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ORIGINAL

EFFECT OF COMBINED COGNITIVE TRAINING AND TMS TREATMENT ON COGNITIVE FUNCTION AND IMAGING INDICATORS IN PATIENTS WITH COGNITIVE IMPAIRMENT IN STROKE

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ABSTRACT

Purpose: To examine the impact of cognitive training and trans phenomenal magnetic stimulation (TMS) on cognitive function and imaging indicators in cognitively impaired patients following post-stroke. **Method:** Seventy-six stroke patients with cognitive impairment admitted to our institution from January 2020 to 12 December 2021 were chosen and classified into different control and study groups depending on the therapy. The treatment was cognitive training for the control group and transcranial magnetic stimulation (TMS) for the study group on top of the treatment for the treatment for the control group. Compare the MoCA, MBI, MMSE scores, treatment effects, serum thyroid hormone levels and lipid index of the two groups. The transverse axial T2W1 and T1W1 scans were performed by MRI, followed by intravenous injection of gadopenate meglumine salt, and repeated transverse scans were performed to evaluate the imaging index of brain edema volume. **Result:** After treatment, MoCA, MBI and MMSE ratings were markedly higher in both groups, The relationship with the difference for both groups was considered in statistical significance ($p<0.05$); the overall effective efficiency was higher in the treatment group (92.11%) than in the treatment group (71.05%) ($p<0.05$); after treatment, Serum thyroid hormone concentrations of

T3 and TSH were higher in the study group than in the response group and the variance was considered to be statistically meaningful ($p<0.05$); Brain edema volume was reduced in both groups, more significantly in case of the investigation group than the response group ($p<0.05$). With the combined treatment, TCHO, TG and LDL levels decreased in both groups, with an increase in HDL in the research group and a decrease in HDL in the trial group, but they were not markedly different ($p>0.05$). **Conclusion:** Cognitive training combined with TMS treatment is conducive to improving the level of serum thyroid hormone and blood lipid of patients, promoting the improvement of cognitive function of patients, and reducing the volume of brain edema. The treatment effect is good. Therefore, cognitive training combined with TMS is worth popularizing.

KEY WORD: Stroke; Cognitive impairment; Cognitive function; Imaging indexes; Cognitive training; TMS

1. INTRODUCTION

The main group of stroke patients is the elderly. The physical function of the elderly patients is reduced, and most patients will be accompanied by cognitive dysfunction to varying degrees (Burke, Fried, & Pascual-Leone, 2019). At present, it is mainly treated by painless and non-invasive technology, among these, the use of transcranial magnetic stimulation (TMS) is popular. This treatment method mainly uses pulsed magnetic field to act on the cerebral cortex, which will adjust the excitability of nerve cells under current stimulation (Hortobágyi et al., 2021; KABASAKAL & BİLECENOĞLU, 2020). Relevant data show that TMS treatment is of great significance in improving visual space, memory ability and language ability of stroke patients (Todorov, Harris, & Fiske, 2006). However, at present, there is insufficient research on TMS in treating cognitive impairment of stroke, and there is no unified treatment parameter, so it needs to be further studied.

One study pointed out that the combination of TMS treatment with cognitive function training will achieve better therapeutic effect, and the changes of patients' cognitive function after treatment can be evaluated by imaging diagnosis (Li et al., 2020).Based on this, 76 patients with cognitive impairment in stroke enrolled in our institution from January 2020 to November 2021 were selected for this study to analyze the effect of combining the two approaches on improving patients' cognitive function. This is hereby reported as described below.

2. DATA AND METHODS

2.1 General information

Seventy-six stroke patients with cognitive impairment treated at our hospital from January 2020 to as early as December 2021 were included. The control group consisted of 38 cases, including 22 in genders and 16 in ladies, aged 30-72 years, with an average age of (57.36 ± 5.24) years, and years of education of (9.53 ± 2.01) years. The stroke type was 18 cases of cerebral hemorrhage, 20 cases of cerebral infarction, There were 9 combined cases of hyperlipidaemia, 14 diabetes mellitus and 25 hypertension; in the research group, the study group consisted of 20 men and 18 women, aged 30-72 years, with a median age of (63.47±6.27) years and years of education (9.45±2.02). The type of stroke was 17 cases of cerebral hemorrhage, 21 cases of cerebral infarction, and the combined history was 7 cases of hyperlipidemia, 15 cases of diabetes, and 24 cases of hypertension. General data are comparable ($P>0.05$).

