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Awake Craniotomy: Analysis of Complicated Cases

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Awake craniotomy is recognized as a method that can reduce the frequency of neurological complications after surgery for gliomas located near the eloquent brain regions. Unfortunately, even the use of this technique cannot ensure good neurological outcome. This paper discusses the reasons of these complications and possible prevention methods. **Material and methods.** A total of 162 awake craniotomies were performed in our clinic. **Results.** 152 patients were discharged from the clinic with good outcomes. In 10 (6%) cases, there was sustained severe neurological deficit. These complications were associated with anatomic or ischemic injury of subcortical pathways and internal capsule. **Conclusion.** Awake craniotomy is an effective tool for brain language mapping and prevention of neurological deterioration. Severe neurological complications of awake craniotomy are associated with underestimated neurosurgical risks, especially in terms of blood vessel injury and resection depth. Meticulous planning of the surgery and adequate use of mapping facilities are the main ways of prevention of these complications.

Keywords: *awake craniotomy, brain mapping, complications, gliomas.*

The problem of iatrogenic injury of the most functionally important parts of the brain is a pressing issue virtually since the creation of neurosurgery as a separate medical specialty. Resection of the space-occupying lesions of the brain is inevitably associated with the risk of damage to the surrounding intact tissues.

Tumors, especially glial ones, are characterized by wide variety of possible locations in the tissue of the cerebral hemispheres, therefore they can occur either in the areas with lower functional importance of neurons or in the areas with high concentration of cells whose dysfunction leads to apparent disability of a patient. According to classical neurology, the latter refers to the areas of precentral and postcentral gyri responsible for motor and sensory function, as well as postero-inferior portions of the frontal lobe and postero-superior portions of the temporal lobe involved in speech functions. Location of lesions in these regions usually attracts the most attention of neurosurgeons when planning surgery on the cerebral hemispheres.

Modern neurophysiological methods (assessment of motor evoked potentials, transcranial stimulation, etc.) enable quite reliable intraoperative identification (of course, without the use of muscle relaxants) of the location of motor areas of the cortex and corticospinal motor pathways under conventional general anesthesia. However, mapping of language areas and associated pathways requires intraoperative awakening of the patient in order to perform specific tests, i.e. the surgery should be conducted according to “awake craniotomy” method.

It would seem that the implementation of these capabilities can ensure the protection of functionally important areas of the brain during the resection of space-occupying lesions. However, the experience gained during awake craniotomies at our clinic shows that this thesis does not fully represent the facts.

In this paper, we tried to analyze the causes and possible methods of prevention of sustained neurological disorders arising during operation or in the early postoperative period in patients who underwent surgical intervention with intraoperative mapping of language areas of the brain according to awake craniotomy protocol.

Material and methods

During the period from 1996 to 2014, a total of 162 operations for resection of space-occupying lesions of the brain with intraoperative mapping of language areas of the brain were performed at the Burdenko Neurosurgical Institute. Of these, arteriovenous malformations (AVMs) were resected in 4 (2%) cases, foci of focal cortical dysplasia with underlying pharma-coresistant epilepsy were resected in 9 (6%) cases, and tumors, especially gliomas characterized by varying degrees of malignancy and located in the dominant hemisphere were resected in the remaining 149 (92%) cases.

Indications to the surgery with intraoperative mapping of the language areas included location of a lesion near the conventional anatomical boundaries of Broca’s and Wernicke's areas (i.e. postero-inferior portion of the frontal lobe and postero-superior portion of the temporal lobe) according to MRI, as well as sufficient speech functions to perform test tasks at admission. Since 2010, the results of functional MRI with mapping of language areas were also widely used to determine surgical indications. Surgical treatment (operation with intraoperative awakening and electrophysiological mapping of language areas of the dominant hemisphere) was carried out according to the procedure developed at the Burdenko Neurosurgical Institute and reported in our previous works [1—5].

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Results

Among the patients who underwent awaked craniotomy, 152 (94%) individuals have been discharged from the hospital with a positive outcome (improvement or the absence of worsening of neurological status). However, there was apparent increase in neurological deficit in 10 (6%) patients, and therefore these treatment outcomes were determined as worsening at discharge (**Table 1**). It should be noted that none of treated patients had pronounced neurological deficit at the first-time admission. Only some patients had mild right-sided hemiparesis and slight speech disorders (which did not hampered execution of tasks for speech function testing).

