Research Progress of Repetitive Transcranial Magnetic Stimulation in Limb Rehabilitation in Patients with Stroke and Hemiplegia

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Abstract: Stroke, also known as cerebrovascular accident. It is a cerebrovascular disease caused by damage or rupture of cerebral blood vessels, resulting in vascular failure and interruption of blood flow, resulting in cerebral cell ischemia and hypoxia. This kind of injury usually causes local brain dysfunction, and the symptoms last for more than 24 hours, which can lead to death in severe cases. Repetitive transcranial magnetic stimulation (rTMS) is widely used in the field of stroke rehabilitation of the upper extremities, but it is rarely described in the literature of the lower extremities. In order to overcome these problems, the challenges we must face in the future are to determine the best parameters and the most appropriate intervention time through a large number of clinical research centers, so as to provide patients with the best treatment plan in combination with the unity of the curative effect after intervention in various periods and various rehabilitation treatment methods.

Keywords: Repetitive transcranial magnetic stimulation, Hemiplegia, Rehabilitation, Overview.

1. Introduction

Stroke, also known as cerebrovascular accident. It is a cerebrovascular disease caused by damage or rupture of cerebral blood vessels, resulting in vascular failure and interruption of blood flow, resulting in cerebral cell ischemia and hypoxia [1]. This kind of injury usually causes local brain dysfunction, and the symptoms last for more than 24 hours, which can lead to death in severe cases. Stroke mainly affects the elderly aged 50 to 70, and is a common and frequent disease among middle-aged and elderly people. With the rapid development of China's economy and the acceleration of urbanization, people's lifestyles have changed significantly, which have led to the increasing prevalence of high-risk factors in stroke. Stroke has become the leading cause of death and disability among Chinese adults. According to statistics, stroke occurs every year in China. The prevalence rate of people over the age of 40 has increased from 1.89 percent in 2012 to 2.58% in 2019, and the total number of people over the age of 40 who are sick and has reached 17.04 million [2]. Stroke is a disease with a very high rate of disability, so it places an endless mental and economic burden on sick patients and their families, as well as society [3]. Despite early treatment and intervention, about 80% of survivors still have residual motor dysfunction, and the percentage of people with lower limb dysfunction reaches 70-80, and they also have dysfunction while walking [4]. The recovery of lower limb motor function is very important for stroke patients. It not only helps patients restore their daily ability, but also helps them better return to their family and society. Therefore, improving the ability of lower limbs to participate in the labor force and daily life, such as walking, running, standing, is of great significance for the functional rehabilitation of patients. In the face of the youthization trend of stroke and its serious socio-economic burden, effective prevention and treatment measures are needed, especially to strengthen early diagnosis and rehabilitation, to reduce the incidence of stroke and improve the quality of life of patients.

At present, there are conventional gait training methods for lower limb rehabilitation training at home and abroad, weight-bearing rehabilitation training methods, electromyo-biofeedback and comprehensive rehabilitation training methods, acupuncture and moxibustion joint rehabilitation training methods, and electrical stimulation therapy [5]. With the progress of science and technology, new physical therapy means and measures continue to emerge. Professionals in rehabilitation medicine have been exploring to improve the means and measures of rehabilitation treatment. With the progress of science and technology, a non-invasive neuroregulation instrument has been produced through cranial magnetism, which has made a milestone contribution to neurotherapy and made new progress in rehabilitation medicine. Repetitive transcranial magnetic stimulation mainly acts on all relative regions of our human cerebral cortex. After each region receives pulse stimulation, the muscle target organ of its corresponding limb function will make corresponding changes, promoting the improvement of limb muscles caused by stroke in hemiplegic patients, and helping hemiplegic patients to restore motor function, which is a treatment method from the center to the periphery [6]. Its original treatment ideas and concepts cannot be completed by other physiotherapy. Clinical data show that repetitive transcranial magnetic stimulation can promote the recovery of our limb function, and the research on transcranial magnetic stimulation in the field of clinical rehabilitation has also been ongoing. In the field of rehabilitation, experts in rehabilitation medicine are constantly exploring rTMS as a new promising treatment for stroke patients.

