ORIGINAL ARTICLE

The Effectiveness of Repetitive Transcranial Magnetic Stimulation and Theta Burst Stimulation on Selective Attention, Working Memory and Response Time in Suicide

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Abstract

Purpose: Cognitive dysfunction is common in individuals with depression and these cognitive deficits may be associated with a risk of suicide. Therefore, the identification of the cognitive functions of depressed patients and the introduction of effective interventions on these factors are highly important. This study aimed to compare the effectiveness of repetitive Transcranial Magnetic Stimulation (rTMS) and Theta Burst Stimulation (TBS) to improve selective attention, working memory, and response time of depressed individuals with and without a history of suicide.

Materials and Methods: This applied quasi-experimental study was conducted based on a pretest-posttest design. The population included 40 depressed patients referring to the clinics of Mashhad, Iran, in 2020. The samples were divided into four groups, namely individuals with a history of suicide subjected to treatment with rTMS, without a history of suicide receiving treatment with rTMS, with a history of suicide undergoing treatment with TBS, and without a history of suicide administered with TBS (n = 10 each). The data were collected using the Stroop Color and Word Test, Corsi block test, and reaction time tests and statistically analyzed using multivariate analysis of covariance.

Results: The results confirmed the effectiveness of the intervention on the congruent reaction time, incongruent reaction time, working memory, simple reaction time, and selective reaction time in all four study groups (P < 0.05). The results of multivariate analysis of covariance showed that the group had a significant effect on the variables of congruent reaction time, simple reaction time, and selective reaction time (P < 0.05); however, it had no significant effect on the variables of incongruent reaction time and working memory (P > 0.05).

Conclusion: Compared to the rTMS method, the TBS had a greater effect on the variables of congruent reaction time, simple reaction time, and selective reaction time.

Keywords: Transcranial Magnetic Stimulation; Theta Burst Stimulation; Depression; Cognitive Functions; Suicide Attempt.

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1. Introduction

Suicide, which usually occurs in conjunction with mental disorders, is one of the most important concerns of mental health professionals. Suicide-related risk factors include biological factors (reduction of one of the metabolites of serotonin called hydroxy indole acetic acid), cultural, socioeconomic (poverty), and growth factors (inability to resolve age-related conflicts) [1].

One of the areas directly related to suicide attempts is depression. Constant mood swings are the most important symptom of depressive disorder that can last for days, weeks, months or years [2]. The prevalence of depressive disorder is so high that the probability of developing major depression during life is 10 to 25% for women and 5 to 12% for men [3]. About two-thirds of depressed patients think about suicide, and 10 to 15 percent of them end their lives this way. Therefore, identifying effective treatments to reduce it is very important [4].

Cognitive functions relate to clinical areas that examine various aspects of information processing speed, attention, memory, language, and executive functions. Various studies have shown that depressed patients suffer from more cognitive deficits than normal people. These deficiencies may be associated with a risk of suicide [5]. Studies that have examined the relationship between depression and executive functions have shown that depression is associated with deficits in executive functions such as attention, processing speed, and impaired working memory [6].

About 35 to 40 percent of depressed people do not respond to antidepressants. Repetitive Transcranial Magnetic Stimulation (rTMS) is used as a relatively new technique in the treatment of drug-resistant depression [7]. This is a safe and non-invasive method that improves brain function by altering glucose levels and the activity of neurotransmitters. However, this treatment can be associated with complications such as headache, fatigue, and pain / discomfort at the site of stimulation. Also, the effects of this treatment are usually short-lived [8]. Therefore, the need to design a paradigm more effective than rTMS in the treatment of depression seems necessary. Theta Burst Stimulation (TBS) therapy is a new treatment that is able to focus waves with energy and power three times the normal state, which produces strong and stable changes compared to traditional rTMS and causes long-term excitatory and inhibitory changes in the cortex of the brain. Another advantage of TBS over rTMS is its shorter time [9].

Considering the increasing growth of depression and suicide attempts, as well as the adverse psychological, social, and physical effects of this disease, identifying the factors affecting the mental state of patients with depression and providing remedial interventions on these factors is of a great importance. Therefore, the aim of this study was to compare the effectiveness of rTMS and tetanus magnetic stimulation on improving the selective attention, working memory, and response time of depressed individuals with and without a history of suicide.

2. Materials and Methods

The present study was a quasi-experimental applied research (pre-test, post-test) which was performed on 18-50 year old patients referring to clinics in Mashhad in 2020.

