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Case Study

Possibilities of Non-Drug Treatment of Tardive Dyskinesia (Theoretical and Practical Aspects). Description of the Case

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Abstract

Tardive dyskinesia (TD) is one of the most severe complications of psycho- and neuropharmacotherapy. Most often, TD is a complication of antipsychotic treatment. Currently, there are no effective methods and clear algorithms for the treatment of TD. All recommendations are reduced to adherence to preventive measures and avoidance of unjustified and prolonged use of antipsychotics. In the last decade, for the treatment of TD, we have been using various methods of inhibiting the otolith apparatus of the labyrinth. One of the fundamental functions of the otolithic apparatus of the labyrinth is the perception of the gravitational constant. Gravitational sensitivity is basic in relation to all other types of sensing and motor skills. Information about the influence of the otolith apparatus on the activity of the brain is given. The aim of the study is to study the effectiveness of anodic bilateral vestibular galvanization (tDCAS) in TD. The study was carried out on 7 patients. The severity of PD was assessed using the Abnormal Involuntary Movement Scale (AIMS). The presented results are illustrated by a clinical example.

Keywords: *Constant Anodic Current; Labyrinth Otolith Apparatus; Tardive Dyskinesia; Treatment*

Introduction

One of the most common complications associated with drug therapy is tardive (tardive) dysknesia (TD). This disease occurs when taking a variety of drugs (antidepressants, mood stabilizers, anticonvulsants, anticholinergics, dopamine agonists, L-dopa drugs, etc.), but most often against the background of long-term use of antipsychotics [1]. Recent studies show that after one year of taking typical antipsychotics, TD develops in young patients in 4%, and in patients older than 55 years in 26% of cases. After three years of taking antipsychotics, these figures increase according to age groups to 11 and 60%. After three years of taking antipsychotics, these figures increase according to age groups to 11 and 60%. Thus, age plays a significant role in the development of TD. It has been proven that TD occurs 5 times more often in elderly patients than in young patients, and in women it occurs more often [2]. At the same time, cases are described

when TD occurred after several days of taking therapy, or immediately after an incorrectly performed therapeutic "break". It should be noted that with the use of the latest generation of antipsychotic drugs, the incidence of extrapyramidal disorders is slightly lower, on average by 30 - 50% [3].

The pathogenesis of TD is still unclear, it is only known that several major neurotransmitter systems are involved in this process. There are several subtypes of TD, each of which may have its own individual spectrum of neurochemical changes. It is generally recognized that at present there are no effective methods and clear algorithms for the treatment of TD. All recommendations are reduced to the observance of preventive measures and the avoidance of unjustified and prolonged use of antipsychotics [1].

Over the past few years, for the treatment of this disease, we have been using various methods of influencing the vestibular apparatus. Before dwelling in more detail on these methods of vestibular neuromodulation, it is advisable to analyze the significance and degree of influence of the vestibular apparatus on the activity of the central nervous system. One of its important functions is the perception of the gravitational constant, and its phylo- and ontogenesis gives grounds to consider gravitational sensitivity as the main (basic) and organizing in relation to all other sensory and motor formations of the brain. In fact, under the influence of the vestibular apparatus, the growth, formation and functioning of all brain structures occurs [4]. It should be clarified that the organ of gravitational sensitivity is the otolith apparatus of the vestibule (paleolabyrinth). These include the paramedian and posterolateral thalamus, the amygdala, the putamen, the raphe nuclei, the locus coeruleus and the adjacent region of the brainstem pons, the hippocampus and the hippocampal gyrus, the middle, inferior, and superior temporal gyri (Brodmann areas 37, 19, and 22), both hemispheres of the cerebellum, the lower and upper parts of the inferior parietal lobule, the supramarginal gyrus bilaterally - (Brodmann's field 40), all insular gyrus, the lower and middle frontal gyrus (Brodmann's fields 45 and 46), the precentral gyrus (Brodmann's fields 6 and 9), the anterior cingular cortex and anterior part of the insula (Brodmann area 23), prefrontal cortex (Brodmann areas 6, 9), insular and retroinsular areas bilaterally, parietal and occipital lobes [5]. Regarding changes in the cerebral cortex of healthy subjects during vestibular galvanization, we summarized this information in the form of figures (Figure 1 and 2).

