MEDS Clinical Medicine (2022)
Clausius Scientific Press, Canada

DOI: 10.23977/medsc.2022.030616
ISSN 2616-1907 Vol. 3 Num. 6

Progress in TMS in the Diagnosis and Treatment of Vascular Dementia

Ting Hu[1,a,*], Jie Chen[2,b]

[1]Shaanxi University of Traditional Chinese Medicine, Xianyang, Shaanxi, 712046, China
[2]Department of Encephalopathy, Shaanxi Provincial Hospital of Traditional Chinese Medicine, Xi'an, Shaanxi, 710003, China
[a]1091646907@qq.com, [b]cj.doctor@163.com
**Corresponding author*

Keywords: TMS, Vascular Dementia, Diagnosis, Treatment

Abstract: Vascular dementia, as the second most recognized cause of dementia, the incidence is increasing year by year worldwide. Early intervention is of great significance to improve the prognosis of vascular dementia, and studies have found that TMS technology can effectively assist in the prevention and treatment of vascular dementia. The study provides new ideas for the improvement of cognitive function in patients with vascular dementia by exploring the mechanisms of TMS technology and its therapeutic progress in improving vascular dementia.

1. Introduction

Vascular dementia (VD) refers to the cognitive dysfunction syndrome caused by various cerebrovascular diseases that lead to the low perfusion of the brain areas in charge of memory, execution and other functions. It is clinically mainly seen in ischemic stroke, mainly manifested in memory, calculation, understanding, judgment, execution, language and other abilities, especially the decline of memory and execution abilities accompanied by cerebrovascular disease related symptoms. VD is now the second most recognized cause of dementia except for Alzheimer disease (AD). As a major cause in East Asia, it is especially common in elderly patients with lesions based on cerebral atherosclerosis[1]. VD will not only reduce the survival rate and quality of life of patients, increase the social and family economic and mental burden, but also affect the treatment and prognosis of the primary disease due to the cognitive impairment of patients who cannot fully cooperate with clinical rehabilitation assessment and rehabilitation treatment. As the only known preventable dementia, the early identification, diagnosis and intervention of risk factors of cerebrovascular disease (old age, diabetes, hypertension, smoking, etc.) and symptoms of mild vascular dementia can help reduce or even reverse the cognitive dysfunction of vascular dementia patients. Therefore, the treatment targeted for VD is very necessary. At present, China mainly treats VD by using drugs to control the risk factors of cerebrovascular disease (including smoking cessation and alcohol restriction, regulating blood pressure and blood sugar, antiplatelet aggregation, lipid regulation and plaque stabilization), improving cognitive function (nutritional nerve, improving cerebral circulation, applying brain agents and cholinesterase inhibitors) and multistage prevention of cerebrovascular disease. However, only relying on drugs and existing rehabilitation treatment means, the patients' cognitive function is unlikely to recover completely. For patients with severe cerebrovascular injury, it is difficult to achieve satisfactory clinical effects. The development of new and effective treatments is the focus of our attention and research today. Transcranial magnetic stimulation (TMS) is commonly used as an adjunct to the treatment of vascular dementia[2], it has been gradually applied in clinical practice. This study will review the research progress in recent years on the mechanism of transcranial magnetic stimulation in improving vascular dementia and its treatment.

2. Brief Introduction of TMS and its Mechanism of Action

In 1985, Barker et al. successfully developed the first TMS, and since then, TMS theory and technology research has been developed continuously, and now it has been successfully applied in the department of neuropsychology (depression, Anxiety disorders, schizophrenia, sleep disorders), rehabilitation department, pediatrics (cerebral palsy, Pediatric abnormal disorder) and other different fields, have obtained different degrees of recognition[3].

TMS is a kind of non-invasive, simple, safe and efficient, low medical cost of physical therapy. As a non-invasive neuroelectrophy siological technology used to regulate the brain function, its main use of electromagnetic principle to hedge magnetic field on the brain, change the membrane potential of nerve cells, to produce induction current, directly or indirectly on the brain synapses and neurons, thus affect the brain metabolism and nerve electrical activity, and through the connection between neural network and interaction[4, 5]. TMS mainly achieves therapeutic goals either by directly regulating task-related local cortical and cognitive networks or by inhibiting activity in non-relevant areas with task processing. According to the different stimulation mode, TMS can be divided into single pulse TMS (sTMS), pair of pulse TMS (pTMS), repeated transcranial magnetic stimulation (rTMS), and θ short array pulse stimulation (TBS). The sTMS and pTMS patterns are often combined with electroencephalography (EEG) technology, and it is mainly used in the detection of brain electrophysiology and cortical function. The rTMS is a series of TMS pulses that continuously act on the cerebral cortex, which can achieve the purpose of stimulating stimulation or inhibiting local cerebral cortical function by changing the stimulation frequency, and can induce long-range neuroplastic changes[6, 7]. It is generally believed that low frequency rTMS (≤ 1Hz) inhibits local neurons and reduces cortical excitability. In clinical practice, low frequency rTMS is often used to reduce the contralateral hemisphere excitability, thus relieving the inhibition on the affected side. High frequency rTMS (≥ 5Hz) facilitates local neurons and increases cortical excitability, which is usually used clinically to improve the excitability of the affected hemisphere. The mechanism of TBS is similar to that of rTMS. TBS can change the excitability and synaptic plasticity of motor cortex by changing the stimulation and intermittent time. In general, intermittent TBS increases cortical excitability, and continuous TBS decreases cortical excitability[8].

