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Lowering the seizure threshold in electroconvulsive therapy using transcranial magnetic stimulation: A case report

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ABSTRACT

We demonstrate the feasibility of lowering the seizure threshold using a combined approach of electroconvulsive therapy and transcranial magnetic stimulation. High-frequency transcranial magnetic stimulation of the supplementary motor area shortly before each electroconvulsive treatment session resulted in a reduction of the seizure threshold by half in a male patient with a severe psychotic depressive episode of bipolar affective disorder.

Introduction

Electroconvulsive therapy (ECT) is generally viewed as an effective, fast, safe and widely used method of treatment in a variety of severe neuropsychiatric conditions [3,10]. However, it has also been associated with neurocognitive side effects [2].

Transcranial magnetic stimulation (TMS) is likewise a safe, efficacious and well-tolerated method [1], even in resistant cases, but with substantially lower efficacy than ECT [5].

Some patients have a seizure threshold that is near or over the maximum intensity that most devices can deliver, which makes the treatment less effective and increases the risk of adverse effects and cognitive deterioration.

In this article, we outline the case of a patient treated for a pharmacoresistant depressive episode with psychotic symptoms, where we attempted to augment ECT via high-frequency TMS "pre-excitement" (HF-TMS) of the left supplementary motor area (SMA).

Case presentation

A 76-year old right-handed Caucasian male with doctoral education was admitted for a pharmacoresistant depressive episode of bipolar affective disorder with psychotic symptoms. He had already been treated for more than five depressive episodes with various types of medication and once with electroconvulsive therapy resulting in successful remission.

Upon admission, his psychiatric medication consisted of 20 mg of escitalopram and 10 mg of olanzapine. The patient initially refused to undergo ECT and treatment was therefore pharmacological. The daily dose of olanzapine was increased to 20 mg and 30 mg of mirtazapine was added, though without significant effect. The patient had also been diagnosed with several somatic conditions, i.e. hyperlipidemia, hypertension and benign prostatic hyperplasia, but at the time these were fully compensated with pharmacological therapy (5 mg of perindopril, 40 mg of esomeprazole, 20 mg of atorvastatin and 0.4 mg of Tamsulosin). He was classified as ASA 2 with unremarkable laboratory values and a physiological electrocardiogram.

During the first week of hospitalization, the patient's state progressively deteriorated: depression and psychosis worsened, and symptoms of catatonia emerged – mutism, stupor, negativism and waxy flexibility. The patient refused to eat and drink.

ECT was initiated without the patient's consent based on the guidelines of the Czech Psychiatric Association and following the Czech legal requirements for involuntary treatment of life-threatening conditions.

General anesthesia was induced by Propofol (1.5 mg/kg) and myorelaxation by 30 mg of succinylcholine; 0.8 mg of atropine was injected subcutaneously 60 minutes prior to each treatment. We planned to administer right-unilateral ultra-brief ECT three times a week (see Table 1). At the first ECT session, the dose was titrated: we started at a higher charge of 76.8 mC (0.8 A; 0.3 ms; 8 s; 20 Hz) due to the patient's high seizure threshold (ST) during a previous ECT session in 2005. However, no ictal activity on a two-channel electroencephalograph (EEG) was recorded. The seizure threshold was eventually established at 153.6 mC (0.8 A; 0.3 ms; 8 s; 40 Hz) and the subsequent seizure lasted 18 s. The therapeutic dose was established at six times the ST (0.8 A; 0.3 ms; 8 s; 120 Hz).

Starting from ECT session two and up to session seven, the protocol was intensified to everyday application due to the patient's severe catatonic state, which is common practice at our department and in accordance with the guidelines of the Czech Psychiatric Association [8]. The charge during the treatment had to be increased to achieve an adequate duration of 20–60 seconds of EEG epileptiform activity.

The pulse width was gradually elongated to 0.75 ms [4] and a charge of 1152 mC was reached (the maximum of the European version of the MECTA SpECTrum 5000Q®).

The patient's state improved after the fifth treatment and symptoms of catatonia subsided. The patient was no longer legally

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Table 1
Course of treatment. Development of the seizure threshold in ECT. Intensified (daily) regiment for catatonia through session two to seven with gradual increase of the charge to obtain a sufficient EEG seizure endpoint (at least 20 seconds). Combined treatment with pre-excitatory stimulation of dominant SMA by 15Hz HF-TMS shortly before each ECT from session ten.

