Article

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Effects of Transcranial Magnetic Stimulation Combined with Sertraline on Cognitive Level, Inflammatory Response and Neurological Function in Depressive Disorder Patients with Non-suicidal Self-injury Behavior

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Abstract

Background: Depressive disorder is a chronic mental illness characterized by persistent low mood as its primary clinical symptom. Currently, psychotherapy and drug therapy stand as the primary treatment modalities in clinical practice, offering a certain degree of relief from negative emotions for patients. Nevertheless, sole reliance on drug therapy exhibits a delayed impact on neurotransmitters, and long-term usage often results in adverse side effects such as nausea, drowsiness, and constipation, significantly impeding medication adherence. This study aims to investigate the impact of combining transcranial magnetic stimulation with sertraline on the cognitive level, inflammatory response, and neurological function in patients with depressive disorder who engage in non-suicidal self-injury (NSSI) behavior.

Methods: A total of 130 depressive patients NSSI behavior, who were admitted to our hospital from December 2020 to February 2023, were selected as the subjects for this research. The single-group (65 cases) received treatment with oral sertraline hydrochloride tablets, while the combination group (65 cases) underwent repetitive transcranial magnetic stimulation (rTMS) in conjunction with sertraline. The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) was utilized to assess the depression status and cognitive function levels of both groups. Additionally, the enzyme-linked immunosorbent assay (ELISA) was employed to measure serum levels of inflammatory factors, including tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6). Furthermore, serum levels of neurotransmitters (norepinephrine (NE), dopamine (DA), 5-hydroxytryptamine (5-HT)) and neuro-cytokines (brain-derived neurotrophic factor (BDNF), nerve growth factor (NGF), glial fibrillary acidic protein (GFAP)) were assessed. The clinical effects of the interventions on both groups were then evaluated.

Results: Following the treatment, the combination group exhibited significantly higher levels of immediate memory, delayed memory, attention, visual function, and language function compared to the single group, with statistically significant differences ($p < 0.05$). Additionally, the serum levels of TNF-α, IL-1β, IL-6, and GFAP in the combination group were lower than those in the single group, while the levels of BDNF and NGF were higher in the combination group compared to the single group. These differences were also statistically significant ($p < 0.05$). Simultaneously, the total clinical effective rate in the combination group reached 95.38%, surpassing the 84.61% observed in the single group, and the disparity between the two groups was statistically significant ($p < 0.05$).

Conclusions: The combined use of rTMS and sertraline in treating patients with depressive disorder exhibiting NSSI behavior has proven to be effective in enhancing cognitive function, mitigating inflammatory responses, and elevating levels of neurotransmitters and nerve cytokines in the patients.

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Keywords

transcranial magnetic stimulation; sertraline; non-suicidal self-injury behavior; depressive disorder; neurological function

Introduction

Depressive disorder is a chronic mental illness characterized by persistent low mood as its primary clinical symptom, presenting with high prevalence and a tendency for frequent relapses [1]. The incidence of depressive disorder has been increasing in recent years, likely influenced by the accelerating pace of life and rising social pressures. According to surveys, approximately 280 million individuals worldwide are affected by depressive disorder [2]. Studies indicate that cognitive impairment often coexists with depressive disorder, and some patients also display non-suicidal self-injury (NSSI) behavior. In my country, the detection rate of NSSI in adolescent depressive disorder patients is notably higher, estimated at around 58.5% [3,4].

NSSI refers to intentional self-injurious behaviors that do not involve suicidal ideation, and typically do not result in direct fatalities. These behaviors encompass activities such as repeated acupuncture, burning, hitting, cutting, and scratching [5]. This type of behavior frequently reflects the patient's negative emotions, avoidance psychology, and limited emotional and behavioral management capabilities. The age group of 14–24 years old is particularly prone to NSSI behavior, with a higher incidence among women [6,7].

