Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres



Brief report

Borderline personality disorder and rTMS: A pilot trial



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ARTICLE INFO

Article history Received 17 September 2012 Received in revised form 14 October 2013 Accepted 21 January 2014 Available online 30 January 2014

Keywords: Neuropsychological test Prefrontal cortex Smoking cessation

ABSTRACT

A randomized, controlled study was carried out to assess the effect of a series of 10 sessions of highfrequency rTMS to the right DLPFC in 10 Borderline Personality Disorder patients. Patients in the rTMS group showed improvements in anger, affective instability (Borderline Personality Disorder Severity Index) and planning (Tower Of London). Two smoking cessations were observed.

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1. Introduction

The neuromodulatory effects of Transcranial Magnetic Stimulation (TMS) on the cerebral cortex suggest that rTMS may be a potential treatment for some Borderline Personality Disorder (BPD) symptoms. Some recent functional neuroimaging research supports the hypothesis of a dysfunctional frontolimbic network in BPD (Leichsenring et al., 2011; Schmahl and Bremner, 2006; Stein, 2009). PET ([18F]fluoro-p-glucose) studies show hypometabolism in the prefrontal cortex (De La Fuente et al., 1997; Salavert et al., 2011). The involvement of the prefrontal cortex in BPD is also supported by neuropsychological findings (Ruocco et al., 2010; Ruocco, 2005). These studies suggest the presence of a cortical dysfunction that might be normalized by rTMS. Other studies indicate that both electric and magnetic stimulation of the right Dorsolateral Prefrontal Cortex (rDLPFC) affect decision-making (Fecteau et al., 2007; Knoch et al., 2006a, 2006b; van 't Wout et al., 2005). Deficits in decision-making were correlated with BPD symptom severity (Schuermann et al., 2011; Svaldi et al., 2012). These arguments suggest that the rDLPFC may be a potential target for cortical stimulation of BPD patients.

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Our objective was to assess the effect of a series of 10 daily sessions of high-frequency rTMS applied to the rDLPFC on the severity of BPD and the results of neuropsychological tasks in BPD patients.

2. Methods

We performed a randomized, controlled study over 3 months (with blinded evaluation and statistical analysis of results); one group was assigned to active rTMS and the other group received sham treatment. The subjects were assessed at specified time points; before treatment, at week 2, month 1, and month 3.

The main inclusion criteria were as follows: age between 20 and 45 and satisfaction of diagnostic criteria for BPD. A diagnosis of BPD was based on DSM-IV-TR criteria and on the Diagnostic Interview for Borderlines-Revised (DIB-R) (Zanarini et al., 1989, 1990). Exclusion criteria were as follows: bipolar I disorder, alcohol dependency, current major depressive episode or post-traumatic stress disorder (Mini International Neuropsychiatric Interview, MINI) and contraindication to rTMS. Patients in the experimental group underwent two series of 5 sessions of daily rTMS, at 10 Hz, administered to the rDLPFC. These treatments were separated by 2 days without simulation. The protocols for rTMS were as follows: frequency: 10 Hz, intensity: 80% of motor threshold (MT), stimulation site: over the rDLPFC (BA 9/46), 6 cm in front of the motor cortex, duration of daily stimulation session: 20 min, in 5-s bursts of stimulation at 10 Hz, with 25-s breaks, total number of pulses per session: 2000, number of sessions: 10 (one per working day over a 2week period). Placebo stimulation (sham-rTMS) was performed using the same stimulation parameters but with the coil angled at 90°.

We assessed Axis I disorder with the MINI and the revised Symptom Check List 90 (SCL-90) and the Montgomery and Åsberg Depression Rating Scale (MADRS) for the severity of depression. BPD severity was based on the Borderline Personality

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Disorder Severity Index (BPDSI) (Arntz et al., 2003). The Global Assessment Scale (GAS) was used to assess overall functioning. We administered the following two neuropsychological tasks: the Tower of London (TOL), which assesses planning, and the Balloon Analogue Risk Task (BART) (Lejuez et al., 2002), which investigates impulsive behavior and risk-taking. The possible occurrence of side effects was evaluated by a physician before each session of stimulation.

After verification of the quality and completeness of data, we conducted a descriptive analysis of the sample. Data analysis was by intention to treat. The primary endpoint for the TOL was defined by the difference in the average number of movements, at baseline and discharge. We analyzed both the global score of the BPDSI and sub-scores (DSM-IV criteria). End-of-treatment differences and change over time were analyzed using unadjusted analysis (independent sample Student's *t*-test).

3. Results

Enrollment began in January 2010 and ended in January 2011. Analyses were performed on nine subjects (five rTMS and four sham rTMS). The two groups were comparable in terms of age and severity of BPD. The groups differed in terms of sex (one male in the rTMS group).