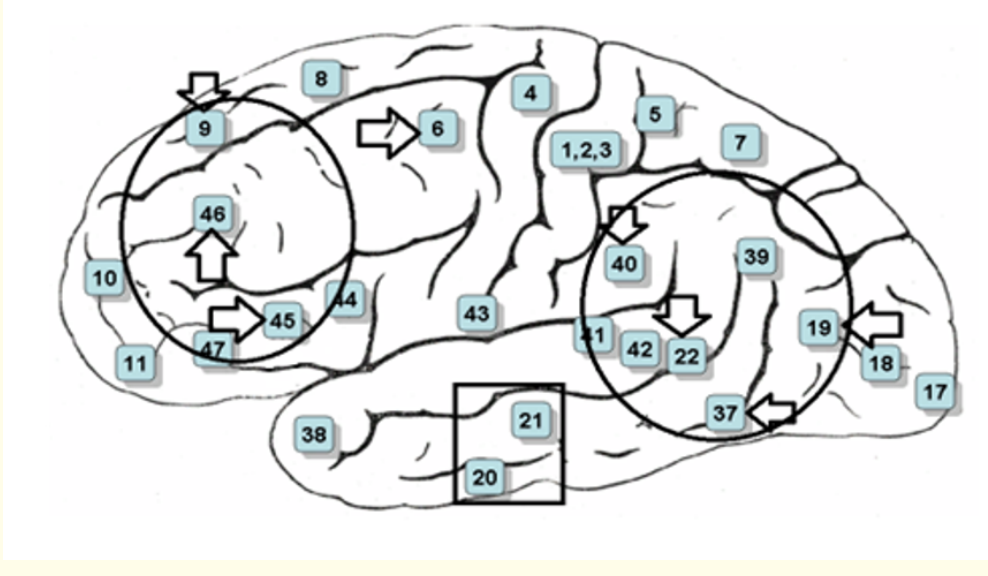

Figure 1: *Zones of increased activity of the cerebral cortex in healthy subjects during anodic galvanization of the vestibular apparatus. The lateral surface of the cortex of the left hemisphere of the brain according to Brodmann. The arrows show areas of the cortex where the increase in activity occurs. Oval outline - front and back associative zones. Rectangular outline - cortical section of the vestibular analyzer.*

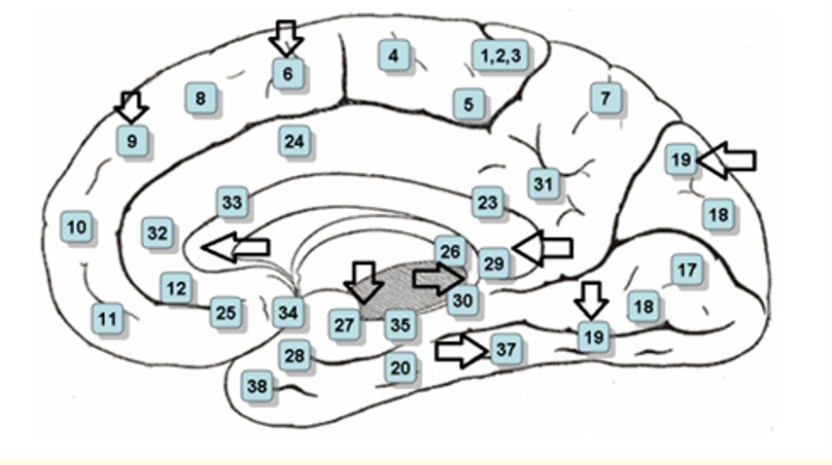

Figure 2: *Zones of increased cortical activity in healthy subjects during anodic galvanization of the vestibular apparatus. Medial surface of the left hemisphere. The arrows show areas of the cortex where the increase in activity occurs.*

Thus, one gets the impression that, unlike other types of sensory modalities, the vestibular analyzer does not have its own clear local representation in the cerebral cortex.

This is wrong. It is necessary, in accordance with the function of the vestibular apparatus, to single out the sections in the cerebral cortex that are involved in the analysis of tangential and linear accelerations.

