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INTRAOPERATIVE SEIZURES OCCURRENCE IN CORTICAL MAPPING OF ELOQUENT AREAS

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ABSTRACT: The effect of structural epilepsy on the frequency of intraoperative convulsive seizures is assessed when mapping functionally significant areas of the cerebral cortex during resection of intracerebral neoplasms. The work is based on the analysis of the results of intraoperative neurophysiological studies at the Polenov Neurosurgical Institute. For the period 2019–2020 87 intraoperative mappings of eloquent cortex were carried out during resections of intracerebral neoplasms: 79 mappings of the motor cortex and 16 mappings of auditory-speech areas during operations with awakening. When mapping the motor zones of the cortex, the frequency of seizures was 5.1%, while mapping the auditory-speech zones with awakening — 18.75%. The division of cases of intraoperative convulsive seizures into two groups: seizures arising from motor mapping and seizures associated with the mapping of auditory zones — reflects differences in factors that affect the excitability of the cerebral cortex. In motor mapping, stimulation occurs against the background of general anesthesia, unlike waking operations. The intensity of stimulation in auditory mapping is higher than in motor mapping. Formally, the current used in motor mapping is significantly higher than in mapping auditory zones. In general, with the development of intraoperative convulsive seizures, the current intensity of cortical stimulation does not exceed the average values required to stimulate functionally significant cortical zones. The presence of epileptic syndrome in patients with intracerebral tumors cannot be considered as a predictor of intraoperative seizure development when performing motor mapping under general anesthesia as well as during surgery with awakening for mapping of motor or auditory verbal zones.

Keywords: intraoperative neurophysiological monitoring; motor mapping; structural epilepsy; neurophysiology; neurosurgery; eloquent cortex.

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ИНТРАОПЕРАЦИОННЫЙ СУДОРОЖНЫЙ СИНДРОМ ПРИ КАРТИРОВАНИИ ФУНКЦИОНАЛЬНО ЗНАЧИМЫХ ЗОН КОРЫ ГОЛОВНОГО МОЗГА

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Резюме. Оценивается влияние структурной эпилепсии на частоту интраоперационных судорожных припадков при картировании функционально значимых зон коры головного мозга в ходе резекции внутримозговых новообразований. В основу работы положен анализ результатов интраоперационных нейрофизиологических исследований в Российском научно-исследовательском нейрохирургическом институте имени профессора А.Л. Поленова. За период 2019–2020 гг. было проведено 87 интраоперационных картирований функционально значимых зон коры головного мозга в ходе резекций внутримозговых новообразований: 79 картирований моторной коры и 16 картирований слухоречевых зон при операциях с пробуждением. При картировании двигательных зон коры частота припадков составила 5,1%, при картировании слухоречевых зон с пробуждением — 18,75%. Деление случаев интраоперационных судорожных припадков на две группы: припадки, возникающие при моторном картировании, и припадки, связанные с картированием слухоречевых зон, — отражает различия в факторах, оказывающих влияние на возбудимость коры головного мозга. При моторном картировании стимуляция происходит на фоне общей анестезии в отличие от операций с пробуждением. Интенсивность стимуляции при слухоречевом картировании выше, чем при моторном картировании. Формально сила тока, используемая при моторном картировании, значительно выше, чем при картировании слухоречевых зон. В целом при развитии интраоперационных судорожных припадков сила тока стимуляции коры не превышает средние значения, требуемые для стимуляции функционально значимых зон коры. Показано, что наличие структурной эпилепсии, ассоциированной с внутримозговыми опухолями, не может рассматриваться как предиктор развития интраоперационных судорожных припадков при выполнении моторного картирования как в условиях общей анестезии, так и при хирургии с пробуждением для картирования слухоречевых зон.

Ключевые слова: интраоперационный нейрофизиологический мониторинг; моторное картирование; структурная эпилепсия; нейрофизиология; нейрохирургия; функционально значимые зоны коры.

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BACKGROUND

A pathological neoplasm localized in the projection of functionally significant areas of the cerebral cortex should be resected according to the principle of “physiological permissibility” formulated by Burdenko [1]. In accordance with this principle, intraoperative mapping of motor areas and mapping of auditory and verbal areas with a conscious patient is widely used in modern intraoperative neurophysiology [2–4]. Intraoperative motor mapping (MM) is a neurophysiological technique based on the direct electrical stimulation of cortical motor areas and registration of evoked responses from target muscles [1, 5, 6]. If during monitoring preservation of higher cortical functions such as speech, spatial sense, and stereognosis is required, a dynamic assessment of the safety of the studied functions is possible only when surgery is performed with a conscious patient during tumor removal [7–10].

