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Chapter

The Role of Nondrug Treatment Methods in the Management of Epilepsy

Natalia Shnayder, Ekaterina Narodova, Valeriya Narodova, Andrey Narodov and Evgeniy Erakhtin

Abstract

The review is devoted to the issue of nondrug epilepsy treatment in the adult population in Russia and abroad. The conducted literature review allowed us to reveal the basic nondrug epilepsy treatment options. However, not all of these options have a sufficient evidence base, and some of them are not always safe. Particularly, methods with low level of evidence include acupuncture and aromatherapy. Further studies are needed to explore the methods aimed to eliminate the epileptic system dominant through the development of a new, more powerful dominant. One of the methods, which can influence the pathogenesis of epilepsy, is physical activity for patients with epilepsy, since epileptiform activity on the EEG is reported to disappear during exercises. The positive results of the application of art therapy (music therapy) are also described in the modern literature. Tempo-rhythm correction methods hold a specific place in neurorehabilitation. There are considerable amount of studies concerning the application of tempo-rhythmic methods in neurology and psychiatry. It can be concluded that these methods are relevant worldwide and can be used in diagnostics and correction of neurological and psychiatric diseases (such as schizophrenia, Parkinson's disease, epilepsy).

Keywords: epilepsy, adults, nonpharmacological treatment, review, tapping

1. Introduction

According to the world statistics, epilepsy takes the third place among overall morbidity after cardiovascular diseases and diabetes mellitus and the third place in neurological morbidity [1]. Therefore, epilepsy is a relevant public health problem both in Russia and abroad [2]. This fact fosters the development and implementation of medicinal and alternative (nondrug) methods of epilepsy treatment around the world. However, current epilepsy treatment options allow achieving remission or reducing the number of seizures only in 60–70% of patients [3].

An important problem of epileptology is ensuring the safety and acceptability of the treatment as well as prevention of adverse drug reaction (ADR) of antiepileptic drugs (AEDs). The emergence of the ASEs can often decrease patients' life quality, thereby offsetting the positive effect of the treatment. Moreover, such ASEs as depression and anxiety (the fear of the coming seizure) may aggravate epileptic seizures [4]. Some ASEs are associated with the AEDs' effects on the liver enzymes.

These effects cause induction or inhibition of the liver enzymes, making other AEDs displaced from protein linkages. These reactions increase the rate of metabolism and cause the reduction of the plasma concentration of ADRs, which may lead to difficulties in the choice of AEDs' dosage. On average, the frequency of ASEs and complications of antiepileptic therapy remains high and varies, according to different authors, from 7 to 25% [5–7].

Therefore, the presence of ADRs requires the immediate withdrawal of AEDs, even if the drug-induced epilepsy remission is achieved. It should be noted that 40% of epileptic patients need polytherapy. This leads to the increase in the ADRs' frequency, adverse drug-drug interactions, and teratogenicity [8]. Also, there are difficulties in assessing the effectiveness of ADRs of a single drug. Drug-drug interactions often decrease antiepileptic treatment efficiency and contribute to the development of ADRs [2, 9, 10].

Consequently, nondrug methods of epilepsy treatment should also be used, both as an additional therapy and (in some cases) as the basic therapy (e.g., vagus nerve stimulation) (see **Table 1**).

The principle of the dominant was introduced in neurophysiology by the outstanding Russian physiologist Uchtomsky in 1911 [11]. Under "the dominant" he meant the dominant reflex system, which determines the integral nature of the functioning of the nerve centers in any period of time and ensures the appropriate behavior of animal and human. He also described the dominants' properties, the main of which were increased excitability, the ability to summation, high resistance, and inertia of excitation. Also, a theory of pathological dominant was suggested. Within this theory, pathological dominant represents sharply enhanced focus of excitation in the central nervous system, caused by "pathogenic effects of the environment."