In the postoperative period, all these patients had severe motor aphasia. It was combined with deep hemiparesis up to and including plegia in 6 cases, deep paresis, mainly in the hand in 2 cases and in the leg in 1 case. In 3 cases, anatomical injury of the cortical (1 case) and subcortical (2 cases) structures are the most probable causes of these disorders, especially the invasion of the internal capsule **(Fig. 1)**. In 5 cases, the unfavorable outcome was likely to be associated with damage to the blood vessels and ischemia of the internal capsule (**Fig. 2**, **3**).

In one case, the deterioration at discharge was associated with progression of the preoperative symptoms after partial resection of the tumor tissue and subsequent edema. Another case of poor neurological outcome was observed in the patient with postoperative hematoma in the immediate postoperative period, which necessitated revision of the surgical wound.

Discussion

Currently, world literature provides quite a lot of publications, reporting the series of resections of disseminated brain tumors with intraoperative mapping of language areas [6—10]. The present article reports the series of case studies performed in our clinic, which is rather large according to international standards and can be included to the aforementioned series. Most professionals, who regularly use awake craniotomy in clinical practice, recognize this approach as a method that can significantly improve treatment outcomes in patients with space-occupying lesions of the brain. According to most researchers, this approach reduces the risk of iatrogenic damage to functionally important areas of the brain (eloquent areas) [7, 11, 12]. Radicality of tumor resection is an equally important aspect of treatment for both benign and malignant gliomas. Its prognostic importance has been proved in numerous studies [13—16]. In this context, the possibility of more confident navigation in the surgical wound, i.e. reasoned efforts towards radical resection, can be considered as another advantage of intraoperative mapping of the language areas of the brain [8, 10].

Of course, within the context of this discussion we can not neglect the fact that there is also skepticism about the influence of the awake craniotomy method on the quality of treatment of patients with gliomas in the literature. In particular, in the study by D. Gupta et al. [6], which was a randomized prospective study including 53 operations, neurological deficit increased in 23% of patients in the awake craniotomy group compared to 15% in the general anesthesia group. At the same time, more radical tumor resection was observed in the 2nd group. No significant differences had been found between these groups. On the other hand, more extensive studies, such as large-scale meta-analysis by De W. Hammer et al. [17], which included 90 studies involving a total of more than 8,000 patients, showed that intraoperative mapping lead to more than twofold better results in terms of the frequency of the newly established post-operative

Table 1. **Clinical manifestations and suspected causes of severe surgical complications in patients who underwent awake craniotomy**

No	Clinical manifestations	Reason	Remark
1	Hemiplegia, motor aphasia	Damage to the fibers of the internal capsule	
2	Severe hemiparesis, aphasia	Acute hematoma in the tumor bed, damage to pathways	
3	Severe hemiparesis of the hand, aphasia	Ischemia of the internal capsule pathways	Recovery of speech in six months. Residual hemiparesis of the hand
4	Motor aphasia, hemiparesis, mainly in the foot	Mechanical damage to pathways	
5	Aphasia and hemiparesis	Small volume of resection	Deterioration with underlying edema after partial resection of the tumor
6	Hemiplegia, aphasia	Ischemia of the internal capsule pathways	Significant regression within 1 month
7	Aphasia	Ischemia of the internal capsule pathways	Significant regression within 1 month
8	Plegia of the hand, paresis of the foot, motor aphasia	Ischemia of the internal capsule pathways	Significant regression within 1 month
9	Aphasia, severe hemiparesis	Damage to cortical centers (hand) and pathways	Absence of movements in the hand during resection. Aphasia manifested in the postoperative period
10	Aphasia, severe hemiparesis	Ischemia of the internal capsule pathways	

neurological deficits (3.4% versus 8.2% in the group without mapping; $p<0.05$), as well as the frequency of complete resection (75% vs 58% in the group without mapping; $p>0.05$).

