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## EVALUATION OF THE EFFECT OF RTMS ON NON-MOTOR SYMPTOMS OF PARKINSON'S DISEASE

**Abstract:** This article describes the nature of non-motor symptoms according to the screening questionnaire NMSQuest with the study of the level of depression according to the Zung scale in patients with Parkinson's disease, as well as the effect of transcranial magnetic stimulation in accordance with the accepted protocols on the dynamics of the development of NMS and depression.

**Key words:** Parkinson's disease, non-motor symptoms, depression, transcranial magnetic stimulation.

**Language:** English

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### Introduction

**Relevance.** The prevalence of Parkinson's disease in recent decades around the world has increased by 1.5 times, including in Central Asia. Parkinson's disease (PD) is a chronic progressive brain disease associated with degeneration of dopaminergic neurons in the substantia nigra, which is manifested by a combination of hypokinesia with rigidity, resting tremor and postural instability, as well as a wide range of non-motor phenomena (mental, autonomic, sensory, etc.) [ 2].

Currently, no complete cure for PD has been identified, however, existing methods of conservative and surgical treatment can improve the quality of life of patients and slow down the progression of the disease [3]. However, the main problem in the management of PD patients is associated with lifelong treatment, which requires constant correction. It is known that treatment is mainly aimed at restoring the activity of the dopaminergic system and correcting

neurotransmitter imbalance [3]. Despite treatment, 40% of patients remain symptomatic. Taking drugs with dopaminergic activity (primarily levodopa) at advanced stages in 28% of PD patients leads to the development of levodopa-induced dyskinesias [11].

It was found that, in addition to motor disorders, non-motor manifestations are noted in 10–50% of patients with PD [6]. It is about cognitive and anxiety-depressive disorders, vegetative disorders, sleep and wakefulness disorders, sensory disorders, etc. [11]. Anxiety-depressive disorders are among the most common psychoemotional manifestations of PD. Thus, depression occurs in 40–90% of patients with PD [1, 12]. It was found that the development of depression aggravates the existing motor deficit and reduces the quality of life of patients even more than motor disorders [13].

Recently, transcranial magnetic stimulation (TCMS) has been increasingly used as an adjunctive treatment [4, 5, 8]. TCMS is a method of

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neurostimulation and neuromodulation based on the principle of electromagnetic induction of an electric field in the brain. The main advantage of the method is its non-invasiveness, no need for surgical intervention or anesthesia. Repeated magnetic impulses for a short time in a specific area of the brain, conducted through a magnetic coil over the head, can modulate cortical excitability, decreasing or increasing it depending on the stimulation parameters. A change in excitability occurs not only at the site of stimulation, but also in areas of the brain anatomically associated with the site of stimulation, which has a great therapeutic potential [7, 9, 10]. The use of TCMS can significantly improve the quality of life without the use of antidepressants and psychoactive drugs [13].

Thus, electromagnetic therapy opens up new possibilities for treating PD patients. Since the main effects of TMS in PD include improvement of motor functions and a decrease in the severity of non-motor manifestations, stimulation may become a new additional therapeutic method for treating patients with PD [4].

Considering the above, the use of TMS requires further comprehensive study, with an analysis of the effect of this method on the non-motor symptoms of Parkinson's disease.

**Materials and methods:** the selection consisted of 34 patients with Parkinson's disease of the akinetic-rigid form with the degree of severity of the disease from 1.5 to 2.5 according to Hen and Yar, the average age of which was  $63 \pm 8.3$  years. Of these, 20 are men and 14 are women. Moreover, the duration of the disease was no more than 3.5 years.

All patients were evaluated for the presence of non-motor disorders using the Parkinson's Disease Quantification Scale (NMS) (NMSQuest). This questionnaire is a screening method for diagnosing

non-motor symptoms of PD. The scale is filled by the patient or a relative, consists of 30 questions with short answers "yes" or "no". The analysis of non-motor symptoms of PD was carried out in the dynamics of the use of TMS (on the first day of the study, at the end of the TMS course). Also, all patients were examined for the presence and level of depression using the Tsung questionnaire.

To assess the effect of rTMS on NMS and depressive disorder, the patients were divided into two groups: the main group consisted of 17 patients who, against the background of basic therapy (levodoposine drugs and / or dopamine receptor agonists) received a course of rTMS, and the control group - 17 patients who received only basic therapy. The samples of the main and control groups were correlatively equal in terms of NMS and the level of depression.

**RTMS protocol:** the magnetic field strength was selected slightly below the motor threshold, in accordance with individual tolerance and amounted to 0.7-1.3 Tesla, the pulse frequency in the series is 10 Hz, the duration of the series is 7 s, the interval between the series is 1.0 s, the duration of the session 5 min., While stimulation of the amplitude of 110-120%. Course - 10 sessions. RTMS was carried out using the Neuro-MS / D apparatus with an amplitude of magnetic induction of up to 4 T, which has several versions. Stimulation types: biphasic.

The rTMS protocol was developed in accordance with the safety requirements of the US National Institute of Neurological Disorders and Stroke, taking into account the technical capabilities of the rTMS apparatus (Neuro-MS.NET software for controlling a magnetic stimulator).

**Results of the study:** analysis of non-motor symptoms during the initial examination of patients with PD revealed the following changes (Table No. 1).

