

DIAGNOSTIC AND TREATMENT METHODS

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STUDY OF THE COGNITIVE PROFILE
IN PATIENTS WITH ESSENTIAL TREMOR

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The clinical picture of essential tremor, in addition to motor symptoms, includes a wide range of non-motor manifestations, which includes cognitive disorders, psychiatric and other disorders. This article presents the results of a study of the cognitive status in patients with essential tremor using the 3-CT scale. As a result of the study, it was shown that patients with essential tremor are diagnosed with cognitive impairment of the dysregulatory profile.

Keywords: essential tremor, trembling hyperkinesia, non-motor symptoms, cognitive disorder.

Introduction. Essential tremor (ET) is a chronic, slowly progressive disease of the extrapyramidal nervous system, the main manifestation of which is trembling hyperkinesia [2]. The initial view that ET is a relatively "simple" and monosymptomatic disease is erroneous. Currently, ET is increasingly considered in the aspect of a neurodegenerative disease with a heterogeneous clinical picture and a wide range of non-motor symptoms (NMS) [10]. Among them, cognitive, psychiatric, sensory and other disorders are actively discussed [7,8,9]. NMS of essential tremor, along with obligate symptoms, constitute a general, rather complex phenotype of the disease [14]. Numerous studies conducted in North America, Europe and Asia demonstrate cognitive deficits in ET patients ranging from mild to moderate cognitive disorder to dementia [8]. Moreover, cognitive disorder can be observed not only in the elderly, but also in young patients. In some cases, it has been shown that changes in cognitive status may precede motor manifestations of the disease [12]. Research shows that mild cognitive deficits primarily affect executive function. Such as fluency of speech,

the ability to solve problems and inhibit reactions [4, 6]. In the development of cognitive disorder, the role of the neurodegenerative process in the cerebellum is also considered. In particular, dysfunction of the connection with the prefrontal cortex [11]. In addition, in patients with rapid progression of cognitive disorder, the spread of the neurodegenerative process outside the cerebellum is assumed [15].

Purpose of the work: to assess the frequency and characteristics of cognitive disorder in patients with essential tremor.

Materials and methods. The study included patients with a confirmed diagnosis of essential tremor according to the diagnostic criteria of the International Society for the Study of Parkinson's Disease and Movement Disorders (MDS, 2017), observed at the Center for Extrapyramidal Disorders and Botulinum Therapy at the NEFU's Clinic. Classical ET was shown when bilateral kinetic-postural tremor of the hands was detected in combination with tremor of another localization, in the case of a combination of classical ET with mild cerebellar signs, ET-plus was diagnosed with other extrapyramidal manifestations.

The 3-CT scale was used to assess the neuropsychological profile of patients with ET and people of the control group [1].

The following cognitive domains were assessed:

1) Test of drawing a clock [3]. The subjects were given the task to draw a dial, arrange numbers and show the specified time with arrows. The result was evaluated on a 3-point scale, 1 point was deducted for each error.

2) Memory was assessed using the visual memory test from the SKT scale [5]. The patient was instructed to memorize 12 familiar drawings. Immediate and delayed reproduction, as well as recognition of previously seen patterns of 48 images, were assessed. Each correct answer was scored 1 point. An indicator of a decrease in short-term memory was considered to

be the reproduction of less than 5 drawings.

3) Research of semantic and phonetic speech activity [13]. For 1 minute, the subjects were asked to name animals (semantic speech) and words with the letter "L" (phonetic speech) in 1 minute. Each correct answer was scored 1 point. Statistical processing of the research results was carried out using the SPSS Statistics 22 software. Descriptive statistics for quantitative data are given as the median and the 25th and 75th quantiles (Me [Q25; Q75]). To compare two independent groups, the analysis was performed using the Mann-Whitney U-test. χ^2 and Fisher's exact test were used to compare qualitative data. The critical level of statistical significance for the two groups was determined at $p \leq 0.05$.

