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Application Value of Multimodal Magnetic Resonance Imaging in Evaluating the Rehabilitation Effect of rTMS Combined with Cognitive Training on Cognitive Impairment in Patients with TBI

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Abstract

Objective: To explore the clinical application of multimodal magnetic resonance imaging in evaluating the effects of rTMS combined with cognitive training on the rehabilitation of cognitive impairment in patients with TBI. **Methods:** A prospective selection of 166 patients with cognitive dysfunction after traumatic brain injury who were in our hospital from January 2018 to January 2020 were divided into observation group and control group according to the principle of randomization, with 83 cases in each group; the former was rTMS + cognitive training, control group cognitive training, observe and compare the changes of GCS score, MRSI examination Cho/Cr, NAA/Cr ratio, cognitive dysfunction score, cognitive impairment grading scale and modified Barthel index. **Results:** The GCS score, Cho/Cr and NAA/Cr ratios of the observation group were significantly lower than those of the control group, while the cognitive dysfunction score, cognitive impairment rating scale and modified Barthel index were better than those of the control group ($P < 0.05$). **Conclusion:** rTMS can improve the rehabilitation effect of patients with cognitive dysfunction after brain trauma, and multimodal magnetic resonance imaging can play a good role in evaluation.

Keywords

Cognitive Dysfunction after Traumatic Brain Injury, rTMS, Cognitive

*These authors contributed equally to this study.
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Training, Observation of Clinical Indicators, Accurate Evaluation

1. Introduction

Traumatic brain injuries (TBI) are increasing and have recently become one of the major causes of death and permanent disability worldwide [1]. In the United States, TBI accounts for 30% of all deaths related to head trauma and 3.2 million disability-related deaths annually [2]. TBI is related to neurological symptoms, such as disorders of consciousness (DoC) and cognitive dysfunction, as well as many co-occurring mental disorders, seriously affecting the quality of life [3]. Studies show that early intervention of cognitive rehabilitation training can effectively improve the cognitive level of patients with head trauma, improve the activity of daily life, and improve the quality of life. In recent years, computer-assisted cognitive training, occupational therapy, exercise therapy, hyperbaric oxygen therapy and drug therapy have been widely studied for the treatment of cognitive impairment, all of which have improved the cognitive impairment of patients to varying degrees [4]. Repetitive transcranial magnetic stimulation (rTMS) can be used to noninvasively deliver powerful and relatively local stimulation to the human brain, and alignment of TMS pulses into specific sequences or patterns can induce long-term neuroplastic effects, which has therapeutic potential [5]. But most studies have focused on a single treatment, with limited results. Therefore, multimodal magnetic resonance imaging was used in this study to evaluate the clinical effect of rTMS combined with cognitive training on the rehabilitation effect of cognitive impairment in TBI patients.

2. Data and Methods

2.1. General Information

A total of 166 patients with cognitive dysfunction after TBI were admitted to our hospital from January 2018 to January 2020 and were randomly divided into observation group and control group according to the principle of random grouping, with 83 patients in each group. It is proposed to use different regiments for treatment. The study meets the standards of the hospital's ETHICS committee and is conducted with the approval of the ethics committee.

2.2. Inclusion and Exclusion Criteria

2.2.1. Inclusion Criteria

It meets the diagnostic criteria for traumatic brain injury. All patients were diagnosed with cerebral contusion or intracranial hematoma by clinical symptoms, MRI or head CT. Duration of illness < 6 months. The patient is conscious, stable and has certain cognitive ability. All patients had mild to moderate cognitive impairment (MMSE score of 10 - 26). All were aware of the study and volunteered to participate.

2.2.2. Exclusion Criteria

Suffering from trauma, ulcers, severe infection, tumor, scalp scar, with metal implants, a history of mental illness in the body, blood disease, serious illness, understanding obstacle, aphasia, severe heart disease, epilepsy, new bleeding lesions or encephalopathy, progression of the disease in patients with infarction patients, and pregnancy and patients were excluded as scheduled.