2.1. Inclusion and Exclusion Criteria

Inclusion criteria were definitive diagnosis of the depressive disorder according to Beck Depression Scale, age range between 18 and 50 years and history of a suicide attempt. History of seizures, history of head surgery, presence of any implants in the head, neck and upper body, having or not having a heart pacemaker, history of drug use and addiction to alcohol and smoking or any other type of drug, pregnancy, lack of normal vision (Color blindness or other eye diseases), schizophrenia, schizoaffective disorder, schizophrenic form disorder, hallucination disorder or psychotic symptoms were the exclusion criteria.

2.2. Research Tools

Stroop test: This test was used to measure the need for selection and cognitive flexibility. In this test, 48 matching color words and 48 inconsistent color words with red, blue, yellow and green colors were displayed. Consonant words mean that the color of the word is the same as the meaning of the word, for example, the word green, which is indicated by the color green. Inconsistent words mean the mismatch of the color of the word with the meaning of the word. The text must specify only the meaning of the word, its apparent color. The presentation time of each stimulus is 2 seconds and the presentation distance of the two stimuli is 800 thousandths of a second. Reliability and validity of this test are required in Iran [10].

Corsi block test: This test is designed to evaluate and measure the capacity of short-term spatial memory and spatial working memory. This test is also suitable for assessing the talents of individuals in various fields related to the performance of the right hemisphere. This test can be measured in both age groups of children and adults and the time required to perform it is between 10 to 15 minutes [11].

Reaction time test: Reaction time can be measured for both simple choices and multiple-choice reactions. Light and sound actuators are available that set the reaction time by selecting red, yellow, or white. This method can be presented in various experimental forms from individual stimuli to a combination of simultaneous or sequential stimuli. Using the break key and the reaction key, the difference between the movement time and the reaction is determined [12].

2.3. Test Design

In this study, after receiving the necessary permits, they referred to the psychiatric services and polyclinics of Mashhad and asked their officials to introduce people with depression with and without a history of suicide. Sampling was done in a purposive and available method. As a result, 40 individuals were selected from the volunteers. Twenty of these individuals had a history of suicide. They were randomly divided into two experimental groups: treated with theta burst and treated with rTMS. Also, 20 individuals without a history of suicide were selected as the control group. They were treated with theta burst and rTMS in two groups.

The Beck Depression Inventory was used to assess depression. Subjects were assessed for cognitive function before performing magnetic stimulation of the brain (rTMS) and magnetic stimulation of theta burst (TBS). In the method of rTMS, a Magestim device was used, which creates excitations in the desired position of the brain by creating magnetic fields. In this study, the frequency of each stimulus was 10 Hz, with an intensity of 120% Resting Motor Threshold (RMT) and the duration of each stimulation was 4 seconds and the inter-train interval was 26 seconds. The number of pulses presented in each session was 3,000 and the number of training was 75. This mechanism was performed on the left Dorsolateral Prefrontal Cortex (DLPFC) for 4 weeks and three sessions of 38 minutes each week. In the TBS method, participants received frequencies of 50 and 5 Hz with coils of 8 Magestim devices for 12 sessions (3 sessions per week for 4 weeks) in the LDLPFC

area. The stimulation intensity was 80% of the patient's motor threshold. The number of trains was 20 and the number of pulses was 600 per session. The duration of each session was 3.3 minutes. TBS was performed according to the recommendations of the International Association for Frequent Magnetic Stimulation of the Brain. One week after the end of the intervention period, the Tower of London tests, Corsi block and reaction time were performed and scored in two groups. Finally, the post-test and pre-test data were compared. Also, all patients used medication in the treatment process and their medications did not change a month before the treatment and their medications did not change during the treatment.

2.4. Statistical Analysis

Data were plugged into SPSS software version 19 and then statistically analyzed. Descriptive data were explained using mean and frequency. The normality of the data was assessed using Kolmogorov-Smirnov. Finally, the data were analyzed using chi-square, paired t-test and multivariate analysis of covariance. The confidence level was considered less than 0.05.

2.5. Ethical Considerations

The present research project has been approved by the ethics committee of the Institute for Cognitive Sciences studies (IR.UT.IRICSS.REC.1399.009). Prior to the study, the conditions were fully explained to the patients and they were assured that their information would remain confidential. Also, written consent was obtained from all patients. Patients were completely free to leave the study at any time. Not participating in the research or not continuing to cooperate did not affect the health care provided to the individual.

