ESSENTIAL TREMOR: MODERN VIEW OF THE PROBLEM AND NEW NEUROSURGICAL TREATMENT OPTIONS

Katunina EA[1,2] ✉, Gryaznev RA[1], Shipilova NN[1,2], Katunin DA[1], Malykhina EA[1,2]

[1] Federal Center of Brain Research and Neurotechnologies of the Federal Medical Biological Agency, Moscow, Russia

[2] Pirogov Russian National Research Medical University, Moscow, Russia

The review is focused on essential tremor (ET), the most common extrapyramidal system disorder. Current understanding of the disease pathogenesis is provided; issues of classification and differential diagnosis are discussed. Modern ET treatment methods include therapeutic approaches and surgical interventions. The benefits of the new ET treatment method, the magnetic resonance-guided focused ultrasound treatment (MRgFUS), are described; the world's experience of using the method, indications and contraindications are summarized.

Keywords: essential tremor, treatment, diagnosis, thalamotomy, MRgFUS

Author contributions: Katunina EA — manuscript writing; Gryaznev RA — literature review, data acquisition and processing, manuscript editing; Shipilova NN, Katunin DA, Malykhina EA — editing, formatting, approval of the final version of the article.

✉ **Correspondence should be addressed:** Elena A. Katunina
Serpukhovskiy Val, 17, Moscow, 115191, Russia; elkatunina@mail.ru

Received: 28.02.2024 **Accepted:** 23.03.2024 **Published online:** 31.03.2024

DOI: 10.47183/mes.2024.015

ЭССЕНЦИАЛЬНЫЙ ТРЕМОР: СОВРЕМЕННЫЙ ВЗГЛЯД НА ПРОБЛЕМУ И НОВЫЕ ВОЗМОЖНОСТИ НЕЙРОХИРУРГИЧЕСКИХ МЕТОДОВ ЛЕЧЕНИЯ

Е. А. Катунина[1,2] ✉, Р. А. Грязнев[1], Н. Н. Шипилова[1,2], Д. А. Катунин[1], Е. А. Малыхина[1,2]

[1] Федеральный центр мозга и нейротехнологий Федерального медико-биологического агентства, Москва, Россия

[2] Российский национальный исследовательский медицинский университет имени Н. И. Пирогова, Москва, Россия

Обзор посвящен наиболее часто встречающемуся заболеванию экстрапирамидной системы — эссенциальному тремору (ЭТ). Приведены современные представления о патогенезе заболевания, затронуты вопросы классификации и дифференциального диагноза. Современные методы лечения ЭТ включают терапевтические подходы и хирургические вмешательства. Описаны преимущества нового перспективного метода лечения ЭТ — терапия фокусированным ультразвуком под контролем МРТ (ФУЗ-МРТ), обобщен имеющийся на сегодняшний день мировой опыт его применения, показания и противопоказания.

Ключевые слова: эссенциальный тремор, лечение, диагностика, таламотомия, ФУЗ-МРТ

Вклад авторов: Е. А. Катунина — написание текста; Р. А. Грязнев — анализ литературы, сбор и обработка материала, редактирование текста; Н. Н. Шипилова, Д. А. Катунин, Е. А. Малыхина — редактирование, оформление, утверждение окончательного варианта статьи.

✉ **Для корреспонденции:** Елена Анатольевна Катунина
Серпуховской вал, д. 17, г. Москва, 115191, Россия; elkatunina@mail.ru

Статья получена: 28.02.2024 **Статья принята к печати:** 23.03.2024 **Опубликована онлайн:** 31.03.2024

DOI: 10.47183/mes.2024.015

Essential tremor (ET) is the most common extrapyramidal system disorder. According to the data of meta-analysis, the average prevalence is 0.9%; it increases with age and reaches 21.7% in the group of patients over the age of 95 years [1]. The ideas about ER have changed considerably in the recent years. This is true for the issues of etiology and pathogenesis, as well as for clinical aspects. ET has been considered as an inherited monosymptomatic disorder associated with the local subcortical structural damage for a long time. To date, the range of ET symptoms has expanded considerably to include both motor and non-motor manifestations. The aim of the review was to summarize the literature data on modern ideas about pathomorphology of the disease as a progressive neurodegenerative process, clinical aspects and treatment methods.

Ethiology and pathogenesis

The term "essential tremor" was first introduced into clinical practice in 1874 by Pietro Burresi, who described the 18-year-old patient with severe action tremor. ET had been regarded as "benign tremor" for a long time. However, today, it is clear that this disorder can have serious functional and psychological consequences: 15% of affected individuals have severe disability; in 80% of patients, tremor significantly limits their daily activity by disturbing the eating process, writing, and execution of target-directed movements [2].

According to the definition issued by the International Parkinson and Movement Disorder Society (MDS) in 2018, ET is an action tremor in the hands with the disease duration of at least 3 years that can be combined with tremor of other localization (for example, head, voice or lower limb tremor) in the absence of other neurological signs, such as dystonia, ataxia or parkinsonism [3].

Based on the etiological principle of distinguishing tremor types, ET can be genetically defined, sporadic or familial (Figure).

ET is commonly inherited by autosomal dominant transmission with incomplete penetrance and had variable in 40–70% of patients [4]. The anticipation phenomenon with the earlier onset and more severe clinical manifestations in subsequent generations is observed in a number of families [5]. The ET familial variants can develop at any age, including at the age over 60 years, however, early onset is more common. According to the data of some studies, familial forms have two age peaks of the disorder onset: early age (including childhood) and older age. No clear incidence peaks are observed among individuals with sporadic forms [6]. The age of onset variability observed in individuals with familial can be

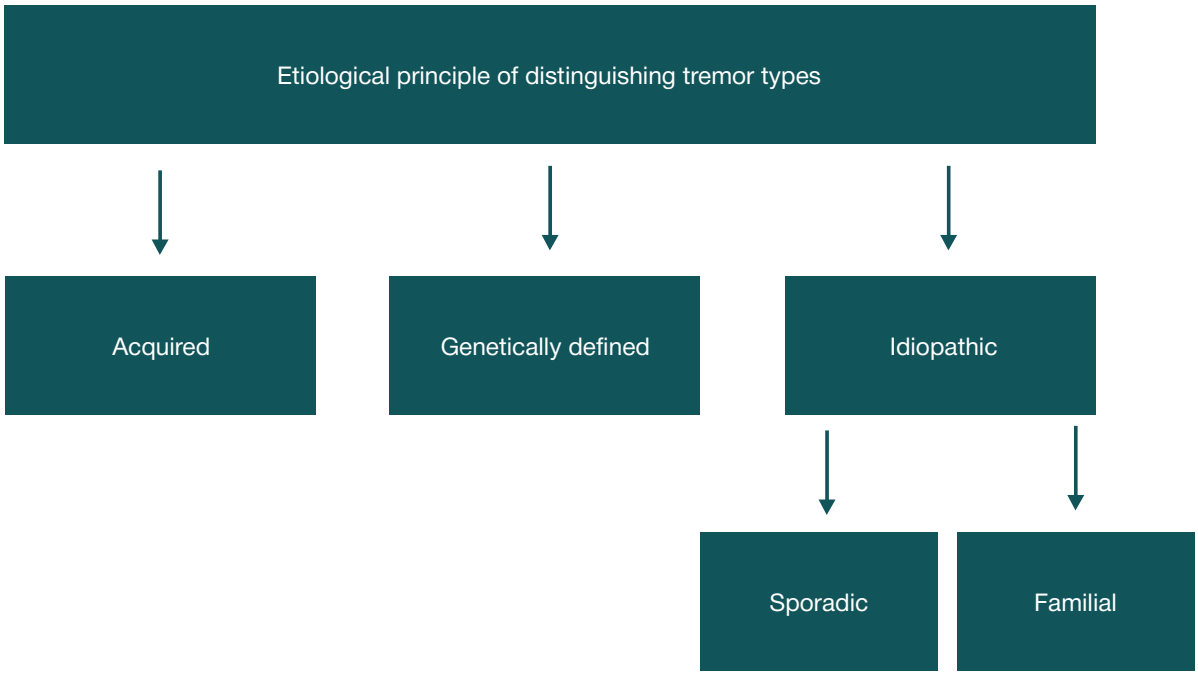

Figure. Consensus classification of tremor compiled by the International Movement Disorder Society in 2018 based on the etiological principle

associated with the diversity of genetic risk factors and the effects of environmental factors on the expression of certain genes [6].

