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ORIGINAL ARTICLE

Result of awake surgery for pediatric eloquent brain area tumors: single-center experience

Mikle Talabaev[1] · Kevin Venegas[1] · Gleb Zabrodets[2] · Volha Zmachinskaya[2] · Alexander Antonenko[3] · Dmitry Naumenko[3] · Hanna Salauyeva[1] · Natalia Churyla[4]

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Abstract

Purpose About half of brain tumors are located in supratentorial regions and 20% of them in eloquent brain cortex areas. The use of fMRI and intraoperative neuromonitoring allows safe surgery of these areas. Carrying out awake brain surgery (ABS) operations provides additional opportunities for direct-function monitoring. In pediatric practice, this method has not been used widely yet.

Methods We present the retrospective analysis of the results of pre-operative examination and surgical treatment of 12 patients with glial tumors located in eloquent cortex areas. Two patients had ABS operations twice. Intraoperative neuromonitoring was used in all the cases.

Results Twelve patients in total underwent fourteen ABS operations. According to histology results, patients with low-grade tumors prevailed, 11 (91.7%) out of 12. Seven (58.3%) patients had the tumor located in the projection of speech cortex area, four (33.3%) patients in the motor cortex area, and one (8.4%) patient in the visual cortex area. The youngest male was 8 years old. Temporary neurological deficit was diagnosed in three (25%) cases. The tumor was removed completely in 66.7% (eight) cases. Three patients were operated upon twice, two of whom had ABS operations twice. The awake phase of the surgery lasted from 30 to 110 min, 61.2 min on average.

Conclusions Our experience has shown sufficient safety of pediatric ABS operations. The achieved functional result and radicality of tumor removal prove that further application and development of this method for children with eloquent brain area tumors (EBATs) is reasonable.

Keywords Pediatric awake surgery · Eloquent cortex areas · Pediatric brain tumor · Brain mapping

Introduction

Modern neurosurgery considers neurosurgical intervention successful only if complete removal of the pathological process is achieved with a minimum risk of developing persistent neurological deficit. About 40% of childhood brain tumors are located in supratentorial regions and about 20% in eloquent areas of cerebral cortex in children [6].

In order to preserve the quality of life, the method of awake brain surgery (ABS) started being applied, first for adult patients with epilepsy, and then for the removal of eloquent brain area tumors (EBATs). Performing direct cortex stimulation to the cerebral cortex during ABS operation allows a neurosurgeon to detect eloquent areas of the cerebral cortex and reduce the risk of neurological deficit [1, 5, 9, 11, 12, 20, 21].

In many modern neurosurgical centers, awake surgery with direct electrical stimulation has become the standard for adult patients. Today, only a few works describe the results in pediatric patients. So, a review article by Lohkamp et al. included the results of 18 publications which brought together 50 pediatric patients [12, 13].

✉ Mikle Talabaev
talabaevm@inbox.ru

1 Pediatric Neurosurgery Department, Republican Research and Clinical Center of Neurology and Neurosurgery, Minsk, Belarus

2 Intraoperative Neurophysiological Monitoring Service, Republican Research and Clinical Center of Neurology and Neurosurgery, Minsk, Belarus

3 Department of Neuroradiology, Republican Research and Clinical Center of Neurology and Neurosurgery, Minsk, Belarus

4 Psychological Service, Republican Research and Clinical Center of Neurology and Neurosurgery, Minsk, Belarus

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Successful ABS operation requires proper preparation and coordinated team work of various specialists: anesthesiologist, neurophysiologist, neuropsychologist, neurosurgeon, neuroimaging specialist, etc. The functional results obtained in the research related to adult patients are quite optimistic. The number of surgical complications did not increase [4, 7, 8, 12, 16, 20].

Safety issues related to pediatric ABS operations, functional outcomes, effects on the radicality of removal, and others are currently being studied.

Material and methods

The article presents a retrospective experience analysis of pediatric ABS operations performed at the Republican Research and Clinical Center of Neurology and Neurosurgery between the years 2016 and 2019. Twelve patients in total underwent fourteen ABS operations related to EBATs (Table 1). Half of the patients were male, half—female, with average age being 14.5 years old. The youngest male was 8 years old and the youngest female—10. The patient with glioblastoma multiforme (GBM) and dysembryoplastic neuroepithelial tumor (DNET) was operated twice.