2.3. Methods

Both groups were given conventional cognitive function training, including functional training for thinking disorders, attention disorders, perceptual disorders, disorientation disorders, and other functions. Meanwhile, all patients were given high-pressure therapy for 45 minutes/time/day for 5 consecutive days, which was regarded as a course of treatment, and a total of 8 courses were completed. Observation group was treated with rTMS and YRDCCY-I magnetic field therapy instrument. The relevant parameters are set as follows: the stimulus intensity is 1.5 - 6.0 T, the output pulse frequency is 0 - 100 Hz, and all parameters can be adjusted continuously. Before treatment, patients were told to relax their whole body, lie on their back, keep their hands flat, use the anterolateral dorsolateral frontal cortex of the affected side as magnetic stimulation site, and use 3Hz as magnetic stimulation frequency. The intensity of magnetic stimulation was adjusted within 30% - 60% of the motor threshold (MT) according to the patient's tolerance, disease status and age. A total of 70 stimulus sequences were performed 10 times consecutively, with 10 intervals between each sequence and a 10-second rest after each sequence. rTMS treatment was performed 20 min/time/day for 5 courses of 8 courses.

2.4. Observation Indicators

2.4.1. Imaging Examination

Image data were collected and analyzed using SIEMENS 3.0T MRI imaging system and standard head coil. Conventional axial, coronal and sagittal SET1WI (TR/TE 2000 ms/9ms) and axial FSET2WI (TR/TE 5000 ms/95ms) scans were performed with a layer thickness of 5 mm, no interval, FOV18 cm × 19 cm, 256 × 256 matrix. A multivoxel MRS scan was performed, and ROI selected the anterolateral dorsolateral cortex of the affected side to measure the areas under NAA, Cho and Cr spectra peaks. The chemical frequency shift positions of NAA, Cho and Cr were 2.02, 3.21 and 3.02 PPM, respectively. ROI was composed of 256 voxels, each with a size of 10 mm × 10 mm × 10 mm. Point analysis was applied to analyze the spectral sequence, and the measurement parameters were as follows: TR/TE 2000 ms/135ms, using automatic and manual mean field, combined modes of receiver—emission gain adjustment, internal voxel uniform field and water inhibition line calibration, signal mean and metabolite identification to measure the required metabolites. A single excited SE-EPI sequence was used in the DTI diagram, with a 30-direction dispersion gradient, TE/TR of 92 ms/9800ms, layer thickness of 4.0 mm, layer spacing of 1.5 mm, layer number of 22, FOV of 240 mm × 240 mm, matrix of 256 × 256, and b value was 1000. The original collected DTI images are processed on Siemens workstation to obtain FA images and color-coded FA images. Set a 10 mm^2 circle and a 6px ROI to avoid blood vessels, brain waves, and cerebrospinal fluid. For each fiber bundle measured by ROI, FA color maps and T1WI stacking techniques were used to track the values of the same fiber bundle in the upper and lower layers of its continuous plane, and the average of these three values was taken as the final result.

2.4.2. Glasgow Coma Score (GCS)

GCS scale was used to score the two groups of GCS (reflecting the degree of brain injury), including the patients' body motor function, language response and eye-opening response. The total score is 15, including 3 - 8 for mild coma, 9 - 12 for moderate coma, and 13 - 15 for severe coma.

2.4.3. Cognitive Dysfunction Score

The Montreal Cognitive Assessment scale [6] was used to compare MOCA between the two groups. The content includes abstract generalization, orientation test, delayed memory test, naming test, language test, attention test, executive function test, visual spatial function test, etc. Out of 30 points, the higher the score, the better the cognitive function.

2.4.4. Modified Barthel Index Score Changes

Modified Barthel Index (MBI) was used to evaluate the activity of daily living (ADL) of each group. The assessment included grooming, stool control, urination control, bathing, eating and drinking, dressing, using the toilet, walking up and down stairs, moving beds and chairs, and walking on flat ground. On a scale of 100, the higher the score, the better the patient's ability to live independently.

2.5. Statistical Analysis

Statistical analysis was performed by SPSS 17.0 software, and count data were expressed by [N (%)]. Comparison between groups was performed by χ^2 test, and bar charts were drawn by GraphPad Prism 5 software. $P < 0.05$ indicates significant difference, and $P < 0.01$ indicates extremely significant difference.

