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Repetitive transcranial magnetic stimulation in a case of atypical parkinsonism

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Dear Editor

Atypical parkinsonism refers to a group of neurodegenerative disorders that include corticobasal degeneration and progressive supranuclear palsy, among other conditions. These are characterised by disabling parkinsonism with poor or absent response to levodopa, as well as non-motor features [1].

Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive neuromodulation technique that has been studied as a potential treatment for Parkinson's disease [2–4] and, recently, for several other neurodegenerative conditions [5–7]. TMS has also been used to study primary motor cortex (M1) excitability and functional connectivity between brain regions in such atypical parkinsonisms as corticobasal degeneration. These studies have reported an increase in the resting motor threshold (RMT) and a planar input/output curve, indicating reduced M1 excitability. A reduction in short-interval intracortical inhibition (SICI) and a significant correlation between the amount of SICI and the degree of atrophy in M1 have also been observed. These findings suggest that M1 has a key role in the development of upper motor and cortical symptoms in these syndromes [8,9].

We report the case of a 77-year-old right-handed man with a diagnosis of non-fluent primary progressive aphasia, who developed atypical parkinsonism during follow-up and was treated with rTMS over M1, displaying an improvement in motor symptoms. The patient started with a progressive language disorder characterised by agrammatism, reduced verbal fluency, and effortful speech. Two years after onset, the patient presented a progressive asymmetrical parkinsonism syndrome, predominantly affecting the right side, with bradykinesia, rigidity, gait and postural instability, and resting and action tremor. Four years after onset, parkinsonism began to have a negative impact on the activities of daily living. MRI and ^{18}F-FDG-PET showed atrophy and hypometabolism in the left frontal and parietal lobes, involving the left motor cortex. Overall, clinical and neuroimaging findings suggest a diagnosis of primary progressive aphasia with clinical progression to corticobasal syndrome. The patient was prescribed levodopa/carbidopa (10 mg/100 mg) 4 times daily for 2 months, with no response. Due to the progression of physical disability, TMS of the M1 region was proposed. The Unified Parkinson's Disease Rating Scale (Part III), Timed 25-Foot Walk, Timed Up and Go test, and Nine-Hole Peg Test were administered at baseline, at the end of the third session, after treatment was completed and one month after the end of the treatment. The patient signed an informed consent form and the study was approved by the Ethics Committee of the Hospital Clínico San Carlos (Madrid).

Six sessions of excitatory 10-Hz rTMS were delivered over the left M1, using a Rapid^2 Stimulator (Magstim, Whitland, UK) and an air-cooled figure-of-eight coil. The target area was identified by neuronavigation (Visor2 neuronavigation software). Thirty trains of 10-Hz rTMS at 100% of RMT were delivered with an inter-train interval of 20 seconds. A total of 1500 pulses were applied in each session. No adverse events were reported. Motor scale scores are shown in Fig. 1. We also observed a decrease in the motor threshold at the end of the 6 sessions (baseline: 90%; final: 75%). Furthermore, the patient reported that he was able to perform some daily living activities that were previously lost (use of eating implements, drinking, dressing).

Primary progressive aphasia is a clinical syndrome of neurodegenerative origin. Although the initial symptom is language impairment, parkinsonism often presents during the course of the disease. In this case, clinical and neuroimaging findings were highly suggestive of corticobasal degeneration [10]. We observed a marked improvement, although transient, in motor symptoms in a patient with atypical parkinsonism. To our knowledge, this is the first report of a favorable response of motor symptoms in a patient with atypical parkinsonism treated with TMS. Motor scale scores revealed improvements in motor symptoms of parkinsonism, mainly contralateral to the stimulated brain hemisphere, but also in the ipsilateral side. Furthermore, the decrease in the motor threshold from high values to near-normal values indicates improved cortical excitability in this patient. We acknowledge that this case report has some limitations, such as the incomplete dosage of levodopa trial, and the short follow-up after the treatment with TMS.

In conclusion, this case report shows an improvement in motor function in a patient with atypical parkinsonism in the context of primary progressive aphasia through treatment with TMS. Further studies and clinical trials involving more patients are needed to study the possible application of TMS to treat motor symptoms in patients with atypical parkinsonism.

