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Стаття надійшла до редакції 21.05.2024;
затверджена до публікації 21.06.2024

UDC 616.714+616.831]-001.31-036.8-06:616.89-008.441]-085.84 https://doi.org/10.26641/2307-0404.2024.3.313673

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TRANSCRANIAL ELECTRICAL STIMULATION IN POST-TRAUMATIC STRESS DISORDER AND BRAIN INJURY: POSSIBILITIES OF TUNING NEURONAL NETWORKS

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Цитування: Медичні перспективи. 2024. Т. 29, № 3. С. 175-183
Cited: Medicni perspektivi. 2024;29(3):175-183

Key words: *posttraumatic stress disorder, traumatic brain injury, functioning, veteran, neuroimaging studies transcranial direct current stimulation*
Ключові слова: *посттравматичний стресовий розлад, черепно-мозкова травма, функціонування, ветерани, нейровізуалізаційні дослідження, транскраніальна електростимуляція*

Abstract. Transcranial electrical stimulation in post-traumatic stress disorder and brain injury: possibilities of tuning neuronal networks. Smashna O.Y. *Transcranial direct current stimulation (tDCS) in the treatment of post-traumatic stress disorder (PTSD) is used to strengthen the inhibitory control of amygdala activity. However, there are still limited meta-analytic studies examining different tDCS protocols on core PTSD symptoms and the relationship between stimulation parameters and effect size. The objective is to investigate the effectiveness of such an intervention, which is a complex combination of a psychotherapy program with tDCS in the treatment of patients with PTSD and mild traumatic brain injury (mTBI) by assessing their level of functioning. 329 veterans (PTSD (n=109), mTBI (n=112), PTSD + mTBI (n=108) were examined using WHODAS 2.0. Standardized treatment was provided as well as psychotherapeutic intervention - a combination of psychoeducation with motivational interviewing and acceptance and commitment therapy for PTSD and tDCS. Clinical targets of therapy in the PTSD group were symptoms of intrusion, avoidance, hyperactivation and protocol of tDCS was dorsolateral prefrontal cortex arousing stimulation. In PTSD + TBI group clinical targets were neurocognitive symptoms, intrusion symptoms, avoidance, hyperactivation and tDCT protocol was motor cortex-supraorbital area inhibitory stimulation. The targest for TBI group was neurocognitive symptoms and tDCS protocol was occipital region exciting stimulation. The long-term effectiveness and the impact on neuroplasticity processes allow considering transcranial direct current stimulation as a promising method of neurorehabilitation of patients with a combination of posttraumatic stress disorder and mild traumatic brain injury.*

Реферат. Транскраніальна електростимуляція при посттравматичному стресовому розладі та черепно-мозковій травмі: можливості налаштування нейрональних мереж. Смашна О.Є. *Транскраніальна електростимуляція (tDCS) при лікуванні посттравматичного стресового розладу (ПТСР) використовується для посилення гальмівного контролю активності мигдалини. Проте метааналітичні дослідження, які вивчають різні протоколи транскраніальної електростимуляції щодо основних симптомів ПТСР і зв'язку між параметрами стимуляції та розміром ефекту, все ще не достатньо вивчені. Мета полягала в тому, щоб дослідити ефективність комплексного втручання у вигляді поєднання психотерапевтичної програми з tDCS у лікуванні пацієнтів із ПТСР та легкою черепно-мозковою травмою (ЧМТ) шляхом оцінки їхнього рівня функціонування. Було обстежено 329 ветеранів (109 з ПТСР, 112 з легкою ЧМТ та 108 з коморбідними ПТСР та легкою ЧМТ) за допомогою опитувальника обмеження життєдіяльності ВООЗ (WHODAS 2.0). Усім пацієнтам було проведено стандартизоване лікування, а також психотерапевтичне втручання – поєднання психоосвіти з мотиваційним інтерв'ю та терапія прийняття та відповідальності, а також tDCS. Клінічними цілями терапії в групі ПТСР були симптоми вторгнення, уникнення, гіперактивації, а протоколом tDCS була стимуляція дорсолатеральної префронтальної кори головного мозку. У групі ПТСР + ЧМТ клінічними цілями були нейрокогнітивні симптоми, симптоми вторгнення, уникнення, гіперактивації, а протоколом tDCT була інгібіторна стимуляція моторної кори головного мозку та супраорбітальної ділянки. Ціллю для групи ЧМТ були нейрокогнітивні симптоми, а протоколом tDCS була збудлива стимуляція потиличної ділянки. Віддалена ефективність і вплив на процеси нейропластичності дозволяють розглядати tDCS як перспективний метод нейрореабілітації пацієнтів із поєднанням ПТСР та легкої ЧМТ.*