3. Results

3.1. Changes in GCS Scores

The results showed that the GCS score of the observation group was significantly lower than that of the control group, indicating that the coma degree of the observation group was better than that of the control group (**Figure 1**), and the difference was statistically significant ($P < 0.05$).

3.2. Comparison of Subpeak Area of 1H-MRS Metabolites

The anterolateral dorsolateral cortex of the affected side was scanned by 1H-MRS and DT. The concentrations of N-acetylaspartic acid (NAA), choline (Cho) and creatine (Cr) were detected, and the ratios of Cho/Cr and NAA/Cr were calculated. The results showed that the ratios of Cho/Cr and NAA/Cr were significantly lower than those of the control group (**Figure 2**), with statistically significant differences (P < 0.05).

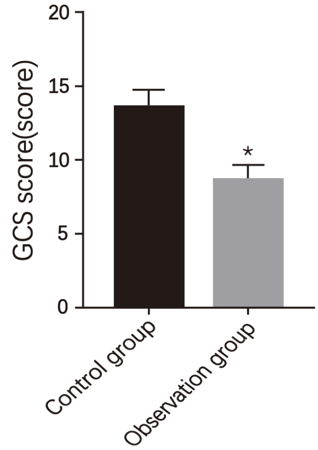
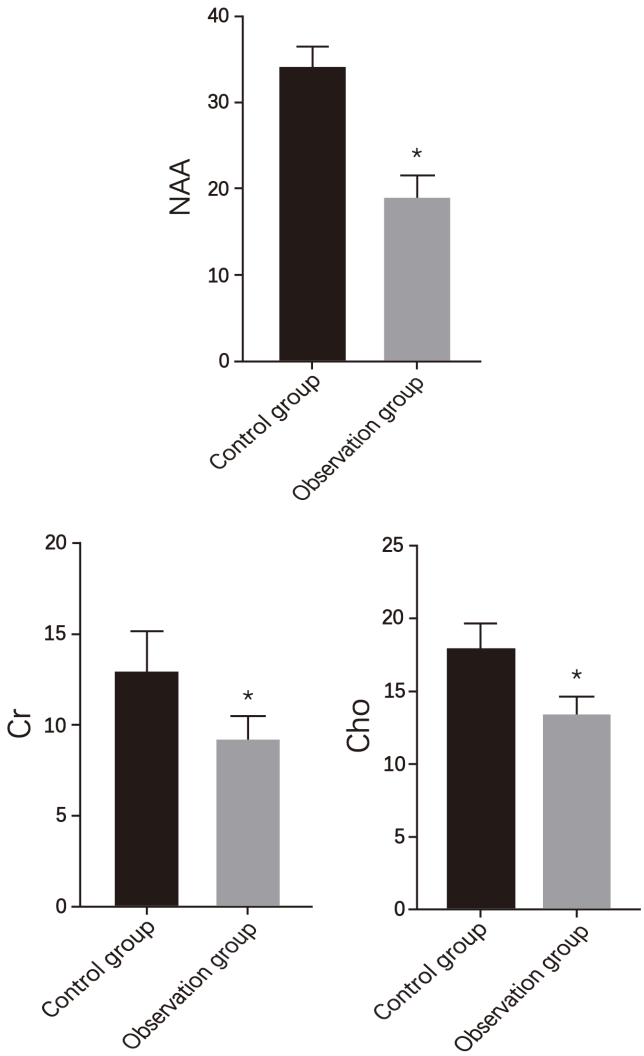


Figure 1. Comparison of GCS between the two groups. Compared with the control: *P < 0.05.