Research results. The main group included 53 patients with ET aged 21 to 89 years, the median age was 67 [55.5; 72.5] years. The distribution by gender was as follows: 19 (35.8%) men and 34 (64.2%) women. Classic ET was detected in 8 (15.1%) patients, and ET-plus variant was detected in 45 (84.9%) patients. ET patients were divided into 2 subgroups. The first subgroup consisted of 22 (41.5%) patients with ET of the Yakut ethnicity. The second subgroup included 31 (58.5%) patients with ET of the Russian ethnicity. The control group consisted of 34 individuals without ET, as well as burdened heredity for extrapyramidal diseases. The age in the control group varied from 30 to 86 years, the average age was 63.4 ± 0.93 years, the median age was 65.0 [59.0; 69.0] years. The main and control groups did not statistically differ in age and gender distribution.

All subjects passed the clock drawing test. Difficulties in copying the cube were found in 6/53 (11.3%) patients with ET, who were associated with writing disorder due to tremor. Statistically significant differences in the study groups were obtained when assessing speech activity and short-term memory ($p < 0.05$). The structure of cognitive disorders accord-

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Table 1

The structure of cognitive disorder on the 3-CT scale

Parameter	The main group, n = 53	The control group, n = 34	p
Clock drawing test	3.0	3.0	-
Copying a cube	49 (92.5%)	34 (100%)	0.15
Semantic speech activity	16.0 [13.5; 19.5]	19.5 [16.0; 25.0]	0.001
Phonetic speech activity	9.0 [6.5; 10.5]	9.5 [7.7; 14.0]	0.03
Instant playback	6.0 [6.0; 8.5]	9.0 [6.7; 10.0]	0.002
Delayed playback	5.0 [5.0; 8.0]	7.0 [6.0; 9.0]	0.01
True recognitions	12.0 [11.0; 12.0]	12.0 [11.7; 12.0]	0.4
False recognitions	0	0	-

ing to individual tests 3-CT is presented in table 1.

The results of a comparative analysis of visual memory are presented in Figure 2. At the same time, all patients coped with the recognition of the previously seen images - 12.0 [11.0; 12.0] and 12.0 [11.7; 12.0], respectively, without statistical differences between groups ($U = 824$; $Z = -0.84$; $p = 0.4$). There were no false recognitions in the ET group and the control group.

A comparative assessment of the results of the 3-CT test was carried out between the first (the Yakut ethnic) and the second (the Russian ethnic) main groups of patients with ET. However, there were no statistically significant differences in the structure of cognitive disorders in the ethnic aspect ($p > 0.05$).

When analyzing the severity of cognitive disorder depending on the clinical variant and the form of ET, there was shown no statistical difference between the groups of patients with ET (Table 2).

As a result of the analysis of the test results, it was shown that in patients with ET in the studied groups, the frequency and severity of cognitive disorder did not

differ depending on ethnicity, form, variant of the disease, and also on the age of ET debut. Evaluation of tests for visual-spatial orientation, drawing of a clock,