2. Overview of Transcranial Magnetism

2.1 Transcranial Magnetic Stimulation (TMS)

Transcranial magnetic stimulation (TMS) is discovered by Baker [7] and others in 1985. Under the transcranial magnetic field, human brain cells will undergo corresponding current changes, mainly due to nerve transmission. The biological stimulation technology of induced cell changes and thus affecting the metabolism of brain cells and the current activity of nerves is mainly used to measure the excitation threshold and motor nerve conduction of the cortex. It is only used in clinical practice for motor examination induction potentials for the diagnosis and evaluation of neurological diseases. Relatively speaking, the application range The periont is relatively narrow. Transcraniomagnetism can be divided into single-pulse TMS (spTMS), double-pulse TMS (ppTMS) and repetitive TMS (rTMS) according to different pulses. Single-pulse TMS refers to the use of a single magnetic pulse, which is usually used to study the physiological functions of the brain, such as measuring motor Dual pulse TMS uses two closely followed pulses to study the interaction of inhibition and excitement between neurons. This review mainly introduces rTMS, which is what we often call repetitive transcranial magnetism. It is most of the cortical region of our human brain in the field of rehabilitation. The time to give repeated stimulation by transcranial magnetic radiation pulses in the cerebral cortex is uninterrupted. It is mainly divided into low frequency and high frequency according to its own pulses. High frequency refers to greater than or equal to 1Hz. Its main role is to stimulate the nerve cells of the brain, thus improving the plasticity of the brain and the balance of the left and right brain. Frequency greater than 1Hz is defined as high frequency, and its effect is the same as the frequency. High and low frequencies are changed through long-range activation or long-range suppression (LTP/LTD). Synaptic plasticity makes this nerve tonic production use far exceed the actual stimulation time [8].

2.2 Mechanism of rTMS on the Central Nervous System

Research shows that the magnetic field pulses of rTMS have a stimulating effect on the nerves of our cerebral cortex and can also reshape and build brain cells. As an important neurotrophic factor widely distributed in the central nervous system, brain-derived neurotrophic factor plays a vital role in brain plasticity and is inseparable from motor learning and functional rehabilitation after stroke [9]. High-frequency rTMS can increase brain-derived neurotrophic factors, activate related signaling pathways, promote nerve cell regeneration and increase motor evoked potential (MEP), while low frequency effect is the opposite [10].

2.2.1 Suppression of the cerebral hemisphere

The principle of bi-way regulation of interhemispherical inhibition of brain excitability, especially interactive inhibition (RIHI), is part of the normal operation between the hemispheres of the brain [11]. This mechanism ensures that the excitability and inhibition on both sides of the brain remain in dynamic equilibrium. However, when a stroke (stroke) occurs, the motor cortex of the affected brain may be less excited, which directly affects the ability to control muscles and leads to abnormal muscle activity. In this case, the motor cortex of the opposite (healthy side) brain may enhance its excitability due to the need to compensate for the lack of function on the affected side, thus making the body movement more obvious. This enhanced excitability may affect the affected side through the inhibitory effect of the transcorpus, further destroying the original interhemispheric balance. This imbalance may lead to further dysfunction of the affected side muscles, and may also increase the burden on the healthy side, which may also lead to functional problems on the side in the long term. rTMS may promote the rehabilitation of nerve function by re-adjusting this inhibition [12].

