E.A. Narodova, N.A. Shnaider, E.E. Erakhtin, A.A.Narodov

# POSSIBILITIES FOR CONTROLLING BILATERAL TONIC-CLONIC SEIZURES USING THE APPLICATION EpiTapp® FOR RESISTANT EPILEPSY WITH THE DEVELOPMENT WITH ARTERIOVENOUS MALFORMATION

DOI 10.25789/YMJ.2023.84.33

УДК 616.853-06:[616.133.33+ 616.145.11]-007-053.1:004.42

Patients with drug-resistant epilepsy (DRE) due to an arteriovenous malformation (AVM) located in a functionally significant area of the brain experience a significant decrease in quality of life and require additional non-drug rehabilitation methods aimed at controlling epileptic symptoms.

Aim. To present a clinical observation of the use of the Epi-Tapp® application in a 29-year-old patient with an AVM. Materials and methods. We used the author's wrist tapping method EpiTapp® (RF patent No. 2606489 dated January 10, 2017). Results. Using the EpiTapp® application allowed a 29-year-old man with an AVM to reduce the severity and duration of focal seizures in 85% of cases and prevent secondary bilateral transformation of incipient bilateral tonic-clonic seizures in more than 50% of cases. Conclusions. This clinical case demonstrates the possibility of effectively using the EpiTapp® application in a patient with drug-resistant epilepsy as an element of a rehabilitation program aimed at controlling epileptic seizures.

**Keywords:** epilepsy, wrist tapping, EpiTapp®, rehabilitation.

**Introduction.** Arteriovenous malformations (AVMs) are congenital vascular anomalies that result from shunting between high-capacity arteries and low-capacity venous vessels, forming a dysplastic vascular lesion in the brain parenchyma [10]. The prevalence rate of cerebral AVMs in the population varies from 1.12 to 1.42 cases per 100 thousand population. However, one of the most common complications of all primary brain AVMs (up to 68% of cases) is hemorrhage [8]. The second most common complication of AVM, which occurs in 20–45% of patients, is the development of structural focal epilepsy (SFE). The mechanisms of occurrence of epilepsy in AVM are diverse. On the one hand, epileptic seizures can develop directly as a result of hemorrhages and hemosiderosis, on the other hand, the cause may be the phenomenon of vascular brain steal [5]. The absolute indications for invasive treatment of AVM are hemorrhage due to rupture of the malformation. The issue of treatment of unruptured AVMs is still controversial. In neurosurgical practice, the classification according to Spetzler-Martin (1986) (Table 1) is widely used, which allows one to assess the possible risk of surgical intervention.

Today, symptomatic therapy and observation, endovascular embolization, microsurgical removal of the malformation and radiosurgery are used to treat patients with AVMs. The opinions of neurosurgeons often differ on the tactics of managing patients with AVMs. According to some experts, patients with AVM always require surgical intervention, other experts choose conservative treatment tactics, and others argue that this group of patients should simply be observed, since the risk of negative consequences

**NARODOVA Ekaterina Andreevna** – Candidate of Medical Sciences, Associate Professor of Voino-Yasenetsky Krasnoyarsk State Medical University, Krasnoyarsk, eLibrary.EN SPIN: 9353-6628. http://orcid.org/0000-0002-6184-9206 , katya_n2001@mail.ru; **SCHNAIDER Natalia Alekseevna** – Doctor of Medical Sciences, Professor, head of Scientific Research, Deputy Head of the Institute of Personalized Psychiatry and Neurology of the Federal State Budgetary Institution Bekhterev National Medical Research Centre for Psychiatry and Neurology of the Ministry of Health of the Russian Federation, St. Petersburg, eLibrary.RU SPIN:6517-0279, http://orcid.org/0000-0002-2840-837X, nascnaider@yandex.ru; **ERAKHTIN Evgeny E.** – neurosurgeon of Karpovich Krasnoyarsk Interdistrict Clinical Hospital of Emergency Medical Care, eepn2014@gmail.com; **NARODOV Andrey Arkadyevich** – MD, Professor, Voino-Yasenetsky Krasnoyarsk State Medical University, Ministry of Health of the Russian Federation, eLibrary.RU SPIN: 781225. http://orcid.org/0000-0001-7384-0682, narodov_a@mail.ru.