Despite apparent genetic predisposition, the gene responsible for the development of ET has not yet been identified. The whole genome sequencing has shown that ET is associated with polymorphism of the LINGO1 gene playing an important role in the mechanisms underlying neuroplasticity. The protein associated with this gene is involved in axonal regeneration and cell differentiation [7]. It has been shown that the LINGO-1 expression increase following the neuronal damage is associated with demyelination of axons. The decrease in the LINGO-1 activity can contribute to the recovery of neurological deficit with increasing survival rate of neurons and dendritic growth [8].

In recent years, there is growing evidence that ET is a neurodegenerative disorder. The most prominent alterations are found in the cerebellum and inferior portions of the brainstem. Progressive Purkinje cell death, degenerative changes affecting the dentate nucleus, white matter atrophy are observed in the cerebellum. The axonal “torpedoes” that represent proximal axonal swellings on Purkinje cells and contain altered neurofilaments are a common nonspecific pathomorphological marker of ET [9]. Furthermore, Lewy bodies are found in the brainstem of individuals with ET, primarily in the locus coeruleus, the axons of which form synapses with the cerebellar Purkinje cells [9]. Perhaps, damage to the locus coeruleus cells reduces the stimulating noradrenergic effect on the Purkinje cells and leads to the secondary Purkinje cell dysfunction. Thus, the results of morphological studies together with the functional neuroimaging data suggest the important role of the cerebellum in the ET pathogenesis [10]. At the same time, primacy of the tremorogenic role played by the cerebellum is still a matter of debate. There is an opinion that abnormal activity of the cerebellar structures can be secondary to the pacemaker activity of the inferior olivary or thalamic nuclei capable of generating spontaneous bursting oscillation [11]. Abnormal activity of the inferior olivary and/or cerebellar nuclei is transmitted to the motor cortical areas through the dentato-rubro-thalamic tract and realized in the form of alternating or synchronous contraction of the agonist and antagonist muscles manifested by tremors [12]. The thalamic nuclei (primarily the Vim nucleus) play a role of a kind of the relay station between the subcortical structures and the motor cortex. That is why the Vim nucleus is the most common target for tremor neurosurgery (deep brain stimulation, magnetic resonance-guided focused ultrasound treatment (MRgFUS), radiofrequency ablation).

Purkinje cells, Golgi cells, dentate nuclei, cerebellar basket cells are GABAergic neurons having the inhibitory function. The role of GABAergic systems in the ET development has been confirmed by the efficacy of such drugs, as primidone, gabapentin, pregabalin, topiramate, benzodiazepines, targeting the GABA receptors. The well known beneficial effect of alcohol in individuals with ET can be also explained by the indirect agonistic effect on the GABA receptors. Its effect on tremor is likely to be realized through reduction of aberrant synchronization of the inferior olives. The antagonistic effect on the low-voltage-activated calcium channels resulting in the increase in the T-type current in the inferior olive can represent one more mechanism underlying the effect of ethanol in ET [13].

Peripheral mechanisms are also likely to be involved in tremor mechanisms. The effect of nonselective beta-blockers used as the first-line drugs for treatment of ET is realized due to the effect on the skeletal muscle β_2-receptors found in the muscle spindles [14].

Clinical features and diagnostic criteria

The clinical features of the disorder include postural tremor (tremor of outstretched hands) and kinetic tremor. Tremor usually develops symmetrically and predominates in the distal limbs. In a number of cases, the asymmetric onset is possible, when the second hand is involved within months. The tremor frequency is stable; it is in the range of 4–12 Hz. The amplitude is very variable, it shows daily fluctuations and depends on the patient’s emotional state and fatigue severity. In contrast to Parkinson's disease (PD), the feature of the ET-associated postural tremor is that it occurs immediately after outstretching the hands, with no delay typical for PD. Kinetic tremor tends to increase in the terminal point of targeted

Table. Diagnostic criteria for ET, ET plus and exclusion criteria for ET, ET plus issued by the International Parkinson and Movement Disorder Society (2018)

Criteria for ET	Criteria for ET plus	Exclusion criteria for ET and ET plus
1. Isolated bilateral kinetic hand tremor 2. Persisting for at least 3 years 3. Tremor can be combined with tremor of other localization (for example, in the head, vocal cords, lower limbs) 4. No other neurological symptoms, such as dystonia, ataxia, parkinsonism)	1. Tremor compliant with the ET characteristics in the presence of additional neurological symptoms of undefined clinical significance: tandem gait impairment, disguised dystonic attitude, memory impairment or other mild neurological symptoms that are not enough to diagnose an additional syndrome or disorder 2. Essential tremor with added resting tremor	1. Isolated focal tremor (head, voice) 2. Orthostatic tremor with the frequency exceeding 12 Hz 3. Tremor associated with execution of certain tasks or manifesting itself in a certain position 4. Sudden onset, stepwise progression

movement (terminal tremor). Hand tremor can involve proximal parts and go with tremor in the head ("yes-yes" or "no-no"), chin, vocal cords, trunk, lower limbs. The isolated head/voice tremor that was earlier considered as an ET variant is currently a reason for exclusion of the diagnosis considered to be a manifestation of focal dystonia. According to the international criteria, individuals with ET should have no other neurological symptoms (parkinsonism, ataxia, dystonia). In case of postural tremor combined with bradykinesia, one should first think about PD.

The disorder tends to progress, which confirms its neurodegenerative nature. However, the ET progression rate is highly individualized. In some patients, tremor persisting for many years does not disturb their daily activity. In other patients, it results in the reduced working capacity, capability of writing and working on the computer, disturbed eating and self-care at home. Some patients show not only growing tremor severity and involvement of other parts of the trunk, but also accession of other symptoms, such as parkinsonism (rigidity, resting tremor, mild hypokinesia), cerebellar disorders (mild intention tremor, dysmetria, impaired tandem gait), dystonia of various localization. These are usually minor "mild" symptoms. According to the international criteria, ET plus is diagnosed in such cases [3] (Table). Moreover, in some patients, such symptoms can be identified during the first years of the disease.

The epidemiological research conducted shows that ET plus is more common than "pure" ET, especially among individuals with the late-onset disease [15]. In this regard, there is an ongoing debate, whether ET plus is a separate disease entity, separate syndrome or it represents the later-stage ET, in the group of experts [16, 17]. The lack of pathomorphological differences from ET is the most significant argument in favor of the fact that ET plus is not a separate disease entity [18]. Interpretation of ET plus as a separate syndrome that is a possible transitional form between ET and such disease entities, as PD, spinocerebellar ataxia, different variants of dystonia, seems to be more potent [3, 16, 17, 19]. The cases of postural tremor combined with resting tremor are the most challenging in terms of differential diagnosis between ET plus and PD. In contrast to PD, the resting tremor associated with ET plus has the same frequency as the postural-kinetic tremor and, which is more important, there is no bradykinesia and rigidity.

Positive response to low doses of alcohol as a diagnostic sign was excluded from the list of international criteria for ET (2018) as a non-specific and non-permanent symptom, however, the 3-year follow-up period remains in the list [3]. Such a time period is essential to reduce the likelihood of the erroneous diagnosis of other neurological syndrome (for example, dystonia, parkinsonism or ataxia). The term "indeterminate tremor" can be found in the literature, which is used in cases of shorter disease duration [20].

