

Objective Evaluation of the Efficacy of Traditional Chinese Medicine Intervention in Mild Cognitive Impairment: Research Progress Based on EEG-Brain-Computer Interface

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Abstract

Background: Mild cognitive impairment (MCI) is a critical transitional stage between normal aging and dementia, especially Alzheimer's disease (AD), characterized by memory or cognitive impairment and a decline in daily living abilities. It has become a major global medical issue and a significant public health challenge worldwide. Current modern medical treatment options are limited, and traditional efficacy assessment methods based on neuropsychological scales have limitations such as strong subjectivity and insufficient sensitivity. Traditional Chinese medicine (TCM), with its multi-dimensional intervention strategies including herbal medicine, acupuncture, and Tai Chi, has shown unique potential in the prevention and treatment of MCI. With the development of neuroscience technology, electroencephalogram (EEG)-based brain-computer interface (BCI) technology, featuring non-invasive, high temporal resolution, and dynamic monitoring capabilities, provides a powerful tool for objectively quantifying brain function. **Objective:** This review aims to systematically explore how EEG-BCI technology, as a potential objective electrophysiological biomarker and brain function assessment tool, can be used to evaluate the regulatory effects of TCM interventions such as herbal medicine, acupuncture, and Tai Chi on the neuroelectrophysiological activities of MCI patients from the perspective of the intersection of TCM rehabilitation medicine and brain science. **Findings:** Through a review of existing evidence, this paper finds that EEG-BCI can sensitively capture the positive changes in the electroencephalogram of MCI patients after TCM intervention, such as enhanced alpha rhythm, reshaped abnormal brain network connections, and improved P300 potential. These objective indicators provide a basis for explaining the neuroelectrophysiological basis of TCM intervention in improving cognitive function beyond subjective scales. **Conclusion:** EEG-based BCI technology provides a new research perspective and potential tool for the objective evaluation of the efficacy of TCM intervention in MCI. Although there are still challenges in research design, standardization of indicators, and consistency of evidence, this technology is expected to become an important bridge connecting the holistic regulation theory of TCM with modern brain science and provide support for the precise assessment of the intervention effects on MCI.

Keywords

Mild Cognitive Impairment; Traditional Chinese Medicine; EEG; Brain-computer Interface; Efficacy Evaluation; Rehabilitation.

1. Overview

1.1. Clinical Definition, Epidemiology and Public Health Implications of Mild Cognitive Impairment (MCI)

MCI is a transitional stage between normal aging and dementia, which is mainly characterized by mild impairment of memory or other cognitive functions [1], accompanied by a decrease in the ability to support daily life. According to the *Chinese Guidelines for the Diagnosis and Treatment of Dementia and Cognitive Impairment: Diagnosis and Treatment of Mild Cognitive Impairment*, the diagnostic criteria of MCI include cognitive complaints are from patients and/or family members; the patient or informant reports a decline in cognitive function relative to the prior within the past 1 year; cognitive impairment is confirmed by clinical assessment as the presence of impairment in memory and/or other cognitive domains, and the memory impairment does not correspond to age and education; functions of daily life are preserved, and complex instrumental functions are unimpaired or only slightly impaired; there is no dementia. Meanwhile, patients with MCI usually exhibit age-incompatible cognitive decline, but it has not yet reached dementia, and their daily activity capacity remains largely intact [2]. Epidemiological studies have shown that the incidence of MCI has increased significantly with the acceleration of the aging process of the global population, especially in the elderly population, where the prevalence of dementia is 15% in people aged 68 years and older [3]. This high incidence not only has a serious impact on the life quality of patients, but also poses a huge burden on social medical resources. Given that MCI is a vital prodromal stage of Alzheimer's disease, about 10%-15% of MCI patients convert to AD within two years, and AD may subsequently manifest as progressive amnesia, aphasia, agnosia, apraxia and visual-spatial disorders, etc., accompanied by mental and behavioral symptoms such as anxiety, depression, agitation and impulsivity, which severely affects the life of patients and their families. In addition, this disease features complex risk factors, which are difficult to detect at onset, and the probability of progression to AD is extremely high. Thus, it is of important clinical value to explore safe and effective targeted therapy for MCI [4]. However, the current intervention methods for MCI still lack specificity with many shortcomings in the efficacy evaluation system, which hinders the effective treatment of MCI in the current medical field.