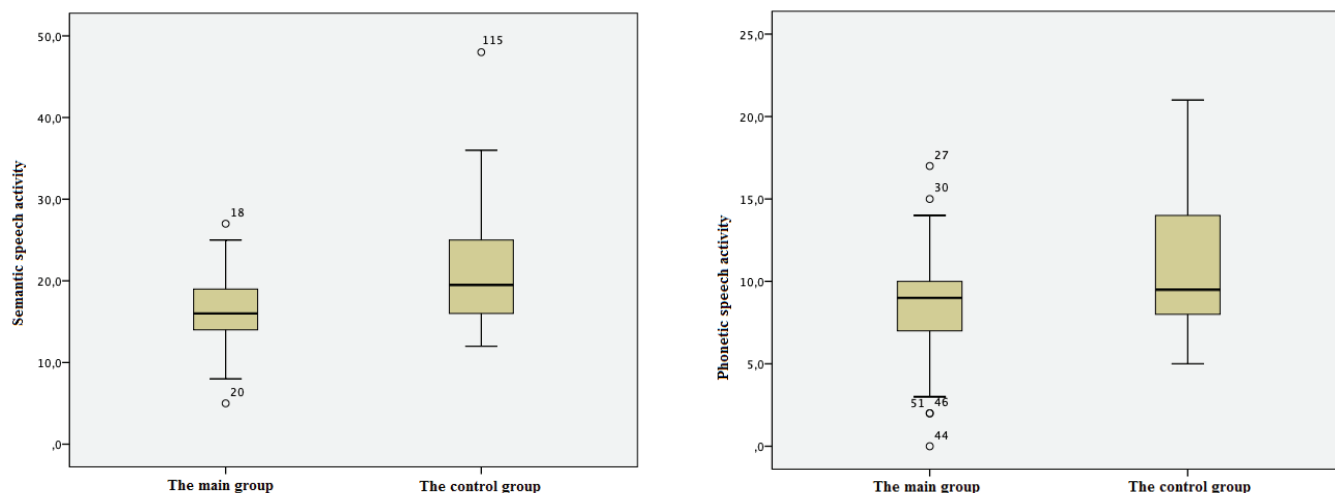


Fig. 1. Assessment of speech activity in patients with ET and the control group

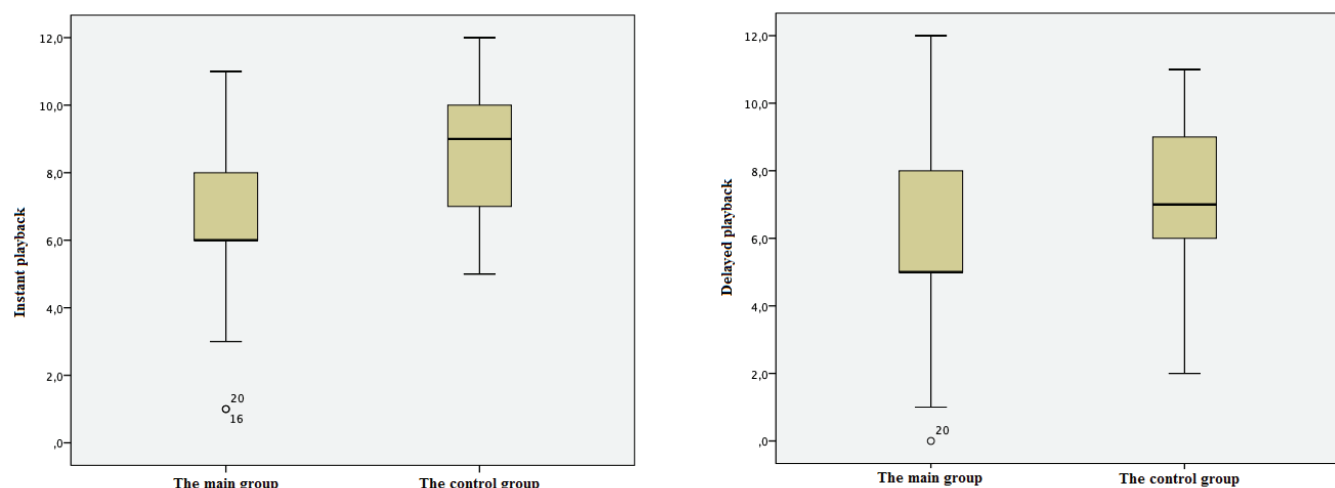


Fig. 2. Comparative assessment of visual memory in the group of patients with ET and persons in the control group.

Table 2

The structure of cognitive disorders by 3-CT subscales depending on the clinical variant and the form of ET, Me [Q25; Q75] points

Parameter	Форма заболевания					
	Classic ET, n = 8	ET-plus, n = 45	p	Familial form, n=28	Sporadic form, n=25	p
Semantic speech activity	16.0 [13.0; 16.0]	16.0 [13.8; 20.3]	0.59	16.0 [14.25; 22.0]	15.0 [11.5; 18.0]	0.08
Phonetic speech activity	9.0 [9.0; 14.0]	9.0 [6.0; 10.0]	0.1	9.0 [8.0; 10.75]	9.0 [6.0; 10.5]	0.48
Instant playback	6.0 [6.0; 7.0]	6.0 [6.0; 9.0]	0.82	6.0 [6.0; 8.75]	6.0 [6.0; 8.5]	0.83
Delayed playback	5.0 [4.0; 5.0]	5.0 [5.0; 8.0]	0.35	5.0 [5.0; 7.75]	5.0 [5.0; 8.0]	0.89
True recognitions	12.0 [12.0; 12.0]	12.0 [11.0; 12.0]	0.25	12.0 [11.0; 12.0]	12.0 [11.0; 12.0]	0.42
False recognitions	0	0	-	0	0	0.55

speech activity and visual memory revealed a decrease in speech activity and short-term memory in patients with ET. However, the results did not show any ethnic differences. ET revealed a dysregulatory profile of cognitive disorders.