Seven (58.3%) patients had the tumor located in the projection of speech cortex area, four (33.3%) patients in the motor cortex area, and one (8.4%) patient in the visual cortex area. According to histology results, patients with low-grade tumors prevailed, 11 (91.7%) out of 12.

Seven (58.2%) patients were diagnosed with DNETs, two (16.7%) patients with ganglioglioma (GG), two (16.7%) patients with pilocytic astrocytoma (PA), and one (8.4%) patient was diagnosed with GBM.

MRI preoperative planning

Preoperative structural MRI and functional MRI (fMRI) were performed on a Tesla 3.0 Discovery MR750w 3.0T scanner manufactured by General Electric Company (USA). Structural MRI was performed for all patients, fMRI—for eight (66.7%) patients. These are five patients with tumors in the projection of speech areas, two patients with tumors in the precentral gyrus, and one patient in the projection of visual cortex area. The results of the structural MRI scan were used to determine the location, etiology, and degree of tumor malignancy, as well as to carry out intraoperative navigation (Fig. 1).

Using fMRI, the dominant hemisphere as well as the location of speech and motor cortex areas were precisely specified. Its results made it possible to detect the necessary eloquent areas of seven (87.5%) out of eight patients. We detected that one 8-year-old male (right-handed) with a tumor in the posterior third of the left upper temporal gyrus had a bilateral location of the Wernicke's area (Fig. 2). It was not possible to detect the Wernicke's area of one patient with DNET located in the posterior third of the superior temporal gyrus, which was an additional indication for awake operation.

It is interesting that an fMRI performed 6 months after the operation perfectly found the location of the Wernicke's area, which was located along the edge of the postoperative cyst, where it was detected by direct cortical stimulation during the operation. In all cases, MRI DTI was performed. Tractography data were taken into account during subcortical stimulation and access planning when removing tumor.

Anesthetic technique (local anesthesia)

Before entering the operating room, all patients received an age-adjusted dosage of diazepam. Before head positioning into Mayfield clamp, total anesthesia of head soft tissues

Table 1 Description of EBAT patients

No.	Age	Sex	Right handed/left handed	Location	Initial symptom	Histology
1	16	F	Right handed	Precentral + postcentral	Seizures	DNET
2	15	M	Right handed	Wernicke	Seizures	PA
3	13	F	Right handed	Wernicke	Seizures	PA
4	16	M	Right handed	Broca	Seizures	DNET
5	17	M	Right handed	Precentral	Seizures	GBM
6	16	F	Right handed	Precentral	Seizures	GG
7	16	F	Right handed	Wernicke	Seizures	DNET
8	14	M	Right handed	Wernicke	Seizures	DNET
9	8	M	Right handed	Wernicke	Seizures	DNET
10	10	F	Right handed	Wernicke	Seizures	GG
11	16	M	Left handed	Precentral	Seizures	DNET
12	17	F	Right handed	Visual cortex	Seizures	DNET

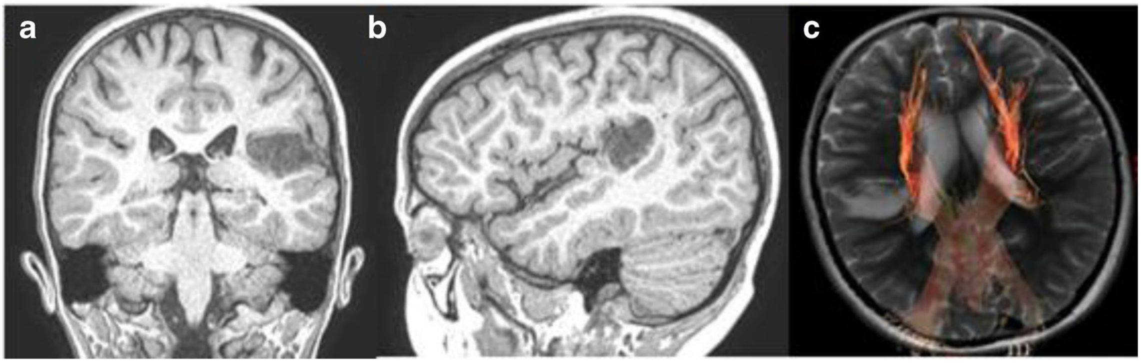

Fig. 1 Tumor in the projection of posterior third of superior temporal gyrus (Wernicke's area). T1-MRI coronal (**a**), sagittal (**b**), and T2-MRI axial with corticospinal tract (**c**)

was performed from 12 standard points. The anesthetic was additionally injected to the Mayfield clamp fixation points as well as along the incision of soft tissues. We used bupivacaine for this purpose. In addition, the anesthetic was injected into the base of the dura mater flap just before it was opened. Local anesthesia was performed under intravenous injection of fentanyl and propofol [2, 15, 16].