It is well known that these include areas of the temporal cortex (fields 21, 20 according to Brodman). Since no motor influences are produced during vestibular galvanization, the ongoing changes in the brain can be explained by the effect of direct current on the activity of the vestibular nerve and hair cells of the labyrinth. In this case, the hair cells undergo inhibition, and the nerve increases its activity [6]. As mentioned earlier, the otolith apparatus of the vestibule provides the perception of gravitational information. It is known that the number of hair cells in the macula of the elliptical sac is 33,000, and that of the spherical sac is 18,000, while the cupulae of the three semicircular canals of the otolithic apparatus account for only 17,000 hair cells [7]. Thus, about 75% of the hair cells are contained in the otolith apparatus of the vestibule. This figure coincides with the number of regular fibers of the vestibular nerve with constant activity [6]. The constant activity of the vestibular nerve confirms the participation of the otolith apparatus in the analysis of the gravitational field. It is this fact that can explain the increased activity of other areas of the cerebral cortex during galvanization of the vestibular apparatus. It is no coincidence that cortical activity increases in the anterior and posterior association zones, in the cingulate sulcus, as well as in the anterior and posterior sections of the insula, which in recent years has been considered one of the leading regions involved in the organization of the integrative activity of the cerebral cortex [8]. Above, we shared our experience in the treatment of tardive dyskinesia by vestibular dereception [1], the mechanism of action of which is similar to vestibular anodic galvanization (decrease in the excitability of receptor-cell formations of the otolith apparatus) [9]. The method of vestibular galvanization is successfully used, unfortunately, not very widely, in many brain diseases, including extrapyramidal pathology [8].

Aim of the Study

The aim of the study was to test anodic vestibular galvanization for the treatment of TD.

Materials and Methods

The study group included 7 people suffering from PD. All patients suffered from various forms of procedural disease and took antipsychotics for a long time. The group consisted of 3 men and 4 women aged 32 ± 0.2g. The duration of PD disease ranged from 1.5 months to 6 years (average 4 ± 0.43 years). Despite its presence, all patients continued to take antipsychotics in various doses due to the underlying disease.

The performed procedure is the impact of a small current (3 - 5 mA, depending on individual tolerance), through the anodes located on the mastoid processes of the temporal bone (transcranial direct current anodal stimulation - tDCAS) bilaterally. The course consisted of 10 - 14 procedures performed daily. The duration of the procedure was 30 minutes.

In addition to clinical assessment before treatment and during further follow-up, patients were examined using the Abnormal Involuntary Movement Scale (AIMS), which allows assessing the severity of involuntary movements [10].

Results

After 2 - 3 procedures, a positive effect was noted from several hours to a day, in the form of a decrease in the amplitude and frequency of involuntary muscle contractions. Gradually (as the course continued), the duration of the positive effect increased. After the end of the first course, the positive effect in the patients of the whole group persisted for an average of 4-5 weeks. An increase in symptoms, although in a less pronounced form, was the reason for repeated courses of treatment. With each subsequent course, this effect increased and manifested itself after the first procedure, and its duration increased. After 4 - 5 courses of tDCAS, the positive effect persisted up to 5 - 6 months. Characteristically, with the return of extrapyramidal disorders, they acquired a local character, differed in lesser severity and duration. At the same time, "light" intervals increased, and painful manifestations appeared more often at the end of the day against the background of fatigue, or were provoked by stressful situations. In general, throughout the group, the duration of remission ranged from 2.5 months to 6 months, and then relapse occurred. It should be noted that even with the return of motor disorders, they were characterized by significantly less pronounced motor disorders (according to the AIMS scale), and 2 - 3 tDCAS procedures were enough to eliminate them. In the future, to maintain the achieved effect, it was enough to carry out one exposure once every two weeks. The maximum effectiveness of tDCAS (both in terms of the time of occurrence and the severity of positive changes) was noted in cases where the duration of the anamnesis of TD did not exceed 10 - 12 months. The goal of the ongoing treatment is to achieve a stable complete clinical remission (SCCR). By SCCR, we mean the absence of even minimal manifestations of TD for more than one year [11]. As an illustration, here is the case history of one of our patients.