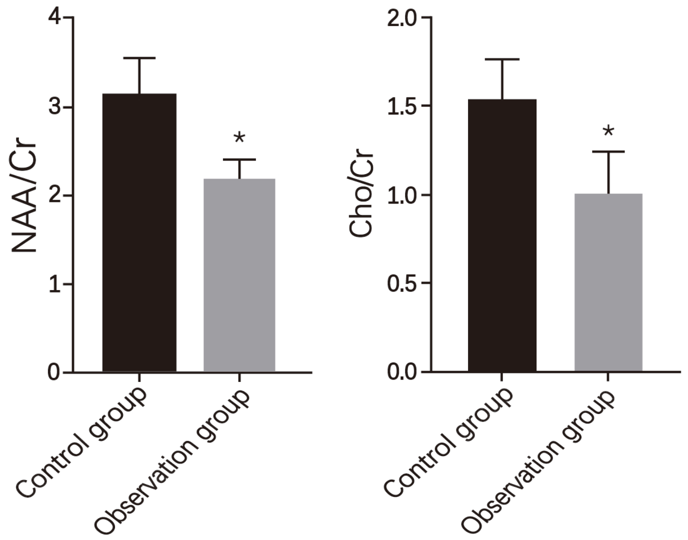


Figure 2. Comparison of subpeak area of 1 H-MRS metabolites between the two groups. Compared with the control: *P < 0.05.

3.3. Comparison of Cognitive Dysfunction Scores

The score of cognitive dysfunction showed that the score of the observation group was higher than that of the control group (**Figure 3**), with statistically significant difference (P < 0.05).

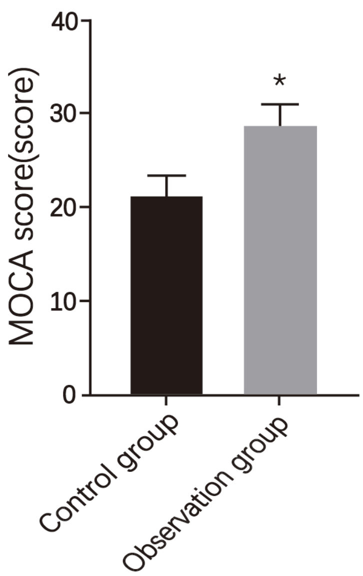


Figure 3. Comparison of MOCA between the two groups. Compared with the control: *P < 0.05.

3.4. Comparison of MBI Scores

MBI results showed that MBI scores of the combined treatment group were better than those of the cognitive training group (**Figure 4**), with statistically significant differences (P < 0.05).

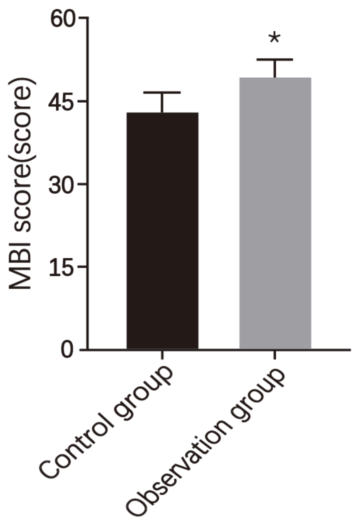


Figure 4. Comparison of MBI scores between the two groups. Compared with the control: *P < 0.05.

4. Discussion

TBI is common in clinical practice and is mainly caused by accidents. After injury, patients may have different degrees of cognitive dysfunction, neurological dysfunction, motor dysfunction, etc. In recent years, the number of patients with craniocerebral trauma has been on the rise, which attracts more researchers' attention. With the progress of medical technology, the mortality rate of patients with TBI has gradually decreased, but the proportion of survivors with related functional disorders is still very high [7]. There are differences and similarities in the spatial distribution of brain injury in TBI patients. In many patients, the damage is isolated and relatively severe. However, when the shock concentration is poor, the diffuse axon damage is more evenly distributed. In addition, animal studies have shown that deep brain regions may be vulnerable regardless of the amygdala [8]. TBI may overlap with co-occurring psychotic symptoms [9], and it is estimated that 70% of patients with TBI suffer from at least one psychotic disorder [10], and major depression is also a common psychiatric disorder associated with TBI [11]. Neurological symptoms of mild or moderate TBI include headache [12] and cognitive deficits, and in severe cases, loss of consciousness. Cognitive function consists of memory, spatio-temporal orientation, executive ability, attention, calculation, etc. It is a psychological process of individual independent understanding and subjective perception of things. Clinically, many diseases can lead to cognitive dysfunction, such as cerebrovascular disease, Alzheimer's disease, Parkinson's disease, etc., among which TBI is also one [13]. As a result of the damage to different brain regions, these patients' brains react differently when they take in, store and reorganize information, and then behave differently accordingly. Examples are attention deficit, judgment deficit, executive deficit and memory deficit. Studies have shown that early detection and treatment can improve the cognitive function of patients to varying degrees, which is very important for reducing the mortality and disability rate of TBI and alleviating the burden of family and social economy [14]. At present, the drugs used for the treatment of cognitive dysfunction patients include calcium antagonists, excitatory amino acid receptor antagonists, cholinesterase inhibitors and so on. Rehabilitation training methods include computer-aided training, group cognitive training, one-to-one manual training and so on. To date, there have been no successful randomized controlled trials (RCTs) of TBI. The lack of effective treatments necessitated the development of more effective treatments.

