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Awake craniotomy

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Awake craniotomy is a neurosurgical intervention aimed at identifying and preserving the eloquent functional brain areas during resection of tumors located near the cortical and subcortical language centers. This article provides the review of the modern literature dealing with this issue. The anatomical rationale and data of preoperative functional neuroimaging, intraoperative electrophysiological monitoring, and neuropsychological tests, as well as the strategy of active surgical intervention are presented. Awake craniotomy is a rapidly developing technique aimed at both preserving speech and motor functions and improving our knowledge in the field of speech psychophysiology.

Keywords: *awake craniotomy, intracerebral tumors, functional area, Broca's area, Wernicke's area, electrophysiology*.

"Awake craniotomy" is a quite well-established term in the scientific literature and implied neurosurgical interventions, which are carried out using patient's awakening from anesthesia in order to control the preservation of certain functions (speech, movement, vision, counting, writing etc.), typically using electrophysiological brain stimulation techniques. The technique of intraoperative electrical stimulation in modern neurosurgery was first published by W. Penfield [1] in 1937, who used it during interventions for epilepsy near the speech cortical areas. In the 1970s, N. Whitaker and G.A. Ojemann [2, 3] improved the technique, using pulse biphasic impulses, and optimized intraoperative tests. In the 1990s, V. Berger [4, 5] applied the awake craniotomy in the surgery of brain tumor near the speech cortical areas. Finally, N. Duffau [6] pointed out the importance of protection of not only the cortical centers, but also axonal pathways connecting the speech centers with motor areas and other areas of the cortex. During the next two decades, the method became widely used in the neurosurgical clinics worldwide. V.A. Loshakov, A.Yu. Lubnin, and G.A. Schekut'ev were the pioneers of awake craniotomy in Russia; they implemented this technique in the surgical practice at Burdenko Neurosurgical Institute at the turn of XXIth century [7, 8].

Indications for the use of surgical techniques with intraoperative awakening and identification of language areas include space-occupying lesions located in the projection or in the immediate vicinity of the cortical speech centers (including tumors and arteriovenous malformations), and epilepsy surgery, such as temporal lobectomy in the dominant hemisphere.

Limitations (contraindications) for this technology include mainly patient's incapability of performing appropriate tests as a result of severe speech disorders or other reasons, such as fear of intraoperative awaking and pronounced mental disorders, which prohibit required intraoperative interactions. Relative contraindications include anatomical features of diffuse tumor growth directly in the projection of functional areas of the left hemisphere. In this case, the operation is actually limited to the open biopsy of the tumor.

Neuroanatomy of the language cortical areas

In the context of current trends of microneurosurgery, using furrows, brain cisterns, or the projectional local incision of certain gyri to access the pathological lesions, understanding of anatomy and functional significance of certain sulci and gyri is absolutely essential. Since we discuss awake neurosurgery for mass lesions located near the speech centers, we should outline typical anatomical structures of the brain associated with language function.

In most people, motor (Brocka's) and sensory (Wernicke's) speech centers are located on the lateral surface of the cortex of the dominant hemisphere (mostly the left one) near the Sylvian fissure [9, 10]. In this case, the most important anatomical landmarks include **(Fig. 1)**:

— Sylvian fissure (denoted as SF in the picture);

— Rolandic fissure, which in its lower part projectionally "splits" the Sylvian fissure into two roughly equal parts (SulC);

— precentral (SulPrS) and postcentral (SulPoC) gyri located anterior and posterior to the Rolandic fissure;

— inferior frontal gyrus (we will discuss its structure in more detail).

The structure of the inferior frontal gyrus is variable, but it is typically split by the terminal bifurcation of the Sylvian fissure to form triangular and opercular portions. Thus, it consists of (in the anterior-posterior direction) orbital, triangular, and opercular parts. In its anterior portion, inferior frontal gyrus merges with the anterior portion of the medial frontal gyrus. In its posterior portion, it is connected to the inferior part of the precentral gyrus. The horizontal and the ascending anterior rami of the Sylvian fissure, originating at the same point, form the triangular part of the inferior frontal gyrus, which is usually more anatomically distinguishable than the opercular and orbital parts. Opercular part is U-shaped. The point where Sylvian fissure bifurcates to the ascending and horizontal rami is called ***the anterior Sylvian point.*** Consequently, the anterior Sylvian point is located inferior to the triangular portion and anterior to the base of the opercular part of the inferior frontal sulcus.