After the main stage of tumor removal was completed, additional propofol was administered to the patient intravenously and the patient slept.

Surgery technique and direct cortex stimulation

All patients underwent routine antibiotic preventive treatment. We used intraoperative navigation (Brainlab AG) in all cases, both when planning trepanation and during tumor removal. After the patient woke up and was able to communicate well with a neurophysiologist and neuropsychologist, the dura mater was opened. The awake phase of the surgery lasted from 30 to 110 min, 61.2 min on average (Table 3).

In all cases, the trepanation size was sufficient to remove the pathological process completely. As a rule, the size of the "opening" in the dura mater was not more than 1.0 cm from the intended border of the tumor. In other words, we avoided a large-scale craniotomy. We based this on the fact that it is essential to determine the location of the eloquent area of the cerebral cortex directly in the region subject to surgical intervention. Its location outside this region did not matter.

After the dura mater was opened, we additionally performed ultrasound navigation, which is especially relevant for low-grade gliomas (LGG), when the tumor differs little from the non-pathological brain tissue. After that, we carried out mapping of the cerebral cortex in the encephalotomy area with a bipolar probe having 5 mm interelectrode distance. Stimulation was performed according to Penfield for 3–4 s having 50 Hz frequency and 0.2 ms stimulation pulse. We used 4 mA initial current rate followed by further 1 mA increase, usually up to 5–10 mA (maximum 20 mA).

In addition, we carried out subcortical stimulation during removal in order to detect eloquent white matter conducting pathways responsible for speech and motion. Except for the above-mentioned technique, during tumor removal and subcortical stimulation, we also used a short-train technique (Taniguchi): series of (train) 5–7 pulses lasting 0.3–0.5 ms with 4–5 μs interpulse interval having 1 Hz frequency both with a bipolar probe and monopolar Mapping Suction Probe by Raabe. Monopolar cathodal stimulation started with 4 mA, followed by further increase of 1 mA, usually up to 10 mA (maximum 20 mA). In the case of motor responses at 5 mA current rate, we stopped tumor removal in this point. If necessary, we carried out test stimulation using ball-tip bipolar Fork probe at the same current rate.

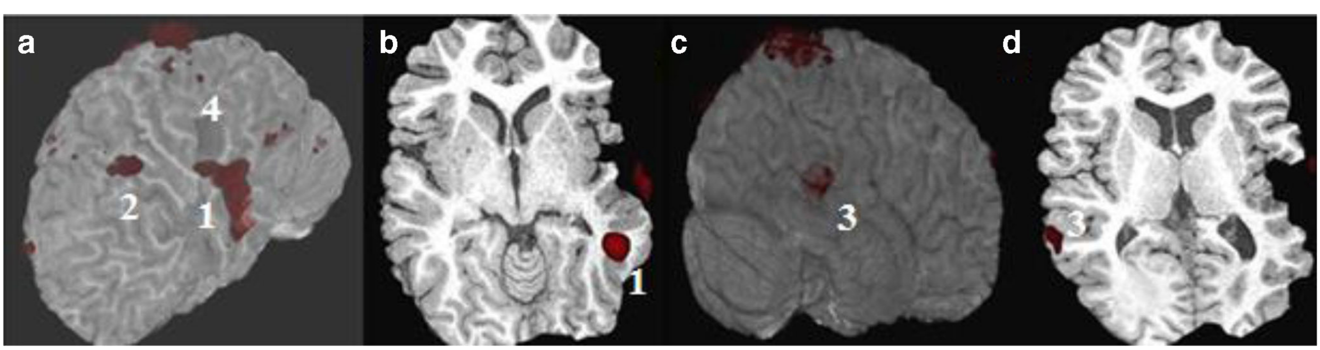

Fig. 2 fMRI of the patient with two-side location of the Wernicke's area. 1, Wernicke's area, on the left (**a**, **b**); 2, language area, on the left (**a**); 3, Wernicke's area, on the right (**c**, **d**); 4, tumor (**a**)

Patients requiring speech function testing were tested in those languages which they speak or study at school. Usually, these are two languages, native (Russian) and English or German. Included was an 8-year-old male who passed elementary testing in English. The features of speech function testing, depending on tumor location are presented in Table 2.