Neuroimaging studies of posttraumatic stress disorder (PTSD) have focused on dysfunctional executive function systems, contextual processing, threat detection, fear learning, and emotional regulation [1, 2, 3].

The most common medical comorbidity of PTSD and mild brain injury in modern realities leads to the addition of cognitive disorders of the organic register [4, 5], mental fatigue, changes in personality and behavior in the form of a combination of impulsivity and apathy caused by multiple axonal brain damage to the classic symptoms of PTSD [5, 6].

Therefore, in the comorbidity of PTSD and mild traumatic brain injury (mTBI), there is hyperactivity in the emotional processing network and hypoactivity in the dorsal network of executive functions [7, 8] and are characterized by a disturbance of adaptive processing systems, which is associated with changes in the functional and even morphological structures of the brain, which is confirmed by fMRI studies [9, 10].

Medical treatment of patients with PTSD and mild TBI is characterized by low compliance due to a large number of side effects of treatment, resistance of symptoms to psychotropic drugs [4, 5, 10]. Cognitive impairments become an obstacle to the involvement of PTSD patients in effective methods of providing psychotherapeutic care, because to obtain a positive result from interventions based on cognitive control of emotions and changing maladaptive thoughts and behaviors to adaptive ones, sufficient executive function is required [8, 10, 11, 12]. And the actual deficit of executive function or inefficient functioning of neural networks reduces the effectiveness of trauma-oriented and evidence-based psychological interventions for PTSD patients [13, 14, 15, 16].

Neuromodulation (or neurostimulation) is one of the most modern areas of science and is a technology of influencing the functional state (bioelectrogenesis) of the brain and spinal cord [17]. Transcranial direct current stimulation has some clinical and practical advantages compared to other methods of brain stimulation – it is cheap, easy to use, and has minimal side effects [18, 19].

Transcranial direct current stimulation (tDCS) in the treatment of post-traumatic stress disorders is used to strengthen the inhibitory control of amygdala activity [20, 21, 22, 23].

However, there are still limited meta-analytic studies examining different tDCS protocols on core PTSD symptoms and the relationship between stimulation parameters and effect size[24].

The objective is to investigate the effectiveness of such an intervention, which is a complex combination of a psychotherapy program with transcranial direct current electrical stimulation in the treatment of patients with posttraumatic stress disorder and mild traumatic brain injury by assessing their level of functioning.

MATERIALS AND METHODS OF RESEARCH

We searched MEDLINE/PubMed and Web of Science databases CrossRef, PubMed, Google Scholar, Directory of Open Access Scholarly Resources (ROAD), Bielefeld Academic Search Engine (BASE), Directory of Open Access Journals (DOAJ) for the period 2012-2022 by keywords: post-traumatic stress disorder, mild traumatic brain injury, transcranial indirect electrical stimulation (tDCS), neuromodulation, tDCS mounting, comorbidity with the aim of selecting tDCS mounting as an augmenting combined therapy in the structure of medical management of PTSD, TBI and comorbid conditions of mild TBI+PTSD. 12 studies were selected for analysis of tDCS mounting for PTSD and mTBI.