3. Results

The frequency of demographic variables is shown in Table 1. Based on the findings, there was no significant difference between the four groups in terms of any of the demographic variables, including age, education, gender, and marriage ($P > 0.05$).

Group comparisons were performed using analysis of covariance. Bartlett sphericity test was used to check the sufficient correlation between dependent variables ($P = 0.231$; Bartlett sphericity = 523.74). The results of the correlated t-test to evaluate the effectiveness of intervention methods

Table 1. Frequency of demographic variables in four study groups

Variable		Theta burst		rTMS	
		Without suicide history	**With suicide history**	**Without suicide history**	**With suicide history**
		Frequency	Frequency	Frequency	Frequency
Gender	**Female**	6	7	7	5
	Male	4	3	3	5
Age	**21-30**	4	4	5	3
	31-40	3	4	3	3
	41-50	3	2	2	4
Marital status	**Married**	7	8	6	7
	Single	3	2	4	3
Education	**Diploma**	5	4	4	3
	Associate Degree	3	3	2	4
	Bachelor	2	3	4	3

on each of the variables of cognitive function of depressed people are shown in Table 2. The results showed the effect of the variables of consonant reaction time, inconsistent reaction time, working memory, simple reaction time, and selective reaction time on depression in all four study groups ($P < 0.05$).

Mean and standard deviation of pre-test and post-test of cognitive functions, including selective attention (consonant reaction time and inconsistent reaction time), working memory and processing speed (simple reaction time and selective reaction time) are shown in groups in Table 3.

The results of univariate analysis of covariance in the text of multivariate analysis of covariance to determine the effectiveness of intervention methods on each of the

Table 2. Correlated t-test results to evaluate the effectiveness of intervention methods on each of the cognitive function variables in depressed individuals

Groups	Variables	Mean differences	Standard estimation error	Statistic T	DF	Significance
Theta burst Without suicide history	consonant reaction time	121	9.49	12.74	9	0.001
	inconsistent reaction time	125.1	9.206	13.58	9	0.001
	working memory	-2	0.21	-9.48	9	0.001
	simple reaction time	75.8	4.17	18.16	9	0.001
	selective reaction time	66.7	4.99	13.35	9	0.001
Theta burst With suicide history	consonant reaction time	187.4	10.94	17.11	9	0.001
	inconsistent reaction time	162.8	12.56	12.95	9	0.001
	working memory	-2.4	0.16	-14.69	9	0.001
	simple reaction time	108.2	3.36	32.17	9	0.001
	selective reaction time	92.1	7.27	12.652	9	0.001
rTMS With suicide history	consonant reaction time	100.9	10.84	9.3	9	0.001
	inconsistent reaction time	121.2	9.09	13.33	9	0.001
	working memory	-1.9	0.23	-8.143	9	0.001
	simple reaction time	69.1	3.23	21.37	9	0.001
	selective reaction time	75.6	3.47	21.73	9	0.001
rTMS Without suicide history	consonant reaction time	151.6	9.79	15.48	9	0.001
	inconsistent reaction time	134.1	7.205	18.61	9	0.001
	working memory	-2.4	0.163	-14.69	9	0.001
	simple reaction time	91.3	3.026	30.17	9	0.001
	selective reaction time	105.6	6.99	15.106	9	0.001

Table 3. Mean and standard deviation of pre-test and post-test of cognitive functions of depressed people by groups

| | | Theta burst | | | | rTMS | | | |
| | | Without suicide history | | With suicide history | | Without suicide history | | With suicide history | |
Variable		Mean	SD	Mean	SD	Mean	SD	Mean	SD
Consonant reaction time	**Pre-test**	960.8	136.85	1011.1	132.74	987.1	148.26	992.2	107.97
	Post-test	839.8	143.01	823.70	153.4	886.2	159.05	840.6	98.48
Inconsistent reaction time	**Pre-test**	1063.4	151.49	1116.70	143.55	1096.2	148.65	1101.5	100.28
	Post-test	938.3	158.64	953.9	129.7	975	136.8	967.4	87.65
Working memory	**Pre-test**	5.9	1.37	6	1.49	6.2	1.31	5.7	1.56
	Post-test	7.9	1.37	8.4	1.71	8.1	1.19	8.1	1.59
Simple reaction time	**Pre-test**	504	21.49	507.8	21.68	496.4	23.88	508.6	24.89
	Post-test	428.2	21.56	399.6	17.51	427.3	25.77	417.3	25.41
Selective reaction time	**Pre-test**	396.7	29.87	410	32.8	409	38.26	416.3	34.19
	Post-test	330	35.59	317.9	31.49	333.4	33.06	310.7	19.77

dependent variables are shown in Table 4. Based on the results, the group had a significant effect on the variables of consonant reaction time and simple reaction time and selective reaction time (P < 0.05), but had no significant effect on the variables of inconsistent reaction time and working memory (P < 0.05).

