rTMS and Suicidality in Adulthood; An Exploratory Open-Labeled Neuromodulative Approach to Battle Suicide

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Abstract

Background: Suicidal attempts are one of the most critical issues with a huge burden on family and health systems all around the world. To decrease the hazardous outcomes of this issue, mental health systems are trying to apply the most effective and safe interventions. In this regard, repetitive Transcranial Magnetic Stimulation (rTMS) as a non-invasive approach could be a proper treatment approach. We investigated the impact of rTMS method on the treatment of the patients with suicidal ideation. For this purpose, the application of rTMS when integrating with Low-Resolution Electromagnetic Tomography (LORETA) data has been assessed.

Methods: As an open-labeled study we enrolled 7 adult men who were recently rescued from suicidal attempts and referred to our psychiatric clinic for three consecutive months (2018). The severity of suicidal ideation was measured by the Beck Scale of Suicidal Ideation (SSI) and brain activity via Low-Resolution Electromagnetic Tomography (LORETA), administered at baseline and the end of the treatment course. Repetitive TMS was delivered to the left and right dorsolateral prefrontal cortices (DLPFC) with a figure-eight solid core coil at 110% motor threshold, 10 Hertz (Hz) and 4 second (s) train duration, (3000 pulses) (total 12 sessions; 36,000 stimuli). Six sessions daily and six sessions within two weeks were scheduled.

Results: According to the results of psychiatric re-interview, LORETA, and SSI scores of all patients revealed an impressive and statistically significant decrease in suicidal ideation. No side effects were seen during the treatment course.

Conclusions: Scheduled three consecutive weeks rTMS course was significantly effective in remitting acute suicidal ideation in adult men regardless of psychiatric diagnosis. Larger double-blinded studies must be conducted to validate the clinical usage of this safe and non-invasive treatment approach in the area of psychiatry.

1. Background

Suicide is a major public health problem that can occur due to several mental, demographic, social, and cultural factors. According to the World Health Organization (WHO), approximately 800000 people die due to suicide each year. Suicide does not just occur in high-income countries, but is a global phenomenon and occurs throughout the lifespan, and is the second leading cause of death among 15-29-years-old globally [1].

It has been estimated by WHO, that around 1.53 million people will die from suicide worldwide in 2020. This represents on average one death every 20 seconds and one attempt every 1–2 seconds [2].

According to the most recent available data originating from the Iranian Legal Medicine Organization (ILMO), nationwide rates of suicide were 5.7 per 100,000 for males and 3.1 for females [3].

Suicidal thoughts and acts are not merely behaviors, but can also be symptoms of a depressive episode and a diagnostic criterion in the diagnosis of Borderline Personality Disorder (BPD), according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5).

Notably, suicidal behavior and ideation has been implicated as a comorbidity of several neuropsychiatric disorders including BPD, schizophrenia (SCZ), bipolar disorder (BD), and major depressive disorder (MDD), and is one of the leading causes of preventable death among people with these disorders [4].

It should be noted that many of the attempters (45.3%) reported at least one psychiatric disorder during their lifetime [5]. Major depressive disorder (22.0%), panic disorder (6.3%), and obsessive-compulsive disorder (6.0%) were the most common psychiatric diagnoses.

In the current study, we aim to propose a novel treatment approach to reduce the probability of re-committing suicide in different etiologies of that.

The most common emergency treatment for people who come with recognizes of suicidal attempts and ideation is Electroconvulsive Therapy (ECT) [6–8].

Although medication therapy is the most recommended treating method in subjects with suicidal attempts and ideation, ECT represents adequate evidence for treatment according to published data[7, 9, 10].

There are some disadvantages related to the application of ECT in the treatment process. The

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most problematic issues are the acceptability of ECT related to repeated general anesthesia, application of an electric charge through the brain, induction of a seizure, and cognitive impairment side effects [11].

Headache, disorientation, and memory complaints are the most common subjective side-effects. Both subjective complaints [12, 13] and objective measures of cognitive impairment can worsen during treatment.

Although, there has been evidence demonstrating the ECT as a first-line treatment for people who have suicidal attempts and ideation [14], according to the mentioned problems still adverse cognitive side-effects of ECT need to be considered.