In the dominant hemisphere, opercular and triangular parts of the inferior frontal gyrus usually form Broca's area, the motor speech center. In its posterior portion, U-shaped part of the opercular zone merges with the inferior portion of the precentral gyrus, which corresponds to the major axonal connections with motor areas of the cortex. In some anatomical

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types, anterior inferior portion of the opercular zone of the inferior frontal gyrus is quite apparent, because the opercular area is split by an additional small ramus of the Sylvian fissure. This additional ramus runs in the anterior-posterior direction, the so-called diagonal sulcus of Eberstaller, and splits the opercular area into two triangles.

Triangular and opercular parts of the inferior frontal gyrus, which are connected to the precentral and postcentral gyri, cover the superior portion of the insula and form a fronto-parietal operculum. Accordingly, fronto-parietal operculum is located between the horizontal and the posterior ascending parts of the Sylvian fissure [12, 13].

Anteriad, frontal gyri are bounded by the fronto-marginal fissure, separating the superolateral and orbital surfaces of the frontal lobe.

Temporal lobe is located inferior to the Sylvian fissure. Its posterior portion is bounded by an imaginary line connecting the superomedial part of the parieto-occipital gyrus with the preoccipital gyrus. The lateral surface of the temporal lobe is represented by the superior, medial, and inferior temporal gyri, which are separated by the superior and inferior temporal fissures (running parallel to the Sylvian fissure). Anteriad, medial temporal gyrus terminates before the superior and inferior ones, which merge to form the temporal pole. Since Sylvian fissure usually terminates in the ascending ramus "embedded" into the supramarginal gyrus, the superior temporal gyrus always terminates at the posterior Sylvian point, the end of the Sylvian fissure. Superior temporal gyrus covers the inferior surface of the insula and thus forms the temporal operculum. Temporal operculum and the posterior portion of the superior temporal gyrus in the dominant hemisphere form the representation of Wernicke's area, sensory speech center. However, there are numerous options for functional cortical representation of the sensory speech center, since this component of speech function involves a lot of other parts of the cortex, such as auditory perception, cortical and subcortical centers of memory, close axonal connection with Broca's area, and the part of the motor cortex that controls facial and lingual muscles. Therefore, the precise anatomical and functional localization of sensory speech representation is very complicated **(Fig. 2)**. It is believed that speech perception often involves the temporal lobes of both hemispheres (particularly in patients with dominant left hemisphere) [14, 15].

We only touched on the most common issues of the anatomy of the cerebral cortex, corresponding to the present knowledge about the anatomical and functional areas of the speech cortex. Meanwhile, additional anatomical, neuroimaging, and neuropsychological studies are in progress. Intraoperative data collected during operations with awakening are being studied in order to further explore the whole complexity of human speech processes. Let us refer the reader to the recently published review of the pathway anatomy [16].

Preoperative neuroimaging

MRI of the brain in normal mode provides almost real preoperative picture of the individual anatomy of patient's brain [17]. In the past two decades, functional magnetic resonance imaging (fMRI) of the brain has been developed and used. It is a non-invasive method to identify functional areas zones of the cerebral cortex, i.e. motor, language, and visual ones, and, in recent years, even more sophisticated functions, such as counting, memory, etc. Technically, these methods are based on determining the changes in blood oxygenation level (blood oxygenation level dependent — BOLD) in the areas of the brain, excited by certain functions, such as motor, speech, etc. Of course, the method itself is quite complicated and requires some technical equipment, such as special software, trained staff for accurate data analysis, including their relationship to the neuroanatomy of gyri and sulci with allowance for the possibility their displacement in the presence of a pathological process. This examination results is alignment of fMRI-derived color maps of speech activation and three-dimensional MR anatomy of the brain, which can significantly improve the pre-operative planning **(Fig. 3)**. Despite the rapid development of fMRI, some features of physical and biophysical processes pose significant limitations. Thus, the maximal available anatomical accuracy of determining the anatomical speech areas is currently 10 mm from the center of received signal. Significant distinctive features occur in dextrosinistrals, ambidexters, and polyglots. Therefore, fMRI with identification of Broca's or Wernicke's areas cannot be a completely accurate landmark in the intraoperative navigation systems [17].

In recent years, magnetoencephalography (MEG) technique is increasingly widely used. Physically, the method is based on magnetic field measurement. Movement of ions in the cells, intercellular space, and blood vessels results in generation of magnetic fields around neurons, a kind of elementary magnetic generators. The electric current generated due to potential difference between the synaptic terminal and the proximal part of the neuron induces magnetic fields, which are summed up together to produce high enough value for extracranial measurements [18].

Magnetic encephalograph, a device for magnetic encephalography, consists of 3—5 sensors to measure magnetic fields, the computer system, which links these signals to MRI geometry similar to neuronavigation system, and, often, an electroencephalograph for simultaneous recording of EEG. These measurements produce voxel magnetic fields around the entire surface of the scalp. Processing of data about changes in these fields, when a patient follows certain instructions, enables recording and localizing the signals from the motor cortex, speech centers, etc. In recent years, this technology competes in its reliability and data accuracy with functional MRI [19].