The mapping of functionally significant areas can be complicated by the development of intraoperative convulsive seizures (ICS). In the literature of the last 10 years, possible factors contributing to ICS developing has been actively investigated. However, no clear and generally accepted concept of epileptogenesis during intraoperative electrical stimulation of the cortex has been formulated yet. One of the factors that could explain the pathological excitability of the cerebral cortex is the presence of structural epilepsy associated with intracerebral tumors. Lesser et al. [11] and Spina et al. [12] have reported an increased risk of ICS during cortical mapping in patients with epilepsy; however, Simon et al. [13] and Seifert [14] did not find such correlation.

The study aimed to evaluate the effect of structural epilepsy on the frequency of intraoperative seizures when mapping functionally significant areas of the cerebral cortex.

MATERIALS AND METHODS

This study was based on medical and statistical analyses of the results of intraoperative neurophysiological studies at the A.L. Polenov Russian Neurosurgical Research Institute (RNRI) in 2019–2020. The incidence of ICS that occurred in intraoperative mapping during resections of neoplasms in the projection of functionally significant areas of the cerebral cortex was analyzed.

To perform MM, monopolar stimulation with trains was used (4 pulses with a frequency of 500 Hz with an interstimulus interval of 1–2 ms and repetition rate of trains of 0.25–1 Hz). Stimulation was started with a current strength of 1 mA and then increased in increments of 1–2 mA until a motor response from the target muscles was received. Motor responses were recorded using subcutaneous needle electrodes placed on the contralateral side of the body above *m. abductor pollicis brevis*, *m. abductor digiti minimi*, *m. tibialis anterior*, and *m. abductor hallucis*. In the absence of responses from the target muscles at a current strength

of 30 mA, the cortical area was considered to not present motor responses.

To exclude false-negative results of motor zone mapping, the level of neuromuscular transmission was monitored using peripheral nerve stimulation with a train-of-four (TOF) stimulus burst. Stimulation was performed with a burst of four electrical stimuli with a duration of 500 μ s and an intensity of 30–50 mA (above the motor threshold) delivered at a frequency of 1–2 Hz. Stimulation needle electrodes were located in the projection of *n. medianus*. Registration was performed with needle electrodes installed above the *m. abductor pollicis brevis*. MM was performed at a TOF level above 70%.

The auditory and verbal zones were stimulated bipolar using the Penfield paradigm, i.e., continuous stimulation for 1–2 with rectangular stimuli at a frequency of 50 Hz [1]. Stimulation was performed at a current strength of 1–10 mA. When performing auditory and verbal tests, symptoms of loss were recorded.

Electrocorticography (ECoG) was performed to verify epileptiform activities during cortical stimulation. Registration was performed with AdTech cortical electrode strips (USA). The bandwidth was 0.5–35 Hz. ECoG was analyzed visually and logically in real time.

Neurophysiological parameters were registered in the IOM ISIS hardware–software complex from Inomed (Germany).

Data are presented as $\bar{X} \pm \sigma$ (mean \pm standard deviation). Student's *t*-test was used to assess the significance of differences in unrelated paired samples. The χ^2 test was used to assess the significance of differences in the empirical and theoretical distribution of ICS cases. Differences were considered significant at $p < 0.05$. SPSS Statistics version 17 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

RESULTS AND DISCUSSION

From 2019 to 2020, 87 intraoperative mappings of functionally significant areas of the cerebral cortex were performed during resections of intracerebral neoplasms. Moreover, 79 mappings of the motor cortex and 16 mappings of auditory and verbal areas were performed during awake surgeries. The average current was 21.6 ± 7.6 mA during MM and 6.9 ± 3.4 mA during mapping of verbal zones.

During the analyzed period, seven ICS cases were registered when mapping functionally significant areas of the cortex. In cases where the surgery was complicated by ICS, the intensity of the stimulation current did not exceed the average values necessary for mapping the motor cortex and the auditory and verbal areas during awake surgeries (Table 1).

During surgeries with conscious patients for mapping speech areas using the bipolar stimulation technique, seizures occurred in three patients, which accounted for 18.75% of

all surgeries using this technique (Table 2). When mapping the motor areas of the cortex under general anesthesia, four cases of convulsions were registered, which accounted for 5.1% of all surgeries during MM. However, the difference in ICS incidence in MM and mapping of auditory and verbal zones was not statistically significant.