To diminish these challenges, a new method entitled repetitive Transcranial Magnetic Stimulation (rTMS) could be recommended as an alternative neuromodulation approach for subjects who have suicidal ideation and attempt, recently [15].

In particular, it has been suggested to carry out rTMS in those patients who are unable to have treatment with ECT. This method has been approved by the FDA in 2008 [16, 17, 18].

The application of rTMS in the area of psychiatry has several advantages such as it is nonconvulsive, requires no anesthesia, hasn't a notably side effects profile, and may even improve cognitive performance [19]. Due to its highly positive impacts, it is being increasingly investigated as a potential treatment approach for distinct neuropsychiatric disorders [20], and several recent meta-analyses have confirmed its overall efficacy and safety for treating MDD [21–23].

This method has been used to treat some neurodegenerative disorders in recent years such as Parkinson's disease (PD) and Alzheimer (AD) [24–26]. In addition to the mentioned disorders, researchers try to treat Migraine [27, 28]; Obsessive–compulsive disorder (OCD) [29, 30], and Anxiety [31, 32] with this kind of new neuromodulation methods during the past two decades.

Due to its minimal side effects and relatively less burden on patients, their families, and the mental health system, rTMS has been considered a potentially attractive therapeutic intervention in the method for psychiatric disorders [33, 34].

This new method as an alternative to ECT can be suggested as a first-line treatment and management tool in a critical situation for individuals who have suicidal attempts and ideation.

In the current study, we aim to report an open-labeled study of using rTMS with a combination of LORETA in adult males who had recently attempted suicide with prominent ideation.

2. Methods

2.1. Participants

In this study, seven adult men patients were included with an average age of 34 years old. They accidentally were referred to the clinic meanwhile of three months period, according to their history, clinical assessment, and diagnosis of a psychiatrist they were selected to enter this project. All the patients had recently survived suicidal attempts and recruited after fully recovered and discharged from emergency wards of general hospitals. At first, all of them were visited by a psychiatrist and diagnostic interview also general physical exams were done. According to the previous medical history and recently performed laboratory testes, all the patients hadn't any medical disease and general medical condition was stable. All the patients were imaged by LORETA scanning via 19 channel EEG device.

The chief complaint about these seven patients was recent suicidal attempt or ideation. All the patients and families have been informed and cautioned for the next three weeks of treatment and intensively were followed by an expert psychologist. A low-dose of Risperidone was prescribed at night for all the patients.

2.2. rTMS treatment protocol

HF-rTMS following the updated safety guidelines was prepared [35], also high-risk written informed consent was obtained from participants as a routine part of treatment in a clinical setting.

Magstim Rapid 2 device [36] with a 70-mm figure-of-eight air-film coil was used to carry out rTMS. The stimulation parameters were optimized on 10-Hz frequency, stimulation intensity at 110% of MT, 4-seconds train duration. The same stimulation protocol over the Rt, Lt-DLPFC, and Lt-OFC was guided by LORETA images, especially at theta and alpha frequencies. In the first session, before starting rTMS treatment, MT was measured and considered as a criterion for determining the power delivered over targeted cortices for each of the patients.

Each session of rTMS consisted of 3,000 pulses delivered, a total of 36000 pulses in 12 sessions during three weeks. A total of 12 sessions of rTMS, six-session of daily stimulation, and six sessions over two weeks were scheduled. The FDA clearance for the Neurotics machine approves 3000 stimuli per day over a course of 4 up to 6 weeks. [37–39]

2.3. Clinical assessment

All patients have referred to the clinical setting accidentally, then the psychiatrist interviewed the patients based on DSM-5. In the following step, all of them were evaluated by LORETA, then analyzed by a psychiatrist. Patients showed deviations from normal brain activity as evidenced by LORETA [40].

Patient-specific protocol based on his LORETA analysis was prescribed. They were assessed by a Scale for Suicide Ideation (SSI). The correlations between the self-reported and clinically rated versions for both inpatients and outpatients were > 0.90, which suggested strong concurrent validity.

The result showed that the Cronbach's alpha coefficients of the screening part and the whole scale were satisfactory (> 0.8) [41–42].