3. Application of rTMS in Lower Limb Motor Function after Stroke

3.1 Application of Low-frequency Lower Limb Motor Function after Stroke

Clinically, the current rTMS stimulation with a frequency of \leq 1Hz is low-frequency stimulation. Low-frequency stimulation can cause long-term inhibition and inhibit the current transmission of local nerve cells, which reduces the current activity of brain cells and reduces the excitability of the brain. According to the hemispheric competition theory of stroke function rehabilitation, the cortical function recombination after stroke, and the coordination and inhibition between the two hemispheres were broken: The affected hemisphere is not only less excited by itself, but also more inhibited by the healthy hemisphere. The asymmetry of this inhibition and excitement is related to the plasticity of the cortex and the degree of recovery of motor function [13-14]. It improves the cerebral cortex and regulates the balance of the cerebral cortex by stimulating nerves in the damaged part of the affected side of the brain. According to the mate analysis of Zhang W [15] and others, they mainly inquired randomized controlled trials (RCT) in PubMed, Embase, Cochrane libraries and other relevant databases to study the efficacy of rTMS in solving lower limb motor dysfunction after stroke. They found that low-frequency rTMS has a significant improvement in the Barthel index (BI) score, while high-frequency rTMS and iTBS have no significant effect, in which patients with stroke time 56 months 515d treatment effect is the best. Maryam [16] can improve the clinical measurement of muscle spasms and motor function through low-frequency rTMS on the LE exercise area. Repeated transcranial magnetic stimulation (rTMS) has a beneficial effect on the reduction of upper limb spasms and the improvement of motor function after stroke, which has been confirmed in previous studies. Their study this time showed that after 5 times a day of inhibitory rTMS treatment of the unaffected brain hemisphere (lasting for at least 1 week after intervention), the lower limb spasm and motor function improved. From H. After reviewing the literature and mate analysis, Sharma, MSc, PhD [17] and others claimed that rTMS post-stroke exercise recovery has a positive effect. Low-frequency rTMS may be better than high-frequency rTMS. They explore the role of low-frequency repeated transcranial magnetic stimulation (rTMS) and conventional physiotherapy in functional recovery of patients with subacute ischemic stroke. Their research results show that the two weeks of low-frequency rTMS and improved Barthel index (mBI) scores have changed significantly, while Fugl-Meyer evaluates upper limbs, Fugl-Meyer evaluates the lower limbs, Hamilton Depression Scale, the improved Rankin Scale and the National Institutes of Health and the Stroke Scale (before and after rTMS). It further shows that the effect of low frequency on stroke is obvious. Jean-Pascal Lefaucheur [18] Evidence-based guidelines on the use of repeated transcraniomagnetic stimulation (rTMS) treatment: update

(2014-2018) rTMS can produce significant clinical improvements in various neurological and neurological diseases, and introduced updated guidelines on the use of rTMS treatment, including 2014-2018 publications. There is higher evidence of efficacy in the field of depression, pain and acute post-motor stroke. The guidelines point out that stroke LF-rTMS (low-frequency repetitive transcranial magnetic stimulation) has a clear effect on the recovery of the hand in the acute stage of stroke. HF-rTMS (high-frequency repetitive transcranial magnetic stimulation) may have an effect on the recovery of the hand in the acute stage of stroke, and the recovery of the hands in the chronic stage of LF-rTMS stroke may be effective. Yu Liu [19] et al. are evaluating the efficacy of repeated transcranial magnetic stimulation (rTMS) to improve the spasm of the lower limbs after stroke. They searched PubMed, Science Network, Cochrane Library, EMbASE, China National Knowledge Infrastructure (CNKI), China Biomedical (CBM) Database, China Science and Technology Journal Database (VIP) and Wanfang Database searched for randomized controlled trials (RCT) online from the beginning to May 2021, involving repetitive transcranial magnetic stimulation for the treatment of lower limb spasm after stroke. From the inclusion of these literature, the improved Ashworth Scale (MAS), the lower limb Fugl-Meyer evaluation (FMA-LE), the improved Barthel index (MBI) and the stand-up walking evaluation (TUG) they observed were effective in improving spasm status and daily activity compared with the post-treatment control conditions. LF-rTMS has a positive clinical effect on the improvement of motor function in patients with lower limb spasm after stroke. In order to better verify the above conclusions, more multi-center, high-quality and double-blind randomized controlled trials are needed. Yan Yulin [20], a domestic scholar, and others studied patients whose low-frequency transcraniomagnetism affected limb function and balance functions caused by stroke. He selected a randomized controlled experiment. The control group was based on conventional rehabilitation and core muscle training interventions, and the observation group added low-frequency repeated transcraniomagnetic. After treatment, the clinical spasm index (CSI) in both groups was lower than that before treatment. The lower extremity scores in the Berg Balance Scale (BBS) and Fugl-Meyer scores were higher than those in the lower extremities before treatment, and the CSI scores in the observation group were lower than those in the control group. The scores of BBS and FMA-LE were higher than those in the control group. Their findings showed that the low frequency of repetitive transcranial magnetic stimulation improved the spasm treatment of limb palsy after stroke, improved lower limb function, balance function and walking function, and was safe. Domestic scholar Tao Feng [21] et al. also selected patients with acute stroke to observe the function of their lower limbs using low-frequency repetitive transcraniomagnetic stimulation and mirror therapy. Studies have shown that the combined effect is better. Gore [22] et al. found significant improvements in lower limb motor function and walking speed in stroke patients with head needle combined with repetitive transcraniomagnetic stimulation further illustrate the effectiveness of repetitive transcraniomagnetic stimulation in patients with stroke. Qin Yin, Liu Xiaoying [23] and others discussed the curative effect of repetitive transcranial magnetic stimulation on upper limb spasm. Studies have shown that low-frequency and high-frequency repetitive transcranial magnetism on upper limb MAS, limb function and MBI score have been significantly improved, indicating that both high and low frequency repetitive transcranial are effective for the improvement of spasm of limbsm in stroke, which providing evidence for the use of repetitive transcranial magnetism and extensive clinical advancement.