Along with fMRI and MEG, MR tractography is a highly valuable method, which facilitates navigation in the anatomy of axonal connections of cortical speech centers with each other and with other functional areas of the cortex, primarily motor tracts.

Clinical and neuropsychological testing

Clinical methods (assessment of neurological deficits, neuropsychological examination, as well as conversation with the patient, explaining the aims and methods of awake intraoperative brain mapping and preparing the patient to cooperate during the surgery [8]) are no less valuable than instrumental techniques in the preoperative examination of patients before operations with awakening.

Neuropsychological examination is the least unified part of this clinical examination complex. However, even in this field, the scientific world tends to normalize preoperative data analysis in order to achieve more accurate assessment of the immediate and long-term post-operative changes in patient's neuropsychological function [20]. The so-called mini-mental state examination (MMSE) is a pretty simple test. Despite its

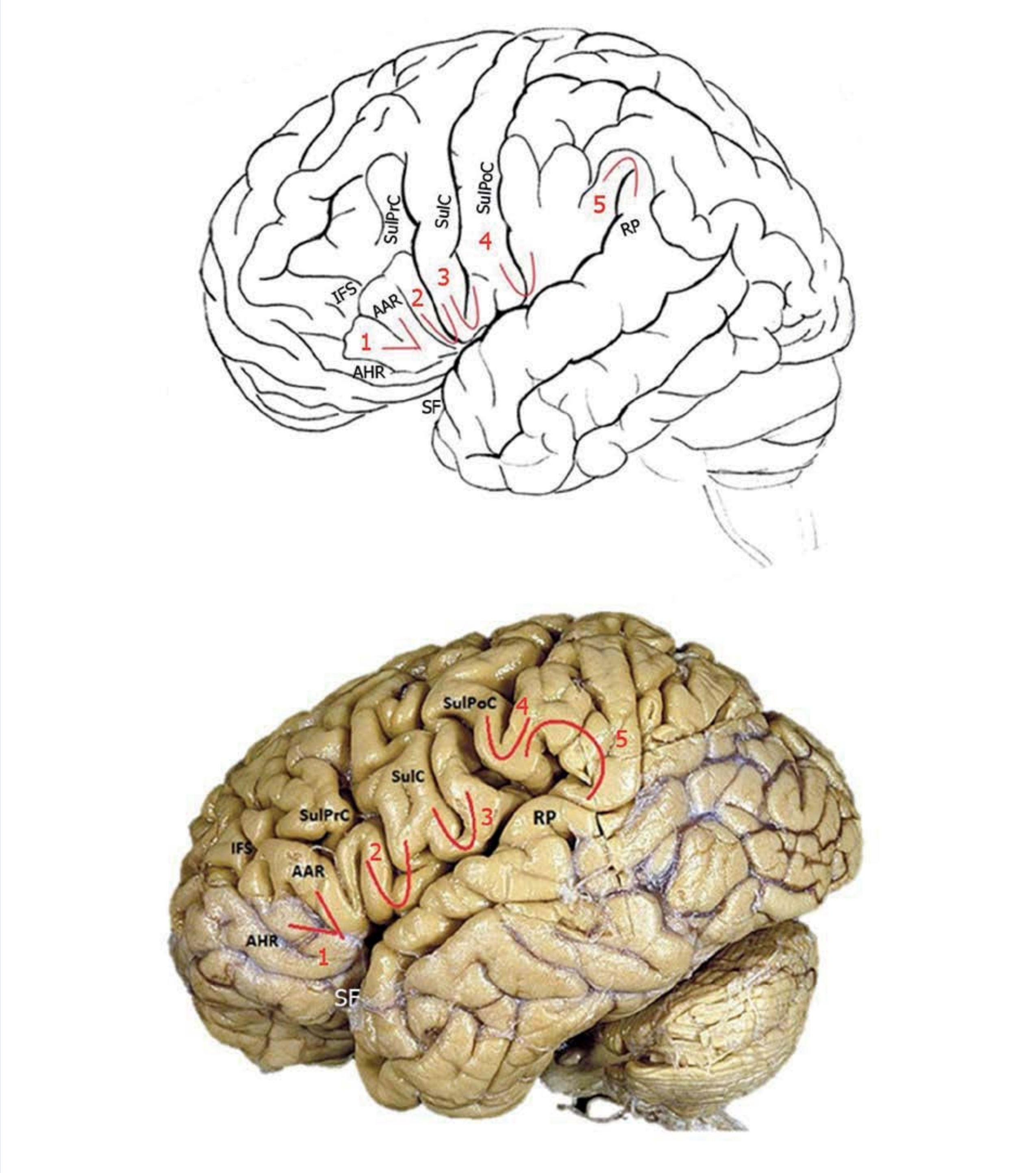

Figure 1. **Anatomical landmarks of speech areas of the dominant hemisphere.**

1 — inferior frontal gyrus (triangular part); 2 — junction of the inferior frontal gyrus (tegmental part) and precentral gyrus; 3 — junction of the precentral and postcentral gyri; 4 — junction of the postcentral and supramarginal gyri; 5 — supramarginal gyrus; SF — Sylvian fissure, SulPrC — sulcus precentralis (precentral sulcus); SulC — sulcus centralis (central sulcus); SulPoC — sulcus postcentralis (postcentral sulcus); AHR — anterior horizontal ramus; AAR — anterior ascending ramus; IFS — inferior frontal sulcus; RP — ramus posterior.

relative primitiveness, it is sensitive to evaluate the progression of malignant gliomas [21].

The following additional options are taken into account in the development and selection of specific test systems and testing [22]:

- demographic characteristics (age, sex, right-handedness/left-handedness, education and occupation, cultural development);
- medical history, including previous treatment;
- data from clinical and instrumental examination methods (neurological examination, CT/MRI, EEG, MEG, etc.);
- results of previous neuropsychological examinations;