It is important to note that the patients were evaluated by standard psychiatric interview, LORETA, and SSI before and after the treatment.

2.4. Data analysis

All statistical tests were performed as two-way models. Alpha < 0.05 was considered as significant level. The normal distribution of the data was evaluated using the Kolmogorov-Smirnov test. Because the data did not follow a normal distribution, a non-parametric test; Wilcoxon two dependent tests, was performed to compare LORETA values before and after rTMS courses.

3. Results

All patients according to their clinical interview, LORETA, and SSI scores showed positive changes. The post-test scores of SSI had decreased significantly in comparison with the pre-test. The result of their LORETA demonstrated impressive recovery in brain signals and cortical function. Tables 1–3 illustrate the results of brain activity in four brain locations; results of SSI scores and demographic information.

Also, Fig. 1 contains images of brain function in Brodmann 9 (L DLPFC), before and after rTMS treatment course.

The demographic and clinical characteristics of the 7 adult men in the current study were presented in Table 1. Mean SSI scores were 24.57 ± 7.27 at baseline (before rTMS treatment course) and then 9.57 ± 2.43 at the end of the treatment course with P value = 0.018.

Table 1
Demographic information

Variables		**Values**	
Age mean (SD)		34.43	7.63
Education N (%)	Diploma	3	42.9
	Bachelor of sciences	2	28.6
	Master	1	14.3
	Doctoral	1	14.3
No of attempt to suicide N (%)	Once	3	42.9
	Twice	3	42.9
	Third or more times	1	14.3

Tables 2 and 3 include the information of brain activities in theta (4–8 Hz) and alpha (8–12 Hz) frequency bands, respectively in these areas: Hippocampus (location 1), Dorsolateral Prefrontal Cortex) DLPFC((location 2), Orbitofrontal cortex (OFC) (location 3), and Inferior Prefrontal Cortex (location 4), in the Right and Left hemisphere (the areas that located in the frontal and prefrontal lobe).

Table 2
Results of LORETA values before and after the application of rTMS (activity of theta band)*

Location		Before rTMS	After rTMS	Mean difference (SD)	P value**
		Mean (SD)	Mean (SD)		
Location 1	Right	-0.800 (0.290)	-0.344 (0.380)	-0.452 (0.270)	0.018
	Left	-0.802 (0.465)	-0.210 (0.480)	-0.592 (0.310)	0.018
Location 2	Right	-0.800 (0.460)	-0.311 (0.305)	-0.480 (0.360)	0.018
	Left	-1.040 (0.600)	-0.270 (0.395)	-0.771 (0.454)	0.018
Location 3	Right	-0.844 (0.360)	-0.164 (0.370)	-0.680 (0.554)	0.018
	Left	-0.990 (0.560)	-0.105 (0.560)	-0.880 (0.629)	0.018
Location 4	Right	-0.791 (0.390)	-0.304 (0.217)	-0.490 (0.492)	0.028
	Left	-1.020 (0.566)	-0.184 (0.266)	-0.835 (0.502)	0.018

***Theta frequency bands on 6Hz

****Dependent non-parametric test

-location 1: Hippocampus, location 2: DLPFC, location 3: OFC, location 4: Inferior, Prefrontal Cortex

-Number of participants: 7

Table 3
Results of LORETA values before and after application of rTMS (activity of alpha band)*

Location		Before rTMS	After rTMS	Mean difference (SD)	P value**
		Mean (SD)	Mean (SD)		
Location 1	Right	-1.107 (0.526)	-0.219 (0.503)	0.889 (0.755)	0.018
	Left	-1.110 (0.520)	-0.127 (0.610)	0.983 (0.786)	0.018
Location 2	Right	-1.115 (0.431)	-0.157 (0.832)	0.959 (0.995)	0.018
	Left	-1.367 (0.527)	-0.408 (0.702)	0.959 (0.849)	0.018
Location 3	Right	-1.094 (0.309)	-0.137 (0.706)	0.957 (0.872)	0.018
	Left	-1.415 (0.612)	-1.728 (0.267)	0.687 (0.593)	0.018
Location 4	Right	-1.052 (0.352)	-0.565 (0.417)	0.487 (0.380)	0.018
	Left	-1.417 (0.557)	-0.567 (0.309)	0.850 (0.644)	0.028
SSI		24.57 (7.27)	9.57 (2.43)	15.00 (5.508)	0.018

***Alpha frequency bands on 9Hz

****Dependent non-parametric test

-location 1: Hippocampus, location 2: DLPFC, location 3: OFC, location 4: Inferior, Prefrontal Cortex

-Number of participants: 7

The results have been provided in two conditions before and after the rTMS treatment course. Finally, results demonstrated that the changes in brain activities are positive and statistically significant. As shown in Tables 2 and 3, LORETA values post-rTMS were significantly changed in all locations.

