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Case Report

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Daily Prefrontal Repetitive Transcranial Magnetic Stimulation (rTMS) Combined with Cognitive Training as a Treatment for Mild Cognitive Impairment: A Case Report

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Abstract

Background: To date, drug treatment for Alzheimer's disease (AD) has little efficacy and is of short duration. Transcranial magnetic stimulation (TMS) was developed as a non-invasive tool to activate the cortex, measure its connectivity and excitability, and assess the integrity of motor pathways. Its use in neurology, clinical neurophysiology and psychiatry has been spread from research to more strictly clinical purposes. Cognitive rehabilitation (CR) is an intervention to treat the overall well-being of the patient, to increase the reactivation of residual powers and slow down functional loss.

Objective/hypothesis: We aimed to explore the consistency and reliability of the effects of rTMS combined with cognitive training rehabilitation has positive results in Mild Cognitive Impairment.

Methods: One patient received treatment consisting of combined sessions of "repetitive" Transcranial magnetic stimulation (rTMS) rehabilitation and CR for 6 weeks, one session each day for the first two weeks (from Monday to Friday), and three days a week from the third to the sixth week.

Results: The results were encouraging, and we recorded improvements in all the tests administered.

Keywords

Transcranial magnetic stimulation; Cognitive impairment; Alzheimer's disease

Introduction

Mild cognitive impairment (MCI) is a syndrome defined as cognitive decline larger than conventional for an individual's age and education level but don't interfere prominently with activities of daily life. Prevalence in population from 3% to 19% in adults older than 65 years.

MCI has a high risk of progression to Alzheimer's disease, and it could constitute a prodromal phase of this disease [1].

The diagnostic process for MCI requires assessment of multiple cognitive functions, with particular attention to episodic and semantic memory.

MCI is an important clinical problem, always more present in the next future. The essentials of management include a thorough estimation directed at etiological determination and counselling and careful use of available therapeutics [2].

Many different studies have found a good improvement of memory skills after a set of rTMS, a single case study reported possible improved cognitive skills after application of rTMS treatment in an AD patient [3].

rTMS produces changes in cognition and behaviour. The present theories suggest that its effects may be produced by changes in focal cortical circulation, an increase in synaptic connectivity (possibly modifying the LTP phenomenon) or modulation of the cognitive reserve [4].

Furthermore, many results demonstrate that rTMS joined to Cognitive Training (CT) provides a significant improvement compared to currently available usual treatment, but also (given the reports in scientific literature) that rTMS-CT results are better than using CT or TMS alone [5,6].

The rehabilitative training consists of 45-minute sessions; the esecitate skills are memory, executive functions and thinking skills and standards-use software that enable you to record and monitor the patient's improvements.

Materials and Methods

Case study

The patient was a 57-year-old right-handed man with a low educational level, selected from the Neuropsychological center of the Hospital of Asti (Italy), without other associated comorbidities. He was diagnosed 3 years ago with probable MCI, his wife had noticed progressive difficulty in remembering recent events and spatiotemporal disorientation for about 3 years associated with word finding problems, that sometimes interfere with daily living activities. A brain mri was performed and demonstrated a single hyperintense focus in the right temporo parietal region (10 mm) on axial t2 weighted images consisting with an ischaemic area, without restriction on diffusion weighted images. A light to moderate diffuse cerebral atrophy was detected, but with no side prevalence.

The diagnostic criteria to identifying the MCI were those of the International Working Group on MCI (Stockholm 2 to 5 September 2003):

a) Exclusion of dementia (not met DSM-IV and ICD-10 criteria for the diagnosis of dementia); contemporary exclusion of normality: the patient is neither normal nor demented.

b) Presence of cognitive decline:

• Patient-reported and / or by a person close to him, confirmed by the finding of objective deficits in specific cognitive areas through appropriate neuropsychological tests and / or

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• Evidence of significant decline in time in objective cognitive tests.

c) No significant functional impact: basic activities of daily life preserved, or minimum decline of complex instrumental functions [7].

Assessment of cognitive functioning measures

To assess the patient's cognitive deficit, we used a battery of tests aimed at defining the degree of decline in cognitive function. The tests used included attentive matrices, Rey auditory verbal learning test, short story, and frontal assessment battery (FAB). Raw scores were used to process the results to allow other researchers to have comparable values.

Application of rTMS

The patient was treated by rTMS for ten stimulation sessions of 20 minutes each spread for the firsts two weeks. From the third to the sixth week was treated with 3 stimulation each week.