Inclusion criteria: (1) First onset; (2) Patients diagnosed as stroke disease by MRI and CT; (3) The total score of MoCA is lower than 26; (4) Those who meet the "diagnostic key points of various cerebrovascular diseases".

Exclusion criteria: (1) Patients with dementia; (2) Persons with psychiatric history; (3) Incomplete liver, kidney, heart and lung functions; (4) Those with obvious emotional fluctuation; (5) Installation of cardiac stent; (6) Aphasia or visual impairment.

2.2 Methods

2.2.1 Cognitive training for the control group: According to the specific conditions of patients, professional rehabilitation therapists should formulate and implement appropriate training plans, mainly including physical therapy, antispasmodic posture, activities of daily living training, hemiplegic limb training and other training programs. Each training time shall be controlled at about half an hour, once a day. Cognitive training shall be conducted from Monday to Friday for a total of 4 weeks.

2.2.2 The study group received transcranial magnetic stimulation (TMS) on the basis of the control group: Before treatment, the patient should be informed of the precautions and operating principles, and the patient should keep relaxed. The patients were treated with transcranial magnetic stimulation instrument (CCY-I, Wuhan Yiruide Group). The "8" shaped coil plane was tangent placed on the scalp. Before treatment, the patient's motion threshold should be detected. The reference and recording electrodes should be attached to abductor pollicis brevis muscle, and the ground wire should be placed on the wrist. The motor cortex area of the upper limbs of the cerebral cortex should be stimulated through the positioning cap of transcranial magnetic stimulation instrument. The stimulation intensity should be adjusted, and the potential evoked amplitude should be recorded. During the treatment, the patient cannot move at will, so as not to affect the accuracy of the stimulation site. Once a day for 4 weeks.

2.3 Observation indicators

2.3.1 MoCA, MBI and MMSE scores: (1) The cognitive function of patients was evaluated with Montreal Cognitive Assessment Scale (MoCA) (Formica et al., 2021). There were 11 items and 30 points in total, and less than 26 points indicated cognitive dysfunction. (2) The modified Barthel index (MBI) (Bikson et al., 2020) Used to assess a patient's ability to live, it consists of 10 items, including modifications to, bathing, toilet use, eating and dressing, with a total score of 100 points. The score was in direct proportion to the living ability of patients. (3) The patient's mental health status is evaluated by the Mini-Mental State Examination (MMSE). (Borisova, Isakova, & Kotov, 2021), which included four items: language ability, time/place orientation, attention, and computational ability, with a total score of 30 points, 25 to 30 points for normal cognitive function, 21 to 24 points for mild cognitive function impairment, 14 to 20 points for moderate cognitive function impairment, and less than 13 points for severe cognitive function impairment.

2.3.2 Treatment effect (Liu et al., 2020): The improvement range of nerve function ≥ 90% is considered as recovery; The improvement range of nerve function is 45%~89%, which is significant; The improvement range of nerve function is between 18% and 44%, which is effective; The improvement range of neural function is less than 18%, which is invalid.

2.3.3 Serum thyroid hormone level: Take 5ml of fasting venous blood, centrifuge, and obtain serum. Chemiluminescence immunoassay (Richard et al., 2020) was used to measure the levels of thyroid stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4), T3 (T3) and thyroxine (T4).

2.3.4 Brain edema volume: The transverse axial T2W1 and T1W1 scans were performed by MRI, followed by intravenous injection of gadopenate meglumine salt, and the transverse repeated scans were performed.

2.3.5 Blood lipid indicators: Low density lipoprotein (LDL), total cholesterol (TCHO), high density lipoprotein (HDL) and triglycerides (TG) were measured by using an enzyme-linked immunosorbent assay (Kolskår et al., 2021) and the instructions were strictly followed.

2.4 Statistical methods

The software package SPSS 24.0 was used to analyse the results.