4. Discussion

The current research study was conducted to assess the effect of high-frequency TMS course in adolescents with Suicide ideation and attempt. Treatment with TMS was safe and feasible in these samples. Findings suggest that suicidal ideation improved throughout TMS treatment with 12 sessions.

The brain activity that has been measured via LORETA, showed a deviation from normal activity; so it positively changed after a treatment course with rTMS.

Also, the patients and their families reported that they returned to their daily routine and work. The SSI had decreased significantly in comparison. The result of their LORETA values demonstrated impressive recovery in brain signals and cortical function as shown in the tables above.

These findings underscore the well-supported relationship between the clinical effectiveness and cost of repetitive transcranial magnetic stimulation versus electroconvulsive therapy [16].

Our results are consistent with those of similar studies with the same features. In this research, ECT is considered a risky treatment and rTMS could be replaced by this kind of risky treatment that sometimes leads to a seizure. Additionally, the use of ECT is often limited by other issues such as the need for anesthesia, while rTMS is noninvasive and no side effects have been reported [43, 44]. We observed a confirmation in other researches that demonstrated the cost-effectiveness of repetitive transcranial magnetic stimulation [45]. Also, we observed a strong association between our results and other researches in improving suicidal ideation throughout TMS treatment [46, 47].

According to the obtained results, applying rTMS could be a suitable alternative treatment approach for those people who are in a critical situation and struggle with suicidal ideation.

One of the most important points of the present study is related to the limited number of rTMS sessions in comparison with other studies focusing on brain stimulation. Also, the lack of drug interactions could be another positive aspect of our study.

It is worth mentioning that the sample size of this study is small and to accurately validate the proposed method the results have to be confirmed in a larger study. Also, we recommend carrying out the same research in other future studies consisting of samples from both women and men gender should be considered two gender men and women and compare them.

5. Conclusions

The current study indicates that rTMS has a significant effect on subjects who had suicidal ideation and attempt recently. Outcomes were positive change in the severity of suicidal thinking as measured by the Beck Scale of Suicidal Ideation (SSI) administered at baseline and then at the end of the last rTMS session, as well as LORETA measures before and after the TMS treatment course. Finally, it suggested that a clinical trial will be carry out for detecting the effect of TMS for patients who are in a critical situation such as suicidal ideation and attempt recently.

Abbreviations

repetitive Transcranial Magnetic Stimulation (rTMS)

Low-Resolution Electromagnetic Tomography (LORETA)

Scale of Suicidal Ideation (SSI)

DorsoLateral Prefrontal Cortices (DLPFC)

World Health Organization (WHO)

Borderline Personality Disorder (BPD)

Diagnostic and Statistical Manual of Mental Disorders (DSM-5)

Schizophrenia (SCZ)

Bipolar Disorder (BD)

Major Depressive Disorder (MDD)

Electroconvulsive Therapy (ECT)

Parkinson's Disease (PD)

Alzheimer's Disease (AD)

Obsessive–Compulsive Disorder (OCD)

Orbitofrontal Cortex (OFC)

Declarations

Ethics approval and consent to participate and publish

All the subjects gave their verbal consent to participate in the current project because the research presents no risk of harm to the subjects and involves no procedures for which written consent is normally required outside of the research context. The mentioned reasons satisfy IRB requirements to provide study participants with a verbal consent.

Human subjects

All procedures performed in the current study involving human participants were in accordance with the ethical standards of the Tehran University of Medical Sciences.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Competing interests

The authors declare that they have no financial and non-financial competing interests.