Our experience confirms the advantages of the method of intraoperative mapping of language areas. Favorable surgical outcomes (according to neurological status) in 94% of patients in the given group of high-risk patients can be safely regarded as proof of advisability of clinical application of awake craniotomy technique.

Interestingly, in the first operations with awakening in our series, there were mainly intraoperative complications such as seizures and brain edema, but the incidence of severe neurological deficit was low [1, 18]. This is probably due to some reasonable caution in tumor resection (possibly due to its radicality) when mastering the method.

However, a large-scale practical application of awake craniotomy unfortunately showed that successful mapping of the cortical language areas does not always guarantee the safety of motor and speech functions of the nervous system, since it does not protect against damage to the subcortical structures. Maintaining patient's consciousness when removing a tumor, which enables continuous neurological monitoring of the patient, does not always protect against unintended iatrogenic damage.

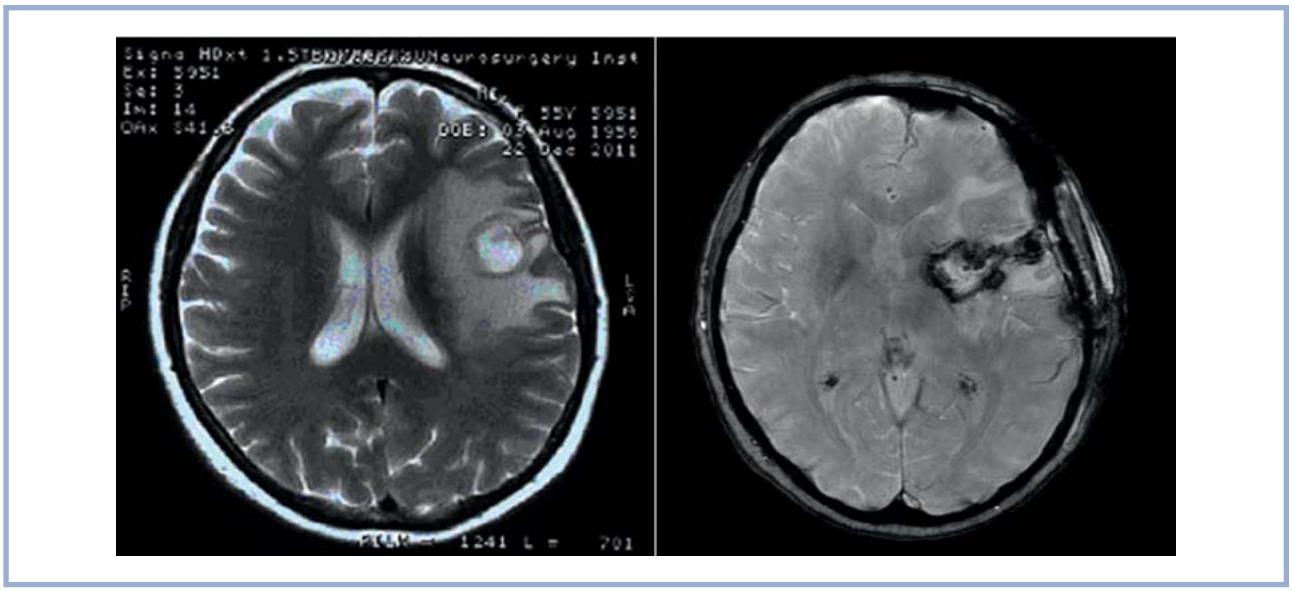


Fig. 1. **Preoperative and postoperative MRI of patient No 1 (expansion of resection area to the projection of the internal capsule can be observed).**