Statistical values was tested using the n (%) χ2 test, and econometric data was tested using the ($\bar{x} \pm s$), t-test was used and statistical meaningful variation was considered at P < 0.05. The graphing software used in the study was GraphPadPrism8.

3. RESULTS

3.1 General data comparison of the two groups

No statistically significant difference between the control and study groups in regard to age, gender, duration of illness, type of stroke, history of comorbidities, or years of education, indicating that the general statistics of the two populations were similar (p>0.05). (see Table 1).

Table 1. general data for two groups compared

data	Control group (n=38)	Study group (n=38)	X^2/t	*P*
Age (years)	57.36±5.24	56.80±5.19	0.597	0.552
Gender (cases, %)				
Male	22（57.89)	20（52.63)	0.213	0.645
Female	16（42.11)	18（47.37)		
Duration of illness (days)	62.14±6.01	63.47±6.27		
Type of stroke (cases, %)				
Cerebral haemorrhage	18（47.36)	17（44.74)	0.053	0.818
cerebral infarction	20（52.63)	21（55.26)		
History of merger (case,%)				
Hyperlipidemia	9（23.68)	7（18.42)	0.263	0.877
Diabetes	14（36.82)	15（39.47)		
hypertension	25（65.79)	24（63.16)		
Years of education (years)	9.53±2.01	9.45±2.02	0.173	0.863

3.2 Comparison of MoCA, 9 and MMSE scores between the two groups

Before surgery, MoCA, MBI and MMSE scores were not visually separated statistically among the two groups (p>0.05). After receiving therapeutic treatment., the MoCA, MBI and MMSE scores were found to be significantly higher in both groups, with a numerical comparison among the both groups (P<0.05) (see Figure 1).

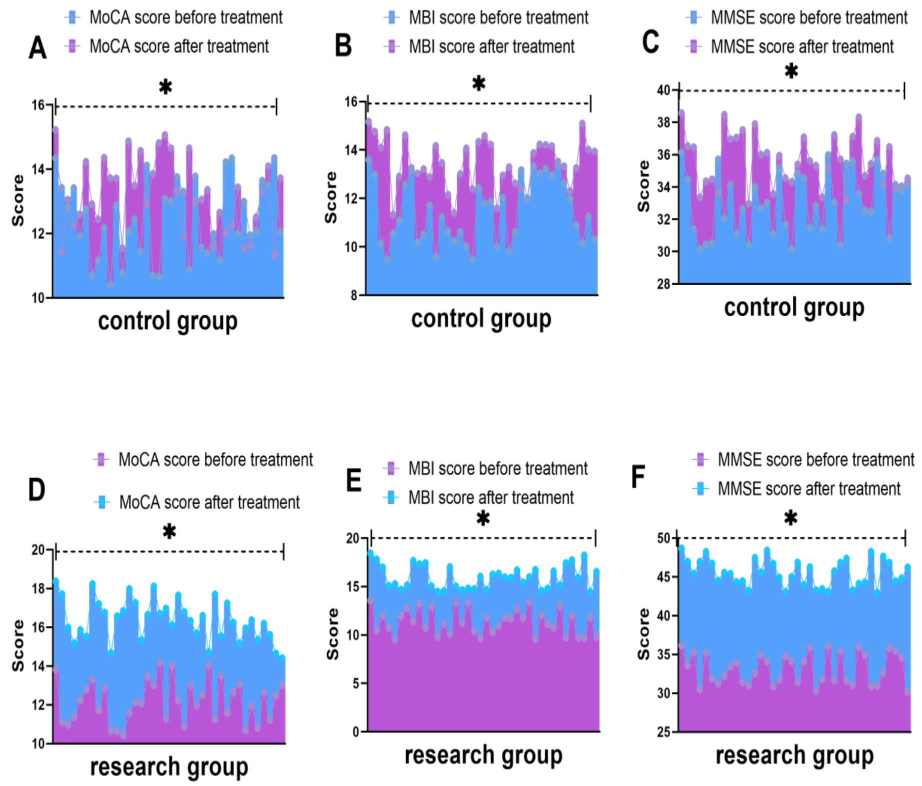

Figure 1. MoCA, MBI and MMSE scores compared amongst the two groups

Note: * P < 0.05 indicates a significant state-of-the-art method for the MoCA, MBI and MMSE scores in the control and study groups.