3.2 Application of High Frequency in Rehabilitation Function in Lower Limb Movement after Stroke

We define the frequency of repetitive transcranial magnetic stimulation greater than 1HZ as high frequency, which has an excitatory effect on cerebral cortex cells. Foreign literature, in 2014, Raffaella Chieffo [24] et al. studied the effect of high-frequency (20 Hz) brain stimulation on lower limb motor function in subjects with chronic (>6months) cortical stroke. They used double-blind and placebo-controlled cross-study to repeat transcranial magnetic stimulation (rTMS) with the H coil, which was specially designed for deeper and larger brain regions. Each subject accepts true and false rTMS in random order. 2 rTMS cycles (real or fake) consist of 11 courses of treatment, each of which is given within 3 weeks, with an interval of 4 weeks of clearance. The main indicators are 10 days before and after the end of each treatment period and 6 weeks of follow-up to evaluate lower limb function through the lower limb Fugl-Meyer scale, 1 m walking test and 4-minute walk test. These data show that 1 week of high-frequency deep rTMS can induce long-term improvement of lower limb function after a chronic stroke that lasts for at least 3 months after a chronic stroke. This shows that high frequency has a good effect on the limbs of chronic stroke. 18 randomized controlled trials were used for lower limb movement recovery from the mate analysis of Xie Yunjuan [25] and others in 2021. According to direct evidence, in terms of motor function, only LF-rTMS is significantly more effective than fake simulation. In contrast, dTMS, HF-rTMS and iTBS do not seem to have a better effect than fake stimulation. For the secondary outcome of speed, 11 randomized controlled trials (307 subjects) were included. The results of paired meta analysis show that there are significant differences between HF-rTMS and fake stimuli. However, dTMS, LF-rTMS and iTBS are not more effective than fake stimuli. For the equilibrium survey, we have included 13 randomized controlled trials. Direct evidence shows that LF-rTMS is significantly better than HF-rTMS, and there is no significant difference in balance improvement between HF-rTMS, LF-rTMS or iTBS compared with fake surgery. In the 2019 literature, Juan Du [26] et al. repeated transcranial magnetic stimulation (rTMS) can regulate cortical excitability, which may be beneficial to motor recovery after stroke. However, in the early stage after stroke, the neuroplasticity effect of rTMS has not been thoroughly studied. Juan Du and others selected 60 hospitalized patients with first ischemic stroke (within 2 weeks after stroke) in addition to standard physical therapy, they were also randomly assigned to receive 5 consecutive courses of treatment: (1) high frequency (HF) rTMS stimulates the primary motor cortex (M1) at 10HZ; (2) 1Hz on the low-frequency (LF) rTMS control group (M1); (3) false rTMS. Among them, the baseline, rTMS scores motor function 1 month after the test and 3 months after the test, and intervened with the excitability and functional image (fMRI) data of

cortical cells in the brain 24 hours before and after the experiment. Through clinical, neurophysiological and functional magnetic resonance imaging tests, comparing the recovery effect of three groups of rTMS. Their study showed that HFrTMS stimulates the nerve cells in the affected cerebral cortex of patients with hemiplegia to induce their movement and activate fMRI, while the LF-rTMS group has an inhibitory effect on the motor area of the healthy side of the brain, thus reducing the excitement caused by the inability of the cerebral cortex of the affected side and reducing the activation of fMRI. After three months of intervention in the experimental patients, it was found that the high-frequency stimulation of the affected side is closely related to the recovery of its motor function, which proves that high-frequency in the acute period has a significant improvement effect on motor function. Tian Fei, Zhao Chenguang [27] and others studied the end limb robot combined with high-frequency repetitive transcranial magnetic stimulation to improve walker function. A number of scores showed that high-frequency repetitive transcranial magnetism was effective in improving gait. In the study of high-frequency and low-frequency controlled cerebral infarction stroke, the rehabilitation function of the lower limbs after high-frequency and low-frequency controlled cerebral infarction was studied. Research shows that high-frequency and low-frequency rTMS can improve motor function by regulating the activation of the motor cortex in the early stage of stroke. These research results show that high frequency is effective in regulating the excitability of the cortex.