A MagVenture, MagPro R20 with an air cooling figure-of-eight coil was used. The rTMS was administered at 20 Hz during 5 seconds, 25 seconds between train, and 90% of the motor threshold (MT) over the left dorsolateral prefrontal cortex (DLPFC) and after over the right dorsolateral prefrontal cortex (DLPFC) per 10 minutes every session (2000 stimuli per day) with the coil angled tangentially to the head. The left and the right prefrontal cortex rTMS stimulation site was determined by measuring 5 cm anterior and parasagittal line from the hand motor area [8].

Cognitive training

The rehabilitative training was administered using the software called "Training of Cognitive Rehabilitation," an Italian version of 2012, translated from the English version by Trevor Powell and Kit Malia [9]. It included several sections, and in each section, the authors proposed various types and exercises of differing difficulties:

Section 1- mnemonic training exercises were given, many of which require a time scale within which the patient has to answer. The patient was asked to recall information, images, lists, alignments, and numbers.

Section 2- The exercises in this section offered activities on thinking skills and were often focused on understanding and linguistic competence.

Section 3- The purpose of these exercises was to improve the ability to summarize concepts or to grasp the essentials [10].

The treatment of the patient has planned 18 rehabilitation sessions, lasting 45 minutes each. We used exercises for the stimulation of memory skills, using the Training Program of Cognitive Rehabilitation. The exercises provide for storage and recall of material is that the semantic, visual and numeric. Also, they have been enhanced executive and problem solving skills, in order to encourage the choice of storage strategy and re-enactment in the moments of greatest difficulties. The patient has proved cooperative and helpful in the various sessions and has not found adverse reactions or waste even in moments of greatest frustration.

Results

The results of this study show a marked increase in performance after the rehabilitation period of combined rTMS and cognitive training.

The subject achieved improvements in both memory skills (the most impaired function) for attentional ability and frontal executive functions.

The attentional matrices test yielded a raw score of 37.5 before the training, equal to 40 after the rehabilitation (Table 1) (Figure 2). The FAB test yielded a raw score of 37.5 in evaluating before the training, equal to 40 after the rehabilitation (Table 1) (Figure 3). The short story test yielded a raw score of 2.5 in evaluating before the training, equal to 6.6 after the rehabilitation (Table 1 and Figure 1). The Rey auditory verbal learning test (immediate recall) yielded a raw score of 20.2 in evaluating before rehabilitation, totalling 31 in that after (Table 1 and Figure 4). The Rey auditory verbal learning test (delayed recall) yielded a raw score of 2.6 in evaluating before rehabilitation, equal to 5 in that after (Table 1 and Figure 5).

This study shows an increase in performance after the period of rehabilitation, combined rTMS and cognitive training.

The patient achieved improvements both as regards memory skills (the most impaired) and in attentional abilities and frontal executive functions.

Discussion

This case study reported possible improved cognitive skills after application of rTMS treatment in an MCI patient.

It is unlikely that the improvements seen were due to practice effects (PE) because also if the patient was reassessed with the same test materials, during the first assessment showed significant mnestic deficits. A long interval between testing reduced already this potential.

In addition, several studies have demonstrated that PE are largely absent in patients with dementia even for those with mild AD for short test-retest intervals, suggesting that the score improvements at time 1 were due to rTMS treatment [11].

We used the standard method of localization (5 cm method) for which lack of precision is reported [12].

Table 1: Results of evaluation before and after the training.

Test	24/10/2016	19/12/2016	24.10.16	19.12.16
Mnesic skills				
15 Rey words	Immediate recall 20,2 Delayed recall 2,6	Immediate recall 31 Delayed recall 5	(deficit) (deficit)	(borderline) (borderline)
Short Story	2,5/16	6,6/16	(deficit)	(borderline)
Attentional skills				
Attentional Matrices	37,5/60	40,0/60	(normal)	(normal)
Executive Functions				
Frontal Assesment Battery	14,4/18	15,0/18	(normal)	(normal)

A group confirmed that 5 daily sessions of HF (20 Hz) rTMS applied over the left then the right DLPFC could improve cognitive function in patients with mild to moderate Alzheimer's

disease for up to 3 months after the stimulation period [5]. The same protocol performed at LF (1 Hz) was ineffective. Finally, a third group investigated the relevance of a 6-week protocol combining daily sessions of HF rTMS delivered over various cortical sites and cognitive training also reported significant improvement on various clinical scales [4,6]. All these results favour the design of further HF rTMS trials in Alzheimer's disease, especially in combination with cognitive therapy, but they are not sufficient, to date, to warrant any recommendation, because of the absence of replicated placebo-controlled studies (with similar stimulation protocols and methods of assessment) reported from independent groups.

