Depression is a disease involving a wide range of brain network abnormalities. The Dorsolateral Prefrontal Cortex (DLPFC) is considered to be the most commonly used target for rTMS in the treatment of depression. The left DLPFC is involved in the generation of positive emotions. Adjustment, the right DLPFC participates in the generation and regulation of negative emotions [8]. In patients with depression, the left DLPFC function is abnormally weakened, and the right DLPFC function is abnormally enhanced. The patient's depression can be alleviated by regulating the DLPFC function [9] .Previous rTMS studies have shown that low-frequency (≤1 Hz) stimulation of right DLPFC is effective in the treatment of depression [10] .In this study, low-frequency rTMS stimulation of right DLPFC was used to treat adolescent depression patients with NSSI behaviour and intention. On the basis of the patient's unified medication, we added rTMS treatment and compared it with sham stimulation treatment to observe the efficacy and safety. At the same time, without medication and psychotherapy, the true and sham stimulation was used to treat another group of depressed adolescents. Contrastive treatment of non-suicidal self-injured adolescents is intended to provide a reference for the clinical treatment of adolescent depression patients with non-suicidal self-injury behaviour and intentions.

2. SUBJECTS AND METHODS

2.1 Participants: 55 Adolescents with depression disorder were selected as subjects in the second ward of the Department of Clinical Psychology of the Fourth People's Hospital of Chengdu from February to August 2019, as well as adolescents with depression were recruited in the outpatient clinic.

2.1.1Enrolment criteria: (1) International organizations have different definition criteria for adolescent age. This study intends to refer to UN standards (young age is defined as 15 to 24 years old) and the statistical standards of public security departments in China (adolescent age is defined as 13 to 25 years old). Patients aged 13 to 22 years old were selected, male or female; (2) met the diagnostic criteria for depression in the American Diagnostic and Statistical Manual of Mental Disorders (DSM-5); (3)24-iterm Hamilton Depression Scale (HAMD24):The total score is more than 17 points, which is assessed by two attending physicians; the Self-rating depression scale (SDS): standard score is 50 or more, and the Adolescent Non-suicidal Self-injury Assessment Questionnaire(ANSSIQ): NSSI behaviour and function scale is used to determine whether to enrol (the number of self-injury behaviours in one year is Not zero, and the number of self-injury behaviours in the first two weeks of enrolment is not zero); (4) no family history of mental illness; (5) informed consent of patients and guardians.

2.1.2Exclusion criteria: (1) compliance with any mental disorder other than depression in DSM-5; (2) with psychotic symptoms; (3) history of substance abuse; (4) severe physical illness and nervous system Disease; (5) history of seizures; (6) installation of pacemakers, prosthetic valves, metal implants in the body.

2.1.3Criteria to discontinue the study: (1) the subject suffered a serious adverse reaction; (2) violated the study protocol; (3) the subject requested termination of the study; (4) the subject developed psychotic symptoms during the study, or seizures (5) The subject has a serious suicidal behaviour during treatment or has to be transferred to a closed ward due to the condition.

The study was approved by the Ethics Committee of the Fourth People's Hospital of Chengdu. All patients signed informed consent and volunteered to participate in the study.

2.2 Research methods: A single-blind design using true and sham stimulation control, except for the research leader and the actual operation staff, the patient itself does not know whether he is receiving true or sham stimulation. (To ensure the patient's treatment effect, the sham stimulation group continued to receive two weeks of true stimulation therapy after two weeks, not included in the study data).