1.2. Understanding of MCI in TCM Theory

Classifying MCI into the “forgetfulness” and “dementia-like disorders”, TCM theory believes that its pathogenesis is the deficiency of the origin and the excess of the standard, the mixture of deficiency and excess. Besides, the core pathogenesis lies in the deficiency of marrow sea and phlegm as well as blood stasis blocking the orifices. The brain is the marrow sea, which depends on the nourishment of kidney essence. If the kidney essence is deficient, the marrow sea will be empty, the brain will lose nourishment, and cognitive function will decline. Meanwhile, pathological products such as phlegm turbidity and blood stasis internally obstruct the clearing of orifices, disturb the circulation of qi and blood in the brain collaterals, and further aggravate the condition [5]. Based on this understanding of pathogenesis, TCM fully reflects the guiding role of “preventive treatment of disease” in the prevention and treatment of MCI, and adopts the hierarchical management and whole-process intervention. The concept of “treating disease before disease” covers three levels: “preventing disease before it occurs”, “preventing disease from degeneration” and “preventing recurrence after disease” [6]. In the stage of “prevention before it occurs”, aiming at the high-risk groups of MCI, attention should be paid to nurturing kidney essence, dredging qi and blood, and advocating diligent use of the brain, moderate exercise, and moderate diet to delay the occurrence of cognitive decline. For patients who have developed MCI, they have entered the

critical stage of “preventing disease from degeneration”, and should intervene as soon as possible to control the progression of the disease and prevent the transformation to dementia. At this stage, TCM comprehensively uses its compound formula, acupuncture and moxibustion, traditional exercises, etc. to carry out overall adjustment. For example, kidney-tonifying and essence-filling drugs are the main drugs, supplemented by products that tonify blood, activate blood circulation, eliminate phlegm and open up the aperture, so as to strengthen the brain and improve intelligence [7]. Acupuncture regulates the movement of qi and blood and dredges meridians by stimulating specific acupuncture points (such as Baihui, Fengchi, etc.) [8]. Traditional exercises such as Tai Chi, as a form of movement combined with static, can harmonize yin and yang, replenish qi and activate blood circulation, thus improving cognitive function [9]. The above-mentioned intervention means reflect the advantages of overall regulation of TCM, that is, comprehensively adjusting the functional state of the body through the mechanism of multi-target and multi-pathway action, rather than simply treating a certain pathological link.

However, TCM therapy still has the following main limitations. First, clinical syndrome differentiation and efficacy evaluation standards have not been unified, which makes it difficult to compare the research results horizontally. Secondly, due to the complexity of compound ingredients of TCM and the particularity of therapies such as acupuncture, there is a shortage of rigorously designed large-sample randomized controlled trials at present to provide high-level evidence-based medical evidence. Furthermore, traditional therapies usually require a long intervention cycle, and patients face challenges in long-term treatment compliance. In practical applications, since the early symptoms are easy to be ignored, the best intervention opportunity of “treating the disease” is often missed, thus affecting the efficacy of the three-stage rehabilitation.

1.3. EEG-Based BCI Technology

A brain-computer interface (BCI) is a communication and control system that realizes the direct interaction between the human brain and external devices by collecting and analyzing brain signals, and incorporates the brain into the loop. It is a new human-computer interaction technology with transformative significance and a crucial branch in the field of human-computer interaction [10] with essential research value and related application potential. In recent years, BCI technology based on electroencephalogram (EEG) has attracted widespread attention from all walks of life, which is regarded as a potential new assessment tool. In the study of MCI, EEG-BCI technology can quantitatively evaluate the brain function status of patients by analyzing indicators such as spectral power, brain network connection and event-related potential. For example, power changes in the Theta, Alpha, and Beta bands can reflect excitability in the cerebral cortex [11]. The synchronization and coherence of brain networks can reveal the functional integration between different brain regions [12]. Event-related potentials such as P300 are considered to be sensitive indicators to assess changes in cognitive function [13]. These characteristics make EEG-BCI technology not only provide an objective basis for the early diagnosis of MCI, but also serve as a new paradigm for evaluating the efficacy of TCM intervention, addressing the strong subjectivity and insufficient sensitivity of traditional scales, and opening up a new direction for the modernization of TCM research.