Currently, psychotherapy and drug therapy stand as the primary treatment modalities in clinical practice, offering a certain degree of relief from patients' negative emotions. However, sole reliance on drug therapy exhibits a delayed impact on neurotransmitters. Prolonged use of medications is often accompanied by side effects such as nausea, drowsiness, and constipation, significantly affecting medication adherence and slowing down the treatment of the disease [8,9].

Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive electrophysiological therapy technique capable of effectively modulating neurotransmitter levels in patients and improving mood disorders through high-frequency stimulation of various brain regions [10]. Some studies have indicated that the combination of rTMS with sertraline offers advantages such as a quicker onset of effect, improved therapeutic outcomes, and fewer side effects compared to single drug therapy. However, there is a limited body of research examining the impact of this combination on the cognitive and neurological functions of depressed patients with NSSI [11].

To contribute novel insights to the clinical treatment of depressive disorders accompanied by NSSI, this study retrospectively selected 130 patients with depressive disorder and NSSI as research subjects. The objective was to observe the influence of rTMS combined with sertraline on the clinical treatment effectiveness, cognitive levels, and neurological functions of these patients. The study also aimed to explore the potential mechanisms of action, providing innovative perspectives for the clinical treatment of depressive disorders associated with NSSI.

Materials and Methods

Research Subjects

A retrospective selection was conducted on a total of 130 patients diagnosed with depression and NSSI who were admitted to the Wuhan Mental Health Center, Wuhan Hospital for Psychotherapy from December 2020 to February 2023. These patients were categorized into two groups based on their treatment methods, resulting in 65 cases in each group: the single group and the combined group. This study received approval from the Wuhan Mental Health Center, Wuhan Hospital for Psychotherapy Medical Ethics Committee and adhered to the principles outlined in the Declaration of Helsinki. Throughout the entire experimental process, informed consent was obtained from the patients or their families.

The study established specific inclusion criteria for participant selection. (1) Patients had to be diagnosed according to the criteria for depressive disorder in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) [12], and simultaneously meet the diagnostic criteria for non-suicidal self-injury in DSM-5. (2) The diagnosis of depressive disorder required confirmation by two attending physicians. (3) Participants were also required to possess the ability to independently complete the self-assessment scale, and those with a similar severity of depressive disorder, as indicated by scale scores, were included. (4) Individuals who had taken antidepressant and sedative drugs within the previous two weeks. These criteria were designed to ensure a well-defined and representative sample for the investigation.

The specific diagnostic criteria for non-suicidal self-injury encompass various facets. (1) Within the past year, an individual must have intentionally inflicted harm upon

their body at least five times. Importantly, these injuries typically result in mild to moderate damage, and the behavior is not motivated by suicidal intentions. (2) Individuals engaging in self-injurious behaviors commonly do so as a means to alleviate negative emotions. (3) These intentional self-injury behaviors are associated with either a perceived difficulty in controlling intentional behavior before engaging in self-harm or frequent thoughts of self-harm. (4) The behaviors must be socially unacceptable, excluding commonplace actions like ear piercing. (5) These behaviors or their consequences cause the individual distress and affect various aspects of their life, including interpersonal, academic, and other social functions. (6) These behaviors occur in situations other than psychotic episodes, delirium, substance addiction, or withdrawal, and are not better explained by other mental disorders or physical illnesses.

The exclusion criteria for participant eligibility were established to refine the study cohort. (1) Individuals with comorbid conditions, including bipolar disorder, schizophrenia, and other mental illnesses. (2) Participants diagnosed with other mental illnesses such as bipolar disorder and schizophrenia by two attending physicians were not considered for inclusion. (3) Cases where depressive disorder was secondary to organic brain disease or a history of craniocerebral trauma. (4) Individuals with abnormal function of major organs. (5) Those with abnormal thyroid function. (6) Those with a history of electroconvulsive therapy within the past two months. These criteria aimed to ensure a focused and homogeneous participant group for the study.