rTMA is a surface stimulation technique, because the TMS induced intracranial electric field (E field) has the greatest "primary activation" effect on the brain surface near the "stimulation coil" and rapidly decays to deeper brain regions [15]. However, activation diffuses from the surface to other brain regions in a white matter connection-dependent manner ("secondary activation") [16], so the TMS networking-level effect depends on primary activation on the surface as well as secondary activation structures throughout the brain, including deep brain [5]. The network of stimulation depends on the coil position relative to the individual brain anatomy and the connectivity pattern of the individual TBI brain [17]. In addition to the stimulation site, TMS also has other parameters, including the frequency or mode of the stimulation; for example, the frequency (low or high) or mode (continuous or intermittent) of the pulse can lead to inhibition or promotion of neuronal excitability, respectively [18]. Under normal circumstances, both hemispheres are balanced by inhibition of the corpus callosum, and once the function of one hemisphere is affected, it affects the function of the other to some extent. rTMS can regulate the balance of bilateral brain function in patients with TBI, further improve the cognitive function of patients, and promote the recovery of daily life and quality of life. Optimizing treatment is challenging given the variability in the anatomical distribution, neurological sequelae, and co-occurring psychotic conditions of TBI.

In this study, patients with cognitive dysfunction after TBI were collected and randomly divided into observation group and control group. The former group received rTMS combined with cognitive training, while the control group only received cognitive training to evaluate the rehabilitation effect of rTMS on cognitive dysfunction of patients with TBI. GCS is a common tool to evaluate the neurological function and state of consciousness of patients with emergency craniocerebral injury. Currently, it has been widely applied in clinical practice with strong objectivity and science, and can reflect the degree of craniocerebral injury of patients by scoring [19]. In this study, the GCS score of the observation group was significantly lower than that of the control group, indicating that the coma degree of the observation group was better than that of the control group. MOCA is a tool for rapid screening of MILD cognitive impairment. As the first neurophysiological and psychological scale in China, it is also widely used in many countries to screen for mild cognitive impairment and vascular cognitive impairment. MOCA has high sensitivity and specificity for the recognition of MILD cognitive impairment, but its disadvantage is poor applicability for illiteracy [20], which is not suitable for patients with poor education level. In this study, the MOCA score of the observation group was higher than that of the control group. MBI is a common method to assess ADL ability in patients. It mainly includes self-care activities, such as dressing, eating and maintaining personal hygiene, as well as physical activities, such as sitting, standing and walking. It is strongly affected by motor function as well as brain functions such as language comprehension, executive function and memory. Functional Independence Measure (FIM), as an international assessment method of independent living ability, pays more attention to the effects of cognitive and social ability on ADL, which may be more suitable for the assessment of cognitive function, which is also the deficiency of this study. In this study, the MBI score of the combined treatment group was superior to that of the cognitive training group. In this study, multimodal magnetic resonance imaging was used to scan the anterior lateral dorsolateral cortex of the affected side to detect the concentration of NAA, Cho and Cr, and calculate the Ratio of Cho/Cr and NAA/Cr. The results showed that the ratio of Cho/Cr and NAA/Cr was significantly lower than that of the control group.

5. Conclusion

In conclusion, rTMS combined with routine cognitive training can help recover the cognitive impairment of TBI patients, which can provide a reference for the early treatment of TBI patients in clinical practice. However, the study area is single, and the sample size is not large enough, so the results lack certain universality. Therefore, validation and follow-up are needed in larger samples.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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