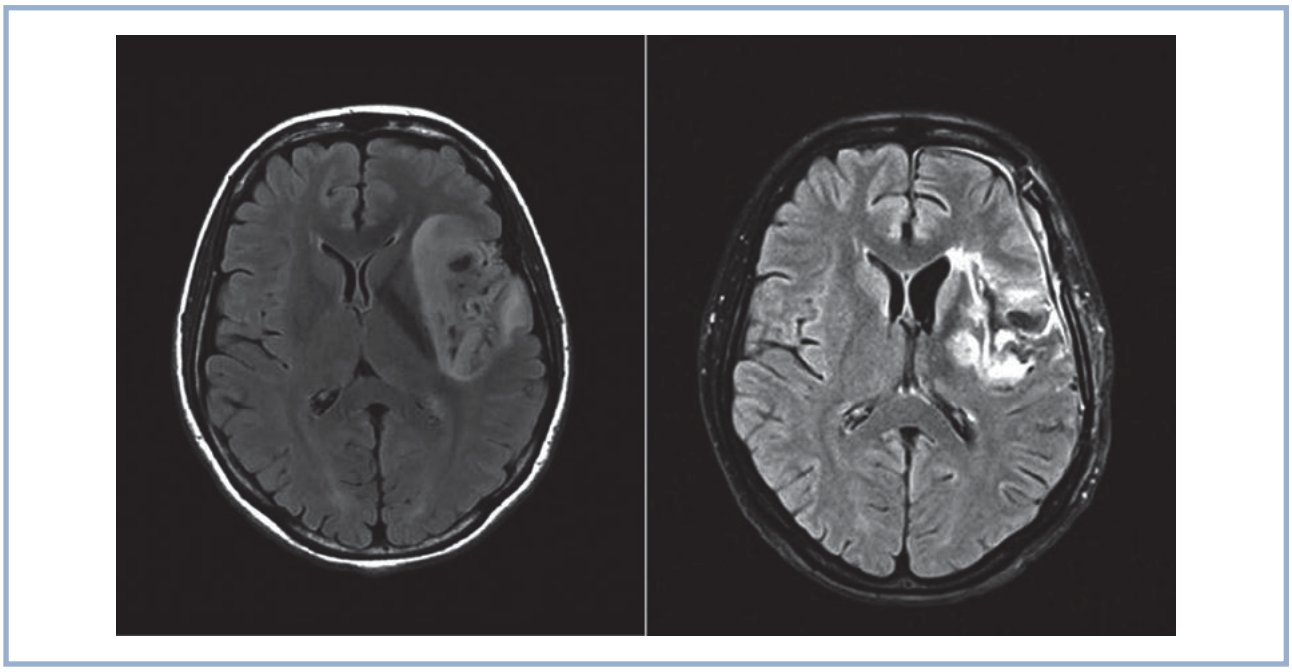


Fig. 2. **Preoperative and postoperative MRI of patient No 8 (right — ischemic foci near the internal capsule).**

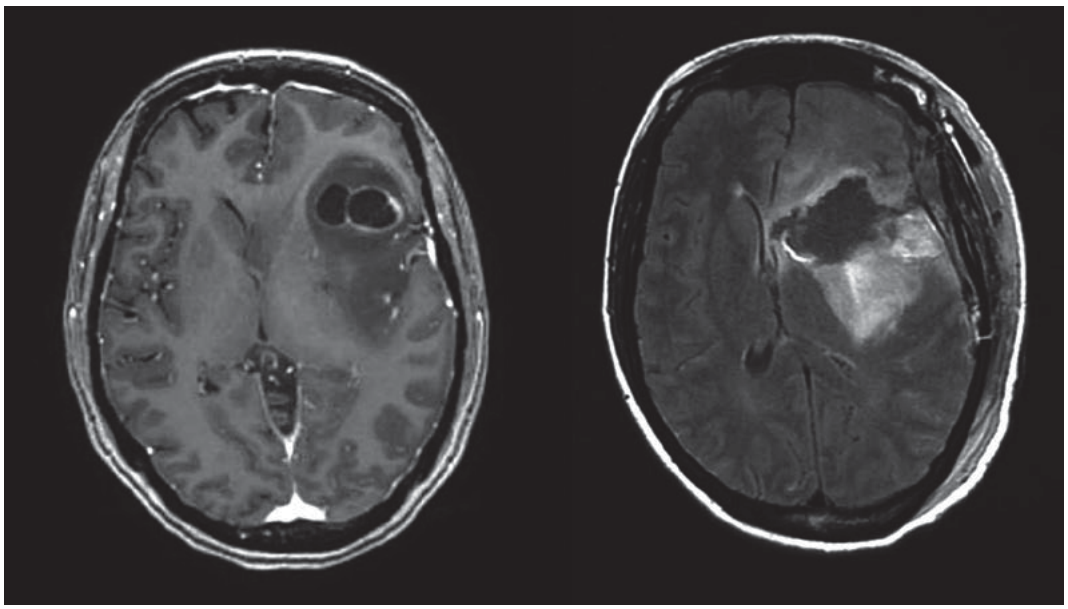


Fig. 3. **Preoperative and postoperative MRI of patient No 10 (large ischemic area near the posterior genu of the internal capsule).**