3.3 Comparison of treatment effects between the two groups

The overall rate of effectiveness was higher in the study group (92.11%) than in the group of controls (71.05%) (p<0.05). (see Figure 2).

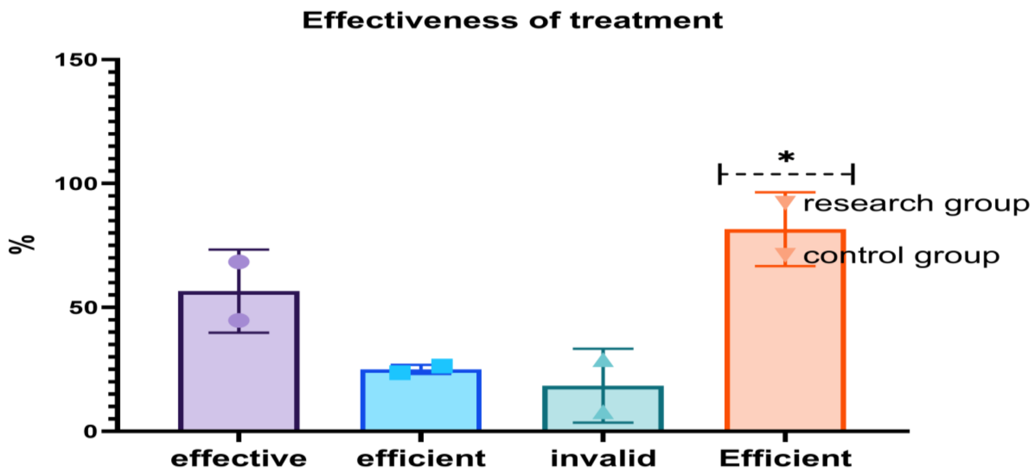

Figure 2. Definition of treatment outcomes of the two groups (cases, %).

Note: The treatment efficiency of the control and research groups were 71.05% and 92.11% correspondingly. The treatment rate in the study group was vastly superior to the treatment rate in the treatment control group, *P<0.05, indicating that there was a statistical variation in the treatment effect between the two groups. (Efficacy rate = (effective + significant + cured)/number of cases, x 100%).

3.4 Serum thyroid hormone levels were matched across these two main groups

Patients' serum thyroid tissue levels before each therapy were not significantly compared between the two groups (p>0.05). After therapy, serum thyroid hormone values of T3 and TSH in the study group were elevated above those in the treatment group, with a significant increase in serum thyroid hormone levels among the two cohorts (p<0.05). (See Figure 3).

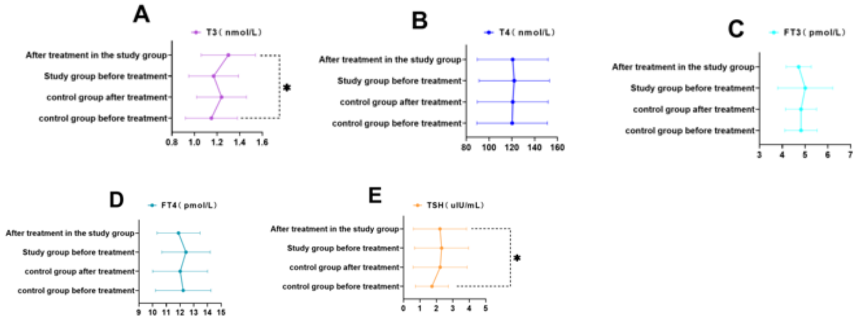

Figure 3. Serum thyroid levels in the two groups compared
Note: * P ＜ 0.05 indicates that there is a statistically significant difference in T3 and TSH serum thyroid hormone levels between the control group and the study group.

3.5 Comparison of brain edema volume between the two groups

No statistically non-significant differences were found in the volume of cerebral oedema prior to treatment in the two groups (p>0.05). There was a trend of decrease in brain edema volume in both groups, And the reduction in brain edema size was greater in the research group versus the control group (p<0.05). (see Figure 4).