**Table 1**

**Classification of AVM (according to Spetzler-Martin, 1986)**

| | |
|---|---|
| *To size:*<br>Less than 3 cm – 1 point<br>3 – 6 cm – 2 points<br>More than 6 cm – 3 points<br><br>*By localization:*<br>Outside the functionally significant zone* – 0 points<br>Within a functionally significant area – 1 point<br><br>*ABM division by nature дренирования:*<br>Absence of deep draining veins – 0 points<br><br>Presence of deep draining veins** – 1 point | Using this classification, most neurosurgeons determine the degree of operability of the malformation.<br>There are 5 gradations of malformation: with gradation I (1 point), the risk of surgical intervention is insignificant, with gradation V (5 points), great technical difficulties arise, and the risk of severe disability and death is high. |

* Functionally significant areas - sensorimotor area, Broca's and Wernicke's centers, occipital lobes, thalamus, deep structures of the temporal lobe, brainstem.
** Deep venous collectors are draining veins that flow into the system of the great cerebral vein, the straight sinus.

Table 2

**Study design of the author's EpiTapp® wrist tapping method in patient A. 29 years old**

| Event | Visit 1 randomization | Visit 2 inclusionin the study | Visit 3 in 3 months | Visit 4 via 6 months |
|---|---|---|---|---|
| Anamnesis of life | + | - | + | + |
| History of the disease | + | - | + | + |
| Analysis of the seizure diary | + | + | + | + |
| Neurological examination | + | + | + | + |
| EEG video monitoring | + | - | - | + |
| MRI of the brain according to the Epilepsy protocol | + | - | - | - |
| Therapeutic drug monitoring of AEDs in the blood | + | - | - | - |
| Scale for assessing the quality of life of patients with epilepsy "Quality of life in epilepsy - QOLIE - 31" | - | + | + | + |
| Author's scale for assessing the effectiveness and safety of EpiTapp® "Research on the effectiveness of the EpiTapp® wrist tapping method" | - | - | + | + |
| EpiTapp® training | - | + | - | - |
| EpiTapp® session | - | + | + | + |

of using any invasive treatment methods exceeds the risks natural course of the disease [9]. It is known that all methods of invasive treatment are aimed at completely eliminating the AVM from the bloodstream in order to eliminate the risk of hemorrhage, eliminate the phenomenon of brain stealing, reduce or regress neurological deficit, and control epileptic seizures [3]. The literature describes data that total shutdown of the AVM using open surgery provides effective control over epileptic seizures with seizure freedom in more than 70% of cases [4]. Considering the fact that structural epilepsy in patients with AVMs is almost always pharmacoresistant, which is associated with the presence of a functioning AVM, the only and most effective way to treat this disease is total resection neurosurgical treatment. However, when an AVM is localized in a functionally significant area (3 - 5 points on the Spetzler-Martin grading scale), great technical difficulties may arise during invasive intervention, and the risk of profound disability and death increases. Thus, this group of patients experiences a significant decrease in quality of life due to drug-resistant epilepsy and needs additional non-drug rehabilitation methods aimed at being able to control epileptic seizures.

The goal is to present a unique clinical observation demonstrating the ability to control bilateral tonic-clonic seizures using the EpiTapp® application in

