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Advances in the application of non-invasive brain stimulation technology in the rehabilitation of patients with cognitive impairment after stroke

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Abstract: *Post-stroke cognitive impairment is a common and serious sequela, which significantly affects the quality of life and independent living ability of patients. In recent years, non-invasive brain stimulation technology, as a new intervention method, has shown a potential effect in improving cognitive function after stroke. This paper reviews two major non-invasive brain stimulation technologies, including the application of transcranial DC stimulation and repeated transcranial magnetic stimulation in the treatment of post-stroke cognitive impairment and their latest research progress. Studies have shown that transcranial direct current stimulation can improve multiple cognitive fields such as memory, attention and executive function by regulating the excitability of the cerebral cortex. Repeated transcranial magnetic stimulation induces current through the magnetic field, which has a higher spatial resolution, which also plays a positive role in promoting neuroplasticity and functional recovery. Although the current research results are encouraging, there is still some heterogeneity between the results of different studies, and the long-term effect and safety need to be further verified. This article also discusses the challenges of non-invasive brain stimulation technology in clinical application, including individual differences, optimal parameter settings, and the combination of other rehabilitation methods. Future research should focus on large-scale, randomized controlled trials to determine the optimal treatment plan, and deeply explore the mechanism and principle of non-invasive brain stimulation technology. In summary, non-invasive brain stimulation technology provides new hope for the treatment of post-stroke cognitive impairment. However, its extensive clinical application still requires more evidence support and optimization strategies, pay attention to the improvement of non-invasive brain stimulation technology for the cognitive function after stroke, and choose the appropriate intervention plan according to the characteristics of the patient's condition.*

Keywords: *non-invasive brain stimulation technology, post-stroke cognitive impairment, application progress*

1. Introduction

Stroke is one of the main causes of disability and death in adults worldwide. It has five characteristics: high incidence, high recurrence rate and high economic burden [1]. 60% of patients after stroke have different degrees of cognitive impairment, which is a key problem affecting patients' quality of life and ability to live independently [2]. It not only hinders the rehabilitation process of patients, but also brings heavy care and economic burdens to the family and society. If not intervened in time, it may even develop into dementia [3]. At present, the treatment of post-stroke cognitive impairment (PSCI) is mostly treated with cognitive behavior therapy, and the effect is relatively limited [4]. Non-invasive Brain Stimulation (NIBS) is an emerging brain stimulation method, which mainly uses non-invasive technologies such as current and magnetic field to regulate the excitement of relevant functional areas of the brain. It is easy to operate and safe. Full, reliable, effective and other advantages, research in the field of neuropsychiatric diseases such as anxiety, pain, Parkinson's disease and schizophrenia has attracted widespread attention [5].This article repeats repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current

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stimulation(tDCS) Two non-invasive brain stimulation methods review the improvement effect of cognitive function in patients with post-stroke cognitive impairment, in order to provide reference for clinical practice.

2. Clinical overview of cognitive impairment after stroke

Post-stroke cognitive impairment refers to a series of syndromes that meet the diagnostic criteria for cognitive impairment within 6 months after the clinical event of stroke [6]. It is a common complication after stroke, which is seen in 50-83% of stroke patients [2] and is associated with poor functional prognosis. PSCI includes several cognitive disorders caused by brain injury, such as attention disorder, memory impairment and executive dysfunction. Clinically, simple intelligent state check scales, Montreal cognitive evaluation scales and evaluation scales for different cognitive fields are often used to screen and evaluate the degree of cognitive impairment in patients [7]. The severity of cognitive impairment is affected by factors such as age, education level, type of stroke, location of damaged brain area, and co-disease. Because the plasticity principle of the brain PSCI is reversible [8], the recovery of PSCI is very important for the improvement of self-care ability and quality of life of stroke patients. Timely treatment of primary diseases, control of risk factors and active cognitive rehabilitation training play an important role in patients, and the use of auxiliary treatment methods is more effective.