The results of Bonferroni post hoc test to compare the effectiveness of intervention methods on consonant reaction time, simple reaction time, and selective reaction time were shown in Table 5. The results showed a decrease in consonant reaction time and simple reaction time in the non-suicide TBS group compared to the suicidal TBS group and a decrease in the consonant reaction time and simple reaction time in the suicidal TBS group compared to the non-suicide rTMS groups and Suicide rTMS group. Also, the data showed the effectiveness of the non-suicide

rTMS group in reducing the consonant reaction time and simple reaction time compared to the suicide rTMS group (P < 0.05). In reducing the selective reaction time, the effectiveness of the non-suicide TBS group was less than that of the suicide TBS and suicide rTMS groups. Also, the effectiveness of the non- suicide rTMS group was lower than the suicide rTMS group in reducing the selective reaction time (P < 0.05) (Figures 1-5).

4. Discussion

The present study is the first study to compare the effectiveness of two methods of rTMS and theta burst stimulation in depressed patients with and without a history of suicide. Based on the findings, in all groups, the intervention reduced the consistent reaction time, simple reaction time and selective reaction time in depressed

Table 4. Results of univariate analysis of covariance in the context of multivariate analysis of covariance to determine the effectiveness of intervention methods on each of the variables

Dependent variable	Source	Sum of squares	Df	Squares Mean	Statistic F	Significance	Effect size	Statistical power
Consonant reaction time	**pre-test**	21655.22	1	21655.22	23.061	0.001	0.45	0.966
	Group	41009.53	3	13669.84	14.55	0.001	0.609	1.000
Inconsistent reaction time	**pre-test**	16396.89	1	16396.89	16.96	0.001	0.377	0.97
	Group	7165.66	3	2388.55	2.417	0.08	0.209	0.55
Working memory	**pre-test**	58.95	1	58.95	153.36	0.001	0.84	1.000
	Group	1.845	3	0.615	1.6	0.21	0.14	0.37
Simple reaction time	**pre-test**	10750.55	1	10750.55	83.78	0.001	0.75	1.000
	Group	7630.76	3	2543.55	19.828	0.001	0.68	1.000
Selective reaction time	**pre-test**	16528.68	1	16528.68	58.615	0.001	0.76	1.000
	Group	7240.59	3	2413.53	8.545	0.001	0.47	0.98

Table 5. Results of Bonferroni post hoc test to compare the effectiveness of intervention methods on dependent variables

Variables	Groups		Mean difference	Standard error	Significance
Consonant reaction time	Theta burst Without suicide history	Theta burst With suicide history	69.139	14.306	0.001
	Theta burst Without suicide history	rTMS Without suicide history	-21.36	14.006	0.830
	Theta burst Without suicide history	rTMS With suicide history	26.28	14.34	0.465
	Theta burst With suicide history	rTMS Without suicide history	-90.504	14.29	0.001
	Theta burst With suicide history	rTMS With suicide history	-42.85	13.92	0.028
	rTMS Without suicide history	rTMS With suicide history	47.65	14.27	0.014
Simple reaction time	Theta burst Without suicide history	Theta burst With suicide history	31.65	5.28	0.001
	Theta burst Without suicide history	rTMS Without suicide history	-6.34	5.17	>0.99
	Theta burst Without suicide history	rTMS With suicide history	13.96	5.302	0.082
	Theta burst With suicide history	rTMS Without suicide history	-37.99	5.28	0.001
	Theta burst With suicide history	rTMS With suicide history	-17.69	5.14	0.011
	rTMS Without suicide history	rTMS With suicide history	20.305	5.27	0.004
Selective reaction time	Theta burst Without suicide history	Theta burst With suicide history	25.13	7.84	0.02
	Theta burst Without suicide history	rTMS Without suicide history	6.76	7.68	>0.99
	Theta burst Without suicide history	rTMS With suicide history	35.95	7.86	0.001
	Theta burst With suicide history	rTMS Without suicide history	-18.36	7.84	0.159
	Theta burst With suicide history	rTMS With suicide history	10.82	7.63	>0.99
	rTMS Without suicide history	rTMS With suicide history	29.19	7.82	0.005