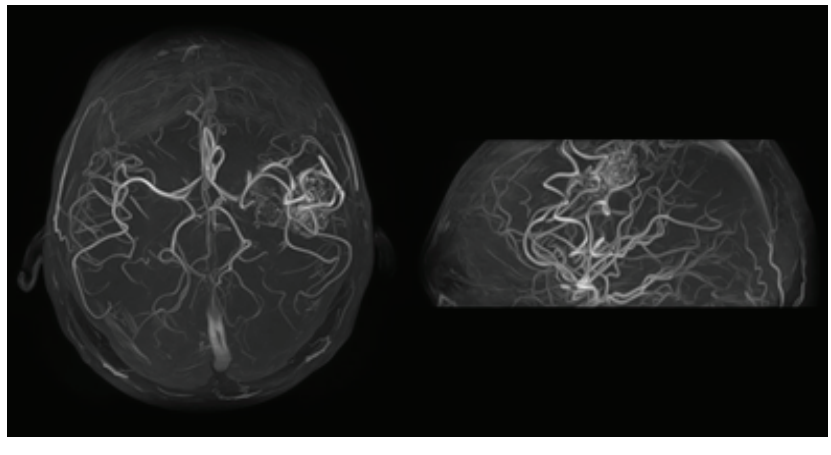

**Fig. 1.** Magnetic resonance angiography of the brain of patient A. (29 years old): AVM in the territory of the left middle cerebral artery

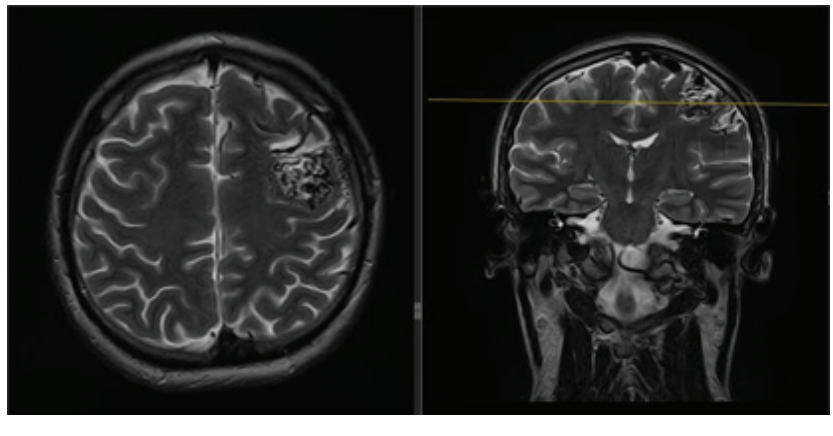

**Fig. 2.** Magnetic resonance imaging of the brain of patient A. (29 years old): Condition after partial embolization of AVM.

a 29-year-old patient with drug-resistant structural focal epilepsy that developed against the background of an AVM located in a functionally significant area of the cerebral cortex.

**Materials and methods.** The work used the author's wrist tapping technique (RF patent No. 2606489 dated January 10, 2017) in the form of the EpiTapp® application for a smartphone. The patient regularly used the EpiTapp® application as an outpatient SFE rehabilitation during the onset of a focal motor hemifacial seizure, or during the focal onset of a bilateral tonic-clonic seizure. Previously, the patient underwent an electroencephalographic study (EEGA - 21/24, elite version "Encephalan - 131 - 03", modification 10 and 11 (Russia) with three-dimensional localization of sources of epileptiform activity (Brain Loc)) and training by a neurologist - epileptologist in the use of the EpiTapp® application on your own at home. The study also used: the quality of life scale in epilepsy - QOLIE - 31 and the effectiveness scale of the author's wrist tapping technique.

**Research procedure.** The patient was installed the EpiTapp® application on a mobile device based on Android OS. The patient then completed three self-calibration tests to automatically configure the application in a therapeutic self-help mode. During the onset of the first signs of an incipient epileptic seizure, the patient independently launched the application and tapped the index or middle finger of the subdominant (left) hand on the smartphone screen, simultaneously with the automatic delivery of sound and vibration signals by this device, programmed by the attending physician in rhythm mode healthy person (1.13 Hz) without epileptic seizures [6].

The design of the present study included 4 patient follow-up visits (Table 2).

**Ethical considerations.** The conduct of this study was approved by the local ethical committee of the Krasnoyarsk State Medical University named after Professor V.F. Voino-Yasenetsky, Krasnoyarsk (protocol No.77/2017 dated June 26, 2017). The patient signed a voluntary informed consent before starting the study. The patient did not receive any remuneration for participating in this study. The researchers did not receive any remuneration for conducting this study.