3. Clinical application of repeated transcranial magnetic stimulation in the treatment of PSCI

3.1. Mechanism of action of rTMS

Transcranial magnetic stimulation (TMS) is a magnetic stimulation technology that uses a pulsed magnetic field to act on the central nervous system of the brain to change the membrane potential of nerve cells in the cerebral cortex, causing it to generate induced currents and affect metabolism and neuroelectric activity in the brain, resulting in a series of physiological and biochemical reactions. Unlike single pulses, repeated transcranial magnetic stimulation is a continuous rhythmic magnetic pulse, so the effect is different. It acts on the cerebral cortex by regulating the excitability of the cortical circuit and thus changing the cell membrane potential to produce an induced current to improve the functional state of patients with stroke. It can non-invasively regulate the excitability of specific areas of the brain and its participation in the network, affecting sensory movement and cognitive ability. Current evidence shows that rTMS acts on the brain and promotes cognition in a variety of ways, including enhancing neuroplasticity, increasing the expression of neurotrophic factors, improving local cerebral blood flow, regulating neural network function connection, reducing pathological electroencephalic activity, anti-inflammatory and antioxidant effects, and improving psychological state. Recovery of functions [9]. Clinically, it is often used to treat depression, schizophrenia and other mental diseases. In recent years, it has also been widely used in the rehabilitation of cognitive function. Transcranial magnetic stimulation has the advantage of non-invasive and painless, which is recognized by patients.

3.2. Research progress of rTMS in the treatment of PSCI

Repeated transcranial magnetic stimulation has advantages in improving lateral neglect, language fluency and execution ability of patients with post-stroke cognitive impairment, and has great clinical development potential. In terms of treatment mode, there is no uniform clinical standard. The dorsolateral prefrontal cortex (DLPFC) is selected for rTMS stimulation sites. The intensity is 80%~120% of the exercise threshold, the frequency is 5~25 Hz, and the time interval is usually 20~30 s. Treatment for more than 3 weeks [10].

Regarding the stimulation frequency, the current clinically used rTMS is mainly divided into high-frequency rTMS and low-frequency rTMS. The former has an excitatory effect on the cerebral cortex, while the latter is considered to have an inhibitory effect. Various studies are more positive about the effect of high-frequency stimulation. Luo Hong et al. [11] found that high-frequency rTMS intervention can effectively improve the cognitive function of patients with hemorrhagic PSCI through resting fMRI examination. The meta-analysis of Liao et al. [12] found that high-frequency rTMS stimulation is more dominant in improving the execution function, while low-frequency rTMS plays a better role in situational memory and visual perception, but the effect of low-frequency rTMS is weaker than that of high-frequency rTMS. Some scholars also believe that the efficacy of the two is comparable. Wang Shiyan et al. [13] divided 45 PSCI patients into low-frequency group, high-frequency group and pseudo-

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stimulation group. After 8 weeks of treatment, the cognitive evaluation table was used to evaluate the cognitive function of the three groups of patients. It was found that after treatment, the MoCA and LOTCA scores of the low-frequency group and the high-frequency group were significantly higher than the level of the pseudo-stimulation group ($P<0.05$), and the improvement trend of the lower-frequency group in the high-frequency group was more obvious, but the difference between the groups was not statistically significant ($P>0.05$), suggesting the treatment of low-frequency rTMS and high-frequency rTMS. The curative effect of PSCI is comparable. Therefore, it is necessary to choose the appropriate stimulation frequency according to the specific situation of the patient. When PSCI patients have a high risk of seizures, they can choose low-frequency rTMS for treatment, while patients with PSCI combined with depression can choose high-frequency rTMS to promote the expression of neurocytokines and the secretion and metabolism of monoamine neurotransmitters. Then it improves its nerve excitability and relieves depression.

In the stimulation site, the rTMS stimulation site is mostly selected in the dorsal lateral prefrontal cortex. The dorsal lateral prefrontal cortex plays an important role in the central execution network [14], which is responsible for advanced cognitive functions, especially the control of attention and working memory. Yin Mingyu et al. [15] After using rTMS to stimulate the patient's left dorsal lateral prefrontal cortex, the patient's overall cognition, execution and daily activity ability were significantly improved. The right lateral dorsal prefrontal cortex is also of great significance in cognitive control and mood regulation [16]. In a study of patients with post-stroke cognitive impairment, Tsai et al. [17] found that patients with 5 Hz rTMS stimulation of DLPFC on the left were significantly better than those in the false stimulation group in terms of total neuropsychological state score and attention and delayed memory. In addition to DLPFC, various studies have also found that high-frequency stimulation of the left lower parietal lobe, anterior wedge and other parts can also improve cognitive function. Another new study shows that [18], under the guidance of event-related potential, the selection of corresponding stimulation sites is of great significance to improve the cognitive function of patients, that is, to determine the corresponding abnormal brain function area according to the abnormality of different waves, so as to carry out more targeted stimulation.

