessary to take into account the effect of volumetric formations on adjacent structures, mediated disorders of liquor dynamics [7].

Rehabilitation measures allowed in most cases to achieve significant results in restoring the higher cerebral functions of neurooncological patients: the average MMSE score upon discharge was 29.0 (27.0, 30.0) points and corresponded to the norm. Total removal of the tumor, especially under conditions of non-traumatic surgical access, allows eliminating the cause of the disease and forms a favorable rehabilitation prognosis [2]. There is also an opinion that the gradual pace of brain tumor development makes it possible to form "flexible" neuron networks, which promotes the active work of compensatory mechanisms during rehabilitation [8].

Conclusion

The structure, severity and rate of recovery of cognitive impairment in neuro-oncological patients depend on the histological structure, size and location of the tumor, disease prescription period, age, educational level and psychoemotional state of patients.

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