A multicenter study in Europe analyzed the results of intraoperative mapping performed in 15 medical centers of neurosurgery [12]. A total of 2098 cases were analyzed, including 1235 (58.8%) cases of mapping under general anesthesia and 863 (41.1%) cases with awakening. The incidence of ICS in different centers ranged from 2.5% to 54%. On average, ICS developed much more often when mapping auditory and verbal areas during awake surgery

($n = 155$; 18.6%) than during MM under general anesthesia ($n = 109$; 8.8%).

Spena et al. [12, 15] provided similar data on ICS incidence when mapping functionally significant areas of the cortex. The incidence of ICS was 11.2% with auditory and verbal awake mapping and 8.2% with mapping of motor areas.

Thus, the incidence of ICS in RNRI during neurophysiological monitoring was close to the minimum values of the incidence of this indicator, as reported by the leading neurosurgical centers in Europe.

The division of ICS cases into two groups, i.e., seizures that occur with MM and seizures associated with mapping of auditory and verbal areas, reflects differences in factors

Table 1. Intraoperative seizures: characteristics of the examined patients

Таблица 1. Интраоперационный судорожный синдром: характеристика обследованных больных

Sex/age, years	Diagnosis/degree of anaplasia	Presence of structural epilepsy/AEP intake	Conditions for mapping	Parameters of cortical stimulation	
				Polarity	Current, mA
F/26	Astrocytoma of the left parietal lobe/grade II	No	TIVA	Monopolar	21
F/31	Astrocytoma of the right insular lobe/grade II	Yes/depakine 750 mg/day	TIVA	Monopolar	7
F/47	Superior sagittal sinus meningioma/grade II	Yes/depakine-chrono 1000 mg/day	Inhalation anesthesia	Monopolar	19
F/31	Astrocytoma of the right frontal lobe/grade II	Yes/carbamazepine 600 mg/day	TBBA	Monopolar	22
M/45	Glioblastoma of the left frontal lobe/grade IV	No	Awake craniotomy	Bipolar	6
M/48	Glioblastoma of the left temporal lobe/grade IV	Yes/depakine-chrono 1000 mg/day	Awake craniotomy	Bipolar	8
M/27	Oligodendroglioma of the left frontal and insular lobes/grade II	No	Awake craniotomy	Bipolar	8

Note: * TIVA, total intravenous anesthesia with propofol, fentanyl, clonidine; AEP, antiepileptic drugs.

Table 2. Frequency of intraoperative seizures during intraoperative mapping of eloquent cortex, abs. (%)

Таблица 2. Частота интраоперационных судорожных припадков при интраоперационном картировании функционально значимых зон коры головного мозга, абс. (%)

Number of cases	Motor mapping under general anesthesia		Mapping of audioverbal zones upon awakening	
	Without ictal event	With ictal event	Without ictal event	With ictal event
Total	75 (94.9)	4 (5.1)	13 (81.25)	3 (18.75)
With structural epilepsy	37 (46.8)	3 (4.1)	10 (62.5)	1 (6.25)
Without epileptic syndrome	38 (48.1)	1 (1.4)	3 (18.75)	2 (12.5)
Without epileptic syndrome	79 (100)		16 (100)	
χ^2	0.44 ($p > 0.05$)		0.49 ($p > 0.05$)	

that affect the excitability of the cerebral cortex. With MM, stimulation occurs under general anesthesia, in contrast to awake surgeries. The intensity of stimulation with auditory and verbal mapping is higher than with MM. The current strength used in MM is much higher than that in mapping auditory and verbal zones. However, according to our calculations, the power of direct stimulation when using trains of 3–5–7 stimuli is significantly lower than with continuous stimulations for 2–5 stimuli with a lower current, but a high frequency. Szelényi, Joksimović, and Seifert [14] adhere to a similar opinion about the lower proepileptogenic activity of train stimulation.

In some patients who developed ICS, an intracerebral tumor was associated with structural epilepsy. There were three such cases in the MM group, and one case in the auditory and verbal zone group. A hypothesis was formulated: the resulting distribution is not random; therefore, the probability of occurrence of ICS in patients with structural epilepsy is higher than in patients without epileptic syndrome. The comparison of the theoretical and empirical distributions with the calculation

of the χ^2 criterion did not lead to the rejection of the hypothesis that the distribution of ICS incidence in patients with or without epileptic syndrome is random both during MM and mapping auditory and verbal zones.