2.2.1Grouping method: a total of 57 eligible adolescents with depression were enrolled in this study. During the process, 2 patients did not complete treatment due to personal reasons, so the final total number of patients was 55.The average age of the patients was 16.75 years (n=55, SD=2.51, range=13-22), and they were all unmarried. As a matter of convenience, we first divided subjects into two groups: 35 patients in the medicated group and 20 patients in the none-medicated group. To note, the inpatients were treated with drugs. The uniform drug regimen from the two weeks after admission was: sertraline 50-200 mg/day, magnesium valproate 250-2000 mg/day, and continued medication for two weeks. Outpatients take a voluntary approach, do not take drugs, and also exclude psychotherapy (the psychological treatment of this hospital usually begins two weeks after the appointment).The two groups of patients were then randomly divided into the true stimulation group (ie the study group) and the sham stimulation group (ie the control group) by random number table method. The final grouping was: Medicated true stimulation group (study group) in 16 cases, male 2 cases, female 14 cases, average age 15.69 ± 1.74 years; Medicated sham stimulation group (control group)in 19 cases, male 3 cases, female 16 cases, the mean age was 16.53±2.63 years; 10 patients were in the None-medicated true stimulation group (study group), 2 males and 8 females, with an average age of 17.00±2.58 years;10 patients were in the None-medicated sham stimulation group (control

group), 2 males, 8 females, an average of 17.00 ± 2.71 years old.

2.2.2Treatment: A Transcranial magnetic stimulator with a figure-o coil (produced by Wuhan Iride Medical Equipment New Technology Co., Ltd.) was used for treatment. Stimulate parameters were as follows: in study group - low frequency rTMs of lHz stimulated the right DLPFC with 80% threshold, 10 pulses / string , string interval 10s, repeated 100 times, a total of 1000 pulses, about 16 minutes / time / day, 5 times a week, continuous treatment for 2 weeks; in control group - using sham stimulation (change the angle between the head plane and the coil , so that it is 45 degrees, so that the magnetic field generated by the magnetic head will not effectively penetrate into the skull, but the patient can still feel the rhythmic tapping[11]) ,and the treatment parameters, time and frequency are the same as the study group.

2.3. Research tools

2.3.1 Self-designed general demographic data questionnaire.

This questionnaire was made to collect population variables, which includes age, gender, ethnicity, education level, job nature, marital status, etc.

2.3.2 Hamilton Depression Rating Scales (HDRS) [12]

This is an objective him-rating scale. In this study we used a revised 24-item version (24-iterm Hamilton Depression Rating Scale), this scale includes 7 factors: anxiety / somatization, weight, cognitive disturbance, diurnal variation retardation, sleep disturbance, hopelessness. The higher the total score, the more severe the depression was.

2.3.3Self-rating depression scale (SDS) [12]:

A Chinese version of the Self-rating Depression Scale (SDS), which was revised according to Zung's Self-rating depression scale. The items include four factors: Psychic-affective disturbance, Physiological disturbance, Psychomoto disturbance and Psychological disturbance [13]. The patient can use this scale to assess his or her own emotional state in the past week. The higher the total score, the more serious the state of depression is.

2.3.4Adolescent Non-suicidal Self-injury Assessment Questionnaire (ANSSIQ) [14]:

A questionnaire compiled by Wan Yuhui et al [14]. This questionnaire was used to assess whether there was self-injury behaviours or intentions in adolescents with depression disorder. The questionnaire was divided into two parts, behavioural questionnaire part and the functional questionnaire part. The behavioural questionnaire has 12 items and two dimensions, and the functional questionnaire has 19 items and seven dimensions.

In order to reflect the comparative timeliness before and after treatment, we added the question of "Did you have the following behaviours in the last two weeks" based on the original question "Did you have the following behaviour within one year" to measure the frequency of self-injury behaviours in the past two weeks. To measure the frequency of self-injury thoughts within two weeks, we added two questions: "the number of self-injury impulses within two weeks", "the intensity of self-injury thoughts within two weeks".

This study looked at efficacy through three perspectives: objective assessment, subjective self-assessment, and behavioural facts.

2.4 Evaluation criteria

2.4.1Hamilton Depression Rating Scale (HDRS): Comparison of total scores and factor scores before and after treatment.

2.4.2 Self-rating depression Scale (SDS): Compare the total scores and factor scores before and after treatment.

2.4.3Adolescent Non-suicidal Self-injury Assessment Questionnaire (ANSSIQ): Assessments were made according to the degree of reduction of the frequency of non-suicidal self-injury behaviours within two weeks and the scores of self-injury impulses and self-injury thoughts.