The investigation was conducted in Ternopil clinical municipal psychoneurological hospital, Ternopil, Ukraine. The material of the research was the results of the examination of 329 employees of the Armed Forces, the National Guard and "volunteer battalions" who took part in combat operations in the Donetsk and Luhansk regions. Based on the results of the collected anamnestic data, the results of the clinical interview and the results of the CAPS-5, the specified contingent was structured into three research groups: 1 – a group of patients diagnosed with post-traumatic stress disorder (PTSD group) – 109 people (33.1% of the examined contingent); 2 group – patients with consequences of craniocerebral trauma (TBI group) – 112 people (34.0%); 3 group – patients suffering from PTSD with comorbid consequences of TBI (TBI group) – 108 people (32.8%). After providing prior informed consent to participate in the study all participants received a course of combined therapy, namely: in addition to standard therapy in accordance with the Unified Protocols for PTSD and mTBI, they received psychotherapeutic intervention (a combination of psychoeducation with elements of motivational interviewing and Acceptance and Commitment Therapy (ACT) for PTSD, and transcranial direct current electrical stimulation (tDCS) with low-frequency electrotherapy device “Radius-01 Cranio”. The duration of treatment was 8 weeks: 10 tDCS sessions daily and 8 weekly psychotherapy sessions lasting 45-60 minutes 1-2 times a week.

All studies of this scientific work meet the requirements and principles of bioethics. When performing the work, safety rules for patients were observed, rights and canons of human dignity were preserved, moral and ethical norms in accordance with the main provisions of GSP (1996), Council of Europe Convention on Human Rights and Biomedicine (on April 04, 1997), Helsinki Declaration of the World Medical association on the ethical principles of scientific medical research with human participation (1964-2000) and the Order of the Ministry of Health of Ukraine No. 281 on November 01, 2000, the ethical code of the scientists of Ukraine (2009).

In accordance with the WHO Disability Assessment Schedule (WHODAS 2.0) (English version) [25], we determined the level of functioning in the following domains: cognition (CW); mobility (MW); self care (SW); relationships (RW); daytime activity (LW); social activity (PW); general level of functioning (WHO). We alson determined a rank correlation between individual criteria of the CAPS-5 scale and domains of the WHODAS 2.0 test.

The obtained results were analyzed using the method of descriptive statistics, calculation of Fisher’s φ*-angular transformation, U-test of Mann and Whitney, W-test of Wilcoxon. IBM SPSS software was used in the work (IBM SPSS Statistics 28). Due to the use of parametric methods of statistical assessment in the reseach work, the normality of data distribution has not carried out. Conclusions with a probability of error of less than 0.5 percent were considered statistically significant [26].

RESULTS AND DISCUSSION

Based on the analysis of search sources, we determined that the issues regarding the algorithms of tDCS application in the comorbidity of PTSD and TBI are quite controversial and ambiguous. To be eligible, studies had to meet the following criteria: experimental studies in adult TBI patients receiving therapeutic tDCS with the primary/research objective of evaluating the outcomes that are clinical (e.g., cognitive, motor, or level of consciousness) or surrogate (e.g., electroencephalogram (EEG)). Transcranial magnetic stimulation (TMS) for any time period was compared to the pre-treatment baseline. We did not take into account the studies that did not meet these criteria, selecting first by title, then by abstract, and then by full text.

When analyzing scientific works that investigated the effectiveness of tDCS in PTSD, they can be

divided into several types depending on the method's application protocol – excitatory and inhibitory, unilateral and bilateral.

The neurobiological premise behind the differential effects of tDCS is the understanding that various neural networks and imbalances in their activity may underlie the four clusters of symptoms which are characteristic of PTSD. To be more specific, changes within and between networks, such as default mode network (DMN), salience network (SN) and central executive network (CEN), have been associated with PTSD. There is a persistent decrease in functional connectivity within the DMN, and disorganization between regions which belong to the DMN is associated with the consolidation of memories which are related to trauma and training to avoid reminders of the trauma.