3. Diagnosis of Vascular Dementia Disease

The diagnosis of vascular dementia requires a combination of clinical symptoms, assessment scale, neuroimaging and pathological diagnosis. Atherosclerosis and cardiogenic embolism are important causes of cerebral vascular injury. A series of changes such as the decrease of cerebral blood flow and small vessel disease are accompanied by atrophy of temporal and frontal lobe neurons, changes in nerve demyelination and glial proliferation cerebral hypoxia and cerebral tissue hypoperfusion, neuroinflammation and oxidative stress will further aggravate the degree of vascular cognitive impairment [9].The recognized pathological classification of vascular dementia includes five types: multiple cerebral infarction, key site infarction, watershed infarction, hemorrhagic and cortical iosclerotic encephalopathy, among which multiple cerebral infarction dementia is the most common. Clinical common apply Mini-mental State Examination (MMSE), Neurobehavioral Cognitive Status Examination (NCSE), the Montreal Cognitive Assessment Scale (MoCA), the Loewenstein Occupational Therapy Cognitive Assessment (LOTCA), and the Activities of Daily Life (ADL) index score scale to assess cognitive function. MMSE is the first clinical choice for general cognitive impairment screening, MMSE is the first choice for clinical screening of general cognitive impairment. Suspected patients cooperate with MoCA and LOTCA as tools for in-depth study of cognitive function [10]. Neuroimaging studies can accurately assess the extent, location, and type of vascular lesions, Clinical technologies now applied include CT, MR, functional magnetic resonance imaging (fMRI), diffusion tensor imaging (DTI), functional near infrared spectroscopy (fNIRS), single photon emission computed tomography (SPECT) and positron emission tomography (PET) class etc.. Through the combined application of TMS, EEG and various imaging technologies, we can observe the specific impact of TMS on the peripheral cortex of the brain in real time, explore neural interaction networks, deep brain functional connections, etc., so as to better diagnose and treat vascular dementia.

4. Possible Mechanism by which TMS Improves Cognitive Impairment

Studies have found that TMS has excitable neurons, thus strengthening cognitive function in normal humans[11]. The TMS not only suppresses the release of glial inflammatory mediators, achieves neuroprotective effects, and interferes in cerebral blood flow and brain metabolism, but also can regulate synaptic plasticity and reconstruct the cortical functional network by mediating the secretion and expression of BDNF, CAMK II, NMDAR and other proteins[12]. Studies have shown that the dorsolateral prefrontal cortex (DLPFC) is associated with executive control and memory functions; The inferior frontal gyrus (IFG), an important brain region associated with emotion and cognitive control circuits. A meta-analysis conducted by ChouY h found that high-frequency rTMS stimulation of the left dorsolateral prefrontal cortex and low-frequency rTMS stimulation of the right dorsolateral prefrontal cortex can significantly improve memory function, and high-frequency rTMS stimulation of the right inferior frontal gyrus can significantly enhance executive ability[13]. Broca District and Wernicke District, which are related to language functions. Parietal somatosensory association cortex (pSAC), relating spatial and geographic orientation functions. Using TMS to stimulate the above related parts can improve cognitive function. The possible mechanisms of TMS promoting the improvement of vascular dementia include: ① stimulating specific functional brain regions to promote synaptic plasticity and functional recovery; ② establishing compensatory network or reconstructing functional balance of brain regions; ③ increasing the expression of BDNF in cerebral cortex, promoting the regeneration of injured neurons or the reconnection of partially deactivated connections; ④Rhythmic stimulation of TMS can reconstruct a new neural network oscillation mode to improve cognitive function [6].