It was believed that ET was a monosymptomatic disease in which there were no non-motor symptoms for a long time. At the same time, a large body of research has emerged showing the development of cognitive impairment, anxiety disorders, and depression in individuals with ET, which further enhances the disease heterogeneity. The cognitive impairment profile is considered to be associated with dysfunction of the frontostriatal or cerebellar thalamocortical systems. The risk of cognitive impairment increases with age. One of the studies focused on assessing the relationship between the ET age of onset and the cognitive impairment has shown that 70% of patients diagnosed with ET had a cognitive deficit at the age of 65 years [21]. Given the neurodegenerative nature of ET and the axonal dysfunction detected, we can assume the possibility of the process expansion from the spinocerebellar structures to the cortical areas.

There are data on higher prevalence of anxiety and depression among patients with ET compared to the group of healthy individuals [22]. The lack of correlation between the tremor severity and the severity of anxiety disorder probably suggests that the anxious personality profile can be a primary disease manifestation, not the consequence of the psychological disorder caused by severe disabling tremor.

The drugs that are currently used to treat ET are symptomatic. These were developed and approved for other indications. Despite numerous attempts to develop new medicinal products, primidone and propranolol remain the first-line drugs for treatment of ET [23]. The drugs are almost equally effective. According to the expert panel of the American Academy of Neurology (AAN), the grade of evidence for their effect is defined as A [24]. According to the research, the use of these drugs does not result in significant reduction of tremor in about 50% of patients [25]. Moreover, in cases of long-term course of the disease, it is almost never possible to achieve complete tremor relief. In an effort to treat tremor, one has to use high doses of drugs, their combinations, thereby increasing the risk of side effects, such as drowsiness, weakness, poor concentration, bradycardia, hypotension, and reducing adherence to treatment. As a result, many patients use subtherapeutic doses or prefer to completely stop taking the drug. The effective dose of propranolol is in the range of 60–120 mg per day. However, there is a need to increase the dose to 240–360 mg/day in a number of patients [26]. It is necessary to monitor bradycardia and arterial hypotension in all dose ranges in order to prevent drug-induced syncope. Furthermore, propranolol should be prescribed with caution to individuals with obstructive lung diseases, bronchial asthma. The effective dose of primidone is in the range of 150–750 mg/day, and the average effective dose is 300 mg/day. Potential side effects include vertigo, instability, drowsiness, fatigue. The combination of propranolol and primidone has a more prominent therapeutic effect [27].

The second-line drugs include topiramate, alprazolam, gabapentin, clonazepam (grade of evidence B). Topiramate is the only drug that has passed a randomized placebo controlled clinical trial [26]. The average effective dose of topiramate varies between 215 and 333 mg/day. Possible side effects include paresthesia, concentration problems, weight loss, nausea,

insomnia, depression. Topiramate should be prescribed with caution to patients with impaired renal and liver function.

The recommended dose of alprazolam is 0.75–1.5 mg/day. In the reviews by AAN and the International Movement Disorder Society (MDS) alprazolam is considered as "probably effective and possibly beneficial" when used for treatment of tremor. The side effects of alprazolam can be represented by drowsiness, vertigo, ataxia, potential addiction. It is more often recommended to use alprazolam from time to time as a supplementary drug.

The risk of addiction syndrome is also typical for clonazepam. Clonazepam is usually recommended for severe head tremor or dystonic tremor. Despite the fact that AAN recognizes gabapentin as a "probably effective" drug [28], and a placebo controlled trial has been conducted showing that gabapentin in a dose of 1200 mg/day is effective against tremor, the drug is rarely used, mostly in combination with other medications, when the first/second-line drugs are ineffective.

It should be noted that the ET treatment goal is not to completely relieve tremor, but to minimize the tremor-associated functional limitations, reduce social maladjustment.

Surgical treatment

In case of tremor refractory to medication, the patient can be referred to surgery [23, 25]. Today, surgical treatment includes deep brain stimulation (DBS), radiofrequency ablation, Gamma Knife, MRgFUS. The advantages of DBS include the possibility of simultaneous bilateral stimulation, adjustment of the stimulation parameters depending on the patient's response or side effects. Prolonged high frequency electrical stimulation, the key "relay" structure (Vim nucleus of the thalamus) is exposed to, functions as an "artificial pacemaker" in the brain, imposing the artificial pattern of neuronal discharges on the stimulated nucleus and thereby ensuring desynchronization of abnormal rhythm in the sensorimotor circles. The DBS efficacy in ET reaches 80% [29]. However, the invasive nature of the procedure creates the risk of hemorrhage and infectious complications reported in about 5–7% of patients [30]. Side effects can be also associated with electrical stimulation itself and be manifested by dysarthria, gait instability, paresthesia. The risk of dysarthria and ataxia increases when bilateral stimulation is applied. Furthermore, the effectiveness of tremor control decreases within a few years, which can be due to the lead migration, developing tolerance to electrical stimulation or the disease progression [31]. The issue of adverse DBS effects on the cognitive function is discussed, along with the increased risk of anxiety disorders and depression [29–31]. There are many contraindications for DBS related to focal brain atrophy, taking anticoagulant drugs, and age limits, which require thorough selection of patients. The patients, who have undergone such surgery, should sometimes contact medical institutions for stimulation mode adjustment and electrical stimulator replacement after 4–5 years.

Radiofrequency ablation is an invasive method (an electrode is introduced into the target point). Despite a significant immediate effect on tremor (reduction by 56.4–90%), it is associated with the risk of intracerebral hemorrhage, developing hemiparesis, dysarthria, ataxia, cognitive decline [32].

The Gamma Knife thalamotomy involves the use of ionizing radiation, despite its non-invasive nature and the fact that it is conducted without anesthesia. The main shortcoming of the method is the lack of intraoperative clinical assessment, along with the unpredictable lesion size and timing of both therapeutic effect (4–8 months on average) and complications [33].

In 2016, the US Food and Drug Administration (FDA) approved a new ET surgical treatment method: destruction of subcortical structures using MRgFUS. In 2017, this treatment method was approved by the Federal Service for Surveillance in Healthcare (Roszdravnadzor) in the Russian Federation. In 2019, the MRgFUS method was included in the evidence-based review of ET treatment methods published by MDS [26]. The MRgFUS advantages over other surgical treatment methods include its non-invasive nature, immediate effect, accuracy of impact on the selected target, and the possibility of monitoring the thermal exposure due to continuous MRI control applied when performing surgery. No implanted devices in the patient, no ionizing radiation, and no need for repeated visits to medical institutions aimed at adjusting the devices are the important features of MRgFUS [34].

The Vim nucleus of the thalamus is the main target for ET treatment using MRgFUS. The effect on the stereotactically verified target point is ensured by initial heating of the selected area (2 mm in diameter) to 40–45 °C with the focused ultrasound through the skull bones (multiple serial short sonications from 1024 sources (650 kHz) placed around the head). Further temperature increase in the target zone causes the ablation damage. The constant visual and verbal contact with the patient is maintained during the procedure in order to estimate the tremor changes upon exposure and record the fact of any adverse effect (for example, paresthesia, dysarthria) after each sonication. Parameters of each subsequent sonication can be adapted to the clinical response during surgery. The temperature is increased and the ultrasound exposure is used until the tremor suppression is achieved. The emergence of paresthesia or any other adverse effect constitutes grounds for the target localization adjustment [35].

