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Research Paper

The effect of bilateral high frequency repetitive transcranial magnetic stimulation on cognitive functions in schizophrenia

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1. Introduction

Schizophrenia is a chronic psychiatric disease that disturbs perception of reality and one's interpersonal relationships, and it has a prevalence of 1% in the population. Cognitive decline by progression of the disease is one of the strongest predictors of functional abilities (Barr et al., 2013; Heaton and Pendleton, 1981; Kraus and Keefe, 2007). Low prefrontal activity is evident in schizophrenia by neuroimaging studies (Shenton et al., 2010). Attention, working memory and executive functions which are among important cognitive functions of prefrontal cortex have been firmly reported as impaired in schizophrenia (Gopal and Variend, 2005; Joyce et al., 2002; Mohamed et al., 1999).

Attention is a set of functions that provides recognition of the stimulus (detection), selectively focusing on the stimulus (selective attention), pursuing of attention on the stimulus (sustained attention) and transferring of the stimulus for more advanced processes, and is critically important in information processing (Soysal et al., 2008). Working memory which can be defined as the ability to store and manipulate information online, is a process that underlies several dimensions of cognitive functions such as language comprehension, learning and reasoning (Barr et al., 2013; Sigaudo et al., 2014). Executive functions refer to a set of cognitive processes including attentional control, inhibitory control, working memory, and cognitive flexibility, as well as reasoning, problem solving, and planning that are necessary for the cognitive control of behavior.

The dorsolateral prefrontal cortex (DLPFC) is an important brain area mostly involved in attention, working memory and executive functions. Decreased DLPFC activity is thought to result in deterioration of these functions (Brown et al., 1999; Sandson and Albert, 1987). Hence, in this study, we used Wisconsin Card Sorting Test (WCST), Digit Span Task (DST) and Stroop Test (ST) to assess DLPFC activity (Drewe, 1974; Mansouri et al., 2009).

Wisconsin Card Sorting Test is used as a tool to measure executive functions (Heaton et al., 1993). It requires strategic planning, organized searching, utilizing environmental feedback to shift cognitive sets, directing behavior towards achieving a goal and modulating impulsive responding. The Stroop Test assesses the ability to inhibit cognitive interference, occurring when the processing of a stimulus feature affects the simultaneous processing of another attribute of the same stimulus (Stroop, 1935). It is also reported that ST can measure some other cognitive functions such as attention, processing speed, and working memory (Leung, 2000; Stroop, 1935). Digit Span Task is a task consisting of two main conditions; forward and backward. It mainly measures attention, short term memory and verbal working memory (Conklin et al., 2000; Lezak, 1995; Reynolds and Powel, 1988).

Although it is evident that antipsychotic drugs are effective on positive symptoms, they do not have a major effect on cognition, in schizophrenia. Therefore, new treatment modalities are needed to be searched for cognitive loss in schizophrenia (Davidson et al., 2009; G. et al., 2009; Harvey and Keefe, 2001; Keefe et al., 2003). Repetitive transcranial magnetic stimulation (rTMS), hence, may be a new line treatment modality for such a goal (Barr et al., 2013; Voineskos and Daskalakis, 2013). rTMS delivers whether low or high frequency trains of magnetic stimuli to the cortical region of interest to induce changes in the function of that area. As it has a central role in attention, working memory and executive functions, DLPFC, has been a target for rTMS practices. In a neuroimaging study with perfusion SPECT on healthy people, 20 Hz rTMS targeted the left DLPFC region has been resulted in increased blood flow in dorsolateral prefrontal, anterior cingulate and orbitofrontal cortices (George et al., 1999). With high frequency rTMS on DLPFC, although, some studies reported an improvement in selective attention (Martis et al., 2003; Rektorova et al., 2005), some found no difference of cognitive functions (Boggio et al., 2005; Huang et al., 2004; Zhuo et al., 2019). In another study, Barr et al. have shown a significant improvement in working memory by applying bilateral 20 Hz rTMS on DLPFC sequentially (Barr et al., 2013). Thus, rTMS

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targeting on DLPFC may be expected to display a positive effect on cognitive functions in schizophrenia.

The main objective of this 4-week randomized double-blind sham-controlled study is to investigate the effect of bilateral 20 Hz rTMS on attention, working memory and executive functions in schizophrenia patients.