3.3 Effects of Combined Use of High and Low on The Rehabilitation of Limbs

In the continuous development of rehabilitation medicine, clinical medical personnel continue to explore the new frequency of rTMS and various combinations of high and low frequencies, such as low-frequency stimulation of healthy cerebral cortex in stroke patients, high-frequency stimulation of the affected cerebral cortex in stroke patients, or high- and low-frequency alternating stimulation of the cerebral cortex to test the effect of exercise rehabilitation. Compared with a single low-frequency or high-frequency stimulus, these stimulation schemes have advantages in improving physical motor function. The domestic literature on the combination of high and low frequency is Xue Hui, Wang Baojun [28] and others studied and compared the high-frequency group, the low-frequency group and the high and low-frequency group respectively to observe the therapeutic effect of motor function in the acute phase of patients with high-frequency (10Hz), low-frequency (1Hz) and high and low-frequency combination of transcranial magnetic stimulation (rTMS) cerebral infarction. He was mainly a stroke patient who studied. The patients included in the study were divided into low-frequency groups, high-frequency groups, high-frequency and low-frequency groups. The research results showed that all four groups used the limb motor function assessment table (Fugel-Meyer), stroke NIHSS evaluation scale, daily life ability assessment scale (BI). The results of the three groups of the results of the three groups were improved before experimental intervention, and the

low-frequency group, high-frequency group and the high-frequency group were higher than the limb motor function evaluation table (Fugel-Meyer) of the control group, the stroke NIHSS evaluation quantification table, and the daily life ability evaluation quantification table (BI), and the differences were statistically significant. Their research finally showed that whether it is high-frequency (10HZ), low-frequency (1HZ), or high-low-frequency combination, it has a significant improvement effect on the limb movement of stroke patients compared with the control group, and the study also found that the movement improvement of the high-frequency and low-frequency combination group is more obvious than the single frequency effect, which promotes the movement and balance of stroke patients and improves their ability to take care of themselves. Subsequent domestic literature continued to be studied in depth in this regard. Zhou Jing [29] and others studied the effect of acupuncture combined with high and low frequency repeated transcranial magnetic stimulation on the motor function of the upper limbs in stroke. The research group adopted the rTMS treatment mode of lesion-side high-frequency and healthy low-frequency. At the same time, the head acupuncture was carried out according to the M1 area of the lesion side of rTMS location. The control group used false head needles on the basis of the research group. The study showed that acupuncture combined with high and low frequency rTMS treatment can improve the motor function of the upper limbs of stroke patients, especially in improving the improvement of hand function and wrist function. However, there is still little research on the joint use of high-frequency and low-frequency in China, so for the effectiveness of high-low-frequency joint use, scientific research data are still insufficient. A large amount of scientific research data are needed to confirm the effectiveness of high-low-frequency joint use, and it is more necessary for scientific researchers to constantly explore and capture.

4. Summary and Outlook

Repetitive transcranial magnetic stimulation (rTMS) is widely used in the field of stroke rehabilitation of the upper extremities, but it is rarely described in the literature of the lower extremities. It is a safer brain stimulation technology, which still has more challenges and limitations in the field of rehabilitation. At present, the research on the therapeutic effect of rTMS lacks long-term tracking, which limits the evaluation of the lasting evaluation of the therapeutic effect. Due to the small sample size of the study and the small statistics, it is difficult to draw universal conclusions. The efficacy evaluation indicators of each study are inconsistent, and the comprehensive curative effect cannot be unified. The diversity of diseases, including stroke time, age and amount of bleeding, all affect the effect of treatment. The inconsistent parameters of each study cannot achieve the unification of big data. In order to overcome these problems, the challenges we must face in the future are to determine the best parameters and the most appropriate intervention time through a large number of clinical research centers, so as to provide patients with the best treatment plan in combination with the unity of the curative effect after intervention in various periods and various rehabilitation treatment methods.

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