It should be noted that these complications occurred in patients during about 15 years of our experience of these operations. Therefore, the awakening technique currently differ from that in "early" patients: in the past years, anesthesia was induced after cortex mapping and the surgery for tumor resection proceeded without the contact with the patient (for this reason, neurological deficit in some our patients was caused by direct damage to conduction paths). Currently, we are committed to contacting the patient during surgery (if the patient can psychologically withstands this approach). During the resection, the patient is requested to move limbs, repeat counting, etc., while we repeat mapping of the brain and association paths from time to time. The experience of these operations in our clinic shows that it is possible to stop resection of the tumor and perifocal zone at the moment of slightest increase in neurological deficit in a significant proportion of patients. It is also possible that the feeling of controllability of the process of abnormal tissue resection and the desire to achieve maximum allowed cytoreduction, which is preconditioned by awake craniotomy, in some cases, can lead to an unjustified extension of the resection zone into the depths of the wound, where the risk of damage is the highest.

On the other hand, the aforementioned severe complications undoubtedly cannot be considered specific to awake craniotomy. They are partially due to the shortcomings of surgical tactics and techniques, i.e. failure to maintain the balance between anatomical capability and physiological permissibility, which are the cornerstones of any surgical intervention regardless of anesthetic conditions of the surgery.

In this regard, it seems advisable to discuss possible ways to prevent severe neurological complications from the standpoint of the aforementioned features of the surgery of hemispheric diffuse tumors.

Unfortunately, the issue of surgical complications of awake craniotomy is poorly covered in the literature. Some authors [19, 20] rather discuss the comparative decrease in the incidence of neurological deficit in the groups of patients where the mapping was successful and functional areas were clearly localized. In particular, N. Sanai et al. [20] report the increase in refractory speech disorders after surgery in 4 (1.6%) of 243 patients who underwent surgery with brain mapping. In all these patients, language areas were not verified according to electrostimulation data. Some other studies demonstrate similar incidence of deterioration in the cases there the areas were not identified during mapping [10, 21]. The authors of these studies suggest that the data on the absence of identified language areas within the trepanation area and the potential benefits of the expansion of trepanation should be interpreted with care for reliable mapping in doubtful cases.

As for the general principles of surgical tactics in resection of diffuse gliomas invading the deep portions of the hemisphere and involving the insula, the data collected by M. Berger et al. [20, 22, 23] at the University of California in San Francisco are quite interesting. Their experience suggests a greater frequency of neurological complications in this group of patients in cases of transsylvian approach to the tumor. For this reason, the authors prefer the transcortical approach. This recommendation is based mainly on the substantially lower risk of damage to the vessels. In the context of the

implementation of the awake craniotomy method, we can also say that manipulations with vessels are often painful, which greatly complicates the process of continuous neurological monitoring and mapping of the subcortical structures during tumor resection. As for the prevention of damage to blood vessels, the recommendation to limit the use of diathermocoagulation and prevent damage to the pia mater during the procedure seems to be important [24].

We should also keep in mind the anatomical studies of the pathways of the brain in general, and fronto-temporal region in particular, which provide the connection between speech centers in the dominant hemisphere [25]. Injury of these pathways in various areas (depending on the direction of tumor growth and therefore surgical manipulations) can lead to various speech disorders and motor loss. In our observations (patients No 1 and 4), there was the injury of a large group of fibers of the internal capsule according to the postoperative imaging, which manifested as severe increase in neurological deficit in the form of hemiplegia, hemianesthesia, and pronounced sensorimotor aphasia. When planning the surgery, one should keep in mind the peculiarities of the anatomical structure of the associative fibers involved in the functioning of the speech centers, since the resolution of MR tractography is currently very high [26—30]. Therefore, careful preoperative planning using MR tractography will reduce the risk of intraoperative events.