2. Materials and methods

The research protocol was approved by Şişli Hamidiye Etfal Training and Research Hospital Ethic Board in accordance with the Declaration of Helsinki. The approval of the study was granted by the Institutional Ethics Committee (Şişli Hamidiye Etfal Training and Research Hospital, decision no: 558/2013).

2.1. Subjects

In this study, subjects with schizophrenia were recruited from Şişli Hamidiye Etfal Training and Research Hospital (İstanbul, Turkey) for six months (between January and July 2014). Age, sex and education-matched right-handed healthy subjects were randomly recruited by face to face interview from Şişli area that the hospital locates. They were screened with Symptom Check List-90-Revised (SCL-90-R) questionnaire, and subjects having a Global Severity Index (GSI) score of < 1.0 were included (Li et al., 2018). Right-handed subjects with schizophrenia between 18 and 65 years old were recorded. In order to exclude a probable comorbid cognitive disorder, the patients performed the Turkish version of Standardized Mini Mental Test (SMMT), and those having a score of 24 or more from SMMT have been included in the study (Güngen et al., 2002). To exclude depression, which is another psychiatric disorder that may disrupt cognitive functions, the patients who has the Calgary Depression Scale for Schizophrenia (CDS) score of 11 or less have been included (Addington et al., 1992). Also, because antipsychotics may cause some extrapyramidal side effects resulting in deceleration of cognitive functions and motor velocity, and because that might affect patients' test performance, those who have a score of 2 (which means that the patient has a mild side effect) or lesser for each item of Extrapyramidal Symptoms Rating Scale (ESRS) were included. Subjects with schizophrenia were excluded if they have any comorbid psychiatric disorder according to Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I), any major neurological (cerebrovascular disease, brain trauma or tumor, encephalitis or meningitis, epilepsy, multiple sclerosis etc.) or medical (diabetes mellitus, hypothyroidism, any infection, hypovitaminoses like B12 or folate deficiencies, myocardial infarction etc.) disease, as well as those with pregnancy, having a cardiac pacemaker or any metal implant. Additionally, because WCST and ST performances require to discriminate colors correctly, color blindness of all participants was excluded. All subjects provided their informed written consent. Inclusion of all subjects rested on volunteering and no payment were done.

2.2. Clinical assessment

Diagnoses were confirmed with SCID-I before the study entry. Symptom severity in schizophrenia patients have been measured with the Positive and Negative Syndrome Scale (PANSS) and Scale for the Assessment of Negative Symptoms (SANS) by a psychiatrist at the day before the first rTMS session and the following day after the 20th session. To assess cognitive functions, subjects with schizophrenia performed WCST, DST and ST at the day before the first rTMS session and at the following day after the last session. Healthy subjects performed the same tests for once. They were control comparison of cognitive status with each of schizophrenia group.

2.3. Randomization and masking

The subjects with schizophrenia were randomized as an active and sham group. They were randomly assigned (1:1) sequentially (first active and then sham). The order of DLPFC hemispheric stimulation was also randomized sequentially (1:1) and counterbalanced (left then right DLPFC followed by right then left DLPFC in each group). In order to prevent any interaction between the patients, we avoided selecting patients who might have any personal relationship with each other. Their appointments for rTMS sessions were organized on remote times. The subjects and the experimenter were masked to the treatment conditions during the study.

2.4. rTMS protocol

Subjects with schizophrenia received a total of 20 sessions of rTMS treatment, during the 5 week days. They were excluded from the study if they missed > 4 sessions of treatment, including weekend days. The rTMS was administered with a Magstim stimulator (Magstim Company Ltd. Whitland, UK), 70-mm diameter figure-of-eight coil sequentially to bilateral DLPFC at 20 Hz, 90% resting motor threshold for 20 trains, 50 pulses/train, inter-train interval of 20 s (1000 pulses/hemisphere, a total of 2000 pulses/session/day) in accordance with safety guidelines (Chen et al., 1997; Rossi et al., 2009). The order of bilateral stimulation (i.e., left then right or right then left) was constant for all 20 treatments. The resting motor threshold was defined as the lowest intensity that produced a motor evoked potential of at least 50 mV in 50% of the trials delivered. It was determined with the minimum motor threshold value method which produces contractions in the abductor pollicis brevis muscle in at least 5 out of 10 sequential single stimulus applications on the area corresponding to the motor cortex. The site of stimulation during the rTMS treatment sessions was defined by a point 5 cm anterior to that required for maximum stimulation of the abductor pollicis brevis muscle for each hemisphere (Pascual-Leone et al., 1996). The subsequent hemisphere was stimulated just after the stimulation of the first hemisphere. Sham stimulation was delivered at the same parameters with the coil held in a single wing-tilt position at 90 degrees, inducing similar somatic sensations as in the active stimulation with no major brain effects. The study treatment was found to be safe and well tolerated.

