Journal of Affective Disorders 150 (2013) 677–681

Contents lists available at ScienceDirect

Journal of Affective Disorders

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

Brief report

rTMS for pharmacoresistant major depression in the clinical setting of a psychiatric hospital: Effectiveness and effects of age

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ARTICLE INFO

Article history:
Received 15 October 2012
Received in revised form
28 March 2013
Accepted 28 March 2013
Available online 11 May 2013

Keywords:
rTM
Major depression
Frequency
Age

ABSTRACT

Background: Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive method of brain stimulation used in the treatment of drug-resistant major depressive disorder (MDD). It has been suggested that the efficacy of rTMS decreases with the age of the patient, but the data are contradictory. Here, we analyze in our clinical setting the efficacy of a 3-week rTMS treatment in drug-resistant MDD during a 3 month period and the potential influence of age on this efficacy.
Methods: Stimulation consisted of 15 sessions of rTMS over the dorsolateral prefrontal cortex. Clinical evaluations included the Hamilton Depression Rating Scale (HDRS), and the Beck Depression Inventory (BDI) at baseline, after 3 weeks of treatment, and 1 month and 3 months after the last session.
Results: Data from 93 patients issued from the 178 patients active file were analyzed. The antidepressant effect observed in the two age groups (<65 and ≥ 65) did not differ at the end of the treatment and 3 months later, with a comparable number of responders (50% decrease in HDRS score from baseline) (53.3% for age <65 versus 46.7% for age ≥ 65, $p=0.51$). The treatment had a significant effect over time. We found no evidence of the age affecting outcome at 3 months after the last session.
Limitations: Previous antidepressant treatments, and therapeutic drug use modifications after rTMS treatment, degree of pharmaco-resistance or duration of current episode are not reported.
Conclusion: RTMS of the DFPLC is effective as an add-on treatment for cases of pharmacologically refractory major depression, independent of the patient age.

1. Introduction

Repeated transcranial magnetic stimulation (rTMS) is a non-invasive method holding promises for treating major depressive disorder (MDD) (Rossini et al., 2005; Slotema et al., 2010). It consists of activating neuronal activity, through strongly focalized stimulation in the dorsolateral prefrontal (DLPFC) cortex either at high frequency (HF) on the left side (10 Hz) or at low frequency (LF) on the right side (1 Hz). The performance of rTMS treatment is better than that of sham treatment (Dell'osso et al., 2012; George et al., 2010), and its combination with routine initial antidepressant treatment seems to provide a significant improvement in 30–50% of subjects with drug-resistant MDD (Hadley et al., 2012; Rossini et al., 2005).

The factors influencing treatment success are not clearly defined, but include the individual susceptibilities, the parameters of the stimulation (frequency, number of pulses, and localization), and the treatment duration (Foucher et al., 2007; Galletly et al., 2012; Herrmann et al., 2006). It has been suggested that the age limits rTMS efficacy (Bigos et al., 2008; Bowie et al., 2007; Ollat, 1992), and the few available data are contradictory (Abraham et al., 2007; Aguirre et al., 2012; Jalenques et al., 2010; Huang et al., 2008; Milev et al., 2009). The effect of age on rTMS treatment outcome is not well known (Jorge and Robinson, 2011). RTMS is routinely administered in our hospital to subjects presenting with drug-resistant depression, without any age restriction. We thus conducted an open study to assess the efficacy of a 3-week rTMS treatment on MDD during a 3 months period (main objective) and to investigate the potential influence of age on this efficacy (secondary objective).

2. Materials and methods

2.1. Subjects

rTMS was administered in the routine practice to patients in hospitalization or ambulatory care. They were over 18 years old,

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http://dx.doi.org/10.1016/j.jad.2013.03.024

fulfilled the DSM-IV criteria for MDD, and had taken courses of at least two antidepressant drugs (doses within the effective therapeutic range, for at least three weeks) without successful reduction in depressive symptoms. They did not present any of the contraindications for rTMS (Lefaucheur et al., 2011). All patients gave their informed consent before receiving the treatment. Their pharmacological treatment was maintained throughout rTMS treatment.

2.2. rTMS procedure

The treatment consisted of 15 stimulation sessions over 3 weeks using a MagPro stimulator (Inomed, La Farlède, France), at 90% of the motor thresholds, corresponding to common conditions (Lefaucheur et al. 2011; Brunoni et al., 2011). The treatment was first HF (10 Hz, on the left prefrontal cortex, 2000 pulses, administered to 4 men and 9 women) and then LF (1 Hz, on the right prefrontal cortex, 1200 pulses, administered to 25 men and 55 women). The LF protocol was used because it was more convenient and practical (less noise and less temperature elevation), and no indication of its inefficiency was found in the literature.