Thus, the results obtained do not enable to consider structural (symptomatic) epilepsy as a factor that increases the risk of a convulsive syndrome during intraoperative mapping of the cortex.

CONCLUSIONS

1. The incidence of intraoperative seizures was 18.75% when mapping auditory and verbal zones during awake craniotomy and 5.1% when mapping the motor cortex zones under general anesthesia.

2. Structural epilepsy associated with intracerebral tumors is not a predictor of the development of convulsive seizures both during MM under general anesthesia and during awake surgery for mapping auditory and verbal zones.

REFERENCES

- Alexandrov MV, Chikurov AA, Toporkova OA, et al. *Nejrofiziologicheskij intraoperacionnyj monitoring v nejroxirurgii*. St. Petersburg: Spetslit LLC; 2019. (In Russ.).
- Saito T, Muragaki Y, Maruyama T, et al. Intraoperative functional mapping and monitoring during glioma surgery. *Neurol Med Chir (Tokyo)*. 2014;55(1):1–13. DOI: 10.2176/nmc.ra.2014-0215
- Simon MV. Intraoperative neurophysiologic sensorimotor mapping—a review. *J Neurol Neurophysiol*. 2013;4(2). DOI: 10.4172/2155-9562.s3-002
- De Witt Hamer PC, Robles SG, Zwinderman AH, et al. Impact of intraoperative stimulation brain mapping on glioma surgery outcome: a meta-analysis. *J Clin Oncol*. 2012;30(20):2559–2565. DOI: 10.1200/JCO.2011.38.4818
- Dineen J, Simon MV. *Neurophysiological tests in the operating room*. In: Simon MV., ed. *Intraoperative Neurophysiology: A comprehensive guide to monitoring and mapping*. NY: Springer Publishing Company, Demos Medical; 2019:1–57.
- Ulitin AY, Alexandrov MV, Malyshev SM, et al. Efficacy of intraoperative motor mapping for resection of brain tumors located in the central gyrus region. *Russian Neurosurgical Journal Named After Professor Polenov*. 2017;9(1):57–62. (In Russ.).
- Ilmberger J, Ruge M, Kreth F-W, et al. Intraoperative mapping of language functions: a longitudinal neurolinguistic analysis. *J Neurosurg*. 2008;109(4):583–592. DOI: 10.3171/JNS.2008.109.10.0583
- Picht T, Kombos T, Gramm HJ, et al. Multimodal protocol for awake craniotomy in language cortex tumour surgery. *Acta Neurochir (Wien)*. 2006;148(2):127–138. DOI: 10.1007/s00701-005-0706-0
- Simon MV. *An introduction to functional mapping*. In: Simon MV, ed. *Intraoperative Neurophysiology: A comprehensive guide to monitoring and mapping*. NY: Springer Publishing Company, Demos Medical; 2019:235–244.
- Zyryanov A, Zelenkova V, Malyutina S, Stupina E. The contributions of the arcuate fasciculus segments to language processing: evidence from brain tumor patients. *Russ J Cogn Sci*. 2019;6(1):25–37.
- Lesser RP, Lee HW, Webber WRS, et al. Short-term variations in response distribution to cortical stimulation. *Brain*. 2008;131(6):1528–1539. DOI: 10.1093/brain/awn044
- Spena G, Schucht P, Seidel K, et al. Brain tumors in eloquent areas: A European multicenter survey of intraoperative mapping techniques, intraoperative seizures occurrence, and antiepileptic drug prophylaxis. *Neurosurg Rev*. 2017;40(2). DOI: 10.1007/s10143-016-0771-2
- Simon MV, Michaelides C, Wang S, et al. The effects of EEG suppression and anesthetics on stimulus thresholds in functional cortical motor mapping. *Clin Neurophysiol*. 2010;121(5). DOI: 10.1016/j.clinph.2010.01.002
- Szelényi A, Joksimović B, Seifert V. Intraoperative risk of seizures associated with transient direct cortical stimulation in patients with symptomatic epilepsy. *J Clin Neurophysiol*. 2007;24(1). DOI: 10.1097/01.wnp.0000237073.70314.f7
- Spena G, Garbossa D, Panciani PP, et al. Purely subcortical tumors in eloquent areas: Awake surgery and cortical and subcortical electrical stimulation (CSES) ensure safe and effective surgery. *Clin Neurol Neurosurg*. 2013;115(9):1595–1601. DOI: 10.1016/j.clineuro.2013.02.006