- prospective patient's view on the neuropsychological tests given the awareness (full or partial) of his/her own deficit and understanding (experience) of testing purposes.
- in clinical trials sponsored by NCCTG[1], RTOG[2], EORTC[3], and some other organizations, the "battery" of preoperative, intraoperative, and postoperative neuropsychological tests listed in **Table 1** was used.

However, the most common intra-operative tests include counting (numbers), naming the days of the week, months, etc., as well as the test for naming the objects, which neuropsychologist shows to a patient (as pictures), who underwent brain electrical stimulation during surgery [21, 22].

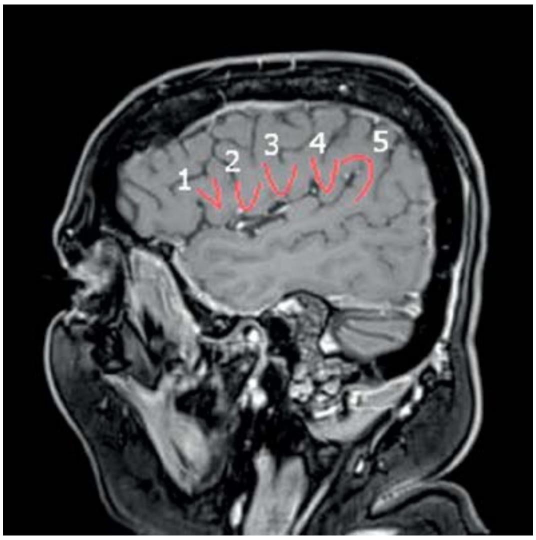

Figure 2. **MR anatomical landmarks of the speech areas of the dominant hemisphere.**

1 — inferior frontal gyrus (triangular part); 2 — junction of the inferior frontal gyrus (tegmental part) and precentral gyrus; 3 — junction of the precentral and postcentral gyri; 4 — junction of the postcentral and supramarginal gyri; 5 — supramarginal gyrus.

Intraoperative brain mapping

Intraoperative functional neuroimaging

Integration of multimodal images in frameless navigation is widely used in the last decades and is called "functional neuronavigation".

However, the only randomized study failed to demonstrate the advantage of the use of navigation in the analysis of postoperative results [23]. This can be explained by limitations of preoperative navigation based on fMRI, as well as intraoperative displacement of anatomical structures of the brain (brain shift), postoperative dislocation of the brain (mass effect), major and vast of operation (especially with large tumors).

In order to reduce the effects of intraoperative dislocation of brain structures, it has been suggested to use certain technical innovations, whose reliability is still being improved: real time three-dimensional intraoperative ultrasound, the use of mathematical models based on the ultrasound data and digital studies capable of cortical shift monitoring, and intraoperative MRI. However, their actual role in the improvement of methods of optimal extent of tumor resection and maintaining patient's quality of life is still to be studied.

Currently, invasive electrophysiological methods are the "gold standard" for operations in the functional areas of the brain.