2. Multimodal Outcome Measures of MCI and Biomarker Roles of EEG-BCI

2.1. Assessment of Multimodal Outcome Measures for MCI

Traditional neuropsychological scales (such as MoCA, MMSE, ADAS-Cog) are classical tools for assessing MCI, which have good sensitivity and specificity. However, they have limitations such as the ceiling effect, susceptibility to subjective factors, inability to reflect

neurophysiological activities of the brain, and limited differential effect between normal elderly people and those with MCI. Neuroimaging biomarkers (such as sMRI, fMRI, and FDG-PET) can detect hippocampal atrophy, abnormal connectivity of default network functions, and reduced glucose metabolism in brain regions, which are helpful for diagnosis and monitoring, but they are expensive with a long scanning duration and require high patient cooperation [14]. Molecular biomarkers (such as A β 42 and p-tau in cerebrospinal fluid or blood) can reflect neuronal damage and synaptic dysfunction, which are valuable for early diagnosis. However, cerebrospinal fluid collection is invasive, complex and expensive to detect, and the specific association with cognitive function is not clear, especially in the context of TCM intervention.

2.2. Relevant Research Perspectives of EEG-BCI

Electroencephalogram (EEG) combined with BCI technology has become a vital electrophysiological biomarker for the evaluation of MCI efficacy due to its high temporal resolution, non-invasive and dynamic monitoring ability. EEG can capture the real-time electrical activity changes of the brain under different cognitive tasks, providing a unique perspective for studying the efficacy of TCM intervention on brain function. In terms of spectral power analysis, relevant studies have shown that patients with MCI usually present an increase in Theta band power, while a decrease in Alpha and Beta band power. These changes are considered intertwined with the decline of cognitive function. The increase in Theta power may reflect the abnormal synchronization between the hippocampus and prefrontal cortex [15], while the decrease in Alpha power suggests a decrease in brain information processing efficiency. EEG-BCI technology is able to sensitively capture these spectral changes and quantify them as objective indicators. When it comes to brain network and functional connection, the brain network of MCI patients often indicates synchronization, coherence and disordered topological attributes, and the global efficiency decreases while the local efficiency increases. EEG-BCI can accurately detect the connection strength of different brain regions through nonlinear interdependence analysis and other methods, and visually demonstrate the remodeling effect of TCM intervention on the brain network [16]. As for event-related potentials (ERPs), P300 is a sensitive indicator to assess changes in cognitive function. MCI patients often have a prolonged incubation period and decreased amplitude. EEG-BCI can capture these subtle changes with high temporal resolution, providing dynamic and objective neuroelectrophysiological evidence for TCM intervention [17]. Such a technique compensates for the shortcomings of traditional scales, and also provides a crucial tool to explore the pathological mechanisms of MCI in depth.

3. Evidence Integration of EEG-BCI in the Efficacy Evaluation of the Specific TCM Intervention MCI

3.1. Evidence of Intervention of Chinese Medicine Compound/Monomer

As an important means of TCM intervention for mild MCI, TCM compounds and monomers have illustrated significant potential in clinical research in recent years. As a classic prescription for tonifying the kidney, Liuwei Dihuang Pill can not only improve the physical strength and immunity of elderly patients, but also significantly boost the memory function of elderly patients [18]. A randomized controlled trial found that taking Liuwei Dihuang Pill in MCI patients can affect the changes of Apo E gene polymorphism in patients with MCI, improve their health condition, delay the progression of the disease, and play an anti-dementia role to enhance the cognitive function of MCI patients [19]. In addition, Zuogui Pill, as a prescription that can enhance the filling of essence and marrow, nourish the kidney, strengthen the brain, and warm and tonify the kidney yang, has also been confirmed to

effectively improve the memory and serum NGF and BDNF of MCI patients. According to relevant studies, based on EEG analysis, the frequencies of brain waves α and β in the control group and the medication group after treatment are lower than those before treatment. The frequencies of θ and δ frequencies of brain waves are higher than those before treatment, and the frequencies of α and β bands in the medication group are lower than those in the control group. The frequencies in the θ and δ bands are higher than those in the control group [20]. These results indicate that the Chinese medicine compound has a profound impact on the brain function of MCI patients through multi-target and overall regulation, which provides corresponding new neuroelectrophysiological evidence for future research on EEG-BCI technology and its new efficacy.