The assessment of self-injurious behavior involved a comprehensive examination of NSSI among all enrolled subjects. The Chinese version of the Ottawa Self-Injury Inventory (OSI), as revised by Zhang Fang, was employed for this purpose. This scale comprises 10 self-injurious behavior patterns, and participants assessed the frequency of their self-injurious behavior over the past year, specifically without suicidal intent. The scoring system ranged from 1 (none) to 4 (5 times or more), allowing for the detection of patients' NSSI behavior based on their individual circumstances. This structured approach facilitated a nuanced evaluation of the frequency and nature of self-injurious behaviors among the study participants.

Evaluation Environment

Half a month prior to the commencement of the study, the personnel responsible for questionnaire assessments underwent uniform training and consistency testing for the scales. The goal was to ensure a reliability threshold of $\geq$0.8 for the scale assessments. On the first day of hospitalization, the Montgomery Depression Scale was employed to assess the degree of depression among prospective patients, and those meeting the enrollment criteria were selected [13]. A self-developed clinical data questionnaire was then utilized to gather personal information, including gender, age, and years of education, along with general clinical data such as the first onset of the disease and the age of first onset for all eligible patients.

Subsequently, the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) was distributed to the patients. Prior to the assessment, patients were briefed on the methods and precautions for completing the questionnaires. The assessments were conducted in a quiet environment, and the questionnaires were collected on-site upon completion. Given the extensive content coverage of the Ottawa Self-Injury Scale, the study primarily employed it to collect information regarding the age at which patients in both groups first engaged in self-injurious behavior, the frequency of self-injury in the past month, and the motivations behind their self-injurious behavior.

Treatment Method

In the single-group intervention, patients received oral treatment with sertraline hydrochloride tablets (Specification: 50 mg, approved by the State Drug Administration: H10890141, Zhejiang Huahai Pharmaceutical Co., Ltd., Zhejiang, China). The initial dose was 25 mg/day, gradually adjusted to 50 mg/day based on the patient's condition, administered orally once a day after meals.

For the combined group, rTMS combined therapy was introduced in addition to the oral sertraline treatment. Transcranial magnetic stimulation (TMS) was utilized as the treatment tool, generating magnetic signals that penetrate the skull to stimulate brain nerves. The depth of stimulation can reach approximately 2.5 cm, enhancing brain metabolism and neural electrical activity. The specific model used in this study was the transcranial magnetic stimulation device NK-01-I, with a frequency band of 0-200HZ, electromagnetic hardness of 1.5 T, and originating from Nanchang, Jiangxi.

During the treatment sessions, patients maintained a relaxed and comfortable position. The magnetic stimulation treatment cap was adjusted to the appropriate size, and the right dorsolateral prefrontal lobe was positioned according to the traditional 5 cm method. The center of the coil was vertically aligned over the right dorsolateral prefrontal cortex throughout the treatment.

The parameter settings for TMS in this study were as follows: a frequency of 10 Hz, a stimulation intensity set at 80% of the resting exercise threshold, and a cyclic treatment approach. Each stimulation lasted for 5 seconds with an interval of 15 seconds. The total treatment time was 15 minutes, administered once per day, and the treatment was sustained for 5 days a week with a 2-day interval. Both the single and combined groups received continuous treatment over a period of 4 weeks.

Detection of Cognitive Function

The cognitive level of both patient groups was assessed before treatment and after 4 weeks of intervention using the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) [14]. Immediate memory assessment comprised story retelling and vocabulary learning, with scores ranging from 0 to 64. Delayed memory assessment included graphic memory, vocabulary memory, story recall, and vocabulary reorganization, with scores ranging from 0 to 62. Attention evaluation covered encoding tests and numerical breadth, with scores ranging from 0 to 105. Visual functions assessment included line positioning and graphic copying, with scores ranging from 0 to 40. Language function evaluation encompassed language fluency and picture naming, with a score range of 0 to 50 points. A lower score on each factor indicated a more severe degree of cognitive impairment.

Detection of Inflammatory Factor Levels

A volume of 5 mL of peripheral venous blood was systematically collected from all patients both before and 4 weeks after treatment, conducted on an empty stomach in the morning. Subsequently, the blood samples were centrifuged at room temperature to obtain separate serum, which was then stored in a –80 °C refrigerator for subsequent testing. Before initiating the testing process, the frozen serum and the ELISA kit were taken out and allowed to return to room temperature.