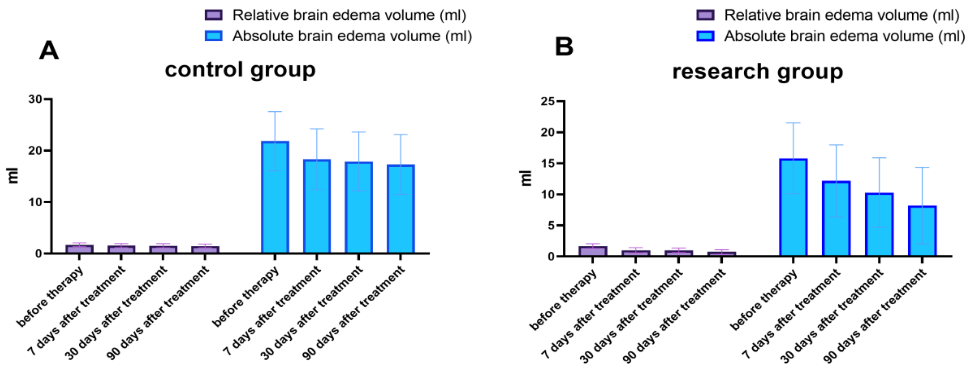

Figure 4. Comparison of brain edema volume between the two groups ($\bar{x} \pm s$)
Note: The difference between the outer edge volume of brain edema and the volume of brain

hematoma is the absolute brain edema volume; The ratio of the peripheral volume of brain edema to the volume of brain hematoma is the relative volume of brain edema.