Later, in 1980, Kryzhanovskii developed the doctrine of "pathological determinant." The latter was described as a "modified formation of the central nervous system, forming a pathological system and determining the nature of its activities" [12]. According to this doctrine, the determinant can form a pathological system in the central nervous system. The feature of the pathological system is the ability to suppress the physiological system. Such pathophysiological mechanisms underlie most neurological disorders. Kryzhanovskii proposed a mechanism of fighting the pathological dominant by introducing another, more powerful dominant [13]. A significant part of the research dedicated to the hand tapping is based on this mechanism.

According to Rudnev, the cyclical nature of movements in wrist tapping is a natural statistical regularity that is a standard you can compare different parameters

Noninvasive methods	Invasive methods
Physical activity	Vagus nerve stimulation
Transcranial magnetic stimulation	Deep brain stimulation
Psychotherapy	Percutaneous stimulation of the trigeminal Nerve
Music therapy	Surgery
Aromatherapy	
Acupuncture	
Referential bioadaptation	
Tapping	

Table 1.
Nondrug methods of epilepsy treatment.

to. Consequently, the study of these biologically appropriate movements makes it possible to establish a pattern of certain rates and rhythms that occurs in the pathology at different levels of the human nervous system [14].

2. Results and their discussion

2.1 Nonpharmacological noninvasive therapy

2.1.1 Psychotherapy

Currently, it is the practice to distinguish three fundamental categories of psychotherapeutic techniques, used in epileptology: rewards/sanctions, self-control, and neurofeedback. "Rewards/sanctions" and "self-control" categories are used for self-induced seizures and for so-called reflective attacks as well as for epileptic seizures, amplifying under the influence of emotional factors. Neurofeedback is a nonpharmacological method of epilepsy treatment with objective registration, amplification, and "feedback" of physiological information to the patient. This method is based on the principle of self-identification of one's own EEG data.

Based on the information from different authors, using neurofeedback can lead to a great reduction in the number of seizures in 50% cases of patients with epileptic risk factors. From this 50%, in 10% of cases, it is possible to completely discontinue AEDs without reappearance of epileptic seizures for 2–3 years and more, and in the remaining 40–50% of cases after the use of the neurofeedback method, it is possible to have pharmacological treatment [15].

2.1.2 Art therapy

There are also art therapy options for epilepsy treatment. For example, there is an actively developing method, based on the creation of therapeutic music to reduce the number of epileptic seizures. This method is based on the theory that epileptic seizures occur because of abnormal synchronization of the brain's electric activity, and the majority of them stop spontaneously. The effect of structured auditory stimuli provides noninvasive galvanic cortex stimulation, which can reduce epileptiform activity [16].

To prove this hypothesis, authors conducted a randomized research, which explored the effectiveness of music therapy for patients diagnosed with epilepsy [17]. Patients were exposed to Mozart's music every night for 1 year. Based on the results of the research, a 17% reduction in the number of epileptic seizures was noticed. The achieved effect remained stable during the next year [18, 19]. In another randomized research, which studied both children and adult patients with epilepsy, it was revealed that 85% of patients had a positive response to music therapy with an average reduction of epileptiform activity index by 31% during the music listening and by 24% after it [20–28].

2.1.3 Aromatherapy

Aromatherapy can be useful (for achieving a state of relaxation) as a component of epilepsy behavioral treatment. However, its use is more justified for the treatment of conditions, accompanying epilepsy, such as anxiety and depression. In the application of aromatherapy for patients with epilepsy, camphora, sage, and rosemary should be avoided because these substances are known to aggravate patients' condition and increase the number of epileptic seizures [10].

In Asia-Pacific region, they actively use acupuncture as a nonpharmacological method of epilepsy treatment. There is data on the use of acupuncture for patients with stroke in order to avoid poststroke epilepsy. Weng et al. showed that patients with stroke receiving acupuncture had significantly less probability of poststroke epilepsy compared to those who did not receive such treatment ($p < 0.0001$). However, defensive effects, associated with acupuncture, need further exploration [29].

Some authors report neuroprotective, anti-inflammatory, and neurotrophic effects of acupuncture and electroacupuncture. These effects are explained by the amplification of recurrent inhibition of the brain cortex and hippocampus with the liberation of different neurotransmitters, including gamma-aminobutyric acid (GABA) and serotonin. However, due to the lack of controlled clinical trials, those methods cannot be recommended as reliably effective and safe in epileptology [30].