2.5 Statistical processing

The data obtained in this study were analysed by SPSS 24.0 statistical software. The count data was taken for Chi-square test, and the measurement data was taken for t test. For the result, the mean value was expressed by ($x \pm s$), while differences was statistically significant when $p< 0.05$, $p< 0.01$, $p < 0.001$.

3. RESULTS

3.1 Comparison of demographic data

There were no significant differences in gender, age, ethnicity, job and education level between every study group and control group ($p>0.05$).

3.2 Comparative results in the data from HDRS scale before and after treatment in the study group and the control group (see Table 1）

Hamilton Depression Rating Scale (HDRS)in medicated group

	Study group		Control group									
item	before	after	before	after	t1	p1	t2	p2	t3	p3	t4	p4
total	25.75±6.84	11.94±5.13	29.89±9.52	19.47±7.02	10.971	0.000***	11.984	0.000***	-1.453	0.156	-3.564	0.001**
Anxiety/somatization /somatization somatization	4.81±3.45	2.19±2.01	6.32±3.86	2.74±2.60	3.543	0.003**	7.875	0.000***	-1.204	0.237	-0.689	0.496
weight	0.69±0.87	0.19±0.54	0.79±0.92	0.68±0.89	2.449	0.027*	0.809	0.429	-0.335	0.740	-1.953	0.059
Cognitive disturbance	4.25±2.46	1.25±0.93	5.26±3.59	3.26±2.62	5.403	0.000***	3.376	0.003**	-0.955	0.347	-2.915	0.006*
Diurnal variation	0.56±0.73	0.06±0.25	1.11±0.94	0.79±0.86	2.449	0.027*	1.837	0.083	-1.886	0.068	-3.278	0.002**
retardation	5.63±2.16	3.44±1.63	6.00±2.40	4.89±1.73	4.869	0.000***	2.840	0.011*	-0.482	0.633	-2.548	0.016*
Sleep disturbance	3.19±2.51	1.38±1.40	4.47±2.14	1.95±1.88	3.093	0.007**	6.985	0.000***	-1.636	0.111	-1.006	0.322
Hopelessness	6.25±2.11	3.31±1.74	6.32±2.14	5.11±1.29	7.929	0.000***	2.582	0.019*	-0.091	0.928	-3.499	0.001**

Hamilton Depression Rating Scale (HDRS)in non-medicated group

	Study group		Control group									
item	before	after	before	after	t1	p1	t2	p2	t3	p3	t4	p4
total	27.6 ± 8.74	13.90±4.20	28.00±9.30	20.80±5.80	8.059	0.000***	4.859	0.001**	-0.099	0.922	-3.044	0.007**
Anxiety/somatization	4.80±3.65	1.50±1.78	5.90±2.42	3.90±1.45	3.374	0.008**	2.410	0.039*	-0.795	0.437	-3.307	0.004**
weight	0.80±0.92	0.60±0.70	0.80±0.79	1.00±0.68	1.000	0.343	-0.802	0.443	0.000	1.000	-1.309	0.207
Cognitive disturbance	5.80±2.74	1.80±1.48	6.20±3.19	3.60±2.95	5.721	0.000***	2.940	0.016*	-0.301	0.767	-1.725	0.102
Diurnal variation	1.40±0.70	0.10±0.32	0.70±0.68	0.80±0.63	6.091	0.000***	-0.361	0.726	2.278	0.035*	-3.130	0.006**
retardation	6.50±1.43	4.10±0.99	4.90±2.08	5.10±1.37	7.060	0.000***	-0.318	0.758	2.003	0.060	-1.868	0.078
Sleep disturbance	2.70±1.41	1.50±1.08	3.20±0.23	2.20±1.81	2.714	0.024*	2.739	0.023*	-0.842	0.411	-1.049	0.308
Hopelessness	5.90±2.33	4.30±1.06	5.00±2.68	5.60±2.22	2.228	0.053	-0.896	0.394	0.804	0.432	-1.671	0.112

Table 1:t1 was compared before and after of the study group, t2 was compared before and after of the control group, t3 was compared the score before treatment in two groups, and t4 was compared the score after treatment in two groups. * indicates p < 0.05, ** indicates p < 0.01, and *** indicates p < 0.001. And the same below.