Alternatively, functional connection within the SN appears to be enhanced, and a relative dominance of the SN over the DMN has been suggested. It is true that increased connection between the DMN and regions belonging to the SN and CEN, particularly between the amygdala and the hippocampus, and decreased connectivity between the amygdala and the medial prefrontal cortex have been shown to be associated with memory intrusion and re-experiencing traumatic events.

Decreased functional connection between the amygdala and the medial prefrontal cortex was also associated with excessive fear, while hyperactivation of the islet and the right prefrontal cortex, as well as general neural sensitization, were associated with hyperarousal. Thus, it is quite possible that by affecting various neural networks and associated clusters of symptoms, stimulation which is both excitatory and inhibitory would lead to a general positive effect. This is consistent with the studies which directly compare excitatory and inhibitory DLPFC stimulation.

Arousal stimulation. Six studies examined the effects of arousal stimulation on reducing PTSD symptoms in 107 experimental patients and 103 control patients. Despite the fact that individual study estimates were highly heterogeneous, the meta-analysis found a significant effect of symptom reduction with a large effect size (g Hedges = -1.161).

Four studies used stimulation of the right DLPFC. Despite the fact that the effect estimates were highly heterogeneous (I2 = 83.32%), the meta-analysis found a significant positive effect with a large effect size (Hedges' g = -1.225). Two studies using bilateral DLPFC stimulation did not reveal any significant positive effect. Four studies examined the effect of excitatory stimulation on the left DLPFC, and three of them revealed a pronounced effect and one a moderate effect of using such assembling.

Inhibitory stimulation. The effects of inhibitory stimulation on PTSD symptoms were studied five times with a total of 84 patients in the experimental group and 79 patients in the sham group, and in all of them exposure to the right DLPF was applied. The heterogeneity of individual effect estimates was low (I2 = 3.85%). A meta-analysis revealed a significant positive effect of active versus sham stimulation or no stimulation with a medium effect size (Hedges' g = -0.680).

The effectiveness of tDCS as an augmentative or adjuvant therapy has also been investigated. Six studies were included in the analysis, when patients underwent psychopharmacological and psychotherapeutic treatment during tDCS neuromodulation. The other four studies, in contrast, showed the results of tDCS monotherapy. Meta-regression did not show any significant difference (p=0.149) between studies that studied tDCS as mono-therapy or as augmentation therapy. A separate meta-analysis for the two groups showed that both tDCS and adjunctive therapy revealed significant positive effects with medium (Hedges' g = -0.649) and large (Hedges' g = -1.446) effect sizes, respectively.

Two studies examining the effects of active versus sham tDCS showed a considerable reduction in PTSD symptoms when the anode and cathode were placed over the left and right DLPFC, respectively. Several studies reveal that right stimulation is associated with significant improvement in core PTSD symptoms, whereas left stimulation results in improved mood but only moderate improvement in core trauma symptoms. This corresponds to the notion that PTSD is associated with right-sided pathology and is consistent with the study by Cirillo et al., which demonstrates the superiority of right prefrontal neuromodulatory exposure to reduce anxiety and PTSD symptoms and relative symptom severity in patients with comorbid PTSD and the decision to use a left or right stimulation protocol should be determined by depressive disorders.

Moreover, studies on the efficacy of tDCS as an augmentation showed that both mono- and augmentation therapy produced significant positive effects, although effect sizes for augmentation therapy were smaller compared to the control group. This may be due to the fact that control patients benefited from psychopharmacological and/or psychotherapeutic treatment.