Figure 1: Short story test results.

Figure 2: Attentional Matrices test results.

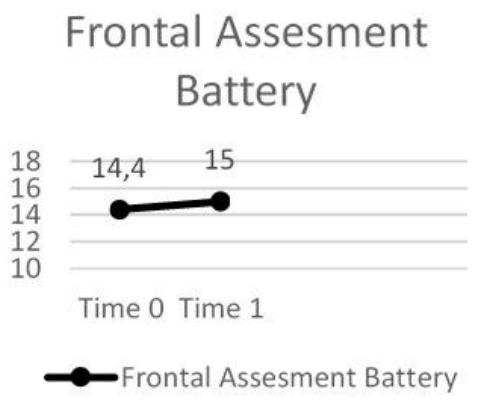

Figure 3: Frontal assesment battery.

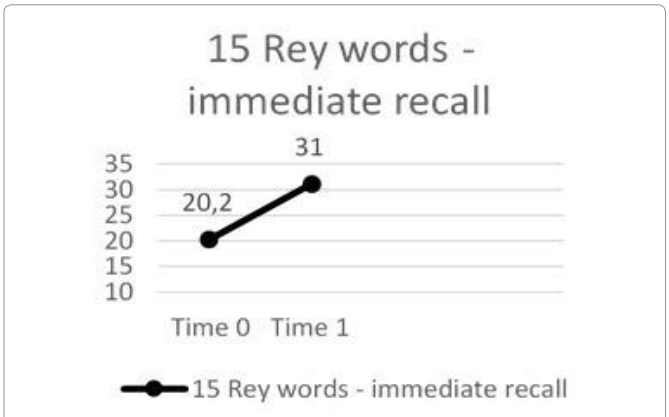

Figure 4: 15 Rey words test results (immediate recall).

Figure 5: 15 Rey words test results (delayed recall).

Conflict of Interest

The authors of the research certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

References

1. Gauthier S, Reisberg B, Zaudig M, Petersen RC, Ritchie K, et al. (2006) Mild cognitive impairment. Lancet 367: 1262-1270.
2. Feldman HH, Jacova C (2005) Mild Cognitive Impairment. Am J Geriatr Psychiatry 13(8):645–55.
3. Haffen E, Chopard G, Pretalli JB, Magnin E, Nicolier M, et al. (2012) A case report of daily left prefrontal repetitive transcranial magnetic stimulation (rTMS) as an adjunctive treatment for Alzheimer disease. Brain Stimul 5: 264-266.
4. Bentwich J, Dobronevsky E, Aichenbaum S, Shorer R, Peretz R, et al. (2011) Beneficial effect of repetitive transcranial magnetic stimulation combined with cognitive training for the treatment of Alzheimer's disease: a proof of concept study. J Neural Transm 118: 463-471.

5. Ahmed MA, Darwish ES, Khedr EM, El Serogy YM, Ali AM (2012) Effects of low versus high frequencies of repetitive transcranial magnetic stimulation on cognitive function and cortical excitability in Alzheimer's dementia. J Neurol 259: 83-92.

6. Rabey JM, Dobronevsky E, Aichenbaum S, Gonen O, Marton RG, et al. (2013) Repetitive transcranial magnetic stimulation combined with cognitive training is a safe and effective modality for the treatment of Alzheimer's disease: A randomized, double-blind study. J Neural Transm 120: 813–819.

7. Albert MS, DeKosky ST, Dickson D, Dubois B, Feldman HH, Fox NC, et al. (2017) The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimer's Dement J Alzheimer's Assoc 7: 270-279.

8. Beam W, Borckardt JJ, Reeves ST, George MS (2009) An efficient and accurate new method for locating the F3 position for prefrontal TMS applications. Brain Stimul 2: 50-54.

9. Powell TJ, Malia KB (1999) The Brain Injury Workbook: Exercises for Cognitive Rehabilitation, Italy.

10. Powell TJ, Malia KB (2012) Training di Riabilitazione Cognitiva, Erickson.

11. Cooper DB, Epker M, Lacritz L (2001) Effects of practice on category fluency in Alzheimer's disease. Clin Neuropsychol 15: 125-128.

12. Sparing R, Buelte D, Meister IG, Paus TFG (2008) Transcranial magnetic stimulation and the challenge of coil placement: a compar- ison of conventional and stereotaxic neuronavigational strategies. Hum Brain Mapp 29: 82-96.

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