2.1.4 Physical activity

Patients with epilepsy experience a range of social restrictions, leading to their external and internal stigmatization. These limitations include the employment problem, driving prohibition, and restriction of *physical activity*. However, it is a well-known fact that physical exercises lead to better functional adaptation [31]. Patients with epilepsy, involved in sport, can receive the same benefits of physical activity as healthy people, including increase in performance efficiency and tolerance, weight loss, and cardiovascular system functioning normalization. Physical activity is also a critical factor in reducing the risks of diabetes mellitus, arterial hypertension, coronary heart disease, obesity, and osteoarthritis. As for psychological advantages, the research in this field found out that physically active patients have better mental health than those leading a sedentary lifestyle [32–34].

Physical activity in early age can cause neuronal reserve's formation, which then will be used during the life course. Consequently, physically active patients have lower risk of developing cognitive impairments associated with epilepsy [35, 36].

Preventive and curative effect of the physical activity in case of epilepsy can be achieved in accordance with several principles, including the principles of consistency, regularity, duration, monitoring, and personalization of the training load. Despite this, it is believed that enhanced muscular activity is accompanied with tachypnea (hyperventilation), which can initiate the seizures.

However, some authors claim that physical activity can reduce the likelihood of seizures. Usually, seizures do not occur while running, swimming, ice skating, skiing, crossing the crowded street, as well as during sport events, although this issue is disputable. On the other side, it is reported that seizures often start when patients are relaxed or sleeping.

The described fact accounts for the development of new dominant excitation areas in the central nervous system (CNS) during vigorous exercises. Due to the negative induction, these areas slow down or inhibit the epileptic area activity, therefore preventing seizure occurrence. It is reported that during physical exercises seizures occur much more rare than during relaxation [31]. The disappearance of epileptiform activity in many patients' EEG during the physical activity proves this theory [37–40].

2.1.5 Ketogenic diet

Ketogenic diet (KD) is a high-fat and low-carbohydrate diet that induces ketosis. Ketosis is a metabolic state where the body uses ketone bodies, made from the breakdown of fatty acids in the liver, rather than carbohydrates as primary source of energy. The classical KD has a fat to carbohydrate plus protein ratio of 3–4:1. Additionally, classical KD can be supplemented with either long- or medium-chain

triglycerides (LCT or MCT) to maintain the appropriate ratio and improve effectiveness. The diets appear to be highly effective as 36–85% of the patients with epilepsy experience more than 50% seizure reduction when on KD [41]. Multiple epileptic syndromes, such as glucose transporter 1 (GLUT1) deficiency, are especially responsive to KD [42].

2.1.6 Tapping

Tapping is a psychomotor test that can be used to assess the psychophysiological brain functions, in particular the time perception**.** Tapping without any external influence reflects the speed of nervous processes and endogenous rhythmic processes of the central nervous system since tapping with the preferred test speed represents a "biological constant" [43, 44].

However, in case of exogenously defined long-term reproduction of the rhythmic intervals, the frequency of stimulation is of importance. A number of studies revealed association between the frequency of exogenous stimulation in case of tapping and body response. Specifically, if stimulation is more than 1 Hz, the leading value is the reaction to time, and at a stimulation frequency less than 1 Hz, the reaction to the stimulus prevails. Therefore, at the frequency of exogenous stimulation of 1 Hz, both reactions acquire an equivalent value.

Despite the long-standing interest in tapping, new developments in this area constantly appear. This is due to the fundamental principles of this technique. In this case we are talking about the doctrine of dominants.

Therefore, tempo-rhythm correction methods hold a specific place in neurorehabilitation. Prototypical techniques of such therapy include movement therapy, music therapy, and logopedic rhythmics [43].

One of the methods of studying the typological features of the nervous system is the "tapping test." The essence of the classical tapping test technique is the application of pencil points on an A4 sheet of paper, pre-drawn into six squares, with the maximum allowable speed. The movement from square to square is carried out by command every 5 seconds, from left to right clockwise [45].