individuals. However, no significant effect was observed on the variables of inconsistent reaction time and working memory. To reduce consonant reaction time, simple reaction time and selective reaction time, TBS intervention was more effective than rTMS in both groups with and without a history of suicide. Also, TBS resulted in a greater reduction in consonant reaction time and simple reaction time in people without a history of suicide than in people with a history of suicide who were treated with rTMS. In both TBS and rTMS, concurrent reaction time, reduced simple
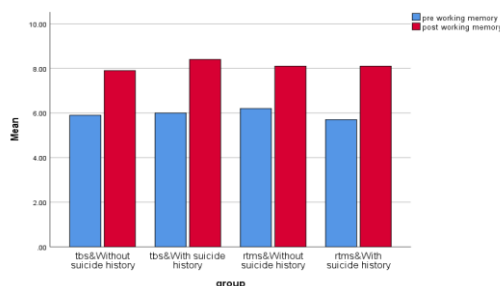

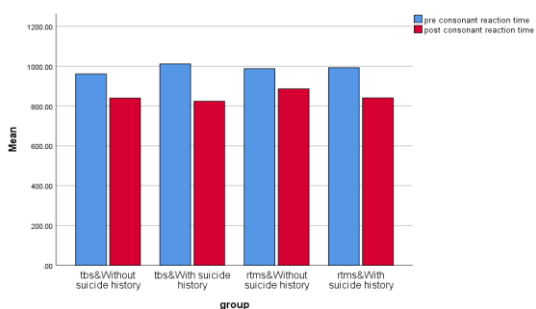**Figure 3.** Comparison effect of working memory in groups

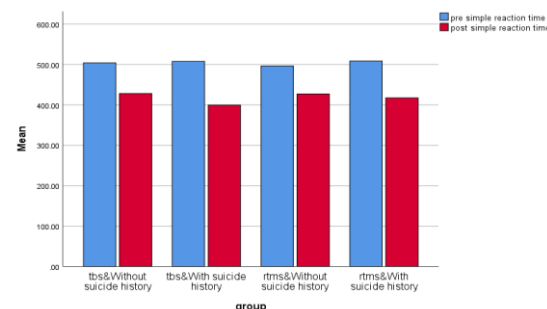**Figure 1.** Comparison effect of consonant reaction time in groups

Figure 4. Comparison effect of simple reaction time in groups
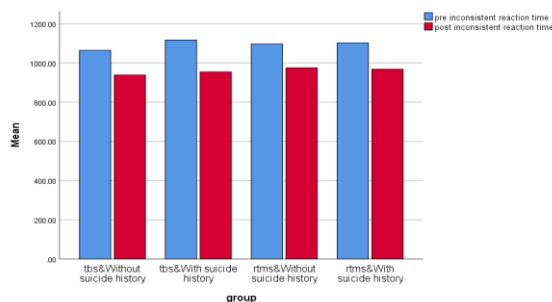

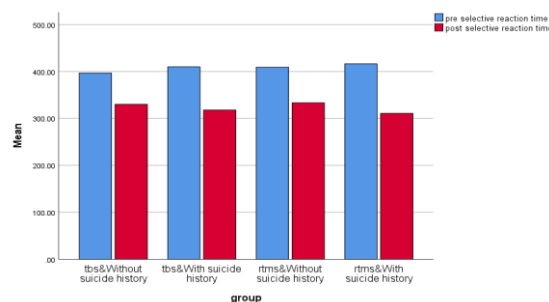**Figure 2.** Comparison effect of inconsistent reaction time in groups

Figure 5. Comparison effect of selective reaction time in groups

reaction time, and selective reaction time were lower in those without a history of suicide than in those with a history of suicide.

Cognitive functions are the same high-level psychological processes that are connected to and integrated into neural networks. Based on the evidence, some neuropsychological functions of depressed people are impaired. Many cognitive functions can be assessed by testing neuropsychological functions. To increase cognitive activity in depressed patients, various therapies are used, including medication, electric shock and transcranial magnetic stimulation. Some findings have shown that transcranial magnetic stimulation in the cortex has the same effect as antidepressants [13].

Our study showed that rTMS is effective in improving the cognitive functions of depressed people who attempt and do not commit suicide. The use of this method led to a decrease in consonant reaction time, inconsistent reaction time, simple reaction time, and selective reaction time and increased working memory in depressed people with and without a history of suicide.