2.5. Statistical analysis

The data was analyzed by Statistical Package for Social Sciences (SPSS for Windows 17.0, SPSS Inc., IL, ABD) computer program. Neuropsychological variables were tested for assumptions of normality (Shapiro–Wilk test) and homogeneity of variances. Descriptive data of all groups has been determined. Differences in demographic and clinical data between the groups were compared with chi-square test for categorical data and independent *t*-test for continuous data. Initially, to test relevance of the groups' data with literature, baseline neuropsychological status between three groups (healthy, active rTMS and sham rTMS) have been compared by One-Way ANOVA test. Comparison of test scores (before treatment, and after treatment) between the schizophrenia groups (active vs. sham) has been done by using independent *t*-test or Mann-Whitney *U* test. Intragroup changes of test scores have been analyzed by paired-samples *t*-test or Wilcoxon test. Effect size measured by Cohen's d. The level of significance *p* was assumed to be below .05.

3. Results

3.1. Patient data

In this study, 21 (11:10; active:sham) subjects with schizophrenia and 11 healthy control subjects were analyzed. Subject selection and

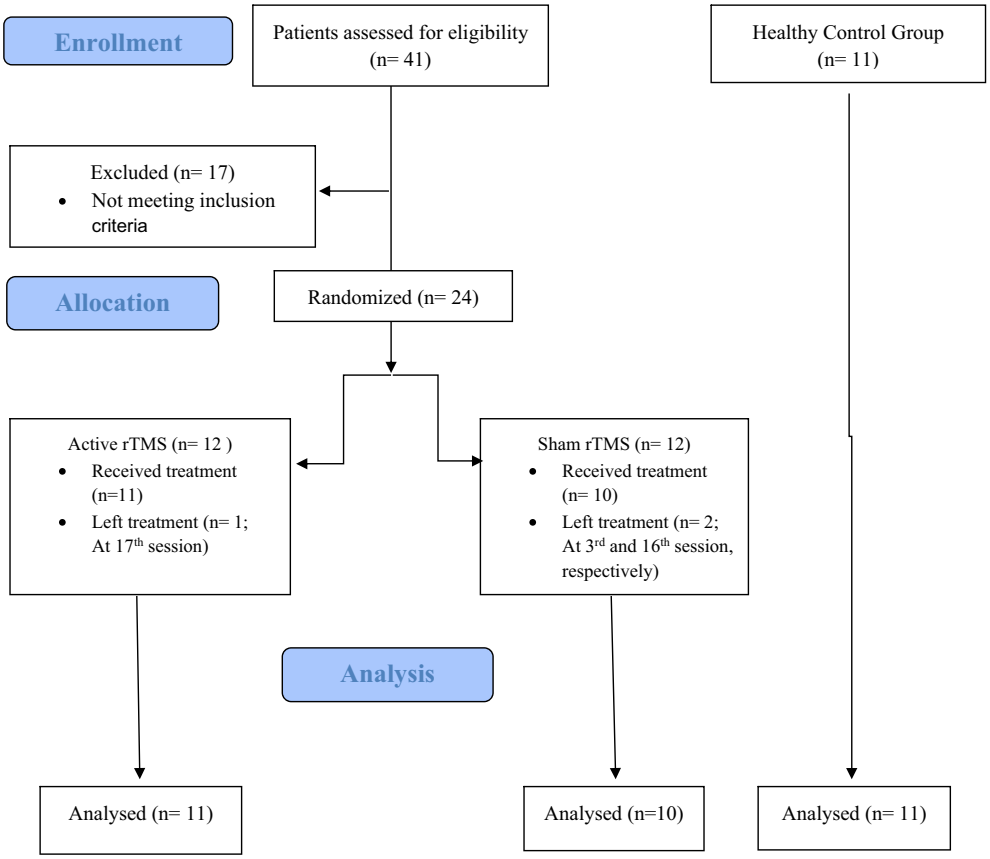

Fig. 1. Flow diagram.

randomization diagram is shown in the Fig. 1. A total of 41 subjects with schizophrenia were recorded. 17 of them did not matched all the criteria, so only 24 subjects have been included. A female subject with schizophrenia had to leave the study at 17th session of the treatment because of a holiday plan with her family, two ones from the sham group left the study at 3rd and 16th sessions relatively, because of their disbelief about the efficiency of the treatment. Ethically, none of patients' medication was changed during the study. Patients who may need a major medical treatment change were also excluded.

