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Research Progress of Transcranial Magnetic Stimulation Combined with Sleep Electrophysiology in Patients with Consciousness Disorder

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Abstract: In recent years, the proportion of patients with consciousness disorder caused by craniocerebral injury caused by many factors continues to rise, which poses a great challenge to society and family. Therefore, a more complete evaluation method and awakening technology are urgently needed to provide assistance. At the same time, in recent years, the application of sleep electrophysiological technology and transcranial magnetic stimulation technology in the field of neurological rehabilitation has been significantly developed and widely used. The wide application of sleep electrophysiological technology provides a further monitoring method for patients with consciousness disorders, and the development of transcranial magnetic technology brings new therapeutic progress and hope for the treatment of patients with vegetative state. At the same time, in clinical practice, the in-depth study of these two technologies is also deepening. The purpose of this paper is to summarize the current research progress of sleep electrophysiological technology and transcranial magnetic stimulation technology, hoping to provide reference for clinical work.

1. Introduction

With the improvement of living standards and the continuous progress of medical technology, the success rate of treatment of patients with craniocerebral injury has been increasing, and most patients have been converted from coma to chronic disorders of consciousness (DOC), commonly known as vegetative[1] patients. DOC includes vegetative state (VS) and minimally consciousness state (MCS). At present, there are more than 500,000 patients with consciousness disorders caused by brain trauma, stroke and hypoxic encephalopathy in our country, with an additional 70,000 to 100,000 patients every year, and an accumulated annual medical expenditure of 30 to 50 billion yuan, bringing huge mental pressure and economic burden to the family and society. Patients are in the difficult situation of "cannot die, cannot be cured" for a long time, which brings great mental pain and heavy economic burden to the family and society. The possible prediction of the patient's

consciousness recovery will directly affect the choice of clinical treatment strategy, and even the choice of relatives for the patient's life or death. However, although the emergence of various assessment scales provides criteria for the prognosis of patients, this method is completely dependent on doctors' clinical observation and personal experience, which is highly subjective and susceptible to multiple factors, and misjudgment of prognosis may lead to serious consequences. [2]Therefore, it [3]is urgent to develop a more objective and effective evaluation method. At the same time, in recent years, the technique of monitoring nervous system, electrophysiological examination, has been developed continuously. Its advantages of objectivity, stability and non-interference have brought new light to the evaluation of vegetative patients. In particular, electroencephalogram technology and its derived sleep spindle technology bring new evaluation criteria for patients with consciousness disorders, while the wide application of transcranial magnetic stimulation brings new hope for vegetative patients to wake up. This paper aims to provide clinical treatment ideas through objective means of electrophysiology.

2. Sleep Electrophysiology

From the perspective of clumsiness, sleep belongs to the normal physiological state of the human body, which is often manifested as the disappearance of various conscious active behaviors within a certain period of time, and awakening can be given appropriate stimulation [4]. Sleep is often closely related to consciousness. In patients with consciousness disorders, sleep disorders often affect the recovery and repair of neurons, and sleep disorders usually further hinder the acquisition of information, thus complicating or even hindering cognitive rehabilitation [5]. Therefore, we often need to monitor the sleep cycle of patients with consciousness disorders to provide important prognostic information for the recovery of consciousness. For comatose patients, there are two important clinical behavioral characteristics: no sleep-wake cycle and unconscious content, that is, behavioral coma. Studies have shown that electrophysiological and behavioral manifestations of comatose patients are different. Currently, the clinical treatment mainly relies on the coma recovery scale to classify unresponsive wakefulness syndrome (UWS) and minimally consciousness state (MCS). While behavioral evaluation relies on the observation of motor output, misdiagnosis between UWS and MCS as well as locks syndrome often occurs [6]. Therefore, although patients with consciousness disorders have behavioral responses, their sleep-wake cycle is separated from electroacoustic sleep-wake cycle, and the existence of sleep-wake cycle cannot be simply judged by opening and closing eyes [7]. Therefore, it is necessary to use sleep electrophysiology to more accurately predict the prognosis of patients with consciousness disorders. According to relevant studies, the sleep spindles of UWS patients have a high sensitivity in predicting the recovery of consciousness within 1 year. The presence of sleep spindles may be related to the preservation of thalamocortical function. Classical sleep elements are not present, showing only monophasic EEG (persistent low-voltage θ/δ activity) or alternating θ and δ activity suggests a poor prognosis [8]. Meanwhile, Jing Yunyun [9] found that EEG sleep spindles had sensitivity (83.25%), specificity (81.82%) and accuracy (82.14%) in the judgment of consciousness recovery in vegetative state patients in her study on the prognostic prediction of sleep spindles in patients with consciousness disorder. Therefore, sleep electrophysiological technology can be used to more accurately analyze the prognosis of patients with consciousness disorders, and improve the probability of awakening promotion for patients with consciousness disorders.