Evoked potentials and electrocorticography

Evoked potential technique aimed at somatosensory and motor mapping is widely used in the past decade. However, the reliability of this method with respect to localization of Rolandic fissure is not optimal; the accuracy of this method is 91 to 94%. Estimated overall sensitivity and adverse effects amount to approximately 79 and 96%, respectively [24]. Furthermore, phase reversal method facilitates finding the location of Rolandic fissure, but provides no information on the distribution of motor functions in the neighboring areas subjected to the surgery. And although the motor evoked potential technique has been improved, it enables evoked

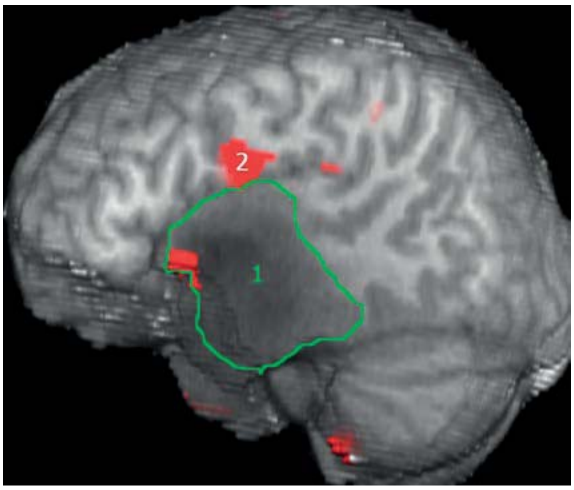

Figure 3. **Functional MRI in a female patient with glioma of the temporal lobe and insula (1); Broca's area (2) is outlined (motor speech center) in the insular operculum above the space-occupying lesion.**

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[1]European Organisation for Research and Treatment of Cancer.

[2]North Central Cancer Treatment Group (USA).

[3]Radiation Therapy Oncology Group (USA).

potential recording only in monitored muscles, but does not allows detection and prevention of possible deficit in the muscles not subject to monitoring. Monitoring of motor evoked potentials does not include the assessment of complex movements and voluntary movements, which are the ultimate goal of patient's physical activity. Further limitation of this method is that it cannot be used to monitor speech functions, memory, and other higher brain functions, which are of key importance for patient's quality of life.

Recent developments in electrophysiological signal interpretation, such as spectral analysis and electrocorticography, evaluating process synchronization, enabled better understanding of the organization of functional cortical areas and studying their interactions. However, extraoperative electrophysiological monitoring involves grids with electrodes located at a distance of 1 cm from each other, which limits the accuracy of the study. Further inconvenience of this method is the need for two surgical procedures: the first one for grid implantation, and the second one for tumor resection. Since the subdural grid is installed for several days, there is a risk of infectious complications [24, 25].

This method is well suited for the surgical treatment of epilepsy, as it allows detecting the epileptic focus. Electrocorticography provides information about the processes occurring in the cerebral cortex, but it provides no information about axonal connections, so there is no way to assess the subcortical structures and this fact limits the use of this technique in neurosurgery, since gliomas can migrate along the white matter fascicles [25].

Electro-stimulation mapping of cortical fields and conduction paths

Given the limitations of the aforementioned techniques, most neurosurgeons currently suggest the additional use of intraoperative electro-stimulation mapping of the functional areas, which may be carried out under general and local anesthesia [26—31]. In patients with tumors affecting the motor area, surgery is performed with cortical field mapping under local anesthesia. However, since movement is more complex process than individual muscle contractions, it is currently recommended to perform intraoperative electro-stimulation mapping with the active participation of the patient in patients with tumors that involve not only the motor area. [32]

This method is based on the use of electro-stimulation mapping to obtain the individual map of the cortical and subcortical levels in order to find out, which of the structures involved in the process are really functionally important (in 15—20% of cases of low-grade gliomas the functional significance of these zones in reduced).

The results obtained in this way enable planning the extent of the surgery in accordance with functional boundaries.

The technique is as follows. Bipolar electrodes conducting biphasic current are spaced 5 mm apart and applied to the brain substance. Current intensity is adjusted individually for each patient. Baseline value is 2 mA followed by 1 mA increment until the response is obtained. Maximum current strength is 6 mA with local anesthesia and 16 mA with general anesthesia. Higher values may cause seizures. The patient is not informed about the time of stimulation. The same area is not stimulated twice in a row to avoid the development of seizures. Each area of the cerebral cortex, which is available for the study, is stimulated three times [26].

Interestingly, according to a recent study, the surgery can be simplified in the case of the refuse to use intraoperative electrocorticography, since electrical mapping provides equivalent reliably and does not increase the incidence of seizures. Nevertheless, in the case of seizures induced by stimulation, the use cold Ringer's solution is advisable to stop seizure activity [27, 28].