The skull is the main obstacle for the ultrasonic wave on its way to the target point, since the bone can both reflect and absorb ultrasonic waves, hampering the acoustic energy transmission and attenuating the MRgFUS therapeutic effect. The skull bone consists of two compact plates (outer and inner) separated by a layer of spongy bone (trabecular or diploe). The coefficient estimating the resolving power of the ultrasonic waves propagating through the skull bone is referred to as Skull Density Ratio (SDR). This parameter calculated based on the head CT scans represent a median ratio between the spongy bone and compact layer of the skull bone in the target area.

The first open-label trial involving the use of MRgFUS in ET was conducted in 2013. The authors of the study reported a significant reduction of tremor and improvement of the quality of life, along with the low number of reversible side effects (paresthesia, dysarthria, ataxia) [36]. In 2016, the results of the blind multicenter randomized trial of parallel groups with the mock surgery used as a control were published. The study involved 76 patients with moderate-to-severe refractory tremor. The tremor severity decreased by 47% within 3 months after unilateral thalamotomy showing significant differences from the mock surgery group ($p < 0.001$). Tremor reduction was accompanied by the daily functioning and quality of life improvement 3 months after treatment. The researchers reported the decrease in tremor severity by 40% relative to baseline and the decrease in maladjustment by 62% [37]. High productivity of the research conducted allowed FDA to approve MRgFUS for treatment of ET. According to the currently available research results, the tremor reduction range is 40–90% [34, 38]. The persistent positive effect on tremor was demonstrated in the 4-year open-label and 5-year retrospective studies [39, 40]. In these studies, paresthesia and numbness, gait instability and mild contralateral muscle weakness that tended to regress by month 3 after surgery were the most frequent adverse events occurring within the first weeks after the MRgFUS thalamotomy. Extinction of postoperative

neurological symptoms is considered to be associated with the reduction and gradual disappearance of perifocal edema.

In 2018, meta-analysis of the outcomes and complications of the MRgFUS thalamotomy used for treatment of ET was conducted. A total of nine studies involving 160 patients published in 2013–2018 were included. Vertigo was noted as the most common intraoperative complication that occurred in 43.4% of cases, it was followed by nausea and vomiting (26.85%). Ataxia (32.8%) and paresthesia (25.1%) were most often detected 3 months after thalamotomy. Regression of ataxia was observed in the majority of patients 12 months after surgery, and paresthesia became the most common permanent complication (15.3%) [41]. According to the results of other studies, no residual side effects were observed by the end of the 4-year follow-up period [42], gait disorders or numbness emerged in 11% of patients by year 5 of follow-up [39].

It should be noted that MRgFUS has no adverse effect on cognitive functions [43]. The recently published meta-analysis provides assessment of the effect of thalamotomy performed using radiofrequency ablation, Gamma Knife, and MRgFUS on cognitive functions. In general, the unilateral thalamotomy safety is emphasized in the review. There was adverse effect on verbal fluency only: the decrease in the number of phonemic associations was mainly observed. The separate sub-analysis performed in the MRgFUS group revealed no cognitive function alteration in any of the areas [44].

The first attempts are made to perform bilateral thalamotomy in order to treat ET using MRgFUS. Thus, in 2014, outcomes of the staged thalamotomy were published. The interval between surgical procedures was 12 months or longer. The tremor severity decreased by 60% after the second surgery; the side effects occurred in 2.6% of patients [45]. Safety of the staged bilateral thalamotomy comparable with that of unilateral surgery was demonstrated in the BEST-FUS trial [46]. Possible adverse events associated with bilateral surgery include transient gait instability, dysarthria, dysphagia, perioral numbness, hemihypesthesia, taste disturbance. The adverse events are mild-to-moderate and regress within 3–6 months [47, 48].

The Vim nucleus of the thalamus is the target of bilateral surgery performed using MRgFUS. However, the papers have emerged reporting the use of the cerebellothalamic tract as a target point for treatment of ET [34], which reduces the risk of side effects. The 12-month prospective study has demonstrated the decrease in hand tremor by 93% and maladjustment by 51% [49].

The MRgFUS method should be recommended to patients with severe disabling tremor that disturbs their daily activity and is resistant to medication. Multiple focal alterations in the brain, preceding brain intervention (DBS, destructive stereotactic surgery, electroconvulsive therapy), high risk of hemorrhage, contraindications to high-field MRI, claustrophobia, mental disorders, severe cognitive impairment, decompensated somatic disorder, SDR $\geq 0.4 \pm 0.05$ (based on the CT data) are contraindications to surgery. It should be noted that density of the skull is a relative contraindication. In the last two years, the papers have emerged that suggest technical feasibility, safety and efficacy of MRgFUS in patients with low skull density (≤ 0.4). Limitation of the number of sonications, adjustment of the maximum impact energy and maximum temperature ensure persistent therapeutic effect [50].

CONCLUSION

ET is among the most common neurological disorders that can be faced by physicians of various specialties. Despite the long history of studying the disorder, many issues of etiopathogenesis are poorly understood and require more extensive epidemiological research with pathomorphological confirmation. The currently available diagnostic criteria for ET are clinical and require monitoring the patient for a certain period, which is sometimes associated with problems in daily clinical practice. In the recent years, the capabilities of neurosurgical treatment have expanded, along with the use of symptomatic agents for treatment of tremor. The results of using such minimally invasive method, as MRgFUS, characterized by high efficacy and safety, are the most encouraging. However, the global and domestic experience of using this technique is only accumulating.

References

1. Louis ED, Ferreira JJ. How common is the most common adult movement disorder? Update on the worldwide prevalence of essential tremor. Mov Disord. 2010; 25 (5): 534–41. DOI: 10.1002/mds.22838. PMID: 20175185.
2. Bain PG, Findley LJ, Thompson PD, Gresty MA, Rothwell JC, Harding AE, et al. A study of hereditary essential tremor. Brain. 1994; 117 (Pt 4): 805–24. DOI: 10.1093/brain/117.4.805. PMID: 7922467.
3. Bhatia KP, Bain P, Bajaj N, Elble RJ, Hallett M, Louis ED, et al. Tremor Task Force of the International Parkinson and Movement Disorder Society. Consensus Statement on the classification of tremors. from the task force on tremor of the International Parkinson and Movement Disorder Society. Mov Disord. 2018; 33 (1): 75–87. DOI: 10.1002/mds.27121. Epub 2017 Nov 30. PMID: 29193359; PMCID: PMC6530552.
4. Illarioshkin SN, Ivanova-Smolenskaja IA. Drozhatel'nye giperkinezy: Rukovodstvo dlja vrachej. Ser. rukovodstv «Dvigatel'nye rasstrojstva». M.: Atmosfera, 2011; 360 s. Russian.
5. Wider C, Ross OA, Wszolek ZK. Genetics of Parkinson disease and essential tremor. Curr Opin Neurol. 2010; 23 (4): 388–93. DOI: 10.1097/WCO.0b013e32833b1f4c. PMID: 20489616; PMCID: PMC3930090.
6. Louis ED, Clark LN, Ottman R. Familial versus Sporadic Essential Tremor: What Patterns Can One Decipher in Age of Onset? Neuroepidemiology. 2015; 44 (3): 166–72. DOI: 10.1159/000381807. Epub 2015 May 7. PMID: 25967236; PMCID: PMC4764084.
7. Stefansson H, Steinberg S, Petursson H, Gustafsson O, Gudjonsdottir IH, Jonsdottir GA et al. Variant in the sequence of the LINGO1 gene confers risk of essential tremor. Nat Genet. 2009; 41 (3): 277–9. DOI: 10.1038/ng.299. Epub 2009 Feb 1. Erratum in: Nat Genet. 2009; 41 (4): 504. PMID: 19182806; PMCID: PMC3740956.
8. Mi S, Hu B, Hahm K, Luo Y, Kam Hui ES, Yuan Q, et al. LINGO-1 antagonist promotes spinal cord remyelination and axonal integrity in MOG-induced experimental autoimmune encephalomyelitis. Nat Med. 2007; 13 (10): 1228–33. DOI: 10.1038/nm1664. Epub 2007 Sep 30. PMID: 17906634.
9. Louis ED, Faust PL, Vonsattel JP, Honig LS, Rajput A, Robinson CA, et al. Neuropathological changes in essential tremor: 33 cases compared with 21 controls. Brain. 2007; 130 (Pt12): 3297–307. DOI: 10.1093/brain/awm266. Epub 2007 Nov 19. PMID: 18025031.
10. Kuo SH, Wang J, Tate WJ, Pan MK, Kelly GC, Gutierrez J, et al. Cerebellar Pathology in Early Onset and Late Onset Essential Tremor. Cerebellum. 2017; 16 (2): 473–82. DOI: 10.1007/s12311-016-0826-5. PMID: 27726094; PMCID: PMC5336493.
11. Long MA, Deans MR, Paul DL, Connors BW. Rhythmicity without synchrony in the electrically uncoupled inferior olive. J Neurosci. 2002;