In terms of security, rTMS is more secure and the incidence of adverse events is low. The main adverse types include convulsions, syncope, one-passing psychotic symptoms and hearing loss or tinnitus, but these events usually improve rapidly with the increase of days of treatment. Patients with first treatment or poor tolerance can appropriately shorten the stimulation time and extend the interval time. Once there is an adverse reaction, it will be stopped immediately and symptomatic treatment.

4. Clinical application of transcranial DC stimulation in the treatment of PSCI

4.1. Mechanism of action of tDCS

Transcranial direct current stimulation (tDCS) significantly stimulates brain tissue by applying weak direct current to the body, which has the positive significance of correcting the action potential of neurons, improving local nerve conduction and improving the cognitive function of patients [19]. The polarization of the membrane is the main mechanism of immediate action after tDCS stimulation, and the treatment effect may be affected by a variety of factors, including current strength, stimulation duration, stimulation position and individual differences. When studying the cognitive reconstruction of stroke patients, Shaker HA et al. [20] found that transcranial direct current stimulation is a safe and effective way of neurorehabilitation, which can effectively improve cognitive dysfunction after stroke and have a positive impact on the performance of daily activities. In addition, tDCS can also improve post-stroke memory and learning disorders, attention disorders, apraxia and agnosia.

4.2. Research progress of tDCS in the treatment of PSCI

tDCS can not only improve cognitive dysfunction caused by disease, but also improve the cognitive level of healthy adults [21]. For example, Shaker et al. [20] was found to significantly improve the attention and logical reasoning ability of patients through tDCS treatment of patients with post-stroke cognitive impairment. Compared with individual cognitive training, anode tDCS combined with cognitive training is more effective in improving the attention and execution function of patients with multiple sclerosis.

In terms of stimulation parameters, tDCS does not have a clear and unified stimulation mode at present. Clinically, the stimulation electrode of tDCSd usually uses a 5 cm × 7 cm anode to stimulate the left dorsal lateral prefrontal lobe or the left frontal lobe. The cathode stimulates the right orbital area, and the electrical stimulation intensity is 1~2 mA. The frequency is 20~30 min/time. Treat 5 times a week for 2 to 4 weeks. The tDCS treatment in the above parameter range is relatively safe and effective [22].

At the stimulation site, tDCS often chooses the dorsal lateral prefrontal cortex as the stimulation target. Relevant scholars also found that stimulating the temporal parietal lobe and other parts also has a significant effect on improving cognitive function. Yu Guo et al. [23] 38 patients with cognitive impairment were treated with tDCS. The stimulation site was the anode placed in the dorsal lateral cortex area of the left prefrontal lobe, and the cathode was placed on the upper edge of the opposite orbit. The results showed that each cognitive index was better than the control group. High-precision tDCS can also further show the stimulation effect of different stimulation parameters. For example, Fiori, etc. [24] studies have found that the high-precision tDCS stimulation of the 2mA group has significantly improved the verb naming of patients in the Broca area. And tDCS combined with electroencephalogram can evaluate the effect in stages, optimize its parameters in the treatment process, and prevent neurological diseases such as seizures.

For safety, tDCS is usually considered safe with mild side effects, mainly including slight headache, skin tingling or burning [25]. However, the safety of its long-term use and high-intensity stimulation still needs to be further studied.