Some authors [29, 30] emphasize the role of “negative mapping” (without identification of eloquent areas). This approach is acceptable in the case of high-grade gliomas (surgery is aimed at removing the bulk of the tumor). However, in the operations for low-grade diffuse gliomas, especially at non-specialized institutions, “negative mapping” can be unsafe. Since low-grade gliomas often have no clear boundary, the extent of resection largely depends on functional criteria. Furthermore, “negative mapping“ method may give false negative results and therefore does not guarantee the absence of functional areas. For example, according to N. Sanai et al. [30], all 4 patients who developed permanent postoperative neurological deficits had no functional areas identified prior to resection. For this reason, other authors suggest making approach with more extensive bone flaps in order to perform more precise systematic mapping before the resection [27, 33, 34]. Importantly, “positive mapping” extends resection boundaries and resection may be performed right up to the eloquent area, i.e. without preserving tissue around these zones. A recent study, including 115 patients with low-grade gliomas located in the left dominant hemisphere, showed that the incidence of persistent neurological deficit did not exceed 2%, despite the fact that resection was carried out close to the speech areas [27]. Indeed, S. Gil Robles and N. Duffau [35] have shown that it is not necessary to keep the distance of 5—10 mm to the functional areas, as recommended in the classical literature. These authors state that it is illogical to leave a small tumorous area of the cortex, when the resection is carried out at the subcortical level and involves the pathways of this area, since, although the cortex remains intact, it is excluded and its physiological processes will not restore in the future.

Intraoperative electro-stimulation mapping of motor functions (under general anesthesia, it causes uncontrolled movements, and in awake operations it causes motor disturbance), somatosensory functions (detection of dysesthesia reported by the patient during awake operation), visual function (development of visual field deficiency), audiovestibular function (dizziness), language function (spontaneous speech, counting, naming objects, understanding of speech, writing, reading, switching from one language to another), as well as the mapping of higher mental functions such as mathematical problem solving, memory, spatial orientation, and emotions. Importantly, speech therapist, neurologist, or neuropsychologist should be present in the operating room in order to accurately interpret the detected disorders caused by intraoperative electrical stimulation, such as speech delay, anarthria, oral apraxia, articulation disorders, semantic paraphasia, anomie, and syntax errors [6, 36, 37]. Therefore, intraoperative electro-stimulation mapping provides preoperative real-time detection of the location of functional areas and facilitates the choice of the best surgical approach of tumor resection within these areas.

Another important task is mapping of the subcortical structures along with examination of the cortex prior to resection. Brain damage studies suggest that damage to the pathways is followed by the development of more severe neurological deficits than in the case of cortex injury. Consequently, the pathways supporting motor, somatosensory,

Table 1. **Control "battery" of tests during awake craniotomy**

Test	Subject for investigation	Assessment of results
Trail-making Test A	Evaluation of thinking speed	Time in seconds (0-300)
Trail-making Test B	Evaluation of attention	Time in seconds (0-300)
Controlled Oral Word Association (COWA)	Evaluation of speech perception fluency	Score in points, depends on age and sex (from 0 and without upper limit)
Hopkins Verbal Learning Test	Memorizing words	Direct memory after listening for 3 times (max points — 36). The number of correctly reproduced words after 20—30 minutes (max. 12 words). Recognizing words heard in a longer list (max 12 words)
Digit Symbol Subtest из WAIS-III	Speed of memorizing digital symbols and numbers	Age-adjusted score from 0 to 20
Grooved Pegboard Test	Psychomotor function	Time in seconds (0—300)

Notes. Trail-making Test is a test to construct a path (test task aimed at assessing attention and speed of thinking); WAIS-III, originally Weschler Adult Intelligence Scale (WAIS), is a testing system and scale suggested by D. Wechsler in 1935—1939 to assess the intelligence level; in 1989, it was upgraded and called WAIS-R, i.e. "revised". In 1997, it was revised once again and called WAIS-III; Grooved Pegboard Test, peg board, a special panel with various holes for attached set of plugs, the task is to match them.

Table 2. **Meta-analysis of the role of intraoperative mapping in operations near the eloquent brain structures**

Parameter	Mapping		*p*
	Used	Not used	
Number of patients	3,230	1,731	
Eloquent area	In all cases	In some cases	
Radicality	75% (66—82%)	58% (48—69%)	>0.05
Exacerbation of neurological deficit	3.4% (2.3—4.8%)	8.2% (5.7—11.4%)	<0.05

visual, auditory, vestibular, speech, and cognitive functions should be identified before the surgery and integrity of these paths should be preserved during the resection [27, 32, 38, 39]. Intraoperative electro-stimulation mapping of the subcortical structures is performed based on the same principle as mapping of cortical areas. Stimulation of pathways enables assessment of the anatomical and functional interaction within the whole surgical area based on functional response of deep association fibers. Additionally, intraoperative electrostimulation mapping provides better understanding of the interaction between various functional areas of the brain and identifies the dynamic cerebral processes in distributing and processing neural networks (so-called hodotopy) [40]. Furthermore, these intraoperative studies facilitate exploration of brain plasticity, which is especially important in surgery of low-grade gliomas.