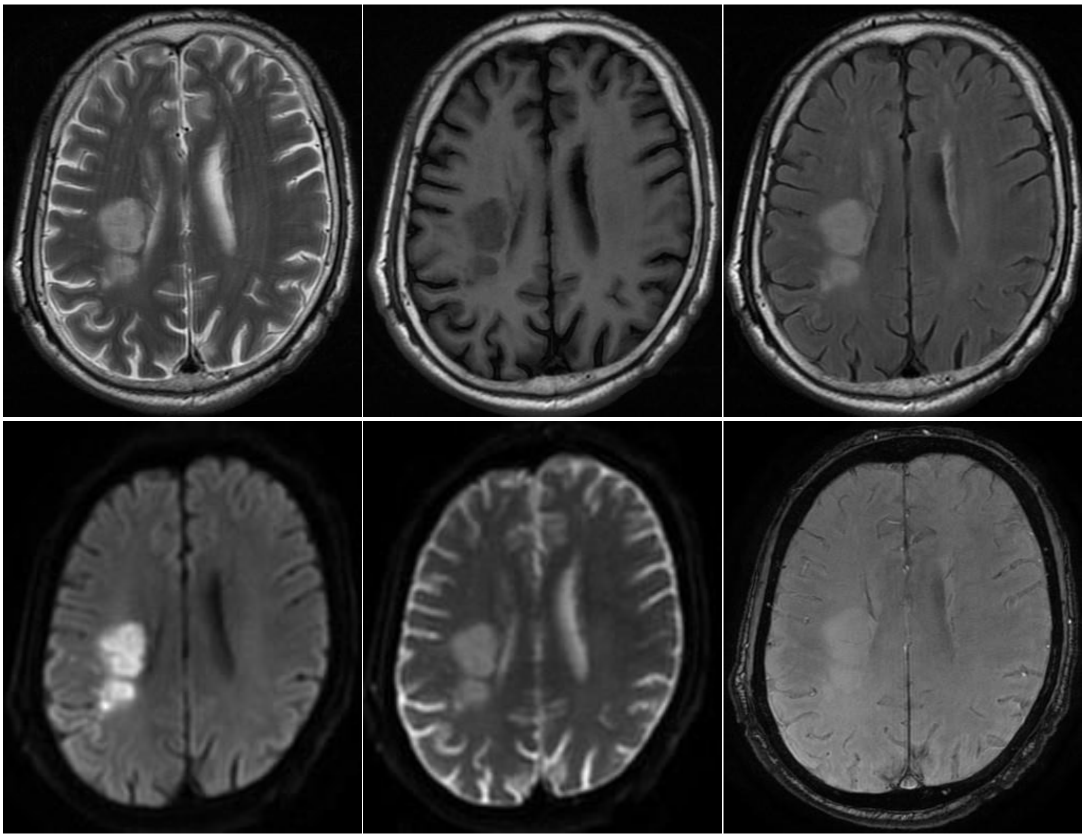

Figure 5. MRI image of brain edema due to acute cerebral infarction

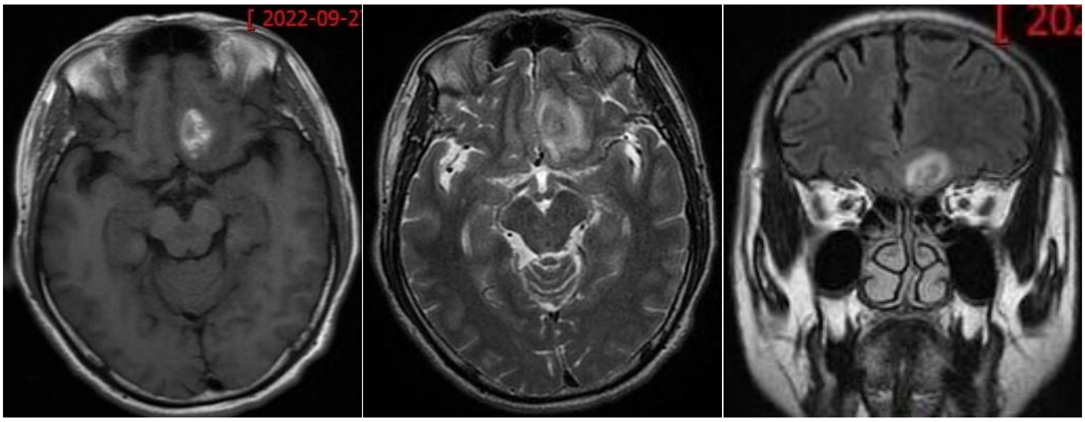

Figure 6. MRI image of cerebral hemorrhage (showing hematoma and perifocal edema)

3.6 Comparison of blood lipid levels between the two groups

Before starting treatment, there was no comparable statistical relationship between the two groups in lipid levels. After treatment, TCHO, TG and LDL levels in both groups decreased. HDL levels increased in the study group, while HDL levels decreased in the control group. However, there was no statistically significant relationship between the two arms ($p>0.05$) (see Figure 5).

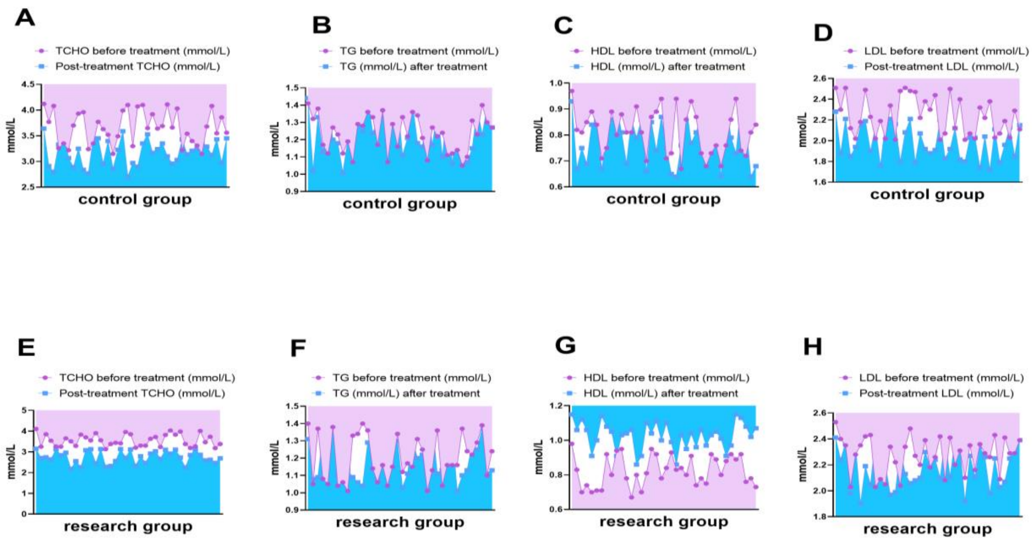

Figure 6. Blood lipid levels compared between groups.