The enzyme-linked immunosorbent assay (ELISA) method was employed to determine the levels of tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6) in the serum. This was achieved by utilizing the following ELISA kits: TNF-α ELISA kit (Shenzhen Kerunda Biotechnology Co., Ltd., Shenzhen, China, Item number: ELH-TNFa) and IL-1β, IL-6 ELISA kit (Shenzhen Hisian Biotechnology Co., Ltd., Shenzhen, China, Product number: HAS-47926, HAS-48678).

Detection of Neurocytokine Levels

A volume of 5 mL of peripheral venous blood was systematically collected from all patients both before and 4 weeks after treatment, conducted on an empty stomach in the morning. Subsequently, the blood samples were centrifuged at room temperature to obtain separate serum, which was then stored in a –80 °C refrigerator for subsequent testing.

The serum levels of Norepinephrine (NE), dopamine (DA) (normal value range: 44–145 pg/mL), 5-hydroxytryptamine (5-HT) (normal value range: 39–361 ng/mL), brain-derived neurotrophic factor (BDNF), nerve growth factor (NGF), and glial fibrillary acidic protein (GFAP) in the two groups of patients were measured using ELISA. The reagent kit for these measurements was procured from Shanghai Zhicheng Biotechnology Co., Ltd. [NE, DA, 5-HT, BDNF, NGF, GFAP ELISA kit (Shanghai Enzyme-linked Biotechnology Co., Ltd., Shanghai, China, Product number: mI077135, mI077133, mI063220, mIS058345, mIS838306, mIS023352)].

Evaluation of Clinical Efficacy

The clinical efficacy of the interventions was assessed using the reduction rate of the Hamilton Depression Rating Scale (HAMD)-24 [15]. The reduction rate of HAMD = (score before intervention – score after intervention) / score before intervention $\times$ 100%. According to the established criteria, a reduction rate of $\geq$75% was deemed basically cured, 50% to 75% was considered markedly effective, 25% to 50% was classified as effective, and a reduction rate below 25% was regarded as invalid.

Statistical Analysis

Initially, the returned questionnaires underwent a meticulous examination, excluding those with incomplete responses, consistent options throughout, or inaccuracies identified during the logical review. Subsequently, the qualified data were entered into an Excel spreadsheet to establish a comprehensive database. Statistical analysis of the data was conducted using SPSS 25.0 statistical software (IBM Corp., Armonk, NY, USA). Normally distributed data were presented as mean $\pm$ standard deviation ($\bar{x} \pm s$), while count data were expressed as [n (%)]. Data comparisons were performed using the χ^2 test, with a significance level set at $p < 0.05$, indicating statistical significance.

Table 1. Comparison of general information of the two groups of patients [$\bar{x} \pm s$, *n* (%)].

Items		Single group ($n = 65$)	Combined group ($n = 65$)	χ^2/t-value	p value
Gender	Male	23 (35.38%)	26 (40%)	0.295	0.587
	Female	42 (64.62%)	39 (60%)		
Age (years)		16.50 ± 2.45	16.35 ± 2.25	0.364	0.717
Duration of disease (years)		1.70 ± 0.50	1.65 ± 0.45	0.599	0.550
Years of education (years)		8.05 ± 1.98	7.72 ± 1.63	1.037	0.302
Degree of depression	Severe depression	46 (70.77%)	42 (64.62%)	0.563	0.453
	Moderate depression	19 (29.23%)	23 (35.38%)		

Table 2. Comparison of cognitive function in the two groups ($\bar{x} \pm s$).