5. Combination therapy of NIBS

The combination of non-invasive brain stimulation technology combined with acupuncture and cognitive training has been proven to improve patients' cognitive abilities in various fields. Guo Xiuxiu et al. [26] used tDCS joint cognitive intervention to treat patients with post-cerebral infarction with cognitive impairment. The results showed that the combined treatment has the effect of synergistic improvement of memory and executive function. Zhang Xueting et al. [27] found in the study of patients with post-stroke cognitive impairment that the use of acupuncture combined with transcranial direct current stimulation significantly improved significantly in terms of the total score of neuropsychological state and memory and executive function of the patients in the false stimulation group. Some scholars have combined the combination of transcranial DC stimulation and repeated transcranial magnetic stimulation to find that combined stimulation can improve patients' memory function. Compared with single magnetic stimulation, combined stimulation has a more significant effect on delayed memory and P300 incubation period. The reason why the combined treatment of rTMS and tDCS produces better therapeutic effects may be related to the interaction of magnetic and electrical simultaneous applications. tDCS can enhance the effect of magnetic stimulation [28].

6. Summary

As a non-invasive and safe treatment technology, non-invasive brain stimulation technology has high research value and broad application prospects. In the treatment of PISCI, non-invasive brain stimulation technology has shown a certain improvement effect on various cognitive fields. In addition, the choice of joint intervention between rTMS and tDCS and other technologies is also an aspect of clinical consideration. However, there are still many problems. For example, the best treatment parameters in various areas of cognitive function are not clear, especially when multiple cognitive fields are damaged at the same time, and there is no consensus on how to choose the most suitable treatment parameters. More high-quality, large sample studies are needed in the future to determine the best treatment plan.

References

[1] Mahon S, Parmar P, Barker-Collo S, et al. Determinants, Prevalence, and Trajectory of Long-Term Post-Stroke Cognitive Impairment: Results from a 4-Year Follow-Up of the ARCOS-IV Study. Neuroepidemiology. 2017; 49(3-4):129-134.

[2] Rost NS, Brodtmann A, Pase MP, et al. Post-Stroke Cognitive Impairment and Dementia. Circ Res. 2022; 130(8):1252-1271.

[3] Filler J, Georgakis MK, Dichgans M. Risk factors for cognitive impairment and dementia after stroke: a systematic review and meta-analysis. Lancet Healthy Longev. 2024; 5(1):e31-e44.

[4] Perng CH, Chang YC, Tzang RF. The treatment of cognitive dysfunction in dementia: a multiple treatments meta-analysis[J]. Psychopharmacology, 2018, 235(5): 1571-1580.

[5] Jiang X, Yan W, Wan R, et al. Effects of repetitive transcranial magnetic stimulation on neuropathic pain: A systematic review and meta-analysis. Neurosci Biobehav Rev. 2022; 132:130-141.