From objective assessment perspective, after 2 weeks of treatment, the patients in the medicated study group had significantly improvement in the aspects of cognitive disturbance, retardation, sleep disturbance, and hopelessness. The medicated control group had significant improvement in the aspects of anxiety/somatization, cognitive disturbance, retardation, and sleep disturbance.

Which can be seen from table1, there were no significant differences in two groups before treatment (t=-1.204, -0.335, -0.955, -1.886, -0.482, -1.636, -0.091, p>0.05). However, after treatment, a significant difference can be seen in cognitive disturbance (t=-2.915, p <0.01), diurnal variation (t=-3.278, p<0.01), retardation (t=-2.548, p<0.05), and hopelessness (t=-3.499, p<0.01). Data analyses showed that the study group was better than the control group.

The none-medicated study group showed significant improvement in the aspects of anxiety/somatization, cognitive disturbance, diurnal variation, sleep disturbance, and retardation. The none-medicated control group also can see improvements in the aspects of anxiety/somatization, cognitive disturbance, and sleep disturbance. There was no significant difference between the two groups before treatment (t= -0.099, p>0.05), and there was a significant difference between the two groups in anxiety/somatization (t=-3.307, p<0.01) and diurnal variation (t=-3.130, p<0.01) after treatment. The study group was better than the control group.

3.3 Changes in SDS scale scores before and after treatment in the study group and the control group (see table 2)

Self-rating depression scale(SDS)in medicated group

	Study group		Control group									
item	before	after	before	after	t1	p1	t2	p2	t3	p3	t4	p4
Standard score	69.61±7.91	52.11±6.77	77.43±11.01	65.75±13.12	10.306	0.000***	9.211	0.000***	-2.01	0.053	-3.755	0.001**
Psychic-affective disturbance	8.98±1.04	4.30±0.91	9.14±0.99	6.05±1.46	12.938	0.000***	1.941	0.000***	-0.434	0.667	-4.174	0.000***
Physiological disturbance	26.33±4.41	18.52±3.98	24.66±4.76	23.49±4.83	7.792	0.000***	1.54	0.002**	-0.818	0.42	-3.279	0.002**
Psychomotor disturbance	6.17±1.33	5.16±1.20	7.19±2.17	6.84±1.79	2.000	0.054	-0.756	0.534	-1.599	0.12	-3.214	0.003**
Psychological disturbance	28.67±5.33	23.28±4.08	33.13±6.55	29.54±7.34	7.442	0.000***	5.094	0.005**	-1.553	0.131	-3.035	0.005**

Self-rating depression scale(SDS)in non-medicated group

	Study group		Control group									
item	before	after	before	after	t1	p1	t2	p2	t3	p3	t4	p4
Standard score	71.63±12.20	54.75±9.50	69.88±11.05	62.00±10.39	7.383	0.000***	2.167	0.000***	0.336	0.74	-3.737	0.002**
Psychic-affective disturbance	7.93±1.86	5.13±1.71	10.42±10.35	5.88±2.20	5.193	0.001**	1.309	0.088	-0.751	0.463	-2.312	0.033*
Physiological disturbance	24.65±9.35	20.25±4.99	36.94±5.27	24.38±5.90	2.042	0.072	1.000	0.162	-0.648	0.525	-2.709	0.014*
Psychomotor disturbance	8.73±6.24	5.38±1.56	6.11±1.32	6.25±1.44	2.253	0.051	1.964	0.471	1.228	0.236	-2.159	0.045*
Psychological disturbance	30.25±4.63	23.62±3.50	31.67±2.58	26.00±3.72	6.943	0.000***	5.094	0.001**	-0.81	0.429	-3.009	0.008**