Tapping test is widely used to study the effect of sleep duration on the level of anxiety of different groups of patients [46, 47].

The technique of meridian tapping [or the emotional freedom technique (EFT)] is used as a clinical procedure to alleviate the psychological and physical suffering of the patient. This method is described as "tapping" and is often combined with other nondrug techniques aimed at relieving patient's emotional stress. Such techniques may include acupuncture and aromatherapy. The EFT includes finger tapping on certain points on the face and hands. More than 60 research articles in various journals report 98% of the effectiveness of this technique in various patients with psychological disorders (such as post-traumatic stress disorder, phobias, anxiety, depression), as well as in patients with various somatic diseases (asthma, fibromyalgia, pain, epilepsy). The advantages of this method are its simplicity and safety. Patients can easily learn this technique and use it as a self-help in various pathological conditions. Also, this technique is used by nurses for patients undergoing inpatient treatment [48].

To study neural mechanisms, lying in foundation of rhythm reproduction, authors conducted an EEG during the tapping test. All subjects were divided into two groups of those who were previously trained and those who were not. EEG analysis showed that beta-rhythm in temporal and hippocampal areas in those who were trained beforehand was higher than in those who were not trained. More than that synchronization between frontal and temporal and hippocampal areas on later training stages was higher than on earlier stage. These results show that frontal,

temporal, and hippocampal beta-neuron schemes can be studied with auditory motor rhythm [49].

In other studies, it was concluded that the decrease in beta-rhythm in temporal areas is connected with rhythmic movements (in this case, rhythmic hand movements) [50]. It is also supposed that temporal areas play an important role in rhythm reproduction, correlating with frontal areas and basal ganglia, forming a link between auditory stimulus and motor response [51]. It is proven that the hippocampus is connected with the processing of rhythmic information. Moreover, EEG showed the beta-fluctuation in the cerebellum during the processing of sensorimotor information [52].

2.1.7 Transcranial magnetic stimulation

Low-frequency rhythmic transcranial magnetic stimulation (rTMS) leads to a decrease in the cerebral cortex neuronal excitability, while high-frequency rTMS increases their excitability [2]. The mechanisms of rTMS are related to its ability to cause long-term effects of postsynaptic inhibition in excitatory neurotransmitter systems and neuronal excitability reduction through inactivation of the voltage-dependent ion channels [53].

2.2 Nonpharmacological invasive therapy

2.2.1 Percutaneous stimulation of trigeminal nerve

Percutaneous stimulation of trigeminal nerve is a minimally invasive method which is based on exposure of the first trigeminal nerve's branches to electricity. To implement this method in practice, a special system is used which consists of external electric impulse generator and electroconductive plasters. There are few studies which report the use of this method, but most of them consider this method to have a positive clinical effect. During preliminary clinical trials, 57% of patients noticed a 50% or more reduction in the number of seizures [54].

2.2.2 Vagus nerve neurostimulation

Vagus nerve neurostimulation (VNS) is one of the nondrug epileptic treatment methods. The principle of this method is in the chronic electrical stimulation of the left vagus nerve, using an implantable stimulator [55]. The primary candidates for the application of this method are patients with drug-refractory epilepsy (DRE), who cannot get resection surgery.

The main contraindications for this method are pregnancy and lactation, cardiac arrhythmia, bronchial asthma, chronic obstructive pulmonary disease, acute peptic and duodenal ulcer, vasovagal syncope, and type 1 diabetes [56]. Against the background of VNS therapy during the period from 3 months to 3 years, a complete cessation of seizures was revealed in 4.8–17.6% of patients. The decrease in the number of seizures by 50% or more was detected in 27.3–47% of patients, while the decrease in the number of seizures by less than 50% was detected in 23.5% of patients [57–59].

2.2.3 Deep brain stimulation

Deep brain stimulation is an effective therapeutic method for DRE treatment, especially for temporal lobe epilepsy. Thus, according to a randomized study, assessing the effectiveness of hippocampal stimulation in patients with temporal lobe DRE, positive effect in the form of complete disappearance of seizures was found in 50% of patients [60]. According to other studies, it was shown that after

11 years of deep brain stimulation, the attacks were not registered for at least 12 months in only 13.8% of the patients [61].