**Results and discussion.** Patient A. at the age of 15 (2009) underwent surgical neurosurgical intervention for a malignant neoplasm (astrocytoma) of the brain. After this, he underwent annual control magnetic resonance imaging of the brain (MRI brain). In 2015, during a routine MRI of the brain, an AVM was discovered in the territory of the left middle cerebral artery (Figure 1). Considering the location of the AVM in a functionally significant area (left frontal and parietal lobes of the brain) of grade III according to Spetzler-Martin, the patient was denied open-access neurosurgical treatment.

In 2018, patient A., aged 24 years, was consulted by neurosurgeons in Novosibirsk. The patient was offered staged partial embolization of the AVM. A year later, in 2019, the first stage partial embolization of AVM occurs. From 2019 - 2022 The patient underwent a total of six staged partial embolizations. At the beginning of July 2022, the last, 6th embolization occurred, after which the patient was recommended for further radiosurgical treatment (Figure 2).

At the end of July 2022, the first focal motor hemifacial epileptic seizure develops. On September 15, 2022, the first bilateral tonic-clonic seizure (BTCS) occurs. Two weeks later, the patient's

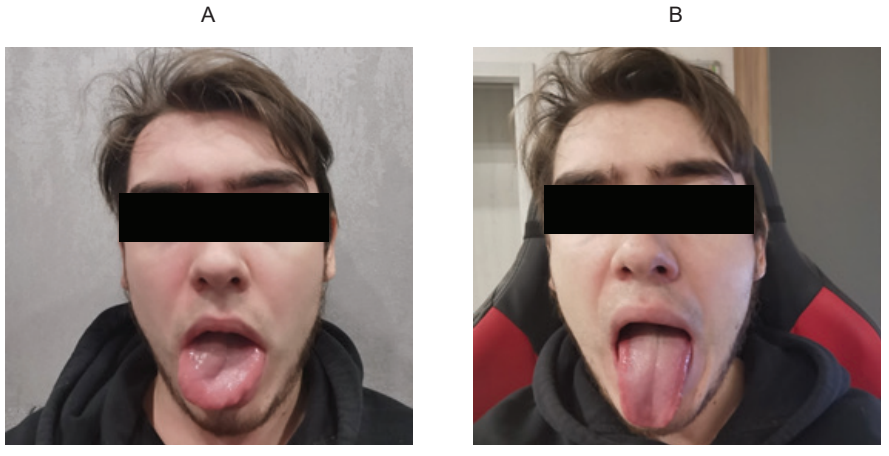


**Fig. 3.** Todd paresis of the tongue muscles after a focal motor hemifacial epileptic seizure: A – immediately after the seizure; B – 15 minutes after the seizure.


**Fig. 4.** Use of the EpiTapp® application by patient A. (29 years old) at home, as an element of urgent self-help in the event of BTCS with focal motor hemifacial onset in the right half of the face: A – onset of focal motor hemifacial seizure; B – stopping an seizure using the EpiTapp® application

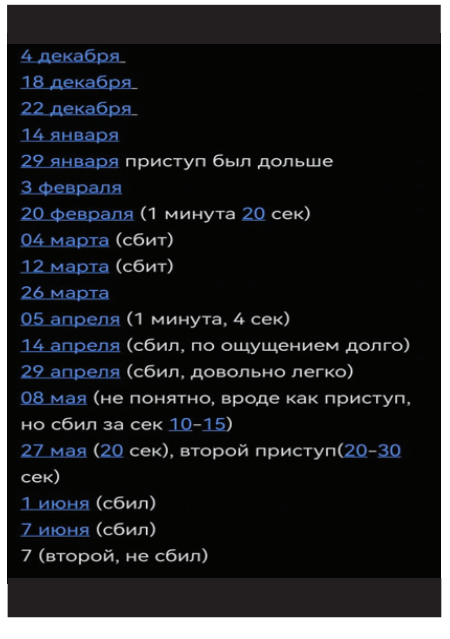


**Fig. 5.** Fragment of the seizure diary provided by patient A. after adjusting the antiepileptic therapy regimen and starting to use the EpiTapp® application