2.3. Clinical assessments

Patients underwent clinical evaluation at baseline, 7 days (5 sessions, E7), 14 days (10 sessions, E14), 21 days (15 sessions, E21), 51 days (one month after the last session, E51), and 111 days (3 months after the last session, E111).

Sociodemographic and current therapeutic treatment data were collected from the patients, and they were evaluated for any psychiatric comorbidities. The Beck Depression Inventory (BDI) questionnaire (Beck et al., 1961; Beck and Beamesderfer, 1974; Delay et al., 1963), and the 21-item Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960; Guelfi, 1993) were used at each evaluation. A HDRS sub-score including the items referring specifically to depressivity and designed as depression sub-score,

Table 1
Data for all patients at baseline and the various evaluations.

	Whole group (n=93 unless otherwise indicated)	< 65 years (n=63 unless otherwise indicated)	≥65 years (n=30 unless otherwise indicated)	p (difference between age groups)
Age (years)	58.7 ± 14.01	51.2 ± 9.8	74.5 ± 6.0	
Sex (male/female)	49/93	20/43	9/21	0.8651 (χ^2)
Previous Ect treatment (n)	17 (18.3%)	9 (14.3%)	8 (26.7%)	0.1487 (χ^2)
Ambulatory care (n)	22 (23.65%)	17 (27.0%)	5 (16.7%)	0.274 (χ^2)
Therapeutic drug use (n)				
Neuroleptics	69 (74.2%)	49 (77.8%)	20 (66.7%)	0.252 (χ^2)
Benzodiazepines	64 (68.8%)	41 (65.1%)	23 (76.7%)	0.2595 (χ^2)
Antidepressant				
Tricyclics	11 (11.8%)	8 (12.7%)	3 (10.0%)	1.000 (F)
SSRI	43 (46.2%)	27 (42.9%)	16 (53.3%)	0.343 (χ^2)
SNRI	32 (34.4%)	22 (34.9%)	10 (33.3%)	0.880 (χ^2)
Others	23 (24.7%)	15 (23.8%)	8 (26.7%)	0.765 (χ^2)
Lithium	2 (2.1%)	1 (1.6%)	1 (3.3%)	0.543 (χ^2)
Na valproate	21 (22.6%)	15 (23.8%)	6 (20.0%)	0.681 (χ^2)
HDRS				
Baseline	18.18 ± 2.78	18.05 ± 3.10	18.47 ± 1.96	0.052[a]
Difference with baseline				
7 days	5.72 ± 3.29	5.52 ± 3.59	6.13 ± 2.57	0.895[b]
14 days	7.84 ± 2.95	7.90 ± 3.02	7.70 ± 2.83	
21 days	9.42 ± 3.64	9.56 ± 3.95	9.13 ± 2.90	
51 days	9.78 ± 3.93 (90)	9.87 ± 4.39 (60)	9.60 ± 2.84	
111 days	9.99 ± 3.65 (77)	10.37 ± 3.74 (51)	9.23 ± 3.40 (26)	
Depression sub-score				
Baseline	8.41 ± 1.87	8.17 ± 1.91	8.90 ± 1.69	0.017[a]
Difference with baseline				
7 days	2.45 ± 1.95	2.43 ± 1.96	2.50 ± 1.96	0.552[b]
14 days	3.26 ± 2.12	3.36 ± 2.19	3.03 ± 1.99	
21 days	4.04 ± 2.40	4.09 ± 2.60	3.93 ± 1.95	
51 days	4.53 ± 2.61 (90)	4.63 ± 2.82 (60)	4.33 ± 2.17	
111 days	4.71 ± 2.62 (77)	4.90 ± 2.76 (51)	4.35 ± 2.33 (26)	
BDI				
Baseline	20.58 ± 5.38	21.32 ± 6.00	19.03 ± 3.42	0.030[a]
Difference with baseline				
7 days	7.00 ± 4.77 (90)	7.13 ± 5.46 (60)	6.73 ± 3.00	0.242[b]
14 days	9.35 ± 5.59 (92)	9.84 ± 6.41 (62)	8.37 ± 3.22	
21 days	10.08 ± 6.55 (91)	10.08 ± 6.55 (61)	9.33 ± 4.10	
51 days	11.86 ± 6.22 (89)	11.86 ± 6.22 (59)	10.10 ± 3.53	
111 days	11.87 ± 6.17 (77)	12.62 ± 6.92 (51)	10.42 ± 4.12 (26)	

HDRS: Hamilton depression rating scale.
BDI: Beck depression inventory.
Difference with baseline: baseline value minus value at each evaluation.
SNRI: serotonin–norepinephrine reuptake inhibitors.
SSRI: selective serotonin reuptake inhibitors.

[a] p-values from Wilcoxon Rank signed test.
[b] p-values from analysis of variance for repeated measures based on ranked data.