Demographic and clinical data is given in Table 1. There was no significant difference between the healthy control group and each schizophrenia treatment group, in terms of age ($p = .857$), gender ($p = .725$) and total years of education ($p = .984$). To assess severity of the illness, the mean duration of illness ($p = .078$), total number of inpatient treatments ($p = .476$), type (typical vs. atypical; $p = .648$) and chlorpromazine equivalent doses of antipsychotic drugs ($p = .318$), and baseline PANSS and SANS total scores (respectively; $p = .568$ and $p = .144$) of schizophrenia treatment groups were not significantly different (Woods, 2003).

3.2. Test performance changes

3.2.1. Baseline test scores

Comparison of baseline test scores of all the three groups (control vs. each schizophrenia treatment group) are summarized in Table 2. Almost all the baseline neuropsychological test mean scores of each schizophrenia treatment group (active/sham rTMS) were poorer comparing with the healthy group, but not all were significant.

3.2.2. Comparison of pre- and post-treatment test scores

There was no significant difference in pre-treatment WCST, ST and DST scores between rTMS groups ($p > .05$). Indeed, post treatment *ST total time* ($p = .045$; *Cohen's* $d = 0.94$), *ST total errors* ($p = .44$; *Cohen's* $d = 0.95$) and *interference* ($p = .021$; *Cohen's* $d > 1.00$) scores of active rTMS group were significantly better than sham (see Table 3). Accordingly, post-treatment *DST forward span* ($p = .045$; *Cohen's* $d > 1.00$) and *DST backward span* ($p = .042$; *Cohen's* $d = 0.98$) scores of active rTMS group were significantly better (See Table 4).

3.2.3. Changes of Test Scores

There was no significant change in WCST scores in both of the treatment groups ($p > .05$). Furthermore, test performance of active rTMS group not significantly regressed after the treatment. In Stroop Test, there were significant improvements in both *ST total time* ($p = .008$; *Cohen's* $d = 0.99$) and *interference* ($p = .013$; *Cohen's* $d = 0.90$) scores of active rTMS group, while no improvement in sham group was determined respectively ($p > .05$). Similarly, improvement in both DST forward and backward scores have been detected in active rTMS group but not sham, while it was significant only in DST backward score change ($p = .046$; *Cohen's* $d = 0.72$: See Table 5).

4. Discussion

In this study, we have found that 20 Hz repetitive transcranial magnetic stimulation targeted to bilateral dorsolateral prefrontal cortices of subjects with schizophrenia does not has any positive effect on some executive functions such as planning, abstract reasoning, concept formation, set maintaining and set shifting (Huang et al., 2016), but it may improve attention, verbal working memory, the competence of switching the perceptional set up under a disruptive effect towards new instructions, and processing speed of information.

First of all, there was no significant change in WCST scores in each rTMS group with the treatment ($p > .05$). Furthermore, test performance of active rTMS group not significantly regressed after the

Table 1
Demographic and clinical data.