The effectiveness of rTMS on reducing the concordant and inconsistent reaction times is consistent with the results of other studies [14, 15]. Also, the effectiveness of rTMS on reducing the simple and selective reaction time as well as working memory has been confirmed by other similar studies [15-19].

In this regard, a study by Kazemi *et al.* in Iran on the effectiveness of repeated bilateral transcranial magnetic stimulation on cognitive function in patients with bipolar depression showed the improved executive function and verbal memory, while no change in selective attention and verbal fluency was observed [20]. In explaining this issue, we can point to the differences in the research community. The study focused on patients with bipolar depression, while the present study was performed on patients with major depression or unipolar depression. In bipolar patients, cognitive deficits increase as the disease progresses and lasts longer. Psychosocial function and psychological functions persist in many bipolar patients even after clinical symptoms have improved. However, patients with unipolar depression have fewer psychological and social problems. It is possible that by increasing the number of repetitive bilateral transcranial magnetic stimulation sessions in people with bipolar disorder, this method will be more effective, which requires more research.

rTMs is a safe and non-invasive method that affects the stimulated area by sending magnetic waves of cortical

activity and changes in glucose levels and neurotransmitter activity. rTMS devices can produce waves with a frequency of 1 to 100 Hz, which can have excitatory or inhibitory effects depending on the type of frequency. This method has a lasting effect on improving cognitive function due to the creation of a long-term potential mechanism, and strong synaptic activity leads to a strong continuous synaptic transmission. This is a powerful technique for enhancing the effects of other interventions, such as drug therapies, which are strongly associated with working memory processes. Another reason could be related to mood improvement (depression). Many cognitive problems in patients with mood disorders improve after a variety of therapeutic interventions. However, many experts believe that this treatment independently improves various aspects of cognitive function.

Other results of this study indicate the usefulness of theta burst stimulation on the improvement of cognitive functions of consonant reaction time, inconsistent reaction time, working memory, simple reaction time, and selective reaction time of depressed people with and without suicide history. The results of other similar studies on theta-burst stimulation on concordance and consonant reaction time and working memory confirm the findings of the present study [21-26].

However, contradictory findings were observed in Hill *et al.*'s study on the effectiveness of theta burst stimulation on cognitive function improvement [26]. This is probably due to the smaller number of intervention sessions (one intervention session) in the study. While in the present study, patients benefited from 12 intervention sessions.

Some findings suggest that even one session of theta-burst stimulated intervention causes long-term excitatory and inhibitory changes in cerebral cortex excitability. The duration of each stimulation in this method is very short and about 3 to 6 minutes. However, this short duration does not only reduce its effectiveness, but can also be even greater compared to the method of rTMS. The findings of the present study showed that the theta-burst stimulation method leads to further improvement of cognitive functions of consonant reaction time, simple reaction time and selective reaction time compared to rTMS method. But there was no difference between the two groups in the variables of inconsistent reaction time and working memory.

In general, both theta burst stimulation and rTMS are safe and non-invasive methods that have been confirmed in various studies. However, theta-burst stimulation method

is a shorter and more effective method for improving cognitive functions compared to rTMS. To date, no study has compared the effects of these two methods on improving cognitive function. However, two studies by Mendlowitz *et al.* and Bulteau *et al.* confirmed the effectiveness of these two methods in reducing depression [27]. Due to the lower cost and time required in the theta burst stimulation method, it seems to be more economical than the rTMS. Bulteau *et al.* showed that despite the effectiveness of both methods, theta burst stimulation had a faster effect compared to rTMS [28].

4.1. Limitations and Suggestions

The most important limitations of this study were the use of purposive sampling method and small sample size. Failure to follow the subjects to evaluate the continuity of the effectiveness of the results and compare the effectiveness of the results in the long run was another limitation of this study. Although the groups were identical in terms of demographic variables, some intervening variables, such as the desire and motivation of some participants, may have affected the test results. Failure to review the results by gender and age was another limitation of this study. Therefore, randomized studies with a larger sample size are recommended, taking into account the intervening variables.

5. Conclusion

In summary, both methods, rTMS and theta stimulation in both depressed groups with and without suicidal history, improved cognitive functions of consonant reaction time, inconsistent reaction time, simple reaction time, and selective reaction time and working memory. Compared with the rTMS method, the theta-burst stimulation method had a greater effect on the variables of consonant reaction time, simple reaction time and selective reaction time. But in terms of inconsistent reaction time and working memory variables, no difference was observed between the two methods.

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