Table 2

From the perspective of self-evaluation, the medicated study group had significant improvement in Psychic-affective disturbance, and Psychological disturbance after treatment (t=12.938, 7.792, 7.442 p<0.001). There were also improvements in Psychic-affective disturbance, Physiological disturbance, and Psychological disturbance (t=1.941, 1.540, p<0.001, t=5.094, p<0.01) in the medicated control group. There was no significant difference between the two groups before treatment (t=-0.434, -0.818, -1.599, -1.553, p>0.05), and the difference was significant after treatment (t=-4.174, -3.279, -3.214, -3.035, p<0.01). The study group was significantly better than the control group. The self-rating scores of the none-medicated study group and the control group all decreased significantly. The study group had significant differences in the scores of Psychic-affective disturbance, and Psychological disturbance (t=5.193, 6.943, p<0.01). There was a significant difference in the score of the Psychological disturbance (t=5.094, p<0.01) in the control group. There was no significant difference between the two groups were significantly different (Psychic-affective disturbance t=-2.312, p<0.05, Physiological disturbance t=-2.709, p<0.05, Psychomotor disturbance t=-2.159, p<0.05, Psychological disturbance t =-3.009, p<0.01), the study group was significantly better than the control group.

3.4 Changes in Adolescent Non-suicidal Self-injury Assessment Questionnaire (ANSSIQ) scores before and after treatment in the study group and the control group. (see table 3)

Adolescent Non-suicidal Self-injury Assessment Questionnaire (ANSSIQ)-in medicated group

	Study group		Control group									
item	before	after	before	after	t1	p1	t2	p2	t3	p3	t4	p4
Behaviors in 2weeks	11.38±12.45	3.31±6.95	15.11±14.92	5.05±7.95	2.317	0.035*	3.716	0.002**	-0.787	0.437	-1.675	0.105
Impulses in 2weeks	4.75±2.72	1.06±0.25	4.67±2.95	2.95±3.15	2.654	0.018*	2.383	0.029*	0.085	0.933	-0.078	0.939
Thought intensity	6.19±2.26	3.25±2.57	7.56±2.06	3.39±2.97	3.918	0.001**	5.141	0.000***	-1.846	0.074	-0.145	0.886

Adolescent Non-suicidal Self-injury Assessment Questionnaire (ANSSIQ)-in non-medicated group

	Study group		Control group									
item	before	after	before	after	t1	p1	t2	p2	t3	p3	t4	p4
Behaviors in 2weeks	6.70±6.11	1.70±2.36	6.80±4.96	4.80±6.94	3.527	0.006**	1.085	0.306	-0.040	0.968	-1.337	0.198
Impulses in 2weeks	3.90±1.97	2.00±2.10	4.90±3.14	4.60±2.37	6.862	0.000***	0.258	0.803	-0.853	0.405	-2.594	0.018*
Thought intensity	5.10±1.73	1.70±1.70	6.30±1.89	4.10±2.89	7.520	0.000***	2.080	0.067	-1.482	0.156	-2.266	0.036*

Table 3

In medicated group, compared with non-suicidal self-injury behaviours and intentions, the number of behaviours, self-injury impulses, and thought intensity of the study group and the control group decreased significantly after treatment. In the study group: number of behaviours ($t=2.317$, $p<0.05$), number of impulses ($t=2.654$, $p<0.05$), thought intensity ($t=3.918$, $p< 0.01$). In the control group: the number of behaviours ($t=3.716$, $p<0.01$), the number of impulses ($t=2.383$, $p<0.05$), the intensity of thought ($t=5.141$, $p<0.01$).There was no significant difference between the two groups before treatment ($t=-0.787, 0.085, -1.846$, $p>0.05$), and there was no significant difference after treatment ($t=-1.675, -0.078, -0.145$, $p>0.05$). The number of behaviours, the number of impulses, and the intensity of thoughts after treatment in the none-medicated study group were significantly decreased ($t=3.527, 6.862, 7.520$, $p<0.01$).There was no significant difference between the none-medicated control group before and after treatment ($t=-1.085, 0.258, -2.080$, $p>0.05$).There was no significant difference between the two groups before treatment ($t=-0.040, -0.853, -1.448$, $p>0.05$).There was no significant difference in the number of self-injury behaviours between the two groups ($t=-1.337$, $p>0.05$). The number of self-injury impulses and self-injury thoughts were significantly different. The study group was significantly lower than the control group ($t=-2.594$, $p<0.05$, $t=-2.266$, $p<0.05$).