22 (24): 10898–905. DOI: 10.1523/JNEUROSCI.22-24-10898.2002. PMID: 12486184; PMCID: PMC2834587.
12. Deuschl G, Petersen I, Lorenz D, Christensen K. Tremor in the elderly: Essential and aging-related tremor. Mov Disord. 2015; 30 (10): 1327–34. DOI: 10.1002/mds.26265. Epub 2015 Jun 22. PMID: 26095699; PMCID: PMC4779797.
13. Mu J, Carden WB, Kurukulasuriya NC, Alexander GM, Godwin DW. Ethanol influences on native T-type calcium current in thalamic sleep circuitry. J Pharmacol Exp Ther. 2003; 307 (1): 197–204. DOI: 10.1124/jpet.103.053272. Epub 2003 Jul 31. PMID: 12893844.
14. Hedera P. Emerging strategies in the management of essential tremor. Ther Adv Neurol Disord. 2017; 10 (2): 137–48. DOI: 10.1177/1756285616679123. Epub 2016 Nov 30. PMID: 28382111; PMCID: PMC5367648.
15. Rajalingam R, Breen DP, Lang AE, Fasano A. Essential tremor plus is more common than essential tremor: Insights from the reclassification of a cohort of patients with lower limb tremor. Parkinsonism Relat Disord. 2018; 56: 109–10. DOI: 10.1016/j.parkreldis.2018.06.029. Epub 2018 Jun 21. PMID: 29958776.
16. Elble RJ. Do We Belittle Essential Tremor by Calling It a Syndrome Rather Than a Disease? No. Front Neurol. 2020; 11: 586606. DOI: 10.3389/fneur.2020.586606. PMID: 33101188; PMCID: PMC7554602.
17. Louis ED, Huey ED, Cosentino S. Features of "ET plus" correlate with age and tremor duration: "ET plus" may be a disease stage rather than a subtype of essential tremor. Parkinsonism Relat Disord. 2021; 91: 42–47. DOI: 10.1016/j.parkreldis.2021.08.017. Epub 2021 Sep 1. PMID: 34482193.
18. Gionco JT, Hartstone WG, Martuscello RT, Kuo SH, Faust PL, Louis ED. Essential Tremor versus "ET-plus": A Detailed Postmortem Study of Cerebellar Pathology. Cerebellum. 2021; 20 (6): 904–12. DOI: 10.1007/s12311-021-01263-6. Epub 2021 Mar 25. PMID: 33768479; PMCID: PMC8972074.
19. Iglesias-Hernandez D, Delgado N, McGurn M, Huey ED, Cosentino S, Louis ED. "ET Plus": Instability of the Diagnosis During Prospective Longitudinal Follow-up of Essential Tremor Cases. Front Neurol. 2021; 12: 782694. DOI: 10.3389/fneur.2021.782694. PMID: 34975736; PMCID: PMC8716461.
20. Erro R, Fasano A, Barone P, Bhatia KP. Milestones in Tremor Research: 10 Years Later. Mov Disord Clin Pract. 2022; 9 (4): 429–35. DOI: 10.1002/mdc3.13418. PMID: 35582314; PMCID: PMC9092753.
21. Benito-León J, Louis ED, Bermejo-Pareja F. Neurological disorders in central spain study group. Elderly-onset essential tremor is associated with dementia. Neurology. 2006; 66 (10): 1500–5. DOI: 10.1212/01.wnl.0000216134.88617.de. PMID: 16717208.
22. Huang H, Yang X, Zhao Q, Chen Y, Ning P, Shen Q, et al. Prevalence and risk Ffctors of depression and anxiety in essential tremor patients: a cross-sectional study in Southwest China. Front Neurol. 2019; 10: 1194. DOI: 10.3389/fneur.2019.01194. PMID: 31803131; PMCID: PMC6873801.
23. Hedera P, Cibulčík F, Davis TL. Pharmacotherapy of essential tremor. J Cent Nerv Syst Dis. 2013; 5: 43–55. DOI: 10.4137/JCNSD.S6561. PMID: 24385718; PMCID: PMC3873223.
24. Deuschl G, Raethjen J, Hellriegel H, Elble R. Treatment of patients with essential tremor. Lancet Neurol. 2011; 10 (2): 148–61. DOI: 10.1016/S1474-4422(10)70322-7. PMID: 21256454.
25. Zesiewicz TA, Elble R, Louis ED, Hauser RA, Sullivan KL, Dewey RB Jr, et al. Quality standards subcommittee of the american academy of neurology. Practice parameter: therapies for essential tremor: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2005; 64 (12): 2008–20. DOI: 10.1212/01.WNL.0000163769.28552.CD. Epub 2005 Jun 22. PMID: 15972843.
26. Ferreira JJ, Mestre TA, Lyons KE, Benito-León J, Tan EK, Abbruzzese G, et al. MDS task force on tremor and the MDS evidence based medicine committee. MDS evidence-based review of treatments for essential tremor. Mov Disord. 2019; 34 (7): 950–8. DOI: 10.1002/mds.27700. Epub 2019 May 2. PMID: 31046186.
27. Koller W, Biary N, Cone S. Disability in essential tremor: effect of treatment. Neurology. 1986; 36 (7): 1001–4. DOI: 10.1212/wnl.36.7.1001. PMID: 2940473.
28. Zesiewicz TA, Elble RJ, Louis ED, Gronseth GS, Ondo WG, Dewey RB Jr, et al. Evidence-based guideline update: treatment of essential tremor: report of the Quality Standards subcommittee of the American Academy of Neurology. Neurology. 2011; 77 (19): 1752–5. DOI: 10.1212/WNL.0b013e318236f0fd. Epub 2011 Oct 19. PMID: 22013182; PMCID: PMC3208950.
29. Flora ED, Perera CL, Cameron AL, Maddern GJ. Deep brain stimulation for essential tremor: a systematic review. Mov Disord. 2010; 25 (11): 1550–9. DOI: 10.1002/mds.23195. PMID: 20623768.
30. Verla T, Marky A, Farber H, Petraglia FW 3rd, Gallis J, Lokhnygina Y, et al. Impact of advancing age on post-operative complications of deep brain stimulation surgery for essential tremor. J Clin Neurosci. 2015; 22 (5): 872–6. DOI: 10.1016/j.jocn.2014.11.005. Epub 2015 Feb 7. PMID: 25669119; PMCID: PMC4512238.
31. Favilla CG, Ullman D, Wagle Shukla A, Foote KD, Jacobson CE 4th, Okun MS. Worsening essential tremor following deep brain stimulation: disease progression versus tolerance. Brain. 2012; 135 (Pt 5): 1455–62. DOI: 10.1093/brain/aws026. Epub 2012 Feb 17. PMID: 22344584.
32. Frighetto L, Bizzi J, Oppitz P. Stereotactic radiosurgery for movement disorders. Surg Neurol Int. 2012; 3 (Supple 1): S10–6. DOI: 10.1007/978-3-642-11151-8_18.
33. Agrawal M, Garg K, Samala R, Rajan R, Naik V, Singh M. Outcome and complications of MR guided focused ultrasound for essential tremor: a systematic review and meta-analysis. Front Neurol. 2021; 12: 654711. DOI: 10.3389/fneur.2021.654711. PMID: 34025558; PMCID: PMC8137896.
34. Gallay MN, Moser D, Rossi F, Pourtehrani P, Magara AE, Kowalski M, et al. Incisionless transcranial MR-guided focused ultrasound in essential tremor: cerebellothalamic tractotomy. J Ther Ultrasound. 2016; 4: 5. DOI: 10.1186/s40349-016-0049-8. PMID: 26877873; PMCID: PMC4752806.
35. Titova NV, Katunina EA, Tairova RT, Senko IV, Dzhafarov VM, Malyhina EA. Farmakorezistentnyj tremor pri bolezni Parkinsona i jessencial'nom tremore. Zhurnal nevrologii i psihiatrii im. S. S. Korsakova. 2022; 122 (10): 24–30. DOI: 10.17116/jnevro202212210124. PMID: 36279225. Russian.
36. Elias WJ, Huss D, Voss T, Loomba J, Khaled M, Zadicario E, et al. A pilot study of focused ultrasound thalamotomy for essential tremor. N Engl J Med. 2013; 369 (7): 640–8. DOI: 10.1056/NEJMoa1300962. PMID: 23944301.
37. Elias WJ, Lipsman N, Ondo WG, Ghanouni P, Kim YG, Lee W, et al. A randomized trial of focused ultrasound thalamotomy for essential tremor. N Engl J Med. 2016; 375 (8): 730–9. DOI: 10.1056/NEJMoa1600159. PMID: 27557301.
38. Halpern CH, Santini V, Lipsman N, Lozano AM, Schwartz ML, Shah BB, et al. Three-year follow-up of prospective trial of focused ultrasound thalamotomy for essential tremor. Neurology. 2019; 93 (24): e2284-e2293. DOI: 10.1212/WNL.0000000000008561. Epub 2019 Nov 20. PMID: 31748250.
39. Sinai A, Nassar M, Eran A, Constantinescu M, Zaaroor M, Sprecher E, et al. Magnetic resonance-guided focused ultrasound thalamotomy for essential tremor: a 5-year single-center experience. J Neurosurg. 2019: 1–8. DOI: 10.3171/2019.3.JNS19466. Epub ahead of print. PMID: 31277064.
40. Schreglmann SR, Bauer R, Hägele-Link S, Bhatia KP, Natchev P, Wegener N, et al. Unilateral cerebellothalamic tract ablation in essential tremor by MRI-guided focused ultrasound. Neurology. 2017; 88 (14): 1329–33. DOI: 10.1212/WNL.0000000000003795. Epub 2017 Mar 8. PMID: 28275083.
41. Mohammed N, Patra D, Nanda A. A meta-analysis of outcomes and complications of magnetic resonance-guided focused ultrasound in the treatment of essential tremor. Neurosurg Focus. 2018; 44 (2): E4. DOI: 10.3171/2017.11.FOCUS17628. Erratum in: Neurosurg Focus. 2018; 45 (1): E16. PMID: 29385917.
42. Park YS, Jung NY, Na YC, Chang JW. Four-year follow-up results of magnetic resonance-guided focused ultrasound thalamotomy for essential tremor. Mov Disord. 2019; 34 (5): 727–34. DOI: 10.1002/mds.27637. Epub 2019 Feb 13. PMID: 30759322.
43. Gasca-Salas C, Guida P, Piredda R, Obeso I, Vela Desojo L, Martínez-Fernández R, et al. Cognitive safety after unilateral magnetic resonance-guided focused ultrasound thalamotomy for essential tremor. J Neurol Neurosurg Psychiatry. 2019; 90 (7): 830–1. DOI:

10.1136/jnnp-2018-320129. Epub 2019 Mar 8. PMID: 30850471.
44. Rohringer CR, Sewell IJ, Gandhi S, Isen J, Davidson B, McSweeney M, et al. Cognitive effects of unilateral thalamotomy for tremor: a meta-analysis. Brain Commun. 2022; 4 (6): fcac287. DOI: 10.1093/braincomms/fcac287. PMID: 36440102; PMCID: PMC9683603.
45. Young RF, Hesselgesser RD, Ahn E, Vermeulen S, Li F, Lee J. Bilateral Gamma Knife thalamotomy for treatment of axial tremor. Transl Cancer Res. 2014; 3 (6): 525–9. DOI: 10.3978/j.issn.2218-676X.2014.11.01.
46. Iorio-Morin C, Yamamoto K, Sarica C, Zemmar A, Levesque M, Brisebois S, et al. Bilateral focused ultrasound thalamotomy for essential tremor (BEST-FUS Phase 2 Trial). Mov Disord. 2021; 36 (11): 2653–62. DOI: 10.1002/mds.28716. Epub 2021 Jul 20. PMID: 34288097.
47. Fukutome K, Hirabayashi H, Osakada Y, Kuga Y, Ohnishi H. Bilateral magnetic resonance imaging-guided focused ultrasound thalamotomy for essential tremor. stereotact funct neurosurg. 2022; 100 (1): 44–52. DOI: 10.1159/000518662. Epub 2021 Sep 7. PMID: 34515233.
48. Scantlebury N, Rohringer CR, Rabin JS, Yunusova Y, Huang Y, Jones RM, et al. Safety of bilateral staged magnetic resonance-guided focused ultrasound thalamotomy for essential tremor. Mov Disord Clin Pract. 2023; 10 (10): 1559–61. DOI: 10.1002/mdc3.13882. PMID: 37868927; PMCID: PMC10585969.
49. Gallay MN, Moser D, Jeanmonod D. MR-guided focused ultrasound cerebellothalamic tractotomy for chronic therapy-resistant essential tremor: anatomical target reappraisal and clinical results. J Neurosurg. 2020; 134 (2): 376–85. DOI: 10.3171/2019.12.JNS192219. PMID: 32032945.
50. Vetkas A, Boutet A, Sarica C, Germann J, Gwun D, Yamamoto K, et al. Successful magnetic resonance-guided focused ultrasound treatment of tremor in patients with a skull density ratio of 0.4 or less. J Neurosurg. 2023; 1: 1–9. DOI: 10.3171/2023.6.JNS23171. Epub ahead of print. PMID: 37657095.