Another advantage of intraoperative electrostimulation mapping (IEM) in adults is that the correct use of this procedure prevents from false-negative results. Indeed, IEM is a highly sensitive method to detect important cortical and axonal structures and also provides a unique possibility to study brain connections, since each area responding the stimulus is a part of a large network, rather than a separately operating structure. However, the use of IEM is not an optimal solution. This is due to possible reverse propagation of electrical stimulus or functional compensation due to brain plasticity, which can lead to false positive results.

IEM is considered the "gold standard" of brain mapping. However, because of the risk of false-positive results, it should be used in combination with new techniques, such as perioperative functional neuroimaging and biomathematical modeling in order to have a coherent idea of which areas of the brain are functionally important, and which can be compensated.

The strategy and tactics of awake operations with intraoperative brain mapping

Preoperative planning and intraoperative neurosurgical strategy

Along with the aforementioned detailed and careful preoperative examination, surgery of mass lesions near or in the projection of speech centers of the brain and pathways of these eloquent functional areas of the brain requires thorough planning of neurosurgical operations, including accurate specification of the extent of the transcranial approach and determining cortical anatomical landmarks (major sulci and gyri, large convexital veins etc.). Thus, N. Duffau, one of the leaders of this trend in neurosurgery [41], suggests the following important objectives of intraoperative electrical stimulation of the cerebral cortex:

• to study individual functional cortical organization prior to resection;

• to understand the pathophysiology of brain areas, located in the projection of the tumor ;

• to compare the subcortical structures in the projection of resection and to study anatomical and functional relationships;

• to analyze the mechanisms of on-line (intraoperative) brain plasticity, using repeated electrical stimulation at all stages of tumor resection;

• to perform resection with allowance for individual disturbance of cortico-subcortical functional boundaries. The

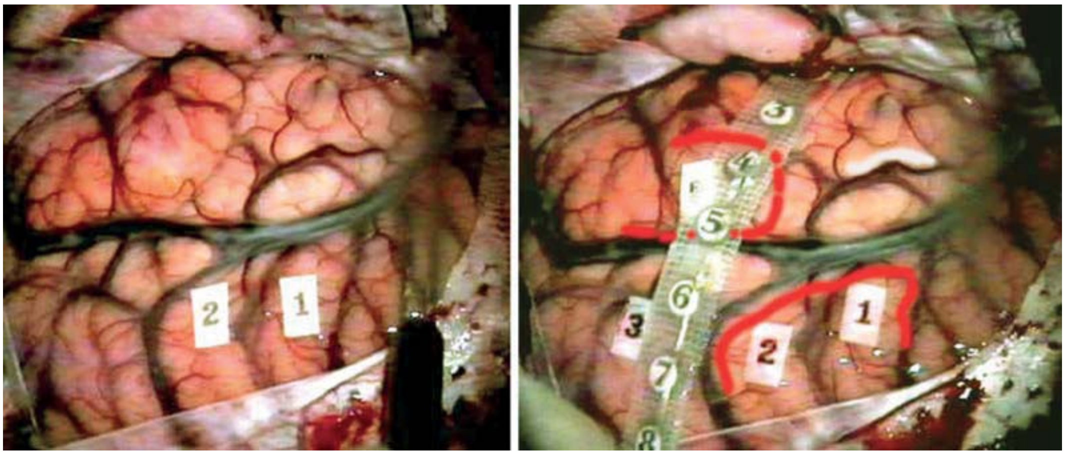

Figure 4. **1 and 2 — the areas, whose stimulation caused motor speech disturbances; 4 and 5 — the areas, whose stimulation caused sensory speech disorders; 3 — the area, whose stimulation caused finger movement on the right hand. Red arcs, the boundaries of speech areas; white arc, the place of cortex incision.**

main objective of this is to optimize the ratio of radicality of the surgery and the risk of exacerbation of neurological deficit.

When using neuronavigation systems, neuronavigation data are used both for planning of trepanation and for the preliminary assessment of the relative location of cortical speech centers after dura mater opening. Furthermore, it is important to compare the results of intraoperative electrical stimulation to the perioperative functional neuroimaging (before and after the surgery) in order to confirm these non-invasive methods and for better understanding of short-term and long-term mechanisms of brain plasticity based on functional cortical reorganization and change in "network" connection [42]. It should be remembered that, because of the virtual neuronavigation technique, the accuracy of neuronavigation data is significantly reduced with mass lesion resection due to displacement of the brain substance.

Dura mater opening during awake operations is carried out in such a way that to open the entire surface of the brain in the projection of trepanation opening with a view of the widest possible intraoperative electrophysiological mapping [43].