ISSN 2616-5791 Vol.5, Issue 7: 9-13, DOI: 10.25236/AJMHS.2024.050702

[6] Wang Kai, Dong Qiang, Yu Jintai, etc. Expert consensus on the management of cognitive impairment after stroke 2021 [J]. Chinese Stroke Magazine, 2021, 16(04):376-389.
[7] Zhuang L, Yang Y, Gao J. Cognitive assessment tools for mild cognitive impairment screening. J Neurol. 2021 May; 268(5):1615-1622.
[8] Dharmasaroja PA, Limwongse C, Charernboon T. Inci-dence and risk factors of vascular dementia in Thai stroke patients. J Stroke Cerebrovasc Dis 2020; 29:1-6.
[9] Zhao CG, Sun W, Ju F, et al. Analgesic effects of directed repetitive transcranial magnetic stimulation in acute neuropathic pain after spinal cord injury[J]. Pain Med, 2020, 21(6): 1216-1223.
[10] Koch G, Bonni S, Pellicciari MC, et al. Transcranial magnetic stimulation of the precuneus enhances memory and neural activity in prodromal Alzheimer's disease[J]. Neuroimage, 2018, 169: 302-311.
[11] Luo Hong, Yu Qian. Based on resting fMRI technology, observe the effect of high-frequency repeated transcranial magnetic stimulation on the cognitive function of hemorrhagic stroke [J]. Chinese Journal of Physical Medicine and Rehabilitation, 2019, 41(4): 279-282.
[12] Liao X, Li GM, Wang AG, et al. Repetitive transcranial magnetic stimulation as an alternative therapy for cognitive impairment in Alzheimer's disease: a meta-analysis[J]. J Alzheimers Dis, 2015, 48(2): 463-472.
[13] Wang Shiyan, Gong Zunke, Chen Wei, etc. Effect of repeated transcranial magnetic stimulation at different frequencies on cognitive impairment after stroke [J]. Chinese Journal of Physical Medicine and Rehabilitation, 2021, 43 (08): 721-723.
[14] Yin M, Liu Y, Zhang L, et al. Effects of rTMS Treatment on Cognitive Impairment and Resting-State Brain Activity in Stroke Patients: A Randomized Clinical Trial. Front Neural Circuits. 2020; 14:563777.
[15] Yin Mingyu, Luo Jing, Hu Xiquan, etc. Effect of high-frequency repeated transcranial magnetic stimulation on cognitive dysfunction after stroke [J]. Chinese Journal of Rehabilitation Medicine, 2018, 33(7):763-769.
[16] Yu LL, Long QS, Tang YC, et al. Improving emotion regulation through real-time neurofeedback training on the right dorsolateral prefrontal cortex: evidence from behavioral and brain network analyses [J]. Front Hum Neurosci,2021,15:620342.
[17] Tsai PY, Lin WS, Tsai KT, et al. High-frequency versus theta burst transcranial magnetic stimulation for the treatment of poststroke cognitive impairment in humans[J]. J Psychiatry Neurosci, 2020, 45(4): 262-270.
[18] Liu Y, McAfee SS, Van Der Heijden ME, Dhamala M, Sillitoe RV, Heck DH. Causal Evidence for a Role of Cerebellar Lobulus Simplex in Prefrontal-Hippocampal Interaction in Spatial Working Memory Decision-Making. Cerebellum. 2022;21(5):762-775.
[19] Park J E, Hong J Y, Lee S Y. Transcranial direct current stimulation and yoga for functional movement disorders[J]. Neurologist , 2021, 26(6):231-236.
[20] Shaker HA, Sawan S, Fahmy EM, et al. Effect of transcranial direct current stimulation on cognitive function in stroke patients[J]. Egypt J Neurol Psychiatr Neurosurg,2018,54(1):32.
[21] Li LM, Violante IR, Leech R, et al. Brain state and polarity dependent modulation of brain networks by transcranial direct current stimulation[J]. Hum Brain Mapp, 2019, 40(3):904-915.
[22] Expert consensus group on the clinical application of transcranial direct current stimulation and stroke rehabilitation in China. Expert consensus on the application of transcranial DC stimulation technology to the rehabilitation treatment of stroke patients [J]. Chinese Journal of Physical Medicine and Rehabilitation, 2021, 43(04): 289-294.
[23] Yu Guo, Sun Qianqian, Xiao Yang, etc. Clinical study of tDCS pre-stimulation to enhance the efficacy of cognitive rehabilitation in patients with cerebral stroke cognitive dysfunction [J]. Rehabilitation in China, 2020, 35(03): 131-134.
[24] Fiori V, Nitsche MA, Cucuzza G, et al. High-definition transcranial direct current stimulation improves verb recovery in aphasic patients depending on current intensity[J]. Neurosci, 2019, 406: 159-166.
[25] Draaisma LR, Wessel MJ, Hummel FC. Non-invasive brain stimulation to enhance cognitive rehabilitation after stroke[J]. Neurosci Lett, 2020, 719: 133678.
[26] Guo Xiuxiu, Xia Siying, Cui Can, etc. Study on the curative effect of transcranial direct current stimulation combined with cognitive intervention on memory and executive function in patients with cerebral infarction cognitive impairment [J]. Chinese Journal of Rehabilitation Medicine, 2022, 37(08):1057-1062.
[27] Zhang Xueting, Zhou Nan, Li Qing. A randomized controlled trial of acupuncture combined with transcranial direct current stimulation for the treatment of stroke with cognitive impairment [J]. World Medicine, 2024,19(01):52-56.
[28] Gong Y, Long XM, Xu Y, Cai XY, Ye M. Effects of repetitive transcranial magnetic stimulation combined with transcranial direct current stimulation on motor function and cortex excitability in subacute stroke patients: A randomized controlled trial. Clin Rehabil. 2021; 35(5):718-727.