AUGMENTATION OF PSYCHOPHARMACOLOGICAL TREATMENT WITH rTMS TO ACHIEVE CLINICAL HEALING: A CASE REPORT

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Summary
Objectives: Repetitive transcranial magnetic stimulation (rTMS) is useful in the treatment of recurrent major depressive disorder but its efficacy in elderly is still controversial. The present study aims to illustrate the outcome of a rTMS treatment in a 68 years old patient.
Materials and methods: rTMS therapy consisted of 30 sessions, six days a week. It was performed placing the butterfly coil over the left prefrontal cortex as defined by 5.5 cm anterior to the motor threshold (MT) site. The first treatment dose was fixed at 80% MT and slowly titrated to 100% within the fourth session; rTMS was applied at 10 Hz. A physiological examination and a clinical and neuropsychological assessment were carried out.
Results: The patient met the DSM-5 diagnostic criteria for recurrent major depressive disorder and generalized anxiety disorder. Her physical, neuropsychological and neurological examinations were normal. She showed an excellent response to the rTMS treatment.
Conclusions: rTMS in combination with pharmacotherapy resulted efficient in an old depressed patient who achieved a full functional recovery.

Key words: rTMS, depression, remission, elderly

Objectives

Repetitive transcranial magnetic stimulation (rTMS) proved to be safe and effective in treating the Major Depressive Disorder in patients who have not achieved improvement from prior antidepressant treatments. By contrast, its efficacy among the elderly (≥ 65 years) is unclear [1].
We report the case of a rTMS therapy in a 68 years old patient, in acute phase of illness.
Mrs A is an Italian housewife living in a country house with her husband. Second to last daughter in a large family, she graduated from primary school. During the young adulthood, she worked as farmer and had two children. In her family history, neoplasias occur but not psychiatric disorders, nor substance use disorders. She had a good health until she was 50, age of her first major depressive episode in association with marked anxiety symptoms. The first episode ended with a partial remission without full interepisode recovery after a SSRI medication. Since then, severe recurrent depressive episodes comorbid with generalized anxiety disorder occurred.
The most recent episode lasted 8 months and was still ongoing when Mrs A came to our Psychiatric Emergency Service.
At admission she looked sufficiently presentable, slow and brief in speech, with an anxious mimicry and decreased spontaneous gesticulation. She complained of a marked fatigue and reported abulia, anhedo-

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nia and lack of appetite, with a mild weight loss. She became easily upset and worried about everything happening around her. Her sleep, pharmacologically induced, was poorly restorative.
She had been taking for two months a stable psychotropic medication made up of venlafaxine 225mg/die, lithium 750 mg/die, risperidone 1.5 mg/die and lormetazepam 1.5 mg/die, obtaining a poor response. Previously, she had even taken multiple treatments with antidepressants (escitalopram, sertraline, trazodone, bupropion), mood stabilizers (lamotrigine and lithium), antipsychotics (quetiapine), benzodiazepines (lorazepam) and other psychotropic drugs, though remaining symptomatic.
Given the refractory nature of her symptoms, with the consent of Mrs A, TMS-naïve, we used a rTMS as augmentation to the pharmacological treatment.

Materials and Methods

The patient was assessed by psychiatrists using the Structured Clinical Interview for DSM-5-Clinical Version (SCID-5-CV) [2] and the Structured Clinical Interview for DSM-5-Personality Disorders (SCID-5-PD) [3]. Electroencephalogram (EEG), Brain Computed Tomography (Brain CT), blood/urine examinations and a neuropsychological assessment were carried out.
We started the rTMS therapy determining the motor threshold (MT, defined as the intensity over the motor hotspot at which 50% of pulses produced a discernible visual motor response in the patient's hand). Following the guidelines [4], we recorded the dose of rTMS administrated as percentage of the MT (80-100% MT).
rTMS therapy was performed using the MagVenture stimulator, MagPro R30, with the butterfly coil CoolDB80. The coil was placed over the left prefrontal cortex as defined by 5.5 cm anterior to MT site. The first treatment dose was fixed at 80% MT and slowly titrated to 100% within the fourth session; rTMS was applied at 10 Hz. The patient received a total of 30 treatments, six days a week. She rated the side effects (discomfort, pain at the point of stimulation, headache, anxiety, sleepiness, eye twitching, facial paraesthesia, epileptic seizures) of each stimulation on a Visual Analogue Scale (VAS). The side effects could be rated from 0 (None), to 2 (Very Mild), 4 (Mild), 6 (Moderate), 8 (Severe) and 10 (Very Severe).
A set of pre- and post- rTMS measures were collected and concerned: anxiety (*Hamilton Rating Scale for Anxiety* [5], HAM-A); depression (*Hamilton Rating Scale for Depression* [6], HAM-D; *Montgomery-Asberg Depression Rating Scale*[7], MADRS; *Beck Depression Inventory-II* [8], BDI-II; *Scala di Autovalutazione per la Depressione* [9], SAD); severity of psychiatric symptoms (*Brief Psychiatric Rating Scale - 4.0* [10], BPRS); improvement in clinical and social functioning (*Health of the Nation Outcome Scale - Rome* [11], HoNOS). The patient self-reported the quality of her life and her health and level of disability using respectively the World Health Organization Quality of Life - BREF [12] (WHOQoL) and the World Health Organization Disability Assessment Schedule 2.0 - 36 items [13] (WHODAS).