5. Clinical Application of TMS in Vascular Dementia

The treatment of TMS for cognitive impairment has been widely studied clinically, and many scholars have confirmed the effectiveness of TMS in treating vascular dementia through various research designs. Zhou M z[14]Studies have confirmed that low-frequency rTMS combined with acupoint application can effectively improve glutathione peroxidase, malonic dialdehyde, superoxide dismutase and vascular endothelial growth factor, endothelin-1, nitric oxide levels, improve the MMSE, ADL score, and 5-30 consecutive rTMS treatment can last for 1 to 3 months[13]. Yao T [15] et al. randomly divided 60 patients with vascular dementia into Jin Sanzhen group and rTMS group. It confirmed Jin Sanzhen and rTMS can improve the cognitive ability of patients, improve bad mood, and the quality of life, and female patients are more willing to accept rTMS. Wang J h[16] et al. found that low-frequency rTMS treatment reduced MDA levels, increased SOD activity, improved spatial cognitive function in vascular dementia rats, inhibited the expression of hippocampal apoptosis-related proteins, and inhibited apoptotic pathway and oxidative stress injury after ischemic injury. Lanza G[17]et al. believe that systemic disease named celiac disease can damage cognitive function and cause dementia, rTMS as an effective non-invasive technology, can help evaluating, monitoring, diagnosis and treatment of celiac disease. Yang Q [18] et al. treated 50 patients with vascular cognitive impairment with cognitive rehabilitation training and cognitive rehabilitation training combined with high-frequency rTMS, and found that the cognitive ability and daily life ability of patients treated with high-frequency rTMS combined with cognitive rehabilitation training improved significantly. Wu R p [19] randomly divided 114 patients with vascular dementia after acute cerebral infarction into routine drug treatment group, nimodipine treatment group and nimodipine plus TMS treatment group. Taking one month as a course of treatment, it was found that the MMSE, MoCA and HDS-R scores in the nimodipine plus TMS group were significantly improved, and the overall effective rate was 87.18%, which was superior to the other two groups. It was confirmed that nimodipine plus TMS comprehensive treatment could significantly improve the clinical symptoms of vascular dementia patients. Zheng S l [20] et al. have confirmed that the application of rTMS combined with Tongqiao Huoxue Decoction in the treatment of vascular dementia can improve patients' Hcy, TCM symptom score and MoCA score.

6. Safety Evaluation of r TMS Treatment

At present, the transcranial magnetic stimulation instrument still has some unfavorable factors, such as high cost, large floor area, fever, need to be equipped with professional and technical personnel who master the relevant knowledge of TMS and neurology, and the patients with metal implants are not applicable. For the moment, some adverse reactions have been found in the clinical application of this device: such as inducing epilepsy, causing transient dizziness, headache and tiredness, muscle twitching and pain, hearing impairment [18], etc.

7. Conclusions

Overall, TMS is currently considered as a non-invasive and relatively safe treatment [4, 5]. In the case of relatively limited effect of drug therapy to improve cognitive function, TMS is expected to become an auxiliary treatment for vascular dementia. Because different stimulation sites, intensities, frequencies, and coil directions of TMS cooperate, different therapeutic effects can be produced. Although most of the current studies on the improvement of cognitive function of VD patients using TMS have achieved good results, due to the small sample size, large differences in individual efficacy, and uncertain duration, the best recognized therapeutic scheme has not been explored yet[6, 7, 19]. Maintenance of therapeutic effect, selection and location of stimulation site, and setting of stimulation parameters are problems to be solved now [20-23]. In the future, more and larger sample multicenter research should be conducted in combination with pathogenesis, TMS mechanism of action, and more scientific and reasonable individualized TMS scheme should be formulated to promote the better promotion and application of transcranial magnetic technology in the field of vascular dementia[24-26].