Groups	Number of cases	Immediate memory		Delayed memory		Attention		Visual function		Language function	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Single group	65	46.42 ± 3.43	52.42 ± 3.13*	41.74 ± 3.72	50.04 ± 3.95*	80.55 ± 5.17	86.25 ± 4.29*	28.04 ± 2.40	33.04 ± 3.25*	31.64 ± 3.32	36.78 ± 3.27*
Combined group	65	46.08 ± 3.54	57.27 ± 2.56*	41.48 ± 3.51	54.71 ± 3.36*	81.47 ± 5.09	91.73 ± 5.33*	27.79 ± 2.28	38.24 ± 3.26*	32.17 ± 3.01	42.82 ± 4.02*
t-value		0.556	10.418	0.652	8.469	0.568	12.113	0.621	11.544	0.594	13.772
p-value		0.579	<0.001	0.546	<0.001	0.640	<0.001	0.584	<0.001	0.557	<0.001

Note: Compared with the same group of patients before treatment, $^*p < 0.05$.

Results

Comparison of General Information

There was no significant difference in general information between the two groups ($p > 0.05$), and they were comparable, as shown in Table 1.

Comparison of Cognitive Function Levels

After treatment, the immediate memory, delayed memory, attention, visual function and language function of patients in the combined group were higher than those of the single group ($p < 0.05$), as shown in Table 2.

Comparison of Inflammatory Factor Levels

After treatment, the serum levels of TNF-α, IL-1β and IL-6 in the combination group were lower than those in the single group ($p < 0.05$), as shown in Table 3.

Comparison of Neurotransmitter Levels

After treatment, the serum levels of NE, DA and 5-HT in the combined group were higher than those in the single group ($p < 0.05$), as shown in Table 4.

Comparison of Neurocytokine Levels

After treatment, the levels of BDNF and NGF in the combination group were higher than those in the single group, and GFAP were lower than that in single group ($p < 0.05$), as shown in Table 5.

Comparison of Clinical Efficacy

Following the treatment, the clinical total effective rate of the combination group exhibited a statistically significant increase compared to the single group ($p < 0.05$), as indicated in Table 6.

Table 3. Comparison of levels of inflammatory factors in the two groups ($\bar{x} \pm$ s, pg/mL).

Groups	Patients	TNF-α		IL-1β		IL-6	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Single group	65	38.43 ± 3.38	31.74 ± 2.62*	21.69 ± 2.15	16.53 ± 1.55*	47.38 ± 4.13	33.82 ± 3.25*
Combined group	65	38.78 ± 3.29	25.32 ± 2.21*	22.17 ± 2.08	11.16 ± 1.03*	46.95 ± 4.25	27.43 ± 2.42*
t-value		0.598	15.101	1.294	23.264	0.585	12.714
p-value		0.551	<0.001	0.198	<0.001	0.560	<0.001

Note: TNF-α, tumor necrosis factor-α; IL-1β, interleukin-1β; IL-6, interleukin-6. Compared with before treatment, $^*p < 0.05$.

Table 4. Comparison of neurotransmitter levels in two groups ($\bar{x} \pm$ s).

Groups	Patients	NE (pg/mL)		DA (pg/mL)		5-HT (ng/mL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Single group	65	75.87 ± 4.85	83.07 ± 6.64*	41.76 ± 3.22	76.47 ± 6.58*	147.27 ± 12.13	223.74 ± 16.25*
Combined group	65	76.37 ± 5.26	92.28 ± 7.19*	42.08 ± 3.19	89.63 ± 7.12*	145.93 ± 13.25	278.65 ± 19.42*
t-value		0.563	7.587	0.569	10.944	0.601	17.483
p-value		0.574	<0.001	0.570	<0.001	0.549	<0.001

Note: NE, norepinephrine; DA, dopamine; 5-HT, 5-hydroxytryptamine. Compared with before treatment, $^*p < 0.05$.

Discussion

The precise etiology and pathogenesis of NSSI remain elusive at present. Influenced by a combination of social factors, complex interpersonal pressures, childhood emotional disorders, adverse childhood experiences, and neurobiological factors, the susceptibility to developing NSSI is significantly heightened [16]. NSSI is particularly prevalent in early to mid-adolescence, a phase characterized by rapid brain development leading to heightened emotional response levels, often persisting into adulthood [17].