4. DISCUSSION

Cognitive impairment of stroke is a kind of cognitive center injury after cerebrovascular disease. Patients will suffer from impairment of visual space, memory and attention ability, which will lead to severe brain tissue damage due to acute onset (Chew et al., 2020). TMS penetrates into the cerebral cortex under the action of magnetic pulse. At this time, current will be generated and the firing process of neurons will be regulated (Wessel & Hummel, 2018). After that, multiple TMS pulses will be sent continuously, and the signals will be superimposed by repetition after being stimulated (Menardi et al., 2021). According to different pulses of signals, they can be divided into low frequency and high frequency. Low frequency pulses will reduce the excitability of cerebral cortex, while high frequency pulses will increase the excitability of cerebral cortex (Chen et al., 2021). Combining TMS-based therapy with cognitive training allows effective rehabilitation measures to be implemented to promote cognitive function according to the individual client's situation (Hong et al., 2021).

In this study, After the combination of TMS and one of the cognitive trainings, the cognitive function of the patients was remarkably better. The main reason for this is that TMS treatment modulates the excitability of the patient's cerebral hemispheres and promotes the re-establishment of a pattern of antagonistic disinhibition balance in the left and injured hemispheres (Lee, Huang, Hsu, Lin, & Tsai, 2022). The following are the main mechanisms of TMS treatment on the regulation of cognitive function of stroke: (1) It can regulate calcium ion channels, increase ion exchange speed and synaptic transmission efficiency, promote the changes of synaptic plasticity, and then improve the overall cognitive ability of patients (Gordon et al., 2021). (2) It can improve the excitability of distant and local brain regions, accelerate the speed of signal transmission between cells, and correspondingly increase the activity of transmission receptors. The speed of cerebral blood flow in cerebral cortex is accelerated, Plays an essential task in the elimination of metabolic waste and harmful substances (Hara, Shanmugalingam, McIntyre, & Burhan, 2021). (3) It can inhibit the expression of apoptotic protein, which is conducive to the reorganization of neural networks in brain damaged areas (Mihelj, Bächinger, Kikkert, Ruddy, & Wenderoth, 2021).

The thyroid hormone level of patients with acute stroke will change significantly. Data show that there is a correlation between the cognitive function of patients and the level of serum thyroid hormone. The decrease of serum thyroid hormone level will increase the degree of cognitive dysfunction of the disease (Fried et al., 2021). Patients with cognitive impairment after stroke will reduce T3 level and oxygen consumption by regulating their endocrine function. This study analysed the variation of blood serum thyroid hormone values in patients prior to and consequent to treatment. After treatment, serum thyroid hormone levels of T3 and TSH were found to be higher in the study cohort than those developed in the treatment control arm ($p<0.05$). The results showed that TMS combined with cognitive training was safe and effective in improving patients' serum thyroid hormone level. However, different individuals have different conditions, so there are some differences in the improvement of serum thyroid hormone indicators. In addition, there was a trend towards a decrease in brain oedema volume in the treatment period in both the control and study groups, The reduction in brain edema volume was more pronounced in the study group than in the review team..（$P<0.05$）, However, it is still hoped that in the future research, we can more comprehensively analyze the imaging features of stroke through functional magnetic resonance imaging technology to provide a good foundation and guarantee for disease treatment.

The DTI technology of MR is very specific to the white matter fiber bundles of the brain. It can reflect the microstructure of living tissues. It can quantitatively analyze the characteristics of Walerian degeneration of white matter fiber bundles under pathological conditions and can effectively supplement the defects of conventional MRI examination. DTI showed a decrease in FA value at the early stage of stroke. The results showed that the early neural cell membrane disintegrated. With the FA value decreasing, the motor function impairment of patients would be aggravated, which was mainly related to the impairment of patients' neural function. If it was not improved in time, the prognosis of patients would be affected. Therefore, DTI technology can be used to evaluate the recovery of patients' motor function, which provides better guidance for clinical rehabilitation.