References

[1] Dichgans M, Leys D. Vascular Cognitive Impairment [J]. Circ Res, 2017, 120(3): 573-591.
[2] Zhou W, Zhang W c, Huang K x. A Meta-analysis of the effect of repetitive transcranial magnetic stimulation on vascular cognitive impairment [J]. General Practice in China, 2020, 23 (31): 3976-3982.
[3] Huang N y, Song L p, Tong Z q, et al. Application progress of repetitive transcranial magnetic stimulation in the treatment of Alzheimer's disease [J]. Rehabilitation Theory and Practice in China, 2019,25 (03): 261-266.
[4] BEGEMANN M J, BRAND B A, ĆURČIĆ-BLAKE B, et al. Efficacy of non-invasive brain stimulation on cognitive functioning in brain disorders: a meta-analysis[J].Psychological medicine, 2020,50(15): 2465-2486.
[5] VITTALA A, MURPHY N, MAHESHWARI A, et al. Understanding Cortical Dysfunction in Schizophrenia With TMS/EEG[J]. Frontiers in Neuroscience, 2020,14.
[6] MINIUSSI C, ROSSINI P M. Transcranial magnetic stimulation in cognitive rehabilitation [J]. Neuropsychological Rehabilitation, 2011,21(5): 579-601.
[7] NARDONE R, TEZZON F, HÖLLER Y, et al. Transcranial magnetic stimulation (TMS)/repetitive TMS in mild cognitive impairment and Alzheimer's disease[J]. Acta Neurologica Scandinavica, 2014, 129(6): 351-366.
[8] Tai J h, Wu J f, Wang T w, et al. Research progress in rehabilitation of dysphagia after stroke with different modes of transcranial magnetic stimulation[J]. Journal of Rehabilitation, 2021,31 (03): 252-257.
[9] FRANTELLIZZI V, PANI A, RICCI M, et al. Neuroimaging in Vascular Cognitive Impairment and Dementia: A Systematic Review[J]. J Alzheimers Dis, 2020,73(4): 1279-1294.
[10] Gong Z k, Wang S y, Chen W. The status and trend of cognitive impairment rehabilitation [J]. West China Medicine, 2019,34 (05): 487-493.
[11] WANG J X, ROGERS L M, GROSS E Z, et al. Targeted enhancement of cortical-hippocampal brain networks and associative memory[J]. Science, 2014, 345(6200): 1054-1057.
[12] Shang Y c, Zhang T. The effect of repetitive transcranial magnetic stimulation on cognitive function and its molecular mechanism[J]. Electrotechnical Journal, 2021,36 (04): 685-692.
[13] CHOU Y, TON THAT V, SUNDMAN M.A. systematic review and meta-analysis of rTMS effects on cognitive enhancement in mild cognitive impairment and Alzheimer's disease[J]. Neurobiology of aging, 2020,86: 1-10.
[14] Zhou M z. Clinical study of acupoint application combined with low-frequency repeated transcranial magnetic stimulation in the treatment of male vascular dementia[J]. New Traditional Chinese Medicine, 2022,54 (16): 171-174.
[15] Yao T, Xu N g, Wang M, et al. Observation on the therapeutic effect of Jin Sanzhen and TMS on vascular dementia [J]. Journal of Guangzhou University of Traditional Chinese Medicine, 2018,35 (04): 659-663.
[16] Wang J h, Ke B x, Chen Y, et al. Effect of low-frequency repetitive transcranial magnetic stimulation on cognitive function of vascular dementia rats [J]. Zhejiang Medical Journal, 2018, 40 (23): 2537-2540.
[17] LANZA G, BELLA R, CANTONE M, et al. Cognitive Impairment and Celiac Disease: Is Transcranial Magnetic Stimulation a Trait d'Union between Gut and Brain? [J]. Int J Mol Sci, 2018, 19(8).
[18] Yang Q, Luo J n, Chen J j, et al. Clinical application analysis of high-frequency repetitive transcranial magnetic stimulation combined with cognitive rehabilitation training in patients with vascular cognitive impairment [J]. Chinese Medical Science, 2019, 9 (11): 17-20.
[19] Wu R p, Zhang H. Effect of transcranial magnetic stimulation combined with nimodipine on vascular dementia after cerebral infarction [J]. Ningxia Medical Journal, 2012, 34 (03): 220-223.
[20] Zheng S y, Li Y m, Zeng K j, et al. Effects of modified Tongqiao Huoxue Decoction combined with repeated transcranial magnetic stimulation on cognitive level and Hcy of patients with vascular dementia [J]. Chinese and Foreign Medical Research, 2022, 20 (06): 44-47.
[21] Zhou L, Guo Z w, Jiang B h, et al. A Meta-analysis of the effect of repetitive transcranial magnetic stimulation on mild cognitive impairment [J]. Chinese Journal of Physical Medicine and Rehabilitation, 2020, 42 (06): 562-569.
[22] Li X x, An J, Ren Y y, et al. Current status of non-invasive transcranial stimulation and treatment of cognitive dysfunction [J]. Chinese general practice medicine, 2017, 20(15): 1804-1808.
[23] Wu Y, Wang L, Chen X g, et al. Research progress in the treatment of social cognitive impairment of common brain diseases by transcranial magnetic stimulation [J]. Chinese Journal of Neuropsychiatric Diseases, 2020, 46 (03): 172-175.
[24] Yu Z y, Zhang W m. Effect of repeated transcranial magnetic stimulation on cognitive dysfunction of stroke patients [J]. Journal of Rehabilitation, 2019, 29 (05): 20-26.
[25] Wen X y, Cao X l, Qiu G r, et al. Effects of repetitive transcranial magnetic stimulation on amnestic mild cognitive impairment [J]. Chinese Journal of Gerontology, 2018, 38 (07): 1662-1663.
[26] KALARIA R N, AKINYEMI R, IHARA M. Stroke injury, cognitive impairment and vascular dementia [J]. Biochim Biophys Acta, 2016, 1862(5): 915-925.