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Case Report Open Access

Repeated Transcranial Magnetic Stimulation (rTMS) to improve Electroconvulsive Therapy (ECT) in Treatment-Resistant Depression: A Report of Two Cases

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Abstract

Major Depressive Disorder (MDD) also referred to as clinical depression, is a significant medical condition that can affect many areas of your life. It impacts mood and behavior as well as various physical functions, such as appetite and sleep. People with MDD often lose interest in activities they once enjoyed and have trouble performing everyday activities. Occasionally, they may also feel as if life isn't worth living. Some people with MDD never seek treatment. However, most people with the disorder can get better with treatment. Medications, psychotherapy, and other methods can effectively treat people with MDD and help them manage their symptoms. The exact cause of MDD isn't known. However, there are several factors that can increase the risk of developing the condition. A combination of genes and stress can affect brain chemistry and reduce the ability to maintain mood stability. Changes in the balance of hormones might also contribute to the development of MDD. MDD may also be trigged by alcohol or drug abuse, certain medical conditions, such as cancer or hypothyroidism, particular types of medications, including steroids. MDD is often treated with medication and psychotherapy. Some lifestyle adjustments can also help ease certain symptoms. People who have severe MDD or who have thoughts of harming themselves may need to stay in the hospital during treatment. Some might also need to take part in an outpatient treatment program until symptoms improve. This article explains how Electroconvulsive therapy (ECT) remains one of the most effective interventions for MDD.

Keywords: Major Depressive Disorder (MDD); Depression; Anxiety treatments; Aripiprazole

Introduction

Major Depressive Disorder (MDD) is an important and worldwide health problem with almost 121 million affected people. Its entire life prevalence is 5% to 15% [1]. Suicide is the major complication of depression. Among the inpatients, the risk of completed suicide is as high as 20-fold compared with the normal population [2]. Approximately 20% of the depressive episodes become chronic and 30% of all the depressions do not respond to antidepressant treatments [3]. The pharmacological resistance, the time needed for drugs to be effective and the severity of complications of MDD (Suicide, under-nutrition or dehydration) are major problematic for MDD caregivers.

Electroconvulsive therapy (ECT) remains one of the most effective interventions for MDD [4]. It is indicated in cases of MDD when adequate antidepressant treatment proves to be ineffective or intolerable or when the severity of symptoms requests a rapid response. However, this response remains partial. A recent meta-analysis showed only a rate of remission under ECT in 48% at the patients presenting a resistant depression maybe due to the fact that some of the patients had a seizure threshold over the maximum intensity able to be delivered by our devices [5]. According to Lysanby, 5% to 10% of the patients would have a seizure threshold particularly raised [6]. Furthermore, ECT can result in both anterograde and retrograde memory impairments. These unwanted effects increase with the number of sessions of ECT and the intensity of the stimulation [7].

High-Frequency Repetitive Transcranial Magnetic Stimulation (HF-rTMS) is a non-invasive instrumental therapy which had proven its efficiency in MDD but its appropriate part in the therapeutic decision tree is not clearly defined to date [8-10]. Nevertheless, rTMS is an accepted, evidence-based treatment option by the American Psychiatric Association (APA), the Canadian Network for Mood and Anxiety Treatments (CANMAT), and the World Federation of Societies of Biological Psychiatry (WFSBP).

We were interested in the possibility to improve the treatment by ECT thanks to rTMS, knowing that rTMS of the left dorsolateral prefrontal cortex (DLPFC) and ECT appear to have a similar cortical GABAergic activity, according to the studies on the neuro excitability. Our hypothesis is that the realization of sessions of HF-rTMS of the left DLPFC would allow to expose in a repeated way the receivers GABA to their substrate and thus to have a role of onset before the realization of ECT sessions which would be more quickly effective.

We present here the cases of two patients treated for refractory MDD. They benefited from a treatment by rTMS in the lapse of time necessary for the implementation of an ECT cure and the obtained results were in the sense of a possible potentiation of these two treatments.

Case Reports

The first patient was a 27-year-old woman with a bipolar disorder type 1 diagnosed at the age of 22. She presented a depressive state evolving for 9 months. She received aripiprazole and lithium, after

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having tested several mood stabilizers and even antidepressants. The symptoms of depression were a major psychomotor retardation, a depressed mood, crying, anxiety and suicidal ideations. She received 10 HF-rTMS sessions of the left DLPFC followed by a bitemporal electroconvulsive therapy. The suicidal ideation disappeared and her mood improved after the third session of ECT.

The second patient was a 39-year-old woman with refractory recurrent depression and histories of suicide attempts. Her current treatment included sertraline, lithium and loxapine. At admission, she presented a psychomotor retardation, anhedonia, anxiety, sleep disturbances and suicidal ideations. She received 7 sessions of HF-rTMS before electroconvulsive therapy. The patient was released from the hospital after the sixth ECT session.