One 17-year-old female who studied painting at the Art Academy and who had a tumor located in visual cortex (Brodman 17) underwent an awake operation too. During primary visual cortex mapping, we received simple responses in the form of white and black spots or light flashes which the patient was telling us about. Stimulation parameters for motor, speech, and visual cortex testing were the same.

In all cases, it was possible to finish ABS operations successfully within the required time. None of the patients had seizures during the surgery. In one case, the patient had cerebral swelling, which required an osmotic diuretic injection. One female patient had a pain response during dissection of Labbe vein, but this did not require additional drug injection.

Results

Functional result

It was possible to detect eloquent areas of the cerebral cortex of seven (58.3%) patients during direct cortex stimulation. Three (75%) out of four patients with motor cortex involvement, three (42.8%) out of seven patients in speech areas, and one patient—with involvement of visual cortex.

Table 2 Features of speech testing depending on pathology location

Location according to MRI	Number of patients	Speech testing
Posterior third of superior temporal gyrus, at the left (dominant) (Wernicke's area)	6	Repetition, semantic tasks, (4th image is odd), semantic judgment (assessment of judgments), reading + semantic sentence completion, naming of objects
Posterior third of inferior frontal gyrus, at the left (Broca's area)	1	Repetition (phonological tests or repetition for motor action), actualization of action names, naming of objects, semantic association
Left frontal + speech cortex	1	Speech dynamics, semantic sentence completion, repetition, motor arrangement of speech

There was no persistent neurological deficit after awake surgical treatment. Temporary neurological deficit was diagnosed in three (25%) cases. None of the four patients with tumor location in the motor cortex projection had motion dysfunctions before surgery. In the postoperative period, one (25.0%) patient with PA in the precentral gyrus and extra motor cortex had mild distal hemiparesis. Postoperative DWI MRI showed a small ischemia area along the front edge of the precentral gyrus. Symptoms completely regressed within a month.

Patients with a tumor in the speech cortex projection did not have function disorder in preoperative period. After surgery, two (28.6%) patients had mild disorders that completely regressed within a month after the intervention.

Radical removal and histology

Eleven (91.7%) patients had LGG. Six patients had DNETs, two patients—GG, and two patients—PA. One patient had GBM. We assessed if surgery is radical based on intraoperative data and according to MRI scans conducted within the first 24 h after the surgery for all the patients (Table 3). Postoperative MRI showed that four patients (33.3%) still have a little amount of the remaining tumor.

All the patients who had non-radical tumor removal, during the direct stimulation had motor (two) and speech (two) responses during the removal. Three patients were operated upon twice, two of whom had ABS operations twice. The postoperative MRI check (FLAIR) of the 17-year-old patient with GBM performed 3 months later revealed the area of changes around the postoperative cyst, corresponding to a diffuse low-malignant tumor. Therefore, we performed the second ABS operation. Histology results confirmed fibrillary astrocytoma. Both operations were performed at the age of 17. The patient underwent adjuvant treatment (radiation treatment and multiagent chemotherapy according to the treatment protocol for GBM) and has already been without the signs of recurrence within 29 months after the first intervention. One patient with PA of the left temporal lobe underwent ABS operation at the age of 15 and 17 years. The third patient with DNET of the posterior third of the left temporal gyrus had surgery under anesthesia for the second time, as fMRI showed the Wernicke's area along the edge of the postoperative cyst but not in the projection of tumor remaining part.

Discussion

The growing interest among neurosurgery specialists for carrying out awake operations, as well as the increasing number of younger patients with indications for this type of operations, demand the development and implementation of ABS operations in pediatric neurosurgery. However, the age-related

Table 3 Radical tumor resection

No.	Histology	Extent of tumor resection	MRI assessment	Reoperation	Time span of the awake phase (min)
1	DNET	STR	PR	No	110
2	PA	TR	TR	No	70
3	PA	TR	TR	No	40
4	DNET	TR	TR	No	60
5	GBM	STR	STR (FS)	Yes	110 (FS)
			TR (SS)		70 (SS)
6	GG	TR	TR	No	50
7	DNET	TR	TR	No	40
8	DNET	TR	STR	Yes	70
9	DNET	TR	STR	No	70
10	GG	TR	TR	No	40
11	DNET	TR	TR	No	30
12	DNET	TR	STR (FS)	Yes	70 (FS)
			TR (SS)		40 (SS)