3.2. Intervention Evidence for Acupuncture Therapy

As a crucial external treatment of TCM, acupuncture and moxibustion present unique advantages in the MCI treatment. During acupuncture stimulation, MCI patients have increased brain neuronal activity in many regions such as the frontal pole, orbitofrontal gyrus, temporal lobe, insula lobe and posterior cerebellum lobe, most of which are closely related to memory and cognitive function [21]. While Baihui, Taixi, Sishencong and other acupoints have been widely used in the clinical treatment of MCI for their regulatory effect on brain function [22]. Relevant studies have manifested that acupuncture at Baihui point can significantly improve the executive function of MCI patients, and fMRI analysis proves that the functional connection strength of the default network is significantly enhanced after its intervention [23]. Acupuncture at the Taixi point can directly affect neuronal activity in brain areas related to cognitive activity in MCI patients and regulate pathologically imbalanced cognitive circuits [24]. As an extraordinary point outside the meridian, the Sishencong point is often used in combination with other acupoints to enhance the curative effect. In addition, the EEG results after acupuncture intervention lead to an increase in α RP and β RP in the whole brain, which suggests that the increase in conscious activity in these brain areas may go through the stimulation of acupuncture points in the frontal area to strengthen the connection between the rich fiber network and each brain area, activate the synergy of each brain area and functional area, provide a good brain state for the body to enter thinking activities, and promote the recovery of patients' brain function and cognitive function [25]. These studies not only verify the effectiveness of acupuncture therapy in the treatment of MCI, but also provide strong support for the application of EEG-BCI technology in evaluating the efficacy of acupuncture.

3.3. Evidence of Tai Chi Intervention

As a traditional exercise therapy, Tai Chi has received extensive attention in the prevention and treatment of MCI in recent years. Relevant studies have shown that Tai Chi practice can significantly improve the cognitive function of MCI patients, including memory, attention and executive function [26]. Moreover, studies combined with EEG-BCI technology further reveal its potential mechanism of action. According to a study that took college students as the research object, brain functional networks were constructed through EEG signals for analysis to understand the effect of practicing Tai Chi on human brain function. The findings prove that participants' Alpha wave power increases significantly after training. Besides, the nodal degree and nodal efficiency of the frontal and temporal lobes of the brain are higher [27], which suggests that Tai Chi may improve cognitive function by enhancing the relaxation state and information processing efficiency of the brain. In addition, Tai Chi practice has been found to modulate the functional connections of brain networks in MCI patients, especially the interaction pattern between the default network and the central executive network. This change may be intertwined with the promotion of cognitive flexibility of patients [28]. It is worth noting that the intervention effect of Tai Chi as a low-intensity aerobic exercise may be

related to its improvement on gait parameters, with gait abnormalities regarded as one of the vital markers of early clinical symptoms of dementia [29]. Thus, the study of the EEG-BCI technique and gait analysis provides a more comprehensive explanation for the action mechanism of Tai Chi in the prevention and treatment of MCI.

4. Discussion and Challenges

4.1. Evidence Integration and Mechanism Discussion

Based on the analysis of the existing literature, different TCM intervention methods showcase common characteristics in improving the cognitive function of MCI patients, including but not limited to prescriptions such as Liuwei Dihuang Pill and Zuogui Pill, acupuncture therapy and traditional exercises like Tai Chi. In addition to improving the gait parameters and default network function of the brain in MCI patients, they are also proven capable of reshaping abnormal brain network connections. These findings not only provide multidimensional support for the efficacy of TCM intervention in MCI, but also reveal its underlying neuromodulation mechanisms. However, because TCM theory emphasizes the treatment plan of individualized syndrome differentiation and treatment, the action path of various intervention methods may be specific, and simple scale evaluation and imaging have their corresponding limitations. Thus, in future research, more attention should be paid to combining EEG-BCI technology with other multimodal biomarkers, and the specific action mechanism of these interventions should be deeply explored. Moreover, it should be confirmed with TCM theory to better understand the advantages of overall regulation of Chinese medicine.