	Healthy (n = 11)	Active (n = 11)	Sham (n = 10)	*p*
Mean age (years)	36.55 ± 8.80	36.45 ± 8.58	34.40 ± 12.11	.857
Gender (M/F)	8/3	8/3	6/4	.725
Mean years of education, n	10.64 ± 1,50	10.73 ± 1.61	10.60 ± 1.89	.984
Mean duration of illness (months)	–	184.55 ± 97.51	133.10 ± 120.77	.078
Number of inpatient treatments	–	4.64 ± 4.24	3.50 ± 3.44	.476
PANSS/SANS scores	–	81.82 ± 8.94/52.64 ± 13.14	79.70 ± 7.61/43.10 ± 15.50	.568/.144
Chlorpromazine equivalent dose of antipsychotic drugs (mg)	–	845.45	661.66	.318
Type of antipsychotic drug (typical vs. atypical)	–	Typical = 1 Atypical = 8 Both = 2	Typical = 0 Atypical = 8 Both = 2	.648
Medication, n: dose (mg)				
Haloperidol	–	n = 2 (20 mg/day, 50 mg/week dekanoat)	n = 1 (10 mg/day)	
Zuclopentixol	–	n = 1 (200 mg/2 week depot)	–	
Flupentixol	–	–	n = 1 (20 mg/2 week depot)	
Chlorpromazine	–	n = 1 (100 mg/day)	–	
Risperidone	–	n = 4 (2 × 3 mg/day, 2 × 50 mg/2 week consta)	n = 3 (2 mg/day, 2 × 50 mg/2 week consta)	
Paliperidone	–	–	n = 3 (6 mg/day, 100 mg/4 week and 150 mg/4 week injection)	
Amisulpiride	–	n = 1 (800 mg/day)	–	
Clozapine	–	n = 2 (2 × 600 mg/day)	n = 4 (2 × 200 mg/day, 400 mg/day, 500 mg/day)	
Olanzapine	–	n = 2 (10 mg/day, 15 mg/day)	n = 1 (5 mg/day)	
Quetiapine	–	n = 5 (3 × 300 mg/day, 400 mg/day, 600 mg/day)	n = 2 (50 mg/day, 300 mg/day)	
Aripiprazole	–	n = 2 (2 × 30 mg/day)	n = 3 (15 mg/day, 2 × 30 mg/day)	

Demographic and clinical data ± SD of healthy control and active and sham rTMS schizophrenia groups. PANSS = Positive and Negative Syndrome Scale; rTMS = repetitive transcranial magnetic stimulation; SANS = Scale for the Assessment of Negative Symptoms.

Table 2
Comparison of baseline test scores between healthy control group and each of schizophrenia treatment group.[a]

Performance	Active (n = 11)	Healthy (n = 11)	Sham (n = 10)
WCST scores (*p*)			
Total trials administered	1.000		0.717
Correct responses	**0.043**		**0.001**
Incorrect responses	**0.036**		**0.003**
Perseverative responses	0.266		**0.039**
Perseverative errors	0.159		**0.027**
Nonperseverative errors	0.092		0.127
% of perseverative errors	0.156		**0.018**
Categories	**0.005**		**0.009**
Trials to complete the first category	0.806		0.513
% of conceptual level responses	**0.012**		**0.002**
Failure to maintain set	0.400		0.974
Learning to learn	0.493		0.651
ST scores (*p*)			
Total time	**0.007**		**0.006**
Total errors	1.000		0.453
Interference	0.060		**0.027**
DST scores (*p*)			
Forward span	0.462		0.120
Backward span	0.555		**0.020**

DST = Digit Span Task; ST = Stroop Test; WCST = Wisconsin Card Sorting Test.
Bold data indicate significance at $p < 0.05$.
[a] One-Way ANOVA test.

treatment. Theoretically, it is evident that WCST performance is biologically mediated by a neural network extending from dorsolateral prefrontal and orbitofrontal cortices to striatum and thalamus and then turning back to prefrontal cortex thus called 'cortico-striato-thalamo-cortical loop' or salience network (Peters et al., 2016). Impaired executive functions in schizophrenia are thought to be related to a defect in this network (Quan et al., 2013). Although, it may be theorized that high frequency rTMS application to dorsolateral prefrontal cortices must improve executive functions by leading to an increased activity in that area, we have not investigated that in our study, indeed. That may be because WCST is a complicated test that needs activation of not only a single brain area but multiple cortical and subcortical areas (Berman et al., 1995). In a neuroimaging study of WCST on healthy people, there was an increased activity during the feedback phase but not at the sorting phase. Subsequently, with a 20 Hz rTMS (250 ms) intervention during feedback phase, an impairment of WCST performance has been observed, whereas there was no change when given during sorting, set maintaining and set shifting phases (Ko et al., 2008). That means firing dorsolateral prefrontal cortex by high frequency rTMS may change some WCST subtest scores, but not all. That may rationalize our findings, and may propose that in order to improve WCST performance, it may not be sufficient to simply increase DLPFC activity. More recent studies with similar evidence have been carried out (Hasan et al., 2016; Mittrach et al., 2010).