The principle of this method is in electrode implantation into certain brain structures (target structures), these electrodes being supplied with low-voltage and high-frequency electric current. Due to the impulses, generated by the neurostimulator, the selected brain structures change their functions. Thus, this high-frequency stimulation of the target structures allows reducing the severity of the symptoms and the amount of AEDs taken by the patients as well as bringing the patient back into the society [56].

3. Conclusion

Based on the conducted literature review results, it can be stated that an adequate number of Russian and foreign studies of the analyzed period are dedicated to nonpharmacological epilepsy treatment. Both methods with proven clinical effectiveness and low-reliable treatment options were found in the studied literature.

Most of the authors emphasize a positive influence of physical activity on epileptic patients, including prevention of epileptic seizures. Besides, physical activity is reported to have a positive influence on patients' psychic function, preventing cognitive disorders. However, up until now, physical exercises as an additional therapy are not included in any treatment program for patients with epilepsy. The analysis of the literature showed that it is due to the current concern of neurologists and epileptologists over the occurrence of epileptic seizures in state of hyperventilation.

Those concerns are not unfounded, because hyperventilation can provoke epileptic seizures in a certain group of patients with epilepsy. As a result, it is reasonable not to ban physical activity for all epileptic patients but to limit its intensity for the group of patients, in whom hyperventilation can provoke epileptic seizures. Meanwhile, the fact is reported that during physical exercising the reduction of epileptiform activity occurs on the epileptic patients' EEG. There are also works that prove a positive effect of music therapy, but the issue is still underinvestigated.

All the options for nonpharmacological epilepsy treatment, represented in the present review, are based on the classical theory of Kryzhanovskii about creation and destruction of pathological systems [62]. The author noted that on early stages of the disease the elimination of pathological determinant leads to liquidation of pathological (and, as a result, epileptic) system.

On late stages the fixation of pathological system leads to chronization of pathological process and corresponding neural disorders. The battle with pathological systems, especially with those with complicated and matured forms, is hard and is not always effective. It requires a complex pathogenetic therapy, focused on elimination of pathological determinant (e.g., the elimination of epileptic focus) and normalization of other links of the pathological system. Activation of antiepileptic system, amplification of overall control, and other genetic mechanisms are important as well. It is also known that there is a constant countdown in living system, on which homeostasis is based [63].

According to the theory of Rudnev [14], the so-called internal time is a genetic core of any motor activity, having both populations' and individual characteristics. Internal time is expressed as an individual rhythm. A lot of studies explore individual rhythm, its "maturation" in late ontogenesis, as well as its breaking in different cases of neural disorders [64]. Individual rhythm is a reflection of harmony of brains' work, and its breaking is a sign of disintegration in brain's work. Since there is an established fact that in case of epilepsy a pathological activation of

brains' neurons occurs, which is a stress for central neural system, it is possible that the epileptic system occurrence can change patients' individual rhythm.

In reproduction of tapping, there are different brain structures concerned, such as the cerebellum. Taking into account the fact that the cerebellum is an antiepileptic device, its activation during tapping can have a therapeutic effect on epileptic patients. Tempo-rhythm studies focused on epileptic patients could be used for the development of new rehabilitative methods. As a fundamental support of this theory, exploration of dominants involving the opportunity to work out a new dominant for this group of patients with tapping exercises makes these studies relevant. Consequently, research on individual rhythm changes in patients with symptomatic post-surgery epilepsy and comparison of these changes with healthy persons' individual rhythm indicators can help to create a new dominant in the absence of pathological focus and reset remaining epileptic system links, imposing the mode of operation closest to the physiological one and activate antiepileptic system. There is also a concept which states that "seizures lead to seizures." First proposed by doctor William Gowers (1881) and reflecting the concept of epilepsy as a progressing disease [65], this concept remains relevant.

Conflict of interest

The authors declare that they have no conflicts of interest to disclose.

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