СПИСОК ЛИТЕРАТУРЫ

1. Александров М.В., Чикуров А.А., Топоркова О.А., и др. Нейрофизиологический интраоперационный мониторинг в нейрохирургии. СПб.: СпецЛит, 2019.
2. Saito T., Muragaki Y., Maruyama T., et al. Intraoperative functional mapping and monitoring during glioma surgery // *Neurol. Med. Chir. (Tokyo)*. 2014. Vol. 55. No. 1. P. 1–13. DOI: 10.2176/nmc.ra.2014-0215
3. Simon M.V. Intraoperative neurophysiologic sensorimotor mapping—a review // *J. Neurol. Neurophysiol.* 2013. Vol. 4. No. 2. DOI: 10.4172/2155-9562.s3-002
4. De Witt Hamer P.C., Robles S.G., Zwinderman A.H., et al. Impact of intraoperative stimulation brain mapping on glioma surgery outcome: a meta-analysis // *J. Clin. Oncol.* 2012. Vol. 30. No. 20. P. 2559–2565. DOI: 10.1200/JCO.2011.38.4818
5. Dineen J., Simon M.V. Neurophysiological tests in the operating room. In: Simon M.V., ed. *Intraoperative Neurophysiology: A comprehensive guide to monitoring and mapping*. NY: Springer Publishing Company, Demos Medical, 2019. P. 1–57.
6. Улитин А.Ю., Александров М.В., Малышев С.М., и др. Эффективность интраоперационного моторного картирования при резекции опухолей центральных извилин // *Российский нейрохирургический журнал им. проф. А.Л. Поленова*. 2017. Т. 9. № 1 С. 57–62.
7. Ilmberger J., Ruge M., Kreth F.-W., et al. Intraoperative mapping of language functions: a longitudinal neurolinguistic analysis // *J. Neurosurg.* 2008. Vol. 109. No. 4. P. 583–592. DOI: 10.3171/JNS/2008/109/10/0583
8. Picht T., Kombos T., Gramm H.J., et al. Multimodal protocol for awake craniotomy in language cortex tumour surgery // *Acta Neurochir. (Wien)*. 2006. Vol. 148. No. 2. P. 127–138. DOI: 10.1007/s00701-005-0706-0
9. Simon M.V. An introduction to functional mapping. In: Simon M.V., ed. *Intraoperative Neurophysiology: A comprehensive guide to monitoring and mapping*. NY: Springer Publishing Company, Demos Medical, 2019. P. 235–244.
10. Zyryanov A., Zelenkova V., Malyutina S., Stupina E. The contributions of the arcuate fasciculus segments to language processing: evidence from brain tumor patients // *Russ. J. Cogn. Sci.* 2019. Vol. 6. No. 1. P. 25–37.
11. Lesser R.P., Lee H.W., Webber W.R.S., et al. Short-term variations in response distribution to cortical stimulation // *Brain*. 2008. Vol. 131. No. 6. P. 1528–1539. DOI: 10.1093/brain/awn044
12. Spina G., Schucht P., Seidel K., et al. Brain tumors in eloquent areas: A European multicenter survey of intraoperative mapping techniques, intraoperative seizures occurrence, and antiepileptic drug prophylaxis // *Neurosurg. Rev.* 2017. Vol. 40. No. 2. DOI: 10.1007/s10143-016-0771-2.
13. Simon M.V., Michaelides C., Wang S., et al. The effects of EEG suppression and anesthetics on stimulus thresholds in functional cortical motor mapping // *Clin. Neurophysiol.* 2010. Vol. 121. No. 5. DOI: 10.1016/j.clinph.2010.01.002
14. Szelényi A., Joksimović B., Seifert V. Intraoperative risk of seizures associated with transient direct cortical stimulation in patients with symptomatic epilepsy // *J. Clin. Neurophysiol.* 2007. Vol. 24. No. 1. DOI: 10.1097/01.wnp.0000237073.70314.f7
15. Spina G., Garbossa D., Panciani P.P., et al. Purely subcortical tumors in eloquent areas: Awake surgery and cortical and subcortical electrical stimulation (CSES) ensure safe and effective surgery // *Clin. Neurol. Neurosurg.* 2013. Vol. 115. No. 9. P. 1595–1601. DOI: 10.1016/j.clineuro.2013.02.006

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