Current therapeutic approaches for adolescents with depression accompanied by NSSI primarily involve psychological counseling and antidepressants. However, it has been observed that the efficacy of psychotherapy is notably lower in adolescents compared to adults, and singular drug treatments often fall short of achieving the anticipated therapeutic outcomes due to substantial individual differences [18].

rTMS presents a non-invasive magnetic stimulation technique facilitated by computerized electromechanical medical equipment. This method induces electrical currents in specific areas of the cerebral cortex through brief, rapid alternating or pulsed magnetic fields. The objective is to ameliorate depression in patients and enhance their overall quality of life [19,20].

The study identified a notable influence of neuroinflammation on the hypothalamus-pituitary-adrenaline axis in depressive patients with NSSI, resulting in significant cognitive function changes and emotional disorders, thereby increasing the incidence of NSSI [21]. This investigation focused on 130 cases of depressive disorder accompanied by NSSI at our hospital. Under the treatment protocols of single drug Sertraline and rTMS combined with Sertraline, the study explored the impacts of different treatment methods on cognitive function, inflammatory factor levels, and neurocytokine levels in patients with depressive disorder and NSSI.

The scores for immediate memory, delayed memory, attention, visual function, and language function in the combined group surpassed those in the single group. This suggests that rTMS, when applied at different frequencies, may induce specific effects in various brain regions, potentially enhancing or reducing cortical excitability through evoked action potentials [22,23]. The RBANS scores in all aspects for the combined group were consistently higher than those for the single group, indicating that the combination treatment involving rTMS had a positive impact on improving the cognitive function of patients. In comparison with single drug treatment, the combined approach exhibited a faster relief of depressive symptoms, showcasing improved clinical efficacy.

Repetitive stimulation of high-frequency rTMS was found to generate a sum of excitatory postsynaptic potentials, inducing abnormal nerve excitability at the stimulation site. This, in turn, enhanced excitability and synaptic plasticity, stimulated hormone secretion and release, improved neurotransmitter function, and contributed to the amelioration of depressive symptoms. The application of

Table 5. Comparison of neurocytokine levels in two groups ($\bar{x} \pm s$, pg/mL).

Groups	Patients	BDNF		NGF		GFAP	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Single group	65	14.65 ± 1.35	19.38 ± 1.59*	7.53 ± 0.71	10.35 ± 1.04*	47.27 ± 4.23	28.74 ± 2.25*
Combined group	65	14.39 ± 1.27	24.39 ± 2.26*	7.47 ± 0.73	15.63 ± 1.52*	46.93 ± 4.15	19.65 ± 1.42*
t-value		1.131	14.617	0.475	23.113	0.463	27.545
p-value		0.260	<0.001	0.636	<0.001	0.644	<0.001

Note: BDNF, brain-derived nerve influence factor; NGF, nerve growth factor; GFAP, glial fibrillary acidic protein. Compared with before treatment, $^{*}p < 0.05$.

Table 6. Comparison of clinical efficacy between the two groups [*n* (%)].

Group	*n*	Basically cured	Markedly effective	Effective	Invalid	Total effective rate
Single group	65	33 (50.76)	8 (12.31)	14 (21.54)	10 (15.38)	55 (84.62)
Combined group	65	49 (75.38)	10 (15.38)	3 (4.62)	3 (4.62)	62 (95.38)
χ^2-value						4.188
p-value						0.003

high-frequency rTMS targeting the prefrontal cortex was observed to reactivate suppressed neural activity, thereby contributing to the improvement of self-injurious behavior in NSSI patients.

It has been observed that the occurrence of depressive disorders is intricately linked to the inflammatory process, marked by microglia activation, increased cytokine release, and heightened oxidative stress [24]. Elevated peripheral inflammation can induce abnormal changes in the central nervous system, contributing to the abnormal increase of pro-inflammatory factors and acute phase proteins in individuals with depressive disorders. This, in turn, triggers neuroinflammation and neurodegenerative processes, ultimately leading to the development of mental illnesses [25,26].