In our study, post treatment *ST total time* and *interference* scores of active rTMS group were better than sham, and there were significant improvements in both *ST total time* and *interference* scores after the treatment. These results led us to hypothesize that application of 20 Hz frequency rTMS to bilateral dorsolateral prefrontal cortices may improve Stroop performance as it increases the competence of switching the perceptional set up under a 'disruptive effect' towards new instructions, and it increases processing speed of information. In Cho and Strafella's study on healthy subjects, they gained PET scans of brain activities of the subjects after applying 10 Hz rTMS targeted to their bilateral DLPFC sequentially. During the rTMS application to right DLPFC, they did not observed any regional brain activity increase, whereas dopaminergic activity of ipsilateral orbitofrontal cortex (OFC) and anterior cingulate cortex (ACC) had increased when applying to left DLPFC (Cho and Strafella, 2009). This increase in dopaminergic activity at OFC and ACC was attributed to the dopaminergic discharge of the neurons extending from ventral tegmental area (VTA) to medial prefrontal cortex via mezocortical tracts caused by rTMS firing of the glutamatergic neurons extending from prefrontal cortex to VTA. Besides this, considering dense connections of DLPFC with OFC and ACC,

Table 3
Comparison of pre- and post-treatment ST scores in between schizophrenia treatment groups.

Performance	Active (n = 11)	Sham (n = 10)	*p*	*Cohen's d*
Pre-treatment				
ST scores				
Total time[a] (mean ± SD)	208.31 ± 40.89	210.34 ± 30.55	.899	
Total errors[b] (mean ± SD; median)	1.09 ± 2.46 (0)	4.00 ± 7.10 (5)	.154	
Interference[a] (mean ± SD)	60.307 ± 23.41	64.09 ± 16.29	.680[a]	
Post-treatment				
ST scores				
Total time[a] (mean ± SD)	177.32 ± 22.52	202.22 ± 30.29	**.045**	**0.94**
Total errors[b] (mean ± SD; median)	0.45 ± 1.21 (0)	2.60 ± 2.98 (2)	**.044**	**0.95**
Interference[a] (mean ± SD)	44.44 ± 10.33	61.08 ± 19.02	**.021**	**> 1.00**

ST = Stroop Test.
Bold indicate significant value.
[a] Student *t*-test.
[b] Mann-Whitney *U* test.

another presumption was that firing these local dopaminergic neurons by rTMS could lead to such a result. Furthermore, some previous studies carried out with schizophrenia patients revealing the relationship between impaired Stroop performance seen with disconnections at ACC (Ungar et al., 2010; Yan et al., 2012) may support this suggestion. Moreover, as Stroop Test, which schizophrenia patients have poorer performance may be an indicator of cognitive flexibility (MacLeod, 1992), it also can be proposed that high frequency rTMS may improve cognitive flexibility in schizophrenia.

Digit Span Task is a well-known neuropsychological task that schizophrenia patients have lower performance than normal population (G. et al., 2009). In this study, it is evident that rTMS has positive effects on DST forward and backward scores which may stand for that it improved attention and verbal working memory of schizophrenia patients. As DST forward performance is assumed to be related to attention and short term memory, there was a non-significant improvement in active rTMS group performance despite the deterioration in sham rTMS group. On the other hand, DST backward scores which is mostly related to verbal working memory, had significantly ameliorated in active rTMS group but not in the sham. In a study, regarding a relation between DST performance and right DLPFC, Aleman had found that repetitive transcranial magnetic stimulation over the right dorsolateral prefrontal cortex disrupted digit span task performances of healthy subjects (Aleman and Van'T Wout, 2008). Similarly, in studies with depression no beneficial effect of rTMS on DST performance could be indicated (Little et al., 2000; Moser et al., 2002; Shajahan et al., 2002). However, Barr et al. achieved an improvement of working memory in subjects with schizophrenia by applying 20 Hz (750 pulses/side) rTMS on bilateral DLPFC. Moreover, as working memory was measured by n-back task in that study, 3-back task scores of active rTMS group and healthy subjects were non-significantly different (Barr et al., 2013). In addition, in a recent meta-analysis investigated effect of high frequency rTMS on neurocognitive functions, authors concluded that high frequency rTMS over left DLPFC with a total of pulses < 30,000 could significantly improve working memory in schizophrenia patients (Jiang et al., 2019). As a result, we have found that 20 Hz rTMS has positive effect on both DST forward and backward scores which implies an improvement in attention and verbal working memory in subjects with schizophrenia (Hauer et al., 2019).