health worsens, repeated BTCS develops, and hemifacial and focal motor seizures become daily. In this regard, patient A. was consulted by an epileptologist with subsequent prescription of antiepileptic therapy (valproic acid 1000 mg per day). No obvious positive effect was observed. Frequent focal motor and bilateral tonic-clonic seizures bothered the patient daily (up to 3-4 times a day), the patient's quality of life and ability to work decreased significantly. Thus, according to the analysis of the results of the questionnaire on the "Quality of Life in Epilepsy - QOLIE - 31" scale as modified by the authors (Narodova E.A. et al. 2021), patient A. had a significant decrease in quality of life due to epilepsy (4 points according to five-point subscale, where 5 points is the worst result). The man rated his health status low (12 points on a 100-point subscale, where 100 points is the best result). Frequent epileptic seizures did not allow the patient to engage in usual work activities, despite the fact that, as a professional programmer, he had the opportunity to work at home.

In October 2022, the patient underwent repeated radiological treatment, after which his dose of valproic acid was increased to 1250 mg per day, and a new generation drug was added - perampanel at a dose of 6 mg per day (with slow titration). Against this background, positive dynamics were observed. However, BTCS continued to bother the patient up to 4 times a month. The focal onset at this time was short-lived (up to 3 seconds) and the patient did not have time to take measures aimed at preventing trauma against the background of the subsequent development of a generalized tonic-clonic seizure. The patient also continued to have frequent focal motor seizures up to 5-10 times a week (Figure 3).

In February 2023, at an appointment with an epileptologist, it was decided to add disease-modifying therapy (Dibufelon at a dose of 400 mg per day, followed by an increase to 800 mg per day according to the regimen) [2], [7], [1] , and also recommended the use of the EpiTapp® application at the first signs of an incipient focal seizure as a rehabilitation program for the self-management of epileptic seizures.

According to the inclusion/exclusion criteria, the patient was included in the study. The date the patient started using the application is February 18, 2023. The duration of using the technique is 7 months. The patient used the EpiTapp® application for focal motor seizures as emergency self-help (at home, on the street, in transport, in a store).

After just a week of regular use of the EpiTapp® application, the patient was able to stop an incipient focal motor seizure. Moreover, against the background of correction of drug therapy, already after 2 weeks the patient experienced a change in the nature of the BTCS, in the form of a lengthening of the focal motor onset. Therefore, the patient was advised to actively use the EpiTapp® app not only during focal seizures, but also during focal motor onset of BTCS (Figure 4).

Figure 4 - Use of the EpiTapp® application by patient A. (29 years old) at home, as an element of urgent self-help in the event of BTCS with focal motor hemifacial onset in the right half of the face: A – onset of focal motor hemifacial seizure; B – stopping an seizure using the EpiTapp® application.

According to the diary of self-observation of seizures, the patient was able to stop the incipient BTCS at the stage of focal onset in more than 50% of cases, which significantly improved the patient's quality of life (Figure 5).

**Discussion.** At visit 4 (6 months from the start of using the EpiTapp® application), according to the study design, patient A. was given a final survey on the scale of the effectiveness and safety of the author's wrist tapping method. Analysis of the data obtained showed that while using the application, the patient noted an improvement in quality of life by 58% due to the ability to stop vocal seizures (FS) and prevent the development of BTCS in more than 50% of cases. In this regard, the patient was able to return to work, and it became possible to work not only at home, but also to travel to the office. In 85% of cases, the patient was able to stop an incipient focal seizure, reducing its severity and duration.

**Conclusion.** Thus, the use of the EpiTapp® application allowed a young man with treatment-resistant FES to reduce the severity and duration of focal seizures in 85% and in more than 50% of cases to prevent secondary bilateral transformation of incipient BTKP. This clinical example demonstrates the possibility of effective use of the EpiTapp® application in a patient with drug-resistant structural focal epilepsy associated with an AVM as an element of a rehabilitation program aimed at controlling epileptic seizures.

