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# Awareness of Symptoms Amelioration Following Low-frequency Repetitive Transcranial Magnetic Stimulation in a Patient With Tourette Syndrome and Comorbid Obsessive-compulsive Disorder

*Dear Editor:*

We report the following case to highlight the importance of keeping into account the patient's awareness of the disease in studies investigating the efficacy of repetitive transcranial magnetic stimulation (rTMS) treatment in patients with Tourette Syndrome (TS) and comorbid obsessive-compulsive disorder (OCD). Reduction of tic severity has been shown following low-frequency rTMS over Supplementary Motor Area (SMA) in TS patients with or without comorbid OCD [1–3]. SMA represents an ideal target for rTMS in these patients, considering that it is richly connected with cortical and subcortical regions involved both in motor control and in TS pathophysiology [2]. Indeed, this site activity correlates with tic production in TS [4]. Furthermore, SMA is hyperactive in OCD patients [5].

We report the case of a 49-year-old right-handed man (13 years of education) with severe TS and comorbid OCD who was referred for rTMS treatment by his neurologist. When the patient was first diagnosed, at the age of 14, he manifested severe motor and vocal tics with strident screams accompanied by violent self-injurious behaviors. At the time of the study, his motor and vocal tics were partially controlled by medications – sertraline (150 mg/d), aripiprazole (10 mg/d), clonazepam (4 mg/d), haloperidol (1 mg/d) with biperiden (2 mg/d), delorazepam (1 mg/d, as needed) and tramadol (50–100 mg/d, as needed) – with the exception of self-injurious behaviors and screams that occurred at least once a day.

The patient signed a written informed consent to participate to the study, which was approved by the Local Ethical Committee. Medications were continued throughout the study. Functional and

**Table 1**

Clinical measures (A) and ad-hoc questionnaire (B) scores collected the week before (Pre) and the week after (Post) two rTMS applications.

	Pre	Post
<b>A.</b>		
YGTSS	85	70
MOVES	12	3
BDI	2	2
BAI	14	9
QOL-AD	23	18
<b>B.</b>		
Number of crises	7	4
Mean daily frequency	1	0.6
Mean intensity <sup>a</sup>	2.1/5	1.4/5
Mean interference <sup>a</sup>	2/5	0.8/5

A. Total tic score for the Yale-Global Tic Severity Scale (YGTSS); Motor tic, Obsessions and compulsions, Vocal tic Evaluation Survey (MOVES); Beck Depression Inventory (BDI); Beck Anxiety Inventory (BAI); Quality of Life in AD (QOL-AD).

B. Results of the ad-hoc questionnaire on weekly self-injurious behaviors.

<sup>a</sup> Intensity and interference were scored on a 0 to 5 points scale (0 = minimum intensity/interference; 5 = maximum intensity/interference).

neuropsychiatric evaluations comprised the Yale-Global Tic Severity Scale (YGTSS), Motor tic Obsessions and compulsions Vocal tic Evaluation Survey (MOVES), Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI) and the Quality of Life in AD (QOL-AD). The patient underwent these evaluations at the end of the week preceding the week of treatment and after one week from the last stimulation. The frequency of weekly self-injurious behaviors, their intensity and interference on everyday activities were quantified using an ad-hoc questionnaire that was completed by the patient, on a daily basis, during the week that preceded and the week that followed rTMS. Before starting the treatment, the patient was worried about having to come every day to the hospital, given his poor control over TS symptoms. rTMS was administered at 1 Hz over pre-SMA [1,6] using a 70 mm figure-of-eight coil and the MagStim Super Rapid stimulator (Magstim Company Ltd., Whitland, UK). EMG monitoring was performed from the right FDI muscle. The intensity of stimulation was set at 80% of resting Motor Threshold. At the end of stimulation the patient was monitored for 30 min. On the first day, he received three trains of 5 min with inter-train intervals of 2 min (900 stimuli). On the second day, he received six trains of 3 min and one train of 2 min with inter-train intervals of 2 min (1200 stimuli). Although the treatment was supposed to include 10 daily sessions, after the second session the patient dropped out. He called reporting he had an “epileptic seizure” after 40 min from rTMS and others seizures after about an hour. However, the patient’s description of the event (self-injurious behaviors with screaming and crying), his responses about specific symptoms (no loss of consciousness, no postictal confusion, no urinary or fecal incontinence, no tongue biting), and the normal EMG led the neurologist to exclude that what occurred were real seizures. They rather appeared to be hysteric or more intense self-injurious crises. The patient preferred not to come to the hospital to undergo EEG or other exams the same day. However, he was willing to complete the second part of the study and to come back after one week to undergo the post-treatment assessment. The day after, one of us brought the ad-hoc questionnaire to his home.

The week subsequent to the rTMS sessions, the patient showed 18% amelioration on the YGTSS, 75% improvement on the MOVES, 36% improvement on the BAI, and a reduction of the number, intensity and interference with daily life activities of the crises. On the other hand, 22% decrease was found on the QOL-AD score, indexing a worsening of the subjectively perceived quality of life (see Table 1). Although some degree of variance in reporting symptoms at the two time points cannot be totally ruled out, the patient’s concern about performing accurately his tasks and

the coherence in reporting a reduction of symptoms across tests in the post-treatment evaluation seem to support a certain reliability.

## Discussion

This case-report shows improvement of TS symptoms following rTMS over SMA [1–3]. It also suggests a dissociation between the clinical condition and the awareness of symptoms amelioration. Although symptoms evaluation on the assessment scales was based on the patient’s description of items and events, he seemed to be not aware of the improvement as he overtly reported no benefits and worsening of quality of life after treatment. Conversely, we may suggest that following rTMS he actually improved his awareness for the disease.

Inhibition of SMA might have reduced the urge to act [7] and TS symptoms. Yet, modulation of SMA might have affected other pre-motor areas belonging to the neural circuit underlying motor awareness [8], consequently improving the patient’s awareness of the disease. Although the presence of anosognosia was not evaluated before treatment, the patient’s high scores on quality of life assessment suggest symptoms underestimation and poor insight. Moreover, comorbidity with OCD may have reduced the patient’s awareness of the disease [9]. On the other hand, rTMS-induced improvement of awareness might have (paradoxically) decreased the patient compliance with the treatment. Indeed, dropouts of TS patients with comorbid OCD from rTMS treatment have been previously reported [1].

Future double-blind placebo-controlled studies on groups of patients are needed to better understand the effectiveness of rTMS over SMA for the treatment of TS and the impact that comorbid OCD and anosognosia may exert on the patients’ compliance.

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