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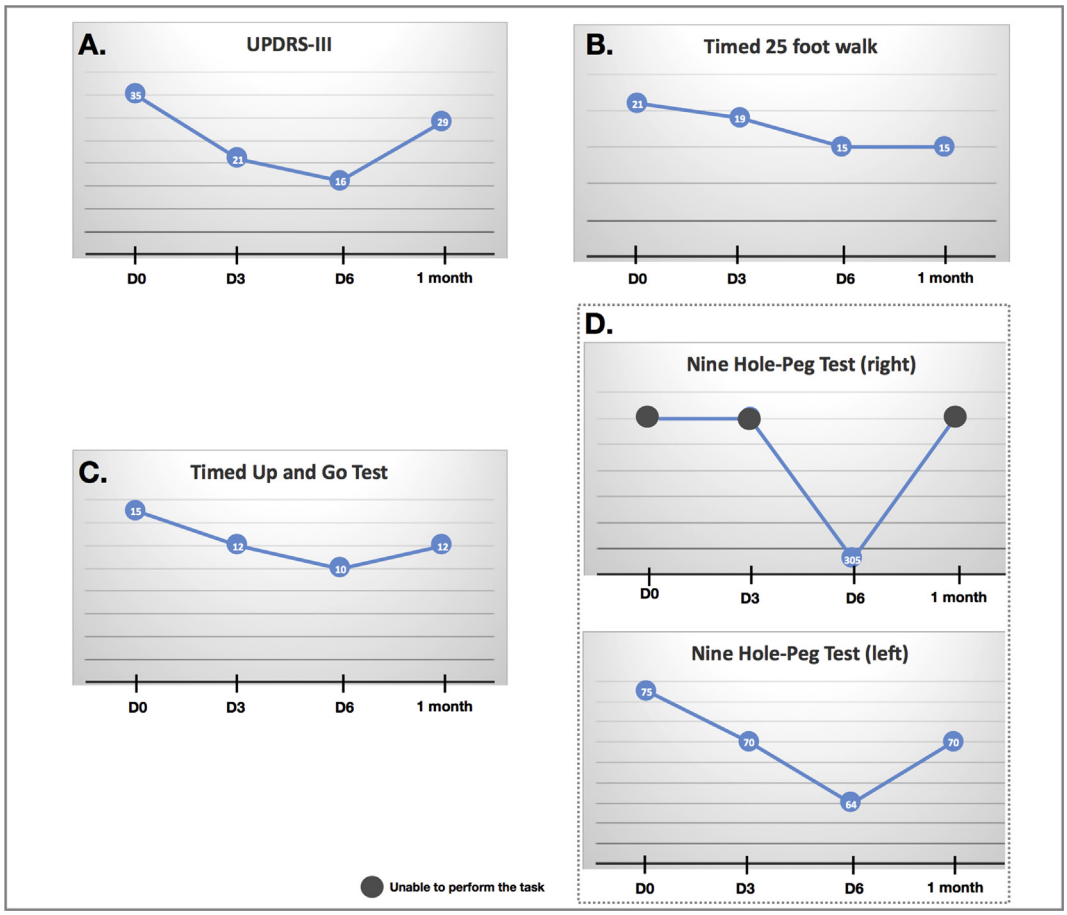

Fig. 1. Motor scale scores at baseline, after 3 and 6 sessions of TMS and one month after the end of the treatment. A. Unified Parkinson's Disease Rating Scale (Part III) (UPDRS-III). Baseline (D0): 35/68; Session 3 (D3): 21/68; Session 6 (D6): 16/68; one month after the end of the treatment: 29/68. B. Timed 25-Foot Walk. D0: 21 seconds; D3: 19 seconds; D6: 15 seconds; one month after the end of the treatment: 15. C. Timed Up and Go Test. D0: 15 seconds; D3: 12 seconds; D6: 10 seconds; one month after the end of the treatment: 12. D. Nine Hole-Peg Test. Right: D0, D3 and one month after the end of the treatment: unable to perform task; D6: 305 seconds. Left: D0: 75 seconds; D3: 70 seconds; D6: 64 seconds; one month after the end of the treatment: 70.

Declaration of conflict of interests

None.

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