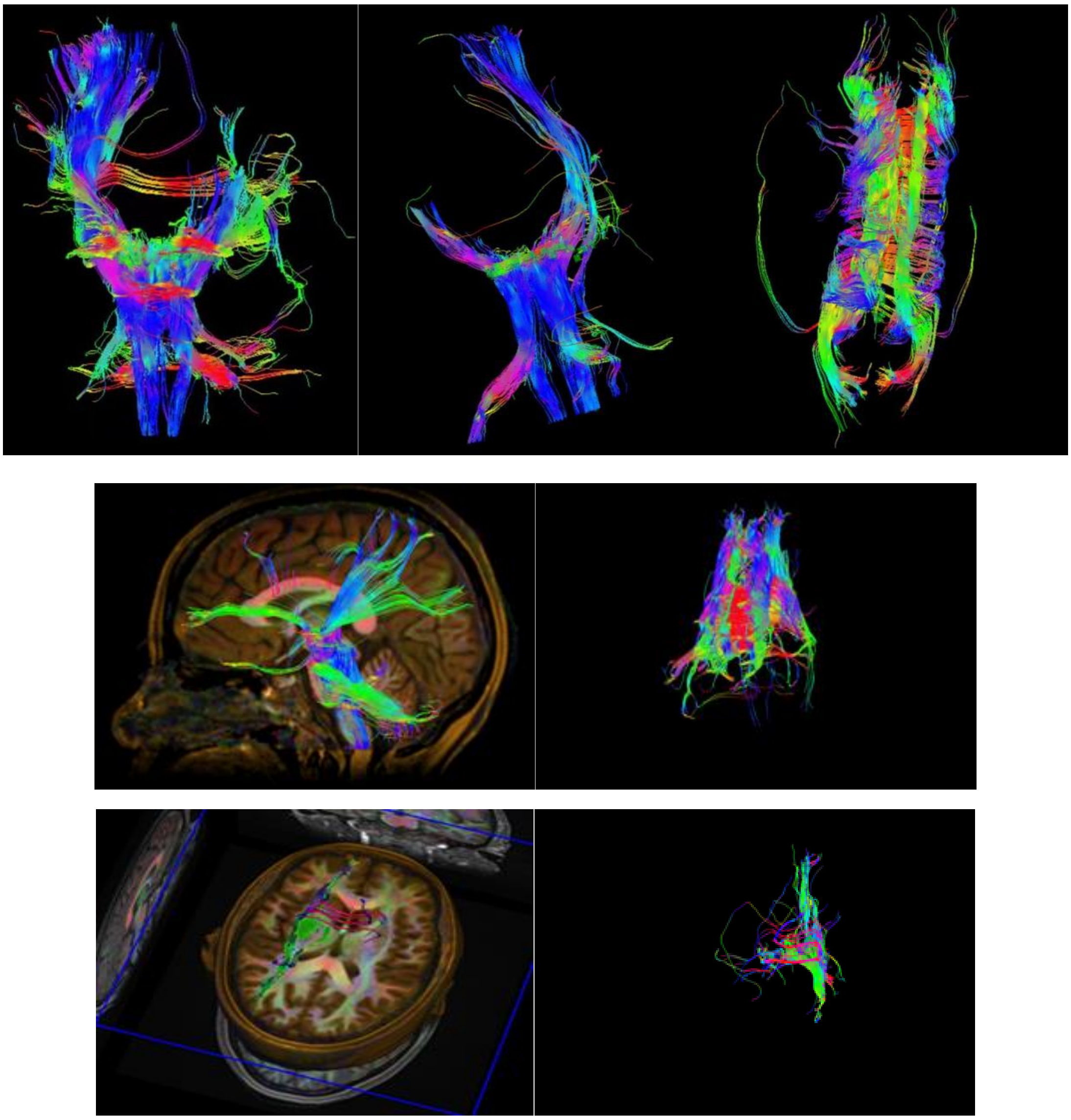

Figure 7. DTI results of stroke patients

5. CONCLUSION

Cognitive training combined with TMS treatment is conducive to improving the level of serum thyroid hormone and blood lipid of patients, promoting the improvement of cognitive function of patients, and reducing the volume of brain edema. The treatment effect is good. Therefore, cognitive training combined with TMS is worth popularizing.

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