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Authors' contributions

SMA designed and supervised the project. SMA, FS, and MYM carried out the clinical part of the project. FS and FP contributed to the analysis results and wrote the manuscript. All authors read and approved the final manuscript.

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Figures

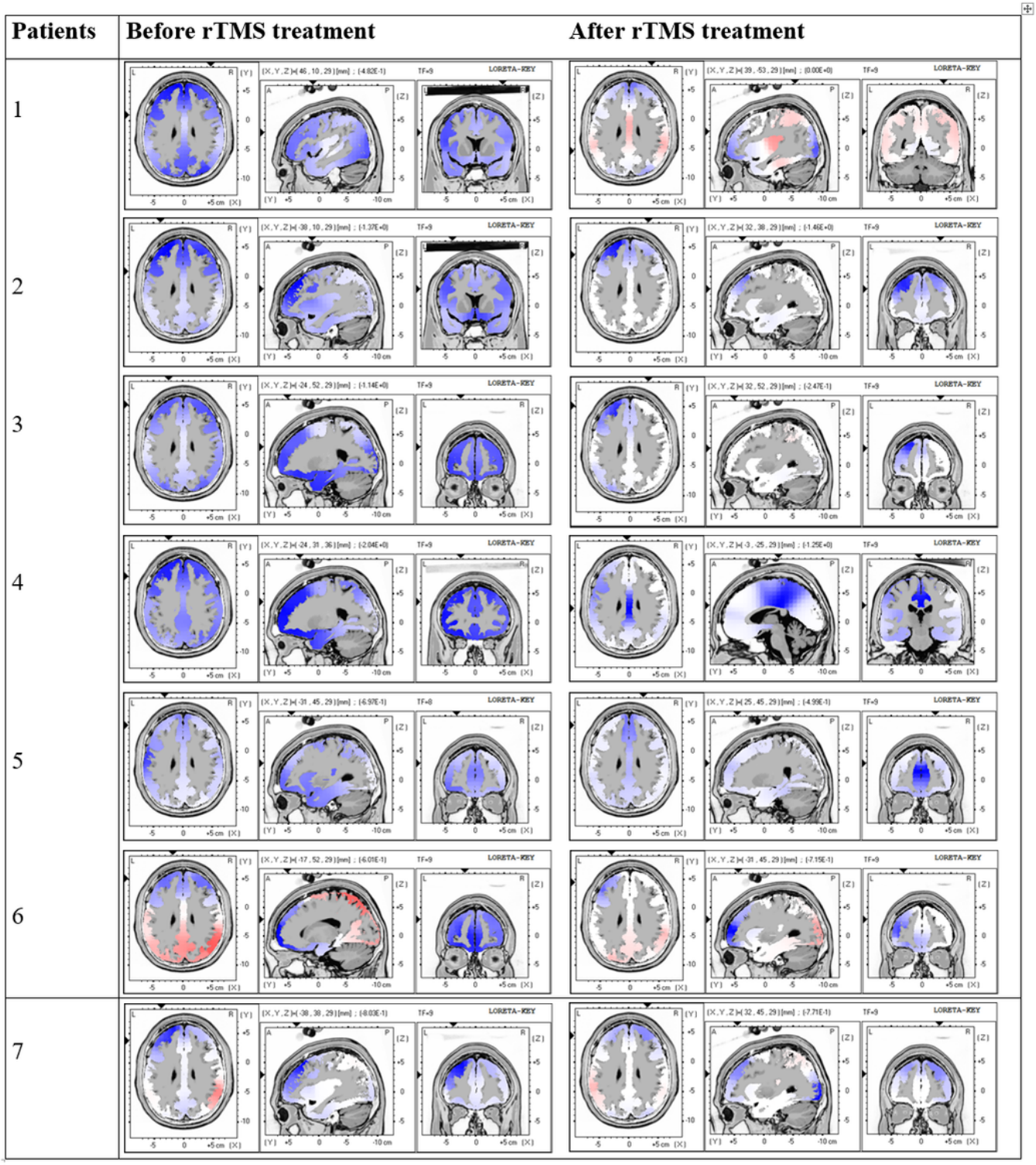

Figure 1

LORETA images in left DLPFC, before and after rTMS treatment course (alpha band 9Hz)