With informed consent, 329 veterans who fully completed the research program (initial examination, treatment program, re-examination) were included in the study, from which three clinical groups were formed: individuals with PTSD (n=109), with mild TBI (n=112) and with a comorbid condition of PTSD+TBI (n=108). All patients received standard therapy according to the Unified Protocols for PTSD

and mild TBI. In addition, they received psychotherapeutic intervention (a combination of psychoeducation with elements of motivational interviewing and acceptance and commitment therapy (ACT) for PTSD) and transcranial electrical stimulation with constant current (tDCS). The duration of treatment was 8 weeks: 10 tDCS sessions daily and 8 weekly psychotherapy sessions lasting between 45 and 60 minutes once or twice a week.

We compared the functioning of patients in separate clinical groups (PTSD, TBI, and PTSD/TBI) after using a treatment program that included standard therapy in accordance with the Unified Protocols for PTSD and mild TBI, as well as a comprehensive intervention program: psychotherapeutic intervention (a combination of psychoeducation including elements of motivational interviewing and acceptance and commitment therapy for PTSD) and transcranial direct current electrical stimulation (tDCS) (Table 1).

Comprehensive intervention program for comorbidity of PTSD and mild TBI was based on the database analisis. Clinical targets of therapy in the PTSD group were symptoms of intrusion, avoidance, hyperactivation and protocol of tDCS was dorsolateral prefrontal cortex (DLPFC) arousing stimulation. In PTSD + TBI group clinical targets were neurocognitive symptoms, intrusion symptoms, avoidance, hyperactivation and tDCT protocol was motor cortex-supraorbital area (MI-SO) inhibitory stimulation. The targest for TBI group was neurocognitive symptoms and tDCS protocol was occipital region (Cz-Oz) exciting stimulation.

Table 1

Comprehensive intervention program for comorbidity of PTSD and mild TBI

Clinical groups	PTSD	PTSD+TBI	TBI
Clinical targets of therapy	Symptoms of intrusion, avoidance, hyperactivation	Neurocognitive symptoms, intrusion symptoms, avoidance, hyperactivation	Neurocognitive symptoms
Protocol of tDCS	DLPFC, arousing stimulation	MI-SO, inhibitory stimulation	Cz-Oz, arousing stimulation
Psychotherapeutic program	Psychoeducation Motivational interview Acceptance and commitment therapies for PTSD		

Notes: DLPFC – dorsolateral prefrontal cortex; MI-SO – motor cortex-supraorbital area; Cz-Oz – occipital region.

In accordance with the WHODAS 2.0 scale, we determined the level of functioning in six domains: cognition (CW); mobility (MW); self care (SW); relationships (RW); daytime activity (LW); social activity (PW); general level of functioning (WHO). We also determined a rank correlation between individual criteria of the CAPS-5 scale and domains of the WHODAS 2.0 test.

As a result of calculating the Mann-Whitney U coefficient when comparing the indicators of the WHODAS 2.0 test of the representatives of the studied groups during the initial and second examination (Table 2), it was established that in both cases the respondents of the PTSD group had significantly ($p \leq 0.032$) higher indicators in all scales of the test, than the respondents of the TBI group, which indicated a more significant impairment of the functionality of patients in the presence of PTSD. At the same time, in comparison with the PTSD/TBI group, respondents of the PTSD group had significantly higher scores only on the RW (relationship) scale at the re-examination ($p=0.016$); on the CW (cognitive sphere) scale at the re-examination and the LW (daily activity) scales and the WHO integral index at the initial examination – on the contrary, significantly lower indicators ($p \leq 0.003$), and on all other scales – no statistically significant differences were recorded at all ($p \geq 0.058$). Therefore, we associate the combination of PTSD and TBI with a more significant and persistent impairment of the cognitive sphere, as well as a decrease in daytime activity. However, the presence of PTSD without somatic burden was associated with more significant impairments in relationships.

The identified features make it possible to assert that the condition of PTSD patients was characterized by significantly more pronounced disturbances in all spheres of life, investigated by the WHODAS 2.0 test, than in patients with TBI. At the same time, the overall level of impairment in patients with comorbid PTSD and TBI at baseline was even more pronounced than in the PTSD group.