For the main clinical outcome measure (the BPDSI), the response rate (at least 30% reduction on the BPDSI) is two of five for the rTMS group and one of four for the sham rTMS group. The nine items of the BPDSI were compared at intake and 3 months. At 3 months we found differences for affective instability (Mean: 0.07 (S.D.=0.13) vs. 1.22 (S.D.=0.82), t=-0.961, d.f.=7, p=0.017) and anger (Mean: 0.6 (S.D.=0.52) vs. 2.1 (S.D.=1.14), t=-2.672, d.f.=7, p=0.032). All other outcomes are provided in Table 1. The performance in the TOL improved significantly in the rTMS group (baseline: 4.17 (S.D.=0.08) and 3 months: 4.11 (S.D.=0.074); t=3.127, d.f.=4, t=0.035, whereas this was not the case in the sham-rTMS group (baseline: 4.15 (S.D.=0.073) and 3 months: 4.10 (S.D.=0.066); t=-0.694, d.f.=3, t=0.54). Data related to the TOL are presented in Table 2. Two patients reported having stopped smoking spontaneously due to loss

of the desire to smoke. No serious side effects were reported by patients in either group.

4. Discussion

This study is the first to examine the potential benefits of rTMS for BPD. It can be used to support the feasibility of this technique for treating the disorder, its acceptability for patients starting the treatment, and its safety. Improvements were observed in both clinical measures and neuropsychological tests. An improvement was observed for all variables, although not to the level of statistical significance. Notably, with the exception of one patient (due to the death of a close relative), all the patients that started the program completed it. The safety of rTMS has been observed in numerous studies (Rossi et al., 2009). The neuropsychological effects of rTMS are challenged by the excellent performance of the sham-rTMS group, which could be due to the moderate severity of our sample. Some technical considerations should be noted. The positioning of the rTMS coil was not based on anatomical criteria. A correction of 1 cm was applied to the "standard" site used to stimulate the rDLPFC, and anatomical variations have been found to affect the precision of this type of positioning system. Furthermore, stimulation efficiency could most likely be optimized by increasing the number of sessions, as is the case for depression (Dell'osso et al., 2011).

The failure of "top-down" control systems in the prefrontal cortex to modulate aggressive acts (Siever, 2008) could be one of the mechanisms that might explain the effect of rTMS on the BPDSI anger subscale. Functional magnetic resonance imaging (fMRI) supports greater differences between healthy controls than BPD patients in the dorsolateral prefrontal cortex related to negative social emotional processes (Koenigsberg et al., 2009).

Table 1 Variables at each visit (Mean (S.D.)).

Time Dependent measures	Baseline		Week 2		Month 1		Month 3	
	rTMS	Sham	rTMS	Sham	rTMS	Sham	rTMS	Sham
BART	29.7 (18.2)	26.3 (16.1)	32.5 (24.9)	37.4 (12)			34.2 (12.1)	36.7 (8)
BPDSI	19.9 (6.6)	24.06 (11.3)			15 (4.5)	22.1 (9.7)	14 (6.5)	20.6 (12.6)
MADRS	16.4 (7.2)	18.7 (14.8)	15.8 (7.1)	12.7 (6.9)	19.6 (5.8)	15 (8.7)	14.4 (11.5)	25.2 (15.2)
SCL-90	118.8 (71.1)	149.7 (59.6)	73.6 (24)	86.5 (54.4)	86.4 (21.7)	121 (73.5)	89.2 (45.1)	143.2 (94.5)
GAS	68.2 (11.3)	73 (19.1)	, ,	, ,	, ,	, ,	69.6 (18)	63 (22.8)

No statistical differences.

BART: Balloon Analog Risk Task; BPDSI: Borderline Personality Disorder Severity Index; MADRS: Montgomery and Åsberg Rating Scale; SCL-90: Symptom Check-List 90 items; and GAS: Global Assessment Scale.

Table 2Mean number of moves per Tower of London test (standard deviation) at each of the 5 visits per allocation group.

	Baseline									
	1	2	3	4	5	6	7	8		
rTMS	1*	2*	3.1 (0.2)	4.1 (0.2)	4*	5.7 (0.3)	5.5 (0.4)	8*		
Sham rTMS	1*	2*	3*	4.1 (0.3)	4*	5.8 (0.3)	5.2 (0.5)	8*		
	Week 2			, ,		, ,	, ,			
	1	2	3	4	5	6	7	8		
rTMS	1*	2*	3.1 (0.2)	4.3 (0.3)	4.1 (0.2)	5.5 (0.3)	5.1 (0.2)	8*		
Sham rTMS	1*	2*	3*	4*	4*	5.6 (0.5)	5.4 (0.5)	7.9 (0.2)		
	Month 1									
	1	2	3	4	5	6	7	8		
rTMS	1*	2*	3*	4.2 (0.3)	4*	5.8 (0.2)	5.3 (0.3)	7.5 (0.4)		
Sham rTMS	1*	2*	3*	4.1 (0.2)	4*	5.6 (0.5)	5.4 (0.2)	7.6 (0.2)		
	Month 3									
	1	2	3	4	5	6	7	8		
rTMS	1*	2*	3*	4.2 (0.3)	4.2 (0.4)	5.4 (4.3)	5.4 (0.2)	7.6 (0.2)		
Sham rTMS	1*	2*	3*	4*	4*	5.7 (0.5)	5.3 (0.3)	7.8 (0.9)		

^{*} For zero standard deviation.

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