In the current study, abnormal elevations in inflammatory factors and sustained low levels of neurotransmitters and neurocytokines were identified, indicating a disrupted immune system, damaged nerve function, and a pronounced neuroinflammatory reaction in the body. The reduction in neurological function was associated with neurotransmitter level disorders, primarily evidenced by decreased levels of NE and 5-HT [27]. 5-HT plays a crucial role in various physiological activities such as body temperature regulation, sleep, mental state, and emotion. The combination of rTMS and sertraline was found to reduce the sensitivity of distal presynaptic membrane receptors, inhibiting the extraction of 5-HT by neurons, thereby increasing the content of 5-HT in the synaptic space and effectively improving neurological function [28,29].

BDNF is capable of crossing the blood-brain barrier, providing nutritional support to brain cells and promoting neuron activity. The decline in cognitive function and the accumulation of negative emotions in depressed patients are often associated with a decrease in BDNF concentration [30,31]. NGF plays a crucial role in promoting the development and differentiation of neurons [32]. GFAP is a vital component of astrocytes, and the abnormal levels of neurotransmitters, coupled with the accumulation of inflammatory factors, can stimulate the atypical structure of astrocytes, leading to dysfunctional synaptic function [33,34].

Following the treatment, a discernible decreasing trend in inflammatory factor levels was observed, with the combination group demonstrating superior effects. Simultaneously, there was an increase in the levels of neurotransmitters NE, DA, and 5-HT, along with elevated levels of nerve cytokines BDNF and NGF, and a decrease in the level of GFAP. These findings suggest that the combined treatment of rTMS and sertraline significantly reduced the neuroinflammatory response in patients, mitigating the impact of inflammatory reactions on nerve function. This reduction is conducive to the restoration of nerve function and improvement of depressive symptoms.

Furthermore, the combined rTMS treatment was found to be beneficial in enhancing the efficacy of antidepressant treatment and accelerating the onset time of the treatment. This underscores the potential of the combined therapeutic approach in achieving comprehensive improvements, addressing both the neuroinflammatory aspects and neurotransmitter levels associated with depressive disorders.

It is important to acknowledge that this study is retrospective, relying on case data from a single center with a relatively small number of included cases. The study lacks a more targeted analysis and does not incorporate dynamic monitoring of serum levels. Consequently, there is a possibility that the study results may be susceptible to a certain degree of inconsistency or bias.

In future investigations, it is imperative to conduct multi-center, large-sample prospective studies to further explore the intricate relationship between changes in peripheral blood inflammatory indicators, neural factor levels, and the occurrence and development of depressive disorders associated with NSSI. Additionally, a more comprehensive approach to treatment options should be examined to enhance the overall quality of life for patients.

Conclusions

In summary, the combination of rTMS with sertraline in the treatment of depressive patients with NSSI demonstrates promising outcomes. This approach not only enhances cognitive function and alleviates depressive symptoms but also reduces inflammation reactions while increasing levels of neurotransmitters and neurocytokines, ultimately leading to a significant improvement in clinical efficacy. Notably, this treatment method is painless, non-invasive, and deemed highly safe. However, it is important to acknowledge that the retrospective nature of this study introduces certain limitations. The uniformity of psychological care across all patients cannot be guaranteed, and methodological constraints are evident. As a result, prospective research is imperative to validate and further explore the effectiveness of this combined treatment approach.

Availability of Data and Materials

The data used to support the findings of this study are included within the article, and during the present study are available from the corresponding author on reasonable request.

Author Contributions

JL and JG made substantial contributions to the conception and design of the study, interpreted the data, wrote and revised the manuscript. JX and FW performed the experiments and collected the data. JX and FW selected the subjects, obtained samples for the study, analyzed as well as interpreted the data and revised the manuscript. All authors read and approved the final manuscript. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics Approval and Consent to Participate

This study was approved by the Wuhan Mental Health Center, Wuhan Hospital for Psychotherapy Medical Ethics Committee (KY201908-3) and complied with the Declaration of Helsinki. The whole process of the experiment was informed consent of the patients or their families.

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Conflict of Interest

The authors declare no conflict of interest.

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