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Литература

1. Левин О.С. Диагностика и лечение когнитивных нарушений и деменции: метод. рекоменд. / Левин О.С., Васенина Е.Е. - М.: МЕДпресс-информ. - 2015; 80 с. [Levin OS, Vasenina EE. Diagnosis and treatment of cognitive impairment and dementia: method. recommendations. M.: Medpress-inform. 2015; 80 (In Russ).]
2. Clark L.N., Louis E.D. Essential tremor: Handbook of Clinical Neurology. 1st ed. - Elsevier B.V. 2018;147:229–239. DOI: 10.1016/B978-0-444-63233-3.00015-4
3. Clock-drawing and dementia in the community: A Longitudinal Study / K. Shulman, G.D. Pushkar, C. Cohen [et al.]. *Geriatr Psychiatry*. 1993;8(6):487–496.
4. Cognition in non-demented Parkinson's disease vs essential tremor: A population-based study. / Sánchez-Ferro Á, Benito-León J, Louis ED [et al.]. *Acta Neurol Scand*. 2017; 136(5):393–400. DOI: 10.1111/ane.12752
5. Evidence of the Cross-Cultural Stability of the Factor Structure of the SKT Short Test for Assessing Deficits of Memory and Attention / H. Lehfeld, G. Rudinger, C. Rietz [et al.]. *Int Psychogeriatr*. 1997;9(2):139–153. DOI: 10.1017/s1041610297004304
6. Frontal lobe dysfunction in essential tremor: a preliminary study / Gasparini M, Bonifati V, Fabrizio E [et al.]. *J Neurol*. 2001; 248(5):399–402. DOI: 10.1007/s004150170181
7. Hearing impairment in essential tremor / W.G. Ondo, L. Sutton, K.D. Vuong [et al.]. *Neurology*. 2003; 61(8):1093–1097. DOI: 10.1212/01.wnl.0000086376.40750.af
8. Janicki S.C., Cosentino S., Louis E.D. The cognitive side of essential tremor: what are the therapeutic implications? *Ther. Adv. Neurol. Disord*. 2013;6(6):353–368 DOI: 10.1177/1756285613489591
9. Louis E.D. Non-motor symptoms in essential tremor: A review of the current data and state of the field. *Parkinsonism Relat. Disord*. 2016; 22:115–118. DOI: 10.1016/j.parkreldis.2015.08.034
10. Louis E.D. The evolving definition of essential tremor: What are we dealing with? 2018; 46:87–91. DOI: 10.1016/j.parkreldis.2017.07.004
11. Rapoport M, van Reekum R, Mayberg H, The role of the cerebellum in cognition and behavior: a selective review. *J Neuropsychiatry Clin Neurosci*. 2000; 12(2): 193–8. DOI: 10.1176/jnp.12.2.193
12. Rate of cognitive decline during the premotor phase of essential tremor: a prospective Study / J. Benito-Leon, E.D. Louis, A. Sanchez-Ferro [et al.]. *Neurology*. 2013;81: 60–66. DOI: 10.1212/WNL.0b013e318297ef2b
13. Short test of semantic and phonological fluency: Normal performance, validity and test-retest reliability / J. Harrison, P. Buxton, M. Husain [et al.]. *Br. J. Clin. Psychol*. 2000; 39(2):181–191. DOI: 10.1348/014466500163202
14. Walterfang M, van de Warrenburg Cognitive impairment in "Other" movement disorders: Hidden defects and valuable clues. *Mov. Disord*. 2014. 29(5):694–703. DOI: 10.1002/mds.25849
15. White matter microstructural changes are related to cognitive dysfunction in essential tremor / Benito-León J, Mato-Abad V, Louis ED [et al.]. *Sci Rep*. 2017; 7(1):2978. DOI: 10.1038/s41598-017-02596-1