**Table No. 1 Average values of NMS in BP (in%)**

Symptomgroup	N=34
Psychoemotionaldisorders	85,3
Vegetativedisorders	55,8
Sleepdisturbance	79,4
Intestinaldisorders	44,11
Sensorydisorders	
Psychoticdisorders	5,8
Cognitivedisorders	97
SexualDisorders	26,4

According to the results of this table, it can be seen that the most frequent NMS in patients with PD are such as psychoemotional disorders (on average 85.3%), sleep disorders (on average 79.4%), and almost all of them had cognitive disorders. And also vegetative disorders were found in half of the patients (on average 55.8%). At the same time, one patient accounted for from 4 (76: 70.5%) to 7 (23.5: 29%).

For a more detailed alignment of the psychoemotional spectrum, a more detailed analysis of psychoemotional disorders was required as one of the leading non-motor symptoms, which leads to a decrease in the quality of life of PD patients, and therefore the patients were further examined for the level of depression (Table 2).

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**Table No. 2 Assessment of the Tsung scale in both groups**

Index	N=34
Milddepression	11,76% (Averagescore54±3,2)
Subdepression	44,1% (Averagescore63±3,6)
Truede Depression	44,1% (Averagescore77±6,7)

The data on the Tsung scale showed that depression was observed in all patients, while subdepressive states and true depression were noted in the overwhelming majority of patients with PD (88.2%).

The use of rTMS was carried out in the prescribed course, upon completion of which, the patients were re-examined for the presence of NMS and assessment of the level of depression (Table No. 3).

**Table No. 3 Dynamics of NMS after application of rTMS**

Symptomgroup / observation	Maingroup		Controlgroup		p
	1.	2.	1.	2.	
Psychoemotionaldisorders	88,3	41,2*	82,3	70,5	0,002
Autonomicdisorders	58,8	23,5*	52,9	52,9	≤0,001
Sleepdisturbance	82,3	58,8*	76,5	70,5	0,002
Intestinaldisorders	47	41,2	52,9	52,9	0,34
Sensoryimpairment	11,7	0	17,6	17,6	0,06
Psychoticdisorders	5,8	0	5,8	5,8	0,09
Cognitiveimpairment	100	70,5*	94	88,2	0,002
SexualDisorders	23,5	17,6	29,4	29,4	0,49

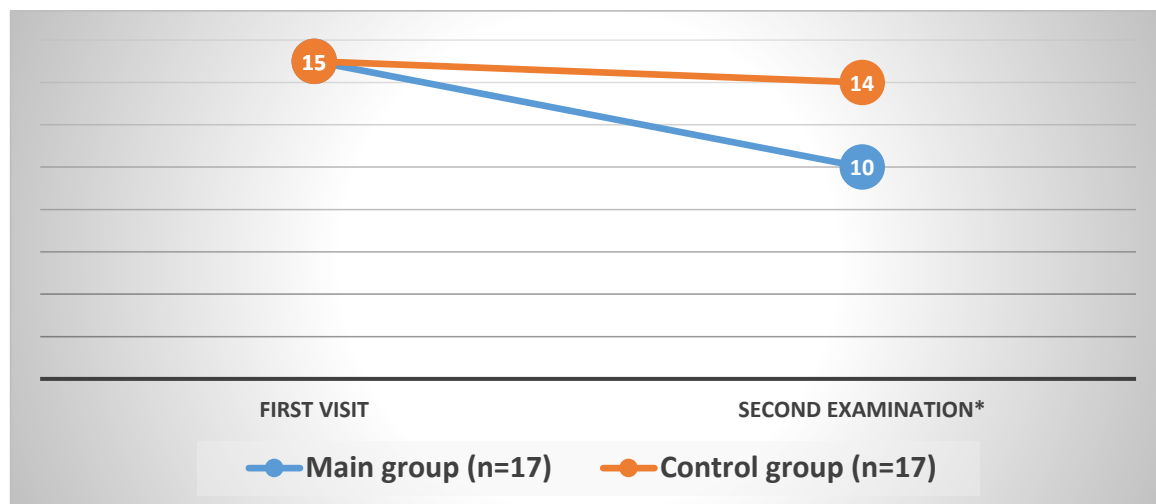
\*Statistically significant differences between groups (p≤0,05)

Statistically significant changes in NMS were observed in the main group, which reliably indicates the effective effect of rTMS on the non-motor

symptoms of PD (p≤0.001), in comparison with the control group, where only basic therapy was used.

Analysis of depression according to Tsung showed the following results (Fig. №4).

**Figure No. 4 Depression dynamics after rTMS application**



\*Statistically significant differences between groups (p≤0,5)

As it can be seen from the diagram, the change in the level of depression is statistically insignificant in both groups (p≤0.5), however, in the main group in 29.4% of patients there is a decrease in subdepression

to the level of mild depression, while in the control group this indicator remains practically unchanged (5.8%).

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**Conclusion:** stimulation of dopamine release by means of transcranial magnetic action significantly improves the non-motor symptoms of Parkinson's disease, namely anxiety, autonomic disorders, sleep disorders and cognitive disorders, which significantly improves the quality of life of patients by reducing the

need for constant drug therapy. However, the effect of rTMS on depression has a statistically insignificant indicator, which leaves room for further study of the effect of rTMS on the psychoemotional spectrum of patients with PD, and also raises the question of the need to take antidepressants regardless of TMS.

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