Session No.	TMS pre-stimulation	Duration delivered [s]	Frequency delivered [Hz]	Pulse width delivered [ms]	Charge delivered [mC]	Dynamic impedance [Ohm]	Energy delivered [J]	Seizure EEG endpoint [s]
titration	no	8	20	0,3	76,8	226	14	**0**
1	no	8	40	0,3	153,6	200	24,6	**18**
2	no	8	120	0,3	460,8	220	82,3	**11**
3	no	8	120	0,45	691,2	215	123,2	**8**
4	no	8	120	0,6	921,6	210	163,8	**7**
5	no	8	120	0,7	1075,2	210	185,8	**12**
6	no	8	120	0,75	1152	196	189	**25**
7	no	8	120	0,75	1152	192	186,6	**20**
8	no	8	120	0,75	1152	210	208,8	**20**
9	no	8	120	0,75	1152	207	201,6	**22**
titration	**yes**	8	20	0,3	76,8	233	14,4	**10**
10	**yes**	8	60	0,3	230,4	204	38,6	**18**
11	**yes**	8	60	0,3	230,4	236	48	**20**
12	**yes**	8	60	0,3	230,4	228	42,1	**20**
13	**half dose**	8	60	0,3	230,4	257	48,4	**10**

considered to be in a life-threatening condition, was re-informed and agreed to continuation of the ECT.

The patient's mood, however, remained severely depressed. Emotivity was flat and the patient experienced episodes of anxious tension, nihilism, paranoia and micromania. We also suspected a cognitive impairment.

A change of approach – a combination of TMS and ECT

We sought a way to lower the seizure threshold of the patient and thus the administered charge during ECT without using standard methods for reducing seizure thresholds (e.g. hyperventilation).

It is widely accepted that high-frequency repetitive transcranial magnetic stimulation (HF-TMS) increases cortical excitability [7] and lowers the ST. Its after-effects may last up to 90 minutes.

The premotor cortex, primary motor cortex (M1) and SMA are all parts of the frontal motoric circuit. SMA has projections to the putamen, subthalamic nucleus and the internal globus pallidus.

Based on these findings, we decided to use HF-TMS of the dominant (in this case left) SMA (rostral region of Brodmann area 6a), as shown in Fig. 1.

The patient agreed to this novel approach and consented to TMS treatment.

The localization of SMA was identified via neuronavigation using the Visor™2ST (with software-based 3D modeling of the native T1 MRI brain scan).

The following parameters of HF-TMS were set: 15 Hz, 900 stimuli in six trains, intertrain 83 seconds. Stimulation intensity was set at 90% of motor-evoked potential (MEP, measured using Medelec Synergy® EMG), or 70% of the device's capacity.

Pre-stimulation took place 70 minutes prior to each ECT (starting at session ten) using the Magstim® Rapid2 with AirFilm® Coil (Rapid version). After the first pre-stimulation of the patient with HF-TMS, the ECT dose was re-titrated. The seizure threshold (ST) was established at 76.8 mC (0.8 A; 0.3 ms; 8 s; 20 Hz), a reduction of the initial seizure threshold by half (see Table 2).

The therapeutic dose was then established based on EEG seizure duration criteria at 230.4 mC (0.8 A; 0.3 ms; 8 s; 60 Hz).

The patient's mood improved. However, paranoid delusions were still present. Halfway through the fourth HF-TMS session, the patient refused to undergo further TMS co-stimulation after the completion of three out of six trains (delusions concerning concrementation of mandible during TMS). The seizure during the last (thirteenth) session of this ECT course lasted comparatively less time (10 s), perhaps because the TMS dose was lowered by half. The clinical state of the patient stabilized and we decided to discontinue the ECT course.

The patient remained cognitively impaired, most likely due to a pre-existing condition correlating with severe frontal and temporal atrophy on an MRI brain scan. There was no alteration of medication throughout the entire course of ECT. No severe adverse effects or complications resulting from this combined protocol were observed throughout the treatment.

Discussion

ECT is a powerful tool in the armamentarium of a psychiatrist. However, it has been associated with adverse neurocognitive effects. Patients with a pre-existing cognitive deficit and those with a high seizure threshold, including the aforementioned patient, might represent a higher risk group.

There are only a handful of case reports in contemporary scientific literature on the topic of combining TMS and ECT [9]. To our knowledge, none of these describe this type of regular pre-stimulation with TMS shortly before each ECT session. Our approach resulted in lowering the seizure threshold by half.

Disadvantages of this approach might include more difficult time and case management and the rare possibility of inducing an epileptiform seizure during the high-frequency pre-excitatory TMS (in localizations close to the primary motor area). Some safety precautions need to be adhered to: an anesthesiology team needs to be on site, a peripheral intravenous line needs to be inserted before the procedure and an EEG needs to be at disposal.