4.2. EEG-BCI Advantages and Values of Methods

EEG-based BCI technology has unique advantages and significant value in evaluating the efficacy of TCM intervention for MCI. Firstly, this technology features high temporal resolution, which can capture subtle changes in the dynamic cognitive process of the brain in real time, thus compensating for the shortcomings of traditional neuropsychological scales in reflecting the disease progression [30]. Secondly, EEG-BCI, as a non-invasive detection method, has high safety and acceptability, especially for the elderly. Furthermore, some vital indexes of EEG-BCI (such as spectral power analysis, brain network characteristics and event-related potential P300) can sensitively quantify brain function changes, providing an objective basis for efficacy evaluation. As mentioned earlier, TCM prognosis of MCI patients will have phenomena such as decreased Theta power, enhanced Alpha power, and strengthened the connection between the rich fiber network and various brain regions, all of which suggest the positive recovery of brain cognitive function. This dynamic, objective and quantitative evaluation method not only helps overcome the subjective limitations of traditional scales, but also provides new technical support for the modernization research of TCM, and promotes the deep integration of TCM and modern neuroscience.

4.3. Current Methodological and Research Challenges

Although EEG-BCI technology has great potential in evaluating the efficacy of TCM intervention for MCI, its application still faces many methodological and research challenges. First of all, most existing studies are small-sample exploratory trials. There are relatively few studies that comprehensively consider the combination of MCI etiology and TCM syndrome types. Besides, the overall mechanism has not been fully clarified, which may trigger insufficient reliability of research results [31].

Furthermore, the lack of uniform standards in the process from EEG acquisition, preprocessing, to feature extraction leads to poor comparability of results between different studies. From the differences in signal acquisition equipment, the selection of data

preprocessing methods, to the diversity of feature extraction algorithms, deviations may result in different results, which in turn affects the accuracy of the research [32]. Secondly, related studies have proved that EEG-BCI has therapeutic effects on the treatment of cognitive function and motor function of MCI patients, but the number of studies on its rehabilitation effect on patients with multiple dysfunctions remains limited. There is still room for further exploration. Finally, the research on the association between the EEG-BCI index and neuroimaging and molecular biomarkers is not complete, and the related mechanism is not yet clear. Thus, future research needs to focus on these issues and deeply reveal the mechanism of TCM intervention in MCI through multimodal fusion analysis.

5. Conclusion and Prospects

EEG-based BCI technology provides a revolutionary objective perspective and a quantitative tool for evaluating the efficacy of TCM intervention for MCI, and its research results have received wide attention in recent years. At present, EEG-BCI technology has been able to sensitively capture the positive impact of TCM interventions such as TCM, acupuncture and Tai Chi on the brain function of MCI patients. TCM therapy also provides new research insights and fresh blood for the main ingredients of EEG-BCI technology. In addition, normalization of event-related potentials (ERPs) such as P300 parameters also provides objective evidence for the efficacy of TCM interventions beyond traditional neuropsychological scales. These findings not only make up for the shortcomings of traditional scales in assessing subtle cognitive changes, but also provide a crucial scientific basis for the modernization research of traditional Chinese medicine.

The shortcomings of this study are: (1) the etiology of MCI and the heterogeneity of TCM syndrome types are not fully considered, which affects the reliability and universality of the research results to a certain extent; (2) many clinical studies are still small sample, single-center studies, and more high-quality clinical trials are needed in the future to confirm the exact efficacy, safety and in-depth action mechanism of TCM in the treatment of MCI; (3) not all the references are core papers and they have uneven quality with insufficient absolute authority.

Overall, due to the uneven quality of the literature and the different depth of related research, only some of the current related clinical studies have adopted large sample size studies, and many remain case-based or small-sample studies. Although EEG-based BCI technology provides a new perspective for the efficacy evaluation of TCM intervention in MCI, high-quality research is still needed in the future to further explore the practical application of EEG-based BCI technology. Meanwhile, it is necessary to make good use of the existing evaluation evidence to mine more specific and sensitive biomarkers from complex EEG data, and strive to provide more evidence for accurate diagnosis and intervention of MCI.

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