The anatomical classification of the location of insular gliomas suggested by N. Sanai and M. Berger [23] is quite interesting from a prognostic viewpoint. The authors state that tumors located mostly anteriad of the "horizontal line" through the foramen of Monro (axial projection) may be subjected to larger volume of resection. Tumor growth in the areas located posteriad of this imaginary line (axial projection) is associated with greater risk of dysfunctions (due to the proximity of the tumor infiltration to the Rolandic fissure and posterior limb of the internal capsule), i.e. manipulations in these areas require the most careful handling of tissues even during awake craniotomy.

An important role in preventing neurological problems undoubtedly belongs to preservation of lenticulostriate arteries supplying the internal capsule and full utilization of intraoperative electrophysiological mapping of pathways to limit the medial margin of tumor resection in order to preserve the fibers of the corticospinal tract [22, 31, 32].

Conclusion

Awake craniotomy is rightly recognized as the method that significantly reduces the incidence of worsening of neurological disorders in the postoperative period after removal of tumors adjacent to the eloquent areas of the brain. The more is the pity, when the use of this techniques, which is difficult to implement and requires the involvement of the team of highly qualified specialists, nevertheless results in adverse neurological outcome. Our experience shows that these cases are most commonly associated with underestimated neurosurgical risk, especially the risk of ischemic damage, insufficient use of the potential of pathway mapping, preoperative planning, and modern neuroimaging tools, in particular MR tractography. These problems should be solved using careful, accurate planning of the intervention and mapping of the structures based on the evaluation of the conventional and specific risks of manipulations, as well as the serious training of specialists to use this technique in centers with sufficient clinical experience.

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Authors declare no conflict of interest.

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Commentary

The term "Awake craniotomy" was proposed in 1959 by De Castro and Mundeleer as a method to optimize the neurosurgery of the pharmacoresistant forms of epilepsy. The experience in application of this method of anesthesia in neurosurgical interventions requiring localization of higher cortical functions by their intraoperative activation, in particular speech, was accumulated over the last years. The authors of this article have the world's greatest experience of these interventions, which enabled them to carry out thorough analysis of failures resulting in postoperative neurological deficit, both their own and reported by other researchers. Since the reviewer is out of practice in this problem, his opinion is reduced to the level of methodological comments.

In this regard, the authors' approach is worthy of respect as it provides analysis performed cooperatively by neurosurgeons and neuroanaesthesiologists. The results of application of this technique are obviously successful, since the deterioration of neurological status was observed only in 6% of patients. When analyzing the causes of complications, they should be divided into avoidable and unavoidable ones. From this viewpoint, the authors reached the limit of safety of anesthetic care, since all problems significant for deterioration of neurological status, such as seizures, nausea, vomiting, and hemodynamic crises, were eliminated under the conditions of routine neurosurgery. Neurosurgeons suggest options to improve the technique by optimizing the approach, but it is the matter of discussion for experts. We suggest that the phrase "...failure to maintain the balance between anatomical capability and physiological permissibility is the cornerstone of any surgical intervention regardless of anesthetic conditions of the surgery" comprehensively defines the problem of interdisciplinary cooperation between neuroanaesthesiologists and neurosurgeons. In fact, the natural desire to achieve optimal cytoreduction, underpinned by the sense of safety due to the direct contact with the patient, brings the operator to the "yellow sector", where the tissue injury results in a deficit after a while, by the time of awakening. All methods used for preoperative correction of the allowed area of neurosurgical activity (navigation mapping, functional MRI, and tractography) provide maximum possible assessment of correlation between the anatomy and functions. Of course, their complex application is appropriate and, along with improvement of neurosurgical approaches, will result in prevention of some complications. However, the following factors still remain out of control: the effects of perfusion-metabolic mismatch, local inflammatory response, and functional remodeling. These processes are the natural physiologically and genetically determined response to any exogenous impact and result in unavoidable complications in

some patients. Our knowledge and counteraction methods are still insufficient to prevent these complications.

The article was written at the highest methodological level, provides the comprehensive picture of the problem, and its publication will be a worthy acquisition for a specialized journal.

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