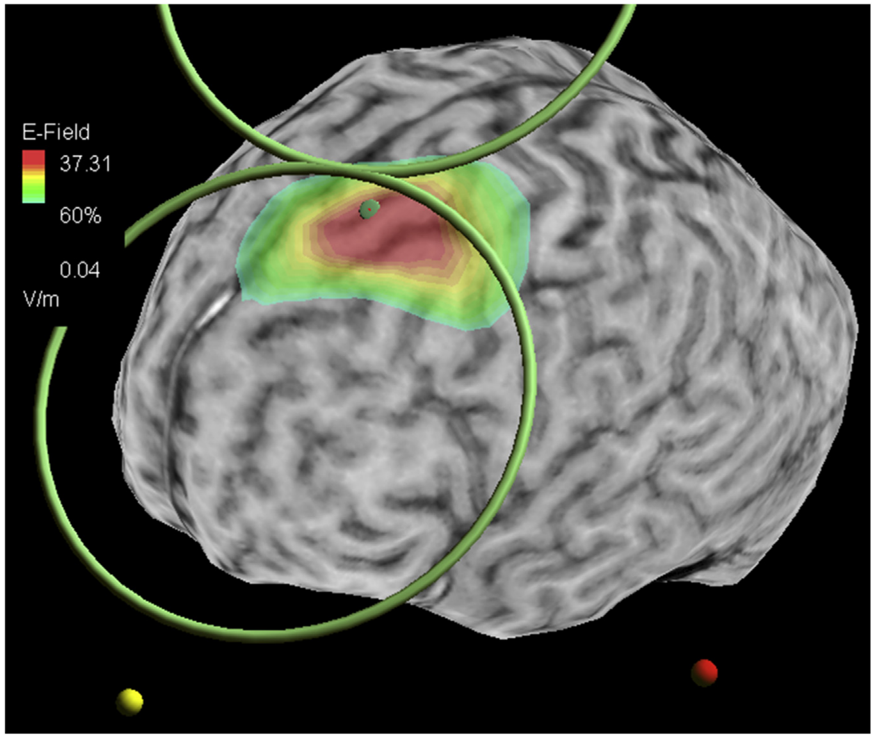
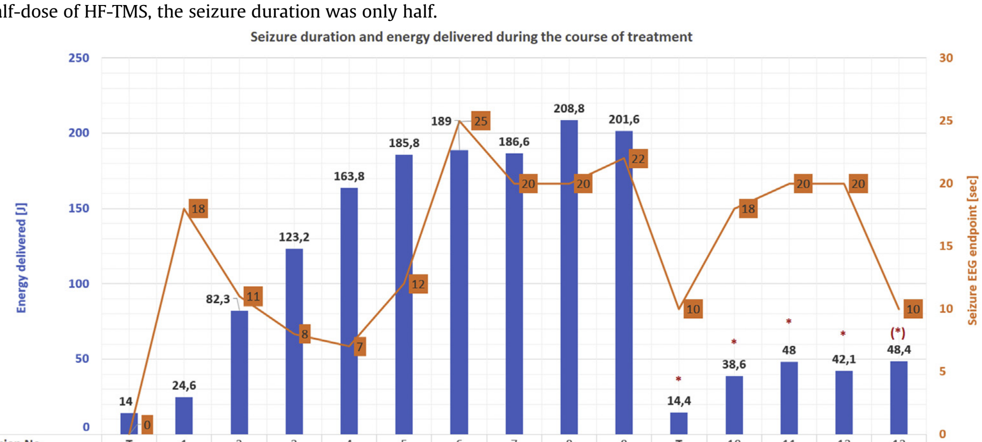


Fig. 1. TMS localization. SMA as identified by neuronavigation using the Visor™2ST with software-based 3D modeling of the patient's native T1 MRI brain scan.

Table 2
Seizure duration and energy delivered during the course of treatment. Titration of energy in session one. Throughout session six to nine, maximal energy was used; however, only minimal epileptiform activity was observed. After HF-TMS pre-stimulation (sessions ten to thirteen), the lower seizure threshold was re-titrated. At the last session (session thirteen), after a half-dose of HF-TMS, the seizure duration was only half.



Session No.	T	1	2	3	4	5	6	7	8	9	T	10	11	12	13
Energy delivered [J]	14	24,6	82,3	123,2	163,8	185,8	189	186,6	208,8	201,6	14,4	38,6	48	42,1	48,4
Seizure duration [sec]	0	18	11	8	7	12	25	20	20	22	10	18	20	20	10
* TMS pre-stimulation															
T titration															

A comparable effect might be expected when ECT is combined with transcranial direct current stimulation. However, we are not aware of any studies on this subject [6].

Conclusion

We demonstrated that it is possible to lower the ST by half using subthreshold HF-TMS in the left SMA prior to each ultra-brief RUL ECT session. We acknowledge that TMS stimulation of other brain areas might lead to different (perhaps even better) results.

Further research on the efficacy of such a treatment is needed. This case demonstrates the feasibility of this combined protocol.

Conflicts of interest

We wish to confirm that there are no known conflicts of interests associated with this publication and no significant financial support for this work has been received. No personal relationships with other people or organizations exist that could have inappropriately influenced our work and its outcome.

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J. Albrecht*, J. Buday, T. Mareš, L. Kališová, J. Raboch, M. Anders
Department of Psychiatry, First Faculty of Medicine, Charles University and General University Hospital in Prague, Czechia

* Corresponding author.
E-mail address: jakub.albrecht@vfn.cz (J. Albrecht).

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