There are some limitations of this study. First of all, the mean years of education in our sample was relatively high (> 10 years), so that we cannot allege the same findings for other samples with lesser mean years of education. In addition, although the schizophrenia treatment groups were similar in our sample, the study was carried out in a unique centre and with a relatively small sample. Indeed, in spite of these limitations, the findings were strongly significant. That means the effect might not be related to sample size. Nonetheless, this study must be replicated in a larger sample.

Consequently, bilateral high (20 Hz) frequency repetitive transcranial magnetic stimulation targeted to bilateral dorsolateral prefrontal cortices of schizophrenia patients does not has any positive effect on some executive functions such as planning, abstract reasoning, concept formation, set maintaining and set shifting. However, it may improve attention, verbal working memory, the competence of switching the perceptional set up under a disruptive effect towards new instructions, and processing speed of information in schizophrenia patients. Future studies with longer treatment duration and larger number of patients are needed.

5. Conclusions

To conclude, the main finding of this study is that 20 Hz repetitive transcranial magnetic stimulation of bilateral dorsolateral prefrontal cortices of schizophrenia patients does not has any positive effect on some executive functions such as planning, abstract reasoning, concept formation, set maintaining and set shifting, but indeed, it may improve

Table 4
Comparison of pre- and post-treatment DST scores between schizophrenia treatment groups.[a]

Performance	Active (n = 11)	Sham (n = 10)	*p*	*Cohen's d*
Pre-treatment				
DST scores				
DST forward (mean ± SD; median)	5.73 ± 0.90 (6)	5.30 ± 1.05 (5)	.269	
DST backward (mean ± SD; median)	4.00 ± 0.63 (4)	3.40 ± 0.96 (4)	.125	
Post-treatment				
DST scores				
DST forward (mean ± SD; median)	5.91 ± 0.94 (6)	5.10 ± 0.56 (5)	**.045**	**> 1.00**
DST backward (mean ± SD; median)	4.36 ± 0.50 (4)	3.70 ± 0.82 (4)	**.042**	**0.98**

DST = Digit Span Task.
Bold indicate significant value.
[a] Mann-Whitney U test.

Table 5
Intra-group changes in ST and DST scores in active rTMS group.

Performance	Time	Test score (mean ± SD; median)	*p*	*Cohen's d*
ST scores				
ST total time[a]	Pre-treatment	208.31 ± 40.89 (194.39)	**.008**	**0.99**
	Post-treatment	177.32 ± 22.52 (171.08)		
ST total errors[b]	Pre-treatment	1.09 ± 2.46 (0)	.414	
	Post-treatment	0.45 ± 1.21 (0)		
Interference[a]	Pre-treatment	60.37 ± 23.41 (57.89)	**.013**	**0.90**
	Post-treatment	44.44 ± 10.33 (41.39)		
DST scores				
DST forward[b]	Pre-treatment	5.73 ± 0.90 (6)	.480	
	Post-treatment	5.91 ± 0.94 (6)		
DST backward[b]	Pre-treatment	4.00 ± 0.63 (4)	**.046**	**0.72**
	Post-treatment	4.36 ± 0.50 (4)		

DST = Digit Span Task; ST = Stroop Test.
Bold indicate significant value.
[a] Paired samples *t*-test.
[b] Wilcoxon test.

attention, verbal working memory, the competence of switching the perceptional set up under a disruptive effect towards new instructions, and processing speed of information.

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CRediT authorship contribution statement

Mehmet Diyaddin Güleken: Formal analysis, Visualization, Writing - original draft, Conceptualization, Investigation, Writing - review & editing. **Taner Akbaş:** Investigation, Formal analysis, Writing - review & editing. **Selime Çelik Erden:** Conceptualization, Investigation, Formal analysis, Writing - review & editing. **Veysel Akansel:** Formal analysis, Visualization, Writing - original draft, Writing - review & editing. **Zeliha Cengiz Al:** Formal analysis, Visualization, Writing - original draft, Writing - review & editing. **Ömer Akil Özer:** Supervision, Writing - review & editing.

Declaration of competing interest

The authors declare that they have no conflicts of interest.

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