Repetitive Transcranial Magnetic Stimulation was administrated by a MagPro magnetic stimulator with a figure 8 coil. The left dorsolateral prefrontal cortex (DLPFC) was stimulated at high-frequency (20 Hz, 90% of the motor threshold, 20 trains of 2 seconds with an intertrain interval of 60 seconds) [11,12]. Before each session, motor threshold (MT) was visually determined over the left primary motor cortex by finding the minimal intensity that produced five abductions out ten stimulations of the right abductor pollicis brevis (thumb). Stimulations were performed over the left DLPFC at a point 5 cm anterior to the point at which the MT was determined. Patients received daily sessions during two weeks (10 sessions in all). The ECT device used was a spectrum 5000Q, MECTA. The anesthetic medications that were used were propofol at 1-2 mg/kg and suxamethonium at 0.3-0.8 mg/kg. The treatment was realized in bitemporal (site of stimulation allowing obtaining a faster efficiency). A titration was realized to define the individual seizure threshold of the patient [13]. Once the seizure threshold determined, the first therapeutic stimulation was then processed. The dose delivered for the therapeutic stimulation was of twice the seizure threshold. In the case of the patient 1, the operator chose to gradually increase the dose delivered by considering that the seizure threshold of the patients increased during the cure of ECT [14]. In the case of the patient 2, the operator preferred to keep the same dose delivered as long as the duration of the electric crisis exceeded 20 seconds.

For both patients, the seizure duration were longer with lower stimulus intensity than expected based on our experience with other patients with the same medical condition (Table 1). Thus, the two patients improved after 3 to 6 sessions of ECT. The ECT sessions were continued as maintenance treatment. Except for stiffness for the first patient after the first session, the patients did not report side effect, including cognitive impairment, during the treatment. The seizure characteristics are shown in the Table 1.

Variables	Patient 1		Patient 2	
	Charge (mC)	Seizure duration (sec)	Charge (mC)	Seizure duration (sec)
ECT 1	33.6	>40	24	>60
ECT 2	72	23	52,8	20
ECT 3	153,6	24	52.8	24
ECT 4	192	21	52.8	> 42
ECT 5	230	32	52.8	29
ECT 6	268	25	52.8	24

Table 1: Seizure characteristics.

Discussion

Neuro-cortical excitability was studied in patients with Major Depressive Disorder. Various studies have demonstrated a decrease in ICI (intracortical inhibition) and CSP (cortical silent period) during MDD, indicating a probable involvement of the GABAergic system as a whole (GABA-A and GABA-B).

Furthermore, the intrathecal administration of the agonist of GABA-B receptors baclofen increased CSP and different authors highlighted decreased GABA concentrations in the occipital cortex and in the prefrontal areas of the brain (including DLPFC) [15-18]. Moreover, the normalization of the prefrontal GABA rate is associated with remission in MDD [19]. All together, these results are in favor of a decrease of GABAergic transmission in depression resulting in changes in measures of neuro-excitability: decrease in CSP and ICI.

Authors showed an up-regulation of the GABA-B receptors in the brain of rats after ECT sessions and an increase of the brain GABA rates as well as an increased activity of the GABA-B after treatment with ECT in humans [20-24]. However, a single session of ECT does not increase CSP 23 while several ECT increase CSP (24), a finding consistent with GABAergic activity of ECT. Transcranial magnetic stimulation also increases the CSP and depressed patients who responded to the high frequency rTMS (20Hz) of the left DLPFC have an increase of CSP and ICI [25-27]. Change of ICI was correlated with improved HAM-D score (Hamilton Rating Scale for Depression) [28].

This results support the view that changes in the CSP are only detectable after a significant activation of inhibitory interneurons, suggesting that activation of GABA-B receptors requires prolonged exposure to GABA or strong GABA concentration [29].

Therefore, left DLPFC High-rTMS and ECT seem to have the same effect on cortical GABAergic activity with an increase in brain GABA rates and neuroexcitability changes. We could expect that high frequency rTMS of the left DLPFC would repeatedly expose GABA receptors to their substrate and it would have a priming role before performing ECT sessions which would be more quickly effective.

Conclusion

For those two patients, we observed longer seizure duration with low electrical charges and an earlier improvement than for those treated by ECT alone. Indeed, the cure of ECT requires 8 to 12 sessions to obtain a sufficient clinical improvement [30]. Our two patients showed an obvious clinical improvement only after only the 3rd and the 6th ECT sessions. These cases suggest that the addition of rTMS sessions in a cure of ECT could represent an efficient and safe treatment for resistant depression.

Conflicts of Interest

The authors of this paper do not have any commercial associations that might pose a conflict of interest in connection with this manuscript.

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