Table 2

Characteristics of clinical groups according to domains of the WHODAS 2.0 test at initial and second examination

No.	scales	CW	MW	SW	RW	LW	PW	WHO
Diagnostic examination	**groups**	**PTSD-TBI**						
	U	**4196**	**3765**	**5126,5**	**1173**	**549**	**406,5**	**76,5**
	p	**5,7E-05**	**1,2E-07**	**0,032**	**1,9E-25**	**9,8E-32**	**9,5E-34**	**7,1E-37**
	groups	**PTSD-PTSD/TBI**						
	U	**5019,5**	**5604**	**5687**	**5562**	**3921,5**	**5110,5**	**4540**
	p	**0,058**	**0,449**	**0,640**	**0,47007**	**1E-05**	**0,089**	**0,003**
	groups	**TBI-PTSD/TBI**						
	U	**3200**	**4060**	**5380**	**1086**	**109**	**509,5**	**22,5**
	p	**1,5E-09**	**7,7E-06**	**0,144**	**3,9E-26**	**6E-37**	**2,4E-32**	**2,4E-37**
Examination after treatment	**groups**	**PTSD-TBI**						
	U	**4049**	**3129**	**3942,5**	**2657,5**	**2233,5**	**1821**	**418,5**
	P	**1,5E-05**	**3,5E-13**	**1,2E-06**	**3,3E-13**	**8,8E-17**	**9,5E-20**	**5,3E-33**
	groups	**PTSD-PTSD/TBI**						
	U	**3882**	**5740,5**	**5693**	**4783**	**5167**	**5786**	**4925**
	P	**1,4E-05**	**0,555**	**0,614**	**0,016**	**0,119**	**0,828**	**0,037**
	groups	**TBI-PTSD/TBI**						
	U	**2264**	**3020,5**	**4129,5**	**3550**	**1020**	**2407**	**151,5**
	P	**1E-15**	**5,4E-14**	**1,7E-05**	**1E-07**	**4,4E-27**	**5,5E-15**	**7,8E-36**

Notes: CW – cognitive sphere; MW – mobility; SW – self-care; RW – relationships; LW – daytime activity; PW – social activity; WHO – total score.

Complex trends were revealed when comparing WHODAS 2.0 test scores in representatives of the TBI and PTSD/TBI groups. During the first examination, on all scales, except for MW (mobility) and SW (self-care), significantly (p≤1.5E-09) higher indicators occurred in the representatives of the PTSD/TBI group. On the MW (mobility) scale, on the contrary, these indicators were higher in the representatives of the TBI group (p=7.7E-06), and no significant differences were found on the SW (self-care) scale (p=0.144). During the re-examination both on the MW (mobility) scale and on the SW (self-care) scale, significantly higher indicators occurred in the respondents of the TBI group (p≤1.7E-05), and on all other scales, on the contrary, these indicators were higher in the respondents of the PTSD/TBI group (p≤1E-07). Therefore, patients in the PTSD/TBI group had lower functional indicators after the therapy with the exception of MW (mobility) and SW (self care).

Discussion. Therefore, the patients of all clinical groups revealed the most pronounced disorders in the cognitive sphere (CW), the sphere of relationships (RW), social (PW) and daytime activity (LW). We associate the combination of PTSD and TBI with more significant and persistent cognitive impairment, as well as reduced daytime activity.

At the second examination, the majority of respondents revealed significantly lower indicators of all

scales of the WHODAS 2.0 methodology than at the first one, which indicated the effectiveness of the therapy. The state of the cognitive sphere proved to be important for the effective psychotherapeutic effect on patients both within the PTSD group and with the PTSD/TBI. Patients in the PTSD/TBI group had lower functional scores than the other groups after the therapy, with the exception of MW (mobility) and SW (self care).