Литература

1. Louis ED, Ferreira JJ. How common is the most common adult movement disorder? Update on the worldwide prevalence of essential tremor. Mov Disord. 2010; 25 (5): 534–41. DOI: 10.1002/mds.22838. PMID: 20175185.
2. Bain PG, Findley LJ, Thompson PD, Gresty MA, Rothwell JC, Harding AE, et al. A study of hereditary essential tremor. Brain. 1994; 117 (Pt 4): 805–24. DOI: 10.1093/brain/117.4.805. PMID: 7922467.
3. Bhatia KP, Bain P, Bajaj N, Elble RJ, Hallett M, Louis ED, et al. Tremor Task Force of the International Parkinson and Movement Disorder Society. Consensus Statement on the classification of tremors. from the task force on tremor of the International Parkinson and Movement Disorder Society. Mov Disord. 2018; 33 (1): 75–87. DOI: 10.1002/mds.27121. Epub 2017 Nov 30. PMID: 29193359; PMCID: PMC6530552.
4. Иллариошкин С. Н., Иванова-Смоленская И. А. Дрожательные гиперкинезы: Руководство для врачей. Сер. руководств «Двигательные расстройства». М.: Атмосфера, 2011; 360 с.
5. Wider C, Ross OA, Wszolek ZK. Genetics of Parkinson disease and essential tremor. Curr Opin Neurol. 2010; 23 (4): 388–93. DOI: 10.1097/WCO.0b013e32833b1f4c. PMID: 20489616; PMCID: PMC3930090.
6. Louis ED, Clark LN, Ottman R. Familial versus Sporadic Essential Tremor: What Patterns Can One Decipher in Age of Onset? Neuroepidemiology. 2015; 44 (3): 166–72. DOI: 10.1159/000381807. Epub 2015 May 7. PMID: 25967236; PMCID: PMC4764084.
7. Stefansson H, Steinberg S, Petursson H, Gustafsson O, Gudjonsdottir IH, Jonsdottir GA et al. Variant in the sequence of the LINGO1 gene confers risk of essential tremor. Nat Genet. 2009; 41 (3): 277–9. DOI: 10.1038/ng.299. Epub 2009 Feb 1. Erratum in: Nat Genet. 2009; 41 (4): 504. PMID: 19182806; PMCID: PMC3740956.
8. Mi S, Hu B, Hahm K, Luo Y, Kam Hui ES, Yuan Q, et al. LINGO-1 antagonist promotes spinal cord remyelination and axonal integrity in MOG-induced experimental autoimmune encephalomyelitis. Nat Med. 2007; 13 (10): 1228–33. DOI: 10.1038/nm1664. Epub 2007 Sep 30. PMID: 17906634.
9. Louis ED, Faust PL, Vonsattel JP, Honig LS, Rajput A, Robinson CA, et al. Neuropathological changes in essential tremor: 33 cases compared with 21 controls. Brain. 2007; 130 (Pt12): 3297–307. DOI: 10.1093/brain/awm266. Epub 2007 Nov 19. PMID: 18025031.
10. Kuo SH, Wang J, Tate WJ, Pan MK, Kelly GC, Gutierrez J, et al. Cerebellar Pathology in Early Onset and Late Onset Essential Tremor. Cerebellum. 2017; 16 (2): 473–82. DOI: 10.1007/s12311-016-0826-5. PMID: 27726094; PMCID: PMC5336493.
11. Long MA, Deans MR, Paul DL, Connors BW. Rhythmicity without synchrony in the electrically uncoupled inferior olive. J Neurosci. 2002; 22 (24): 10898–905. DOI: 10.1523/JNEUROSCI.22-24-10898.2002. PMID: 12486184; PMCID: PMC2834587.
12. Deuschl G, Petersen I, Lorenz D, Christensen K. Tremor in the elderly: Essential and aging-related tremor. Mov Disord. 2015; 30 (10): 1327–34. DOI: 10.1002/mds.26265. Epub 2015 Jun 22. PMID: 26095699; PMCID: PMC4779797.
13. Mu J, Carden WB, Kurukulasuriya NC, Alexander GM, Godwin DW. Ethanol influences on native T-type calcium current in thalamic sleep circuitry. J Pharmacol Exp Ther. 2003; 307 (1): 197–204. DOI: 10.1124/jpet.103.053272. Epub 2003 Jul 31. PMID: 12893844.
14. Hedera P. Emerging strategies in the management of essential tremor. Ther Adv Neurol Disord. 2017; 10 (2): 137–48. DOI: 10.1177/1756285616679123. Epub 2016 Nov 30. PMID: 28382111; PMCID: PMC5367648.
15. Rajalingam R, Breen DP, Lang AE, Fasano A. Essential tremor plus is more common than essential tremor: Insights from the reclassification of a cohort of patients with lower limb tremor. Parkinsonism Relat Disord. 2018; 56: 109–10. DOI: 10.1016/j.parkreldis.2018.06.029. Epub 2018 Jun 21. PMID: 29958776.
16. Elble RJ. Do We Belittle Essential Tremor by Calling It a Syndrome Rather Than a Disease? No. Front Neurol. 2020; 11: 586606. DOI: 10.3389/fneur.2020.586606. PMID: 33101188; PMCID: PMC7554602.
17. Louis ED, Huey ED, Cosentino S. Features of "ET plus" correlate with age and tremor duration: "ET plus" may be a disease stage rather than a subtype of essential tremor. Parkinsonism Relat Disord. 2021; 91: 42–47. DOI: 10.1016/j.parkreldis.2021.08.017. Epub 2021 Sep 1. PMID: 34482193.
18. Gionco JT, Hartstone WG, Martuscello RT, Kuo SH, Faust PL, Louis ED. Essential Tremor versus "ET-plus": A Detailed Postmortem Study of Cerebellar Pathology. Cerebellum. 2021; 20 (6): 904–12. DOI: 10.1007/s12311-021-01263-6. Epub 2021 Mar 25. PMID: 33768479; PMCID: PMC8972074.
19. Iglesias-Hernandez D, Delgado N, McGurn M, Huey ED, Cosentino S, Louis ED. "ET Plus": Instability of the Diagnosis During Prospective Longitudinal Follow-up of Essential Tremor Cases. Front Neurol. 2021; 12: 782694. DOI: 10.3389/fneur.2021.782694. PMID: 34975736; PMCID: PMC8716461.
20. Erro R, Fasano A, Barone P, Bhatia KP. Milestones in Tremor Research: 10 Years Later. Mov Disord Clin Pract. 2022; 9 (4): 429–35. DOI: 10.1002/mdc3.13418. PMID: 35582314; PMCID: PMC9092753.
21. Benito-León J, Louis ED, Bermejo-Pareja F. Neurological disorders in central spain study group. Elderly-onset essential tremor is associated with dementia. Neurology. 2006; 66 (10): 1500–5. DOI: 10.1212/01.wnl.0000216134.88617.de. PMID: 16717208.
22. Huang H, Yang X, Zhao Q, Chen Y, Ning P, Shen Q, et al. Prevalence and risk Ffctors of depression and anxiety in essential tremor patients: a cross-sectional study in Southwest China. Front Neurol. 2019; 10: 1194. DOI: 10.3389/fneur.2019.01194. PMID: 31803131; PMCID: PMC6873801.
23. Hedera P, Cibulčík F, Davis TL. Pharmacotherapy of essential tremor. J Cent Nerv Syst Dis. 2013; 5: 43–55. DOI: 10.4137/JCNSD.S6561. PMID: 24385718; PMCID: PMC3873223.
24. Deuschl G, Raethjen J, Hellriegel H, Elble R. Treatment of patients with essential tremor. Lancet Neurol. 2011; 10 (2): 148–61. DOI:

10.1016/S1474-4422(10)70322-7. PMID: 21256454.
25. Zesiewicz TA, Elble R, Louis ED, Hauser RA, Sullivan KL, Dewey RB Jr, et al. Quality standards subcommittee of the american academy of neurology. Practice parameter: therapies for essential tremor: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2005; 64 (12): 2008–20. DOI: 10.1212/01.WNL.0000163769.28552.CD. Epub 2005 Jun 22. PMID: 15972843.
26. Ferreira JJ, Mestre TA, Lyons KE, Benito-León J, Tan EK, Abbruzzese G, et al. MDS task force on tremor and the MDS evidence based medicine committee. MDS evidence-based review of treatments for essential tremor. Mov Disord. 2019; 34 (7): 950–8. DOI: 10.1002/mds.27700. Epub 2019 May 2. PMID: 31046186.
27. Koller W, Biary N, Cone S. Disability in essential tremor: effect of treatment. Neurology. 1986; 36 (7): 1001–4. DOI: 10.1212/wnl.36.7.1001. PMID: 2940473.
28. Zesiewicz TA, Elble RJ, Louis ED, Gronseth GS, Ondo WG, Dewey RB Jr, et al. Evidence-based guideline update: treatment of essential tremor: report of the Quality Standards subcommittee of the American Academy of Neurology. Neurology. 2011; 77 (19): 1752–5. DOI: 10.1212/WNL.0b013e318236f0fd. Epub 2011 Oct 19. PMID: 22013182; PMCID: PMC3208950.
29. Flora ED, Perera CL, Cameron AL, Maddern GJ. Deep brain stimulation for essential tremor: a systematic review. Mov Disord. 2010; 25 (11): 1550–9. DOI: 10.1002/mds.23195. PMID: 20623768.
30. Verla T, Marky A, Farber H, Petraglia FW 3rd, Gallis J, Lokhnygina Y, et al. Impact of advancing age on post-operative complications of deep brain stimulation surgery for essential tremor. J Clin Neurosci. 2015; 22 (5): 872–6. DOI: 10.1016/j.jocn.2014.11.005. Epub 2015 Feb 7. PMID: 25669119; PMCID: PMC4512238.
31. Favilla CG, Ullman D, Wagle Shukla A, Foote KD, Jacobson CE 4th, Okun MS. Worsening essential tremor following deep brain stimulation: disease progression versus tolerance. Brain. 2012; 135 (Pt 5): 1455–62. DOI: 10.1093/brain/aws026. Epub 2012 Feb 17. PMID: 22344584.
32. Frighetto L, Bizzi J, Oppitz P. Stereotactic radiosurgery for movement disorders. Surg Neurol Int. 2012; 3 (Supple 1): S10–6. DOI: 10.1007/978-3-642-11151-8_18.
33. Agrawal M, Garg K, Samala R, Rajan R, Naik V, Singh M. Outcome and complications of MR guided focused ultrasound for essential tremor: a systematic review and meta-analysis. Front Neurol. 2021; 12: 654711. DOI: 10.3389/fneur.2021.654711. PMID: 34025558; PMCID: PMC8137896.
34. Gallay MN, Moser D, Rossi F, Pourtehrani P, Magara AE, Kowalski M, et al. Incisionless transcranial MR-guided focused ultrasound in essential tremor: cerebellothalamic tractotomy. J Ther Ultrasound. 2016; 4: 5. DOI: 10.1186/s40349-016-0049-8. PMID: 26877873; PMCID: PMC4752806.
35. Титова Н. В., Катунина Е. А., Таирова Р. Т., Сенько И. В., Джафаров В. М., Малыхина Е. А. Фармакорезистентный тремор при болезни Паркинсона и эссенциальном треморе. Журнал неврологии и психиатрии им. С. С. Корсакова. 2022; 122 (10): 24–30. DOI: 10.17116/jnevro202212210124. PMID: 36279225.
36. Elias WJ, Huss D, Voss T, Loomba J, Khaled M, Zadicario E, et al. A pilot study of focused ultrasound thalamotomy for essential tremor. N Engl J Med. 2013; 369 (7): 640–8. DOI: 10.1056/NEJMoa1300962. PMID: 23944301.
37. Elias WJ, Lipsman N, Ondo WG, Ghanouni P, Kim YG, Lee W, et al. A randomized trial of focused ultrasound thalamotomy for essential tremor. N Engl J Med. 2016; 375 (8): 730–9. DOI: 10.1056/NEJMoa1600159. PMID: 27557301.
38. Halpern CH, Santini V, Lipsman N, Lozano AM, Schwartz ML, Shah BB, et al. Three-year follow-up of prospective trial of focused ultrasound thalamotomy for essential tremor. Neurology. 2019; 93 (24): e2284-e2293. DOI: 10.1212/WNL.0000000000008561. Epub 2019 Nov 20. PMID: 31748250.
39. Sinai A, Nassar M, Eran A, Constantinescu M, Zaaroor M, Sprecher E, et al. Magnetic resonance-guided focused ultrasound thalamotomy for essential tremor: a 5-year single-center experience. J Neurosurg. 2019: 1–8. DOI: 10.3171/2019.3.JNS19466. Epub ahead of print. PMID: 31277064.
40. Schreglmann SR, Bauer R, Hägele-Link S, Bhatia KP, Natchev P, Wegener N, et al. Unilateral cerebellothalamic tract ablation in essential tremor by MRI-guided focused ultrasound. Neurology. 2017; 88 (14): 1329–33. DOI: 10.1212/WNL.0000000000003795. Epub 2017 Mar 8. PMID: 28275083.
41. Mohammed N, Patra D, Nanda A. A meta-analysis of outcomes and complications of magnetic resonance-guided focused ultrasound in the treatment of essential tremor. Neurosurg Focus. 2018; 44 (2): E4. DOI: 10.3171/2017.11.FOCUS17628. Erratum in: Neurosurg Focus. 2018; 45 (1): E16. PMID: 29385917.
42. Park YS, Jung NY, Na YC, Chang JW. Four-year follow-up results of magnetic resonance-guided focused ultrasound thalamotomy for essential tremor. Mov Disord. 2019; 34 (5): 727–34. DOI: 10.1002/mds.27637. Epub 2019 Feb 13. PMID: 30759322.
43. Gasca-Salas C, Guida P, Piredda R, Obeso I, Vela Desojo L, Martínez-Fernández R, et al. Cognitive safety after unilateral magnetic resonance-guided focused ultrasound thalamotomy for essential tremor. J Neurol Neurosurg Psychiatry. 2019; 90 (7): 830–1. DOI: 10.1136/jnnp-2018-320129. Epub 2019 Mar 8. PMID: 30850471.
44. Rohringer CR, Sewell IJ, Gandhi S, Isen J, Davidson B, McSweeney M, et al. Cognitive effects of unilateral thalamotomy for tremor: a meta-analysis. Brain Commun. 2022; 4 (6): fcac287. DOI: 10.1093/braincomms/fcac287. PMID: 36440102; PMCID: PMC9683603.
45. Young RF, Hesselgesser RD, Ahn E, Vermeulen S, Li F, Lee J. Bilateral Gamma Knife thalamotomy for treatment of axial tremor. Transl Cancer Res. 2014; 3 (6): 525–9. DOI: 10.3978/j.issn.2218-676X.2014.11.01.
46. Iorio-Morin C, Yamamoto K, Sarica C, Zemmar A, Levesque M, Brisebois S, et al. Bilateral focused ultrasound thalamotomy for essential tremor (BEST-FUS Phase 2 Trial). Mov Disord. 2021; 36 (11): 2653–62. DOI: 10.1002/mds.28716. Epub 2021 Jul 20. PMID: 34288097.
47. Fukutome K, Hirabayashi H, Osakada Y, Kuga Y, Ohnishi H. Bilateral magnetic resonance imaging-guided focused ultrasound thalamotomy for essential tremor. stereotact funct neurosurg. 2022; 100 (1): 44–52. DOI: 10.1159/000518662. Epub 2021 Sep 7. PMID: 34515233.
48. Scantlebury N, Rohringer CR, Rabin JS, Yunusova Y, Huang Y, Jones RM, et al. Safety of bilateral staged magnetic resonance-guided focused ultrasound thalamotomy for essential tremor. Mov Disord Clin Pract. 2023; 10 (10): 1559–61. DOI: 10.1002/mdc3.13882. PMID: 37868927; PMCID: PMC10585969.
49. Gallay MN, Moser D, Jeanmonod D. MR-guided focused ultrasound cerebellothalamic tractotomy for chronic therapy-resistant essential tremor: anatomical target reappraisal and clinical results. J Neurosurg. 2020; 134 (2): 376–85. DOI: 10.3171/2019.12.JNS192219. PMID: 32032945.
50. Vetkas A, Boutet A, Sarica C, Germann J, Gwun D, Yamamoto K, et al. Successful magnetic resonance-guided focused ultrasound treatment of tremor in patients with a skull density ratio of 0.4 or less. J Neurosurg. 2023; 1: 1–9. DOI: 10.3171/2023.6.JNS23171. Epub ahead of print. PMID: 37657095.