Comparison between high and low frequency rTMS in the acute treatment of drug-resistant major depression

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INTRODUCTION

Repetitive transcranial magnetic stimualtion (rTMS) is a non-invasive brain stimulation technique allowing an electrical stimulation of specific cortical areas, in particular the dorsolateral prefrontal cortex (DLPFC), by means of magnetic fields generated by a handheld coil [1]. It is known that prefrontal cortex is involved in the pathophysiology of major depression, in particular showing hypofunction of the left lobe caused by an excessive inhibition exerted by the overactive right lobe [2]. As a consequence, low frequency rTMS (≤ 1Hz) placed on the right DLPFC seems to exert neural inhibition, whereas high frequency rTMS (> 1 Hz) on the left DLPFC induces neural enhacement. In 2008, rTMS has been approved by the FDA as augmentative treatment for major depression and, specifically, for "adult patients who have failed to achieve satisfactory improvement from one prior antidepressant medication at or above the minimal effective dose and duration in the current episode". There is a general consensus on rTMS antidepressant effects for major depression, whereas the debate still goes around its safety and efficacy in bipolar disorder, as well as around the identification of reliable markers for selecting optimal treatment parameters of stimulation. The aim of the present study was, therefore, to assess the efficacy and tolerability of augmentative rTMS in drug-resistant unipolar or bipolar depression.

METHODS

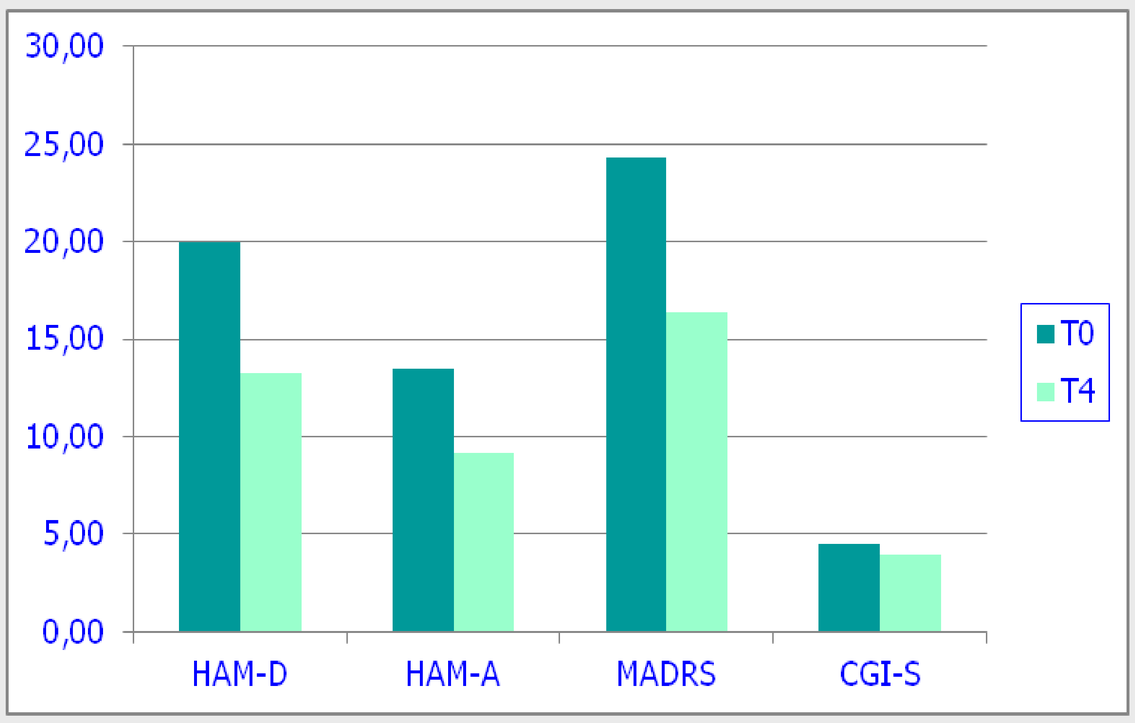
Twenty-eight patients, either inpatients or outpatients, with treatment resistant depression (HAM-D ≥ 18), with a diagnosis of unipolar (43%) or bipolar (I 21%, II 36%) depression, were randomized to an open-label rTMS treatment for 4 weeks with 20 sessions as a whole (Table I). Patients were required to maintain a stable pharmacological treatment for at least four weeks before the beginning of the study and to maintain it for the whole duration of the stimulation. According to stimulation parameters foreseen by recent guidelines [3], patients were randomized to the following three protocols of stimulation:

- DLPFC right, 1 HZ, 110% of the motor threshold (MT), 420 stimuli/day
- DLPFC right, 1 Hz, 110% MT, 900 stimuli/day
- DLPFC left, 10 Hz, 80% MT, 750 stimuli/day

Table I: main socio-demographic variables of the total sample

		TOTAL SAMPLE
Gender	Male	14 (50%)
	Female	14 (50%)
Mean age		51.4 ± 12.6
Mean age at onset		31.3 ± 14.8
Duration of Untreated Illness DUI (months)		24.7 ± 12.9
Diagnosis	Major Depressive Disorder	12 (43%)
	Bipolar Disorder type I	6 (21%)
	Bipolar Disorder type II	10 (36%)
Family history for any psychiatric disorder		57.1 %

Figure I: mean psychometric scores during the 4 weeks of treatment (T0-T4)



Statistics

HAM-D t=7.63, p<0.005; MADRS t=7.80, p<0.005; HAM-A t=7.25, p<0.005; CGI-S t=4.18, p<0.005

RESULTS

Four subjects were not included in the statistical analysis because of treatment discontinuation before the end of the 2nd week. Twenty-four patients completed the treatment, showing a significant reduction of the HAM-D, MADRS, HAM-A and CGI-S scores (t=7.63, p<0.005; t=7.80, p<0.005; t=7.25, p<0.005; t=4.18, p<0.005) (Figure I). Response, considered as a reduction of 50% of the score to the HAM-D compared to baseline, was achieved by three patients, two of whom considered "remitter", achieving a HAM-D score ≤ 8.

A partial response, considered as a reduction of the final score of the HAM-D between 25-50%, was achieved by 10 patients. No significant differences in terms of efficacy and tolerability were found between high vs low frequency. Side-effects were reported by 17% of the sample and were only mild and transient, being represented by headache, local pain and insomnia. Only one patient discontinued the stimulation because of hypomanic switch.

CONCLUSIONS

rTMS appeared to be an effective and well tolerated strategy for the acute treatment of resistant unipolar and bipolar depressive episode in an initial sample of 28 patients, with both high and low-frequency stimulation found to be equally effective and similarly tolerated.

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The authors declare that they have no conflict of interest in relation to the content of the present study