3. Transcranial Magnetic Stimulation (TMS)

TMS uses electromagnetic induction technology to generate magnetic pulses, which pass through scalp and skull without attenuation and generate ring induction current in nerve tissue adjacent to functional area of cerebral cortex, thereby causing excitatory changes of nerve cells and

playing a role in regulating the corresponding physiology of brain tissue. Depending on the Stimulation pulse, TMS is divided into four modes of repetitive Transcranial Magnetic Stimulation (rTMS) and θ rhythmic bursts. When rTMS acts on the cerebral cortex, in addition to affecting the stimulation of cortical function, it also has certain regulatory effects on the function, physiology and biochemistry of the distant cortical region [10]. Moreover, the biological effects of RTMS can continue after the termination of stimulation, so it has the ability to reshape the functional structure of brain networks. TMS mostly adopts this mode in the treatment of DOC [11]. In treatment, rTMS mediates changes in cerebral cortex excitability related to stimulation frequency. Some studies have found that low-frequency (≤1Hz) rTMS has a stimulating effect on patients with consciousness disorders. However, more studies have confirmed that high frequency (≥5Hz) rTMS has a more accurate effect on improving consciousness [12]. Different types of DoC patients have different consciousness recovery conditions after receiving rTMS treatment. The recovery effect of MCS patients is significantly better than that of coma and vegetative state patients, and some MCS may recover by themselves over time. In addition, MCS patients show higher metabolic activity and functional connectivity of resting state in language network [13]. Therefore, different degrees of consciousness disturbance often affect the therapeutic effect. For coma patients, high-frequency rTMS has a significant effect on awakening of coma patients, and can improve the awakening consciousness of patients by improving cerebral hemodynamics and neuroelectrophysiological status. For example, Sun Jie [14] found in the treatment of rTMS that after giving 15HzrTMS to the left dorsolateral prefrontal region in 38 coma patients with severe cranial brain injury, the average power and slow wave ratio of electroencephalogram recorded before treatment were significantly reduced. Chen Dongyan et al. [15] performed high-frequency repetitive transcranial magnetic stimulation combined with hyperbaric oxygen in 88 patients with craniotraumatic coma for 4 weeks and found that serum aquaporin-1 (AQP-1) levels and scores of the Grass Coma Score Scale (GCS) and Coma Recovery Revised Scale (CRS-R) were significantly improved, and the efficacy of the rTMS group was significantly higher than that of the control group. In conclusion, rTMS technology can effectively improve the brain function of comatose patients, so as to achieve the purpose of promoting awakening. For patients with vegetative state, rTMS technology is widely used. Gong Qiuwen [16] found in the application of transcranial magnetic stimulation to unresponsive patients that after 24 patients with vegetative state received high-frequency rTMS treatment in the left posterior parietal cortex after acquired brain injury, 20 patients showed a certain degree of response to rTMS stimulation, among which, 8 patients improved their consciousness and entered the minimal state of consciousness, 2 patients improved their movement and pain scores, and 6 patients improved their eye tracking ability. Therefore, rTMS can regulate the excitability of the cortex, so as to achieve the goal of improving consciousness. As for the stimulation frequency, while most of the high-frequency rTMS had a significant effect, some low-frequency rTMS also had a wakefulness promoting effect. For example, Fan Yingjie et al. [17] conducted 6-week acupuncture combined with 0.5Hz rTMS treatment in the dorsolateral prefrontal region in 54 patients with vegetal state, and found that the CRS-R scores and EEG grading results of the treated patients were better than those before treatment, and significantly better than those of the control group. At present, more and more studies on high frequency rTMS for awakening indicate that the electrophysiological activity of the brain can be effectively improved by rTMS. For example, Zhang Liangxiang et al. [18] applied 20Hz rTMS in the right dorsolateral prefrontal cortex to patients in vegetative state after traumatic brain injury. After 6 weeks of treatment, it was found that the CRS-R score, EEG grading, brainstem auditory evoked potential grading and somatosensory evoked potential grading of patients were significantly improved compared with those before treatment. These studies indicate that rTMS therapy for patients with vegetative state can effectively improve brain electrophysiological activity, regulate synaptic plasticity, improve nerve function, and further promote the recovery of consciousness in patients. At the same time, rTMS therapy is more effective for patients with minimal consciousness state. In Zhu Xi et al. [19] 's magnetic resonance imaging study on severe disorders of consciousness, 24 patients with disorders of consciousness (18