4. DISCUSSION

4.1 Gender differences

Within the participant, a large disparity on gender ratio can be seeing in this study. Among the 55 adolescent participants, 46 were female and 9 were male. Studies have shown [4, 15] that the incidence of non-suicidal self-injury happens more in female adolescent than male. It might because women are more susceptible to external influences, more lack of self-confidence, more intents to have a high emotional response. So female participants were appeared to be more relied on NSSI to alleviate their negative emotions [16].

4.2 Conclusion

Overall, repeated transcranial magnetic stimulation can significantly reduce the clinical depression symptoms of adolescent patients, and rTMS also have a certain inhibitory effect on adolescent reducing non-suicidal self-injury behaviour and self-injury intention.

The result shows that rTMS treatment effect of the study groups was better than that of the control groups as a treatment of depression disorder, regardless of medicated or not. It also shows that rTMS treatment can help adolescents with depression disorder to relieve symptoms within two weeks, clinical symptoms were relived in the aspects of sleep disturbance, cognitive disturbance, anxiety / somatization, retardation and hopelessness. It indicates that rTMS treatment can make up for the lag of anti-depressant drugs (most anti-depressant drugs have an onset cycle of about 2-4 weeks).It can also improve early efficacy in anti-depressant treatment.

The effect of adding rTMS treatment into conventional regimens is superior to the drug-only regimens, this result is the same as the study of Huang ML [7] et al. In the aspect of treating non-suicidal self-injury behaviours and intentions, there was no significant difference in the treatment effect between the medicated study group and the medicated control group. It may be because of all the patients in medicated groups were hospitalized. And in the hospital environment with regular and accompanying status, the implementation conditions of self-injury behaviours are limited, and the comfort effect brought by the companion makes the self-injury intentions suppressed. In both of the non-medicated groups, the self-injury behaviours and intentions were significantly decreased after rTMS treatment, indicating that rTMS treatment increased the patient's treatment compliance, and the participation in the treatment itself brought a comforting effect. After treatment, the self-injury impulse and self-injury thought intensity of the study group were significantly lower than that of the control group, indicating that rTMS treatment reduced the intensity of self-injury impulse and self-injury.

Regarding the relationship between treating depression disorder and reducing self-injury behaviour, some scholars [17] have proposed an experience avoidance model, that is, patient intents to escape or avoid negative emotions through NSSI behaviour. That means, serious negative emotions precedes self-injury behaviours, and negative self-injury behaviours occurs to alleviated the negative emotions, making patients dependent on NSSI behaviours, which may be one of the drivers of depression-induced NSSI behaviour. Lloyd-Richardson et al [18] also believe that causing other people's attention, controlling life and stopping bad emotions are common factors in self-injury behaviour in NSSI patients. In the case of persistent depression in depression disordered patients, these motives may also be one of the mechanisms caused by depression-induced NSSI behaviour. Therefore, the treatment of rTMS can alleviate the depressive symptoms of adolescent patients, so that negative emotions can be alleviated, thereby reducing the incidence of self-injury and intention.

4.3 Insufficient study

This study is a small sample clinical study, using rTMS physical therapy combined with unified drugs and rTMS physical therapy alone, data collected by comparing the study groups and control groups before and after treatment.

In addition to the evaluation tools for depression like SDS and HDRS, the “self-injury number and intention evaluation within two weeks questionnaire” based on the Adolescent Non-suicidal Self-injury Assessment Questionnaire (ANSSIQ) were used. It is an interviewing tool for understanding facts. For the record, we didn’t run enough test on reliability and validity for whether it can truly measure the self-injury intention. A reliability and validity test for further testing tools of the self-injury intention is pending.

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