Case Study

Patient P., age - 33 y.o

Anamnesis: heredity is not burdened. Pregnancy in a mother with toxicosis in the third trimester. Childbirth and early development without features. Up to two years, hypertonicity of the muscles of the neck and ankles. Up to 5 years of hyperactivity. From an early age period, isolation, lack of contacts with peers, and a delay in psycho-speech development were noted. From the age of 7 (after a psychotrauma), verbal hallucinations appeared, at first of a commentary, and then of an imperative nature. Despite this, the patient studied at a comprehensive school until the 5th grade. In the future, due to illness and frequent hospitalizations, he was forced to switch to home schooling. The first hospitalization in a psychiatric hospital (PH) at the age of 10, where active therapy with typical and atypical antipsychotics was carried out, with no visible effect. After 4 months, he was discharged with a diagnosis of paranoid schizophrenia, a continuous form of the course. In subsequent years, despite the constant intake of large doses of antipsychotics, there were frequent (2 - 3 times a year) and long-term (up to 9 months) hospitalizations in the PH. In 2000, he was treated in the children's department of the NRPNI. V.M. Bekhterev, where prof. Kharitonov R.A. At the same time, a rare combination of chronic verbal hallucinosis and mental retardation was noted. In the department he received active antipsychotic therapy - without a visible effect. In the course of further outpatient follow-up, a gradual

withdrawal of broad-spectrum antipsychotics and their replacement with activating antipsychotics was performed. Within about a year, the patient's condition stabilized and drug remission was formed. The state of remission flowed for more than 18 years. The clinical picture was represented by mild manifestations of an emotional-volitional defect and a slight intellectual decline. There were no productive symptoms during the noted period. During this period, the patient recovered to study at a regular school, and at the same time studied at a music school (accordion class). In the future, he successfully completed 10 classes of a regular school, at the same time a music school. For a long time he led an active lifestyle: including composing music, reading, watching TV, attending theater and concert performances, helping his mother with household chores and country work. Repeatedly tried to get a job, but all attempts were unsuccessful, due to the presence of a disability group. All this time the patient was under outpatient supervision, constantly taking maintenance therapy in the form of small doses (1/8 - 1/4 tab. - 0.00025) risperidone in the morning. Since about 2015, seasonal fluctuations in affect began to appear, not reaching the level of cyclothymia. In the autumn of 2016 (29 years), against the background of a slight decrease in mood, which was accompanied by severe irritability and exacerbation of hallucinatory experiences of a commentary nature, the patient's mother turned to another specialist and therapy was prescribed in the form of 3 mg of risperidone and 1.5 mg of phenazepam, and later quetiapine was added. (up to 0.05 per day). Against this background, the patient developed neurolepsy in the form of lethargy, the appearance of a constant large-scale tremor of the hands and fingers, a symptom of a "cogwheel", severe restlessness and dry mouth. After 3 weeks (after changing therapy), tardive dyskinesia appeared in the form of a violent involuntary contraction of various muscle groups of the whole body. Reducing the drug load and conducting detoxification therapy did not have a practical effect. The severity of motor disorders according to the AIMS scale was 33 points. In this regard, it was decided to use tDCAS. The patient underwent the first course of tDCAS, consisting of 10 treatments, which were performed every day. After 6-7 procedures, there was a noticeable decrease in the amplitude and frequency of involuntary muscle contractions. After the end of the first course, the severity of motor disorders was 10 points. Subsequently, the patient underwent 4 more courses of procedures with gradually increasing intervals between them. The last interval reached 7 months, and the last course was carried out with a frequency of one procedure of 10 - 15 days. During the last year, the severity of motor disorders on the AIMS scale was 0 - 2 points. The patient continues to take small activating antipsychotics (risperidone - 0.00025 per day) with episodic addition to antidepressant therapy (fluoxetine - 0.00025 - 0.00012 per day) for 3 - 4 weeks.

Conclusion

Thus, if we compare the effectiveness of tDCAS with the effectiveness of vestibular dereception [1], with the similarity of their mechanisms, then the advantage of tDCAS is its non-invasiveness. While its effectiveness is inferior to vestibular dereception, and in order to maintain the effect, it becomes necessary to conduct ongoing maintenance therapy.

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