In the PTSD group, a tendency to the complete disappearance of the relationship between disturbances in the spheres of mobility and daytime activity and PTSD manifestations after the therapy was determined. Milder severity of self-care problems before therapy was associated with more effective leveling of mobility problems at the end of therapy. In the group of TBI, problems related to daytime activity, mobility after a course of therapy lost connections with any pathological symptoms, but problems related to social activity, on the contrary, after a course of therapy received a clear connection with the presence and expressiveness of distress (especially related to professional activity). In the PTSD/TBI group, the connections of violations in the field of self-care with "intrusion" symptoms and the connections between the expressiveness of violations in the sphere of relationships with the level of cognitive distortion of the feeling of guilt remained, and therefore the recommendations to increase the duration of the therapeutic program are determined specifically for the PTSD/TBI group.

The results of our study indicate that the combination of psychotherapy and transcranial direct current stimulation (tDCS) can be effective in treating patients with PTSD and mild traumatic brain injury (mTBI). However, it is crucial to critically compare and contrast these findings with those from other researchers in the field to contextualize and validate our results.

Previous studies have shown varying effects of tDCS on PTSD symptoms. For example, some researchers have reported significant improvements in core PTSD symptoms with tDCS, particularly in relation to reducing anxiety and enhancing emotional regulation [20, 21]. In contrast, other studies have found limited or no effects, attributing this to differences in stimulation parameters, such as electrode placement, current intensity, and session duration [22, 23]. Our findings align with studies that demonstrate a positive impact of tDCS on emotional processing, but they also diverge from studies where tDCS alone did not show significant improvements. This discrepancy could be due to variations in patient characteristics, including the severity of mTBI and comorbid conditions.

Furthermore, while our study supports the integration of tDCS with psychotherapy, other research has suggested that tDCS's efficacy might be enhanced or diminished depending on the type of psychotherapy employed [24]. Studies comparing different psychotherapeutic approaches combined with tDCS have produced mixed results, highlighting the need for further investigation into the optimal therapeutic protocols [25, 26].

Overall, our results contribute to the growing body of evidence supporting the use of neuromodulation techniques in conjunction with traditional psychotherapeutic methods for treating PTSD and mTBI. Nonetheless, the variability in outcomes across different studies underscores the necessity for additional meta-analytic reviews and well-controlled trials to refine tDCS protocols and better understand the mechanisms underlying its effectiveness.

CONCLUSIONS

1. In the majority of respondents, the indicators of all scales of the WHO Disability Assessment Schedule (WHODAS 2.0) methodology at the second examination were significantly lower than at the first one, which indicated the effectiveness of the therapy. The state of the cognitive sphere turned out to be important for the effective psychotherapeutic effect on patients both within the posttraumatic stress disorder group and with the comorbid posttraumatic stress disorder and traumatic brain injury. Patients in the comorbidity of posttraumatic stress disorder and traumatic brain injury had lower functional scores than the patients in the other groups after the therapy, with the exception of mobility and self care.
2. Transcranial direct current stimulation has some clinical and practical advantages compared to other methods of brain stimulation – it is cheap, easy to use and has minimal side effects. The long-term effectiveness and the impact on neuroplasticity processes allow considering transcranial direct current stimulation as a promising method of neurorehabilitation of patients with a combination of posttraumatic stress disorder and mild traumatic brain injury.
3. There are limited therapeutic options for patients with comorbidity of posttraumatic stress disorder and mild traumatic brain injury which is a complex medical comorbidity, and implementation of transcranial direct current stimulation is considered to be a potential neurorehabilitation adjunct which may improve clinical outcomes (e.g., motor, cognitive, and alertness) in such comorbidity.

Funding. This research received no external funding.

Conflict of interests. The authors declare no conflict of interest.

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Стаття надійшла до редакції 04.12.2023;
затверджена до публікації 11.09.2024