## Reference


1. Yakovlev A.A. [et al.] Antiepileptogennye effekty fenozanovoj kisloty (Dibufelon) na modeli hronicheskoj fokal'noj epilepsii [Antiepileptogenic effects of phenosanic acid (Dibufelon) on a model of chronic focal epilepsy. VolgaMedScience. 2022; 673-675 (In Russ.).]

2. Balimchuk E.V., Kovalenko N.V. Razrabotka strategii prodvizheniya novogo lekarstvennogo preparata na farmacevticheskom rynke na os-nove swot analiza (na primere OOO" PIK-FARMA") [Development of a strategy for promoting a new drug on the pharmaceutical market based on swot analysis (using the example of PIK-PHARMA LLC). INTERNAUKA Founders: Limited Liability Company 'Inter-nauka'. P. 35-37 (In Russ.).]

3. Burd S.G. [et al.] Klinicheskie rezul'taty i perspektivy primeneniya fenozanovoj kisloty u vzroslyh pacientov s fokal'noj epilepsiej [Clinical results and prospects for the use of phenosanic acid in adult patients with focal epilepsy]. Zhurnal nevrologii i psihiatrii im. SS Korsakova [Korsakov Journal of Neurology and Psychiatry. 2021; 121(10): 52-9 (In Russ.).]

4. Narodova E.A., Schnaider N.A., Karnaukhov V.E. Opyt primeneniya prilozheniya EpiTapp pri strukturnoj fokal'noj epi-lepsii [Experience of using the EpiTapp application for structural focal epilepsy]. Epilepsiya i paroksizmal'nye sostoyaniya [Epilepsy and paroxysmal conditions. 2021;13(4):367-376 (In Russ.).] https://doi.org/10.17749/2077-8333/epi.par.con.2021.066

5. Krivoshapkin A.L., Orlov K.Yu., Brusyanskaya A.S., Sergeev G.S., Gaitan A.S., Simonovich A.E. Rezul'taty invazivnogo lecheniya bol'nyh s epilepticheskim tipom techeniya arteriovenoznyh mal'formacij golovnogo mozga [Results of invasive treatment of patients with the epileptic type of arteriovenous malformations of the brain]. Sibirskij nauchnyj medicinskij zhurnal [Siberian Scientific Medical Journal. 2018. No. 6. (In Russ.).] URL: https://cyberleninka.ru/article/n/rezultaty-invazivnogo-lecheniya-bolnyh-s-epilepticheskim-tipom-techeniya-arteriovenoznyh-malformatsiy-golovnogo-mozga

6. Krivoshapkin A.L., Melidy E.G. Microsurgery for cerebral arteriovenous malformation management: a Siberian experience. Neurosurg. Rev. 2005. 28. (2). 124–130

7. Krivoshapkin A., Orlov K., Brusyanskaya A., Berestov V., Gaytan A., Sergeev S. Is first line embolization and subsequent microsurgery a solution to control seizures in patients with cerebral AVMs or not? Controversies and solutions in neurosurgery: abstr. congr., Venice, October 1–5, 2017. Venice, 2017.598

8. Abecassis I.J., Xu D.S., Batjer H.H., Bendok B.R. Natural history of brain arteriovenous malformations: a systematic review. Neurosurg. Focus. 2014 E7

9. Arteriovenous malformations. The Neurosurgeon's Handbook / Ed. G. Saman-douras. Oxford Univ. Press, 2010. 588–598

10. Soldozy S, Norat P, Yağmurlu K, Sokolowski JD, Sharifi KA, Tvrdik P, Park MS, Kalani MYS. Arteriovenous malformation presenting with epilepsy: a multi-modal approach to diagnosis and treatment. Neurosurg Focus. 2020 Apr 1;48(4):E17. doi: 10.3171/2020.1.FOCUS19899. PMID: 32234990