TR, total resection; *STR*, subtotal resection; *PR*, partial resection; *FS*, first surgery; *SS*, second surgery

features of children mental ability, increased psychological fragility and higher risks, in comparison with adult age, development of postoperative psychological adverse reactions with further neurocognitive deficit makes the use of pediatric ABS complicated [10, 12]. Taking into account the absence of clear recommendations for pre- and postoperative neuropsychological evaluation of pediatric patients, we applied an individual algorithm for preparation of each patient and their family. A certified psychologist carried out psychological evaluation and preparation during preoperative meetings. In addition, we provided intraoperative psychological support for patients. Special attention was paid to evaluation of reactive (situational) and personal anxiety, attitude to pain, and tendency to depression; we also practiced intraoperative tasks in order to ensure their correct fulfillment by the patient upon his or her awakening.

ABS operation was considered a potentially traumatic event and a possible reason for development of posttraumatic stress disorder (PTSD), as well as the reason for developing depression when the patients become older [10, 12, 13, 17]. Postoperative patient evaluation was carried out within the nearest postoperative period. In addition, 11 (91.7%) out 12 patients had such an evaluation in 6–12 months.

Within the nearest postoperative period, none of the patients had any negative memories related to ABS operation. Testing done within the long-term postoperative period also did not show any signs of PTSD and depression. Moreover, 7 out of 11 respondents willingly shared their memories of the event and felt proud of it. All the 11 patients reported that they were ready to undergo ABS operation again, as they had no unpleasant memories and were prepared for the event. They were sure about the upcoming outcome as well as ready to recommend ABS operation to other children, if necessary. Within the postoperative period, none of the patients took psychotropic medical drugs.

We were very concerned about a 16-year-old female with signs of behavior disorder. She had a large number of tattoos, some on the most sensitive parts of the body and multiple scars on the inner surface of her left forearm typical for suicide attempt. Behavior disorders could be a precondition for unpredictable behavior during the surgery, as well as become the basis for development of depression at an older age [19]. The key factors that allowed us to offer ABS operation were a low level of situational anxiety and a tolerant attitude to pain.

It is interesting that the youngest of the patients, an 8-year-old boy, tolerated the operation better than others. The decision to carry out ABS operation was based on how easily the patient fulfilled paradigms during fMRI, which, in our opinion, is related to the individual stress resistance of the child and the successful work of the psychologist. In many respects, the success of ABS operations depends on the quality of interaction between the patient and the medical staff. Today, participation of a psychologist at the stage of preparation and carrying out of such operations has become standard [12, 14, 16].

Preserving the quality of life together with radical tumor removal are the main efficiency criteria for neurooncology treatment [3, 9, 14]. Applying the technology of ABS operations, we proceeded from the fact that, first of all, the operation should remain safe enough for the patient.

Before we offered ABS operation to the patient, we used structural MRI scan to find out if the tumor is located in eloquent areas of the cerebral cortex. In order to detect the individual functional structure of the cerebral cortex (location of cerebral cortex areas responsible for motion, speech, and vision), eight (66.7%) patients underwent functional MRI. The remaining four patients did not have fMRI scan for technical reasons not related to the patient.

The next factor ensuring the safety and successful intervention is reliable anesthesia, provided by the local use of bipuvacaine and intravenous injection of propofol with fentanyl. In order to avoid a mistake during soft tissue anesthesia, we used a head phantom where the injection sites and the dose of anesthetic to be injected were marked. One patient showed a short-term pain response while Labbe vein dissection. Intravenous administration of fentanyl and psychologist intervention were sufficient in this case.

The use of intraoperative neuromonitoring made it possible to find the location of eloquent areas of the cerebral cortex of 7 out of 12 patients. Three patients developed neurological disorders after surgery; in all the cases, such disorders were temporary and completely regressed within several weeks.

Our group of patients had no complications described in the literature, such as intraoperative seizures or vomiting and others that might require urgent intubation. Three and half percent of adult patients develop such complications [18].

The achieved gross resection (66.7 %) corresponds to the published data [12].

Conclusion

Our experience of 14 operations upon 12 patients revealed that with proper preliminary preparation and planning of each stage of the operation, ABS operation is quite safe. It allows preservation of the quality of life for the patient upon EBAT removal without reducing radicality of removal.

This successful outcome is possible only in the case of coordinated team work of specialists, including a neurosurgeon, anesthesiologist, neurophysiologist, and neuropsychologist.

In all the cases, strict selection criteria of patients for ABS operation are required.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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