Results

Mrs A met the DSM-5 diagnostic criteria for recurrent major depressive disorder and generalized anxiety disorder. No personality disorder was diagnosed. Biochemistry, complete blood count, urine analysis, thyroid function tests, vitamin B12, folic acid levels were normal. We did not find any neuropsychological or neurological deficit.
After the therapy, Mrs A showed a decrease in the severity of symptoms and achieved the total remission within the 5th week of treatment. Specifically, the scales for depression and anxiety (HAM-D, HAM-A, MADRS) showed a decreased symptoms severity, from "Mild" to "Absent". The self-report scales for depression (SAD, BDI-II) exhibited an amelioration of the perceived symptoms from "Moderate" to "Absent". The severity of symptoms (BPRS) decreased from "Very Mild" to "Absent". At the beginning of rTMS treatment, the health and the psychosocial functioning (HoNOS) showed slight problems, which ceased to exist at the end of the therapy. The scores concerning the quality of life (WHOQoL) and the level of functioning (WHODAS) improved (see Table I).
The patient well tolerated the treatment reporting only "Sleepiness" (2.6/10; Mild - Very Mild) and "Eye twitching" (1.7/10; None - Very Mild) as side-effects of the rTMS treatments.
At the six-month follow-up, the good psychological functioning of Mrs A appeared preserved.

Conclusions

As it is known, the most important international guidelines regarding the management of depression[14] identify the full symptomatic remission and the return to the premorbid social functioning as a necessary goal to achieve. A partial remission should solicit the

Table I. Pre- and post-rTMS scores concerning clinical symptoms, social functioning, quality of life and level of disability.

	First session	After 6 TMS sessions	After 15 TMS sessions	After 30 TMS sessions
HAM-D	13			3
HAM-A	17			3
MADRS	18			2
BPRS	47			27
HoNOS	38			21
SAD	53	45	42	39
BDI-II	27	11	7	5
WHOQoL	61			90
WHODAS	73			37

HAM-D, Hamilton Rating Scale for Depression; HAM-A, Hamilton Rating Scale for Anxiety; MADRS, Montgomery - Asberg Depression Rating Scale; BPRS, Brief Psychiatric Rating Scale - 4.0; HoNOS, Health of the nation Outcomes Scale - Rome; SAD, Scala di Autovalutazionedella-laDepressione; BDI-II, Beck Depression Inventory - II; WHOQoL, World Health Organization Quality of Life - BREF; WHODAS, World Health Organization Disability Assesment Schedule-2.0 36 items.

expert to revise the pharmacotherapy and the overall management of the intervention. Indeed, the persistence of mild or below threshold symptoms correlates with greater rates of disability and with the chronicization of the disorder, increasing the risk for relapses or recurrences and worsening the prognosis.

Until a few years ago, besides the pharmacotherapy, the psychotherapy and the electroconvulsive therapy (either alone or combined with psychotropics) were the only strategies for the treatment of depressive disorders. Currently, even in Italy, research is paving the way for a new physical treatment approach: rTMS.

Despite the high tolerability and safety of the rTMS in elderly, the literature often lacks evidence regarding its efficacy. However, no evidence found that rTMS is not recommended to treat the depression in elderly[15]. In our case, we chose an augmentation of pharmacotherapy with a rTMS therapy due to the poor response to several types of pharmacotherapy, the absence of a cortical atrophy (which may limit rTMS efficacy) and the considerable illness duration characterized by partial remissions and residual, albeit mild, symptoms. The rTMS in combination with pharmacotherapy demonstrated its efficacy in an old patient who achieved the complete recovery with a return to the previous level of functioning.

Conflict of interest

None.

Take home messages for psychiatric care

- rTMS can be used as an augmentation strategy to the pharmacotherapy when it achieves partial responses
- In our case, pharmacotherapy augmentation with rTMS proved its efficacy in an elderly patient

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