

The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided. The patient described in this column gave informed consent for its publication.

## Use of repetitive transcranial magnetic stimulation in the treatment of catatonia

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A 55-year-old woman with paranoid schizophrenia had been hospitalized 17 times since age 25 for psychotic relapses. A steady state had been achieved with clozapine 400 mg/d as monotherapy for the last 5 years. Because of her husband's sudden death, the patient's condition worsened rapidly; she developed a pronounced psychosis, auditory hallucinations, spoke with "God's energy" and regularly tore off her clothes. Within 24 hours of hospitalization, she developed catatonic symptoms, including immobility and mutism evidenced by stupor. Organic causes were excluded. Laboratory results, including creatinine kinase and thyroid-stimulating hormone, were unremarkable. Fever did not occur.

The patient refused intravenous injections, so first-line therapy was diazepam 40 mg/d given orally, in case of nonresponse, followed by zolpidem 40 mg/d. Clozapine 400 mg/d (blood concentration 397 ng/mL) was kept unchanged. After 4 days of nonresponse, we considered electroconvulsive therapy (ECT) to be indicated. Owing to the necessary anesthesia and a pending court order for a constraint treatment, the patient's legal guardian initially refused ECT; however, he gave written informed consent for the patient to undergo repetitive transcranial magnetic stimulation (rTMS). Therefore, she received inhibitory rTMS of the left supplementary motor area (SMA; 8-shaped coil cool-B65, MagVenture) under the following parameters: 1 Hz, pulse width 25  $\mu$ s, 25 series of

40 pulses each (1000 pulses) at 110% of resting motor threshold.

After 3 rTMS sessions, the patient showed partial remission, with speech recovery and increased mobility. One week after completion of rTMS, her stupor gradually disappeared. She experienced no severe adverse effects during the entire course of treatment; however, the psychosis was still present. Therefore, we obtained consent to arrange treatment with ECT. Her psychotic state gradually stabilized during the ensuing 6 months, and she was entirely remitted at discharge.

Our patient's case suggests that inhibitory rTMS of the SMA may have compensated the pronounced motor component of catatonia. This further underscores the explanatory model of SMA hyperactivity,<sup>1</sup> although it is challenging to determine how rTMS alone was responsible for symptom relief. The treatment outcome could also have been a spontaneous improvement or delayed effect of medication.<sup>1</sup>

Benzodiazepines are the most widely studied treatment for catatonia and are usually recommended as first-line therapy.<sup>2,3</sup> If symptoms do not respond substantially, ECT is appropriate as a first-line therapy.<sup>4-7</sup> Patients with chronic schizophrenia are often less responsive to first-line treatments;<sup>8-11</sup> therefore, rTMS has received increased attention in recent years, and is even discussed as a treatment alternative to ECT.<sup>12,13</sup>

Remarkably, rTMS has the potential to treat various symptoms of schizophrenia. Studies have reported successful treatment of auditory hallucinations with inhibitory rTMS over the left temporal lobe.<sup>14,15</sup> For negative symptoms, improvement has been reported with high-frequency rTMS over the left dorsolateral prefrontal cortex.<sup>16,17</sup>

The successful use of rTMS for catatonia has been reported in 9 cases.<sup>1</sup>

Most reports showed an impressive effect. In this context, the practical evidence for the use of rTMS to treat catatonia is particularly noteworthy, especially in consideration of the assumed mechanism.

Recent reviews have highlighted the hyperactivity of premotor areas as an important pathophysiology of catatonia,<sup>13</sup> essential in addressing motor system pathology in schizophrenia. Impairments in neural maturation during the development of schizophrenia indicate a possible dysfunction in cerebral motor networks in catatonia. Hyperactivity within the presupplementary motor area (preSMA) and SMA seems to be the most likely causative factor for catatonia.<sup>13,18,19</sup> Therefore, inhibition of the SMA could improve catatonia in critically ill patients.<sup>19</sup> Based on these findings, the efficacy of rTMS could be improved, especially in patients who do not respond to other treatments.

Although most studies have reported a relatively small number of cases, rTMS may be more effective, especially in cases of nonresponse in catatonia in patients with schizophrenia.

These new developments highlight the need to define the optimal stimulation target and procedure when using rTMS to treat catatonia. More research is required to enhance rTMS efficacy, increase the duration of its beneficial effect, test new therapeutic strategies, and begin a systematic exploration of prefrontal regions as targets for rTMS in psychomotor slowing due to catatonia.

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