in vegetative state, 6 in MCSSS) were treated with 10HzrTMS in the right dorsolateral prefrontal region, and it was found that the activity consistency and synchronization of neurons in the parietal and prefrontal lobes of 7 patients with disorders of consciousness were improved. Compared with the vegetative state group, the improvement was more obvious in the minimally conscious group, so it was speculated that the high frequency of rTMS in the right dorsolateral prefrontal region was conducive to consciousness recovery. Xia Xiaoyu performed 10Hz rTMS treatment on the left dorsolateral prefrontal cortex in 32 patients with minimal conscious state after traumatic brain injury and found that the CRS-R score of the patients improved significantly [20]. A study on patients with minimal conscious state after intracerebral hemorrhage found that rTMS at 10Hz in the right dorsolateral prefrontal lobe could promote the recovery of the damaged brain stem ascending reticular activating system. These results suggest that rTMS plays an important role in the recovery of consciousness in patients with MCS, and that patients with MCS show significantly enhanced brain region connectivity and brain network changes after rTMS treatment compared to patients with vegetative state. It can be seen that rTMS plays a crucial role in promoting consciousness in patients with consciousness disorders. Currently, studies on rTMS combined with other techniques to improve the consciousness promotion rate are widespread. For example, Mi Hongting et al. [21] conducted a study on 52 patients with consciousness disorders after traumatic brain injury using high-frequency rTMS combined with music therapy and found that, Music combined with high-frequency rTMS promoted the recovery of consciousness in patients with consciousness disorder, and the effect of percussion combined with high-frequency rTMS with strong rhythm was significantly higher than that of orchestral combined with high-frequency rTMS with slow rhythm in promoting awakening. Chen Bougan et al. [22] found that after rTMS combined with auditory, visual, smelling, taste, pain, temperature and other stimuli for patients with large-area cerebral infarction, the score of GCS and nerve function deficit of the patients was significantly improved, and the wakefulness promoting effect was obvious. These combined treatment schemes provide a new therapeutic approach for promoting wakefulness in patients with DoC, and are expected to bring more possibilities for clinical treatment.

4. Summary

With the development of society, the number of patients with consciousness disorders caused by various reasons is increasing, and for these patients, an objective, effective and inexpensive assessment means needs to be widely used. The application of sleep electrophysiology based on a technology under the condition of brain electrical changes brings a new dawn for clinical assessment of consciousness recovery of patients with consciousness disorders. At the same time, based on the continuous progress of rTMS technology in promoting awakening, it has brought hope for the clinical awakening of patients with consciousness disorders. At present, although the sleep electrophysiological technology and manager magnetic stimulation technology are relatively mature, they still need to be verified by a large number of clinical trials, especially long-term follow-up studies. Therefore, combined with the current research trend, it can be seen that most studies have begun to transition from a single study to a multi-indicator study, combining a variety of evaluation methods. To comprehensively and objectively analyze and summarize the prognosis of patients with consciousness disorders. It will bring a new dawn to improve the awakening rate of patients with consciousness disorder.

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