Intraoperative electrostimulation technique

After dura mater opening, multipolar electrode for direct corticography is placed (for the purpose of intraoperative control of seizure activity of the cerebral cortex) in such a way that it did not interfere with surgical procedures (it is usually placed subdurally outside the trepanation opening).

Electrophysiological mapping should be carried out with the participation of anesthesiologist, electrophysiologist, neuropsychologist, and operating neurosurgeon.

By the time of electrostimulation of the brain aimed at direct identification of cortical speech centers, the patient must be awaken out of anesthetic sleep. Further, stable verbal and psycho-emotional contact should be established with the patient.

Cortical area remote from tentative Broca's and/or Wernicke's area should be selected to adjust electrostimulation current. After current adjustment, the mapping itself should be carried out.

The entire opened surface of the cerebral cortex should be consistently studied starting from the supposedly "silent" regions to the functional areas. When detecting errors in test execution during intraoperative neuropsychological testing (see relevant sections), the procedure should be paused and then stimulation should be repeated 1—2 times in the area identified as a cortical speech center. Cortical speech areas identified using direct electrical stimulation should be marked with sterile paper (cellulose) labels with numbers **(Fig. 4)** [7, 8].

Seizure activity of the cerebral cortex should be monitored during the entire electrical stimulation procedure. In the case of readiness for convulsions, electrical stimulation of the brain is stopped, and surgical wound is irrigated with prefabricated cooled saline solution, and intravenous anticonvulsants are administered, if necessary (not barbiturates, except for the development of life threatening seizures): sodium valproate and/or levetiracetam [8].

Electrical stimulation of motor areas of the cortex is carried out either during the search for cortical speech areas, or, additionally, motor cortical centers in the case of anatomical spread of space-occupying lesions in the direction of the motor cerebral convolutions. The areas of the motor cortex are also labeled with numbered cellulose piece (**see Fig. 4**).

Postoperative examination

Within 24 hours after the surgery, CT and contrast-enhanced (if the space-occupying lesion accumulated contrast agent) or non-contrast-enhanced (if the tumor was not contrasted according to the preoperative data) MRI of the brain should be carried out in order to exclude intraoperative bleeding complications and complications in the early postoperative period. This postoperative study is aimed at assessing the degree of radicality of tumor resection (including volumetric comparison, if possible). Within the first few days after the operation, repeated neuropsychological study should be done and then it should be repeated during a follow-up examination in 3 and 6 months, and in the long-term follow-up, if possible.

The outcomes of operations with intraoperative awakening

When comparing general results of operations with and without intraoperative awakening in cases with similar anatomical location of the tumor, it should be admitted that the literature provides no clear evidence neither in favor of the use of this technique, nor against it. The case is that in some major neurosurgical centers almost all operations for the tumors located near the speech areas are performed with the awakening, while in the other ones, on the contrary, awake craniotomy is not widely used. And finally, the third group of clinics alternately use both approaches, without giving significant preference to any of them.

To finalize our detailed overview of methodological approaches to the use of the technique of operations with intraoperative awakening and speech area mapping, let us consider the data of meta-analysis performed by a group of researchers, who focused on a wider problem, i.e. the use of intraoperative electrophysiological mapping of both speech areas with awakening and motor areas without awakening compared to operations without the use of intraoperative electrophysiology. The results of this study are shown in **Table 2**.

This meta-analysis shows that the use of intraoperative mapping of eloquent areas of the brain (motor cortex, speech areas, etc.) can provide significantly better results in terms of decreased incidence of persistent neurological deficit (about 2.5-fold) compared to the operations without intraoperative mapping. In this case, better outcome is achieved by no means at the expense of lower radicality of tumor resection. The authors of these works concluded that intraoperative electrophysiological mapping has become the gold standard for operations near the eloquent areas of the brain [45].

Conclusion

Prospects of the development of surgical methods with intraoperative awakening

Currently, the accumulated experience of awake operations, development of functional neuroimaging techniques, and rapid development of intraoperative electrophysiological mapping enables the use of awake operations not only for the purpose of cautious handling cerebral centers and pathways of speech and motor structures, but also to preserve the visual centers and pathways of the visual analyzer.

In this review, we deliberately did not touch the issues of anesthetic management of awake craniotomy, since this part of the problem is covered in the works of our colleagues [7, 8]. However, let us note that our neuroanaesthesiologists have priority in publication of materials on the use of xenon anesthesia for awake operations in the scientific world. [46]

It should be emphasized that awake neurosurgical operations near speech areas and other functional centers of the brain using the active multidisciplinary approach contribute to the development of our knowledge in the field of functional structure of the brain centers of speech, memory, counting, writing, hearing, and visual perception and other higher neural functions.

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