Case Report and Case Series

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Long-term intermittent low-frequency repetitive transcranial magnetic stimulation effectively controls seizures in two drug-free adolescent patients

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Abstract

Recently, repetitive transcranial magnetic stimulation (rTMS) has been widely used for treating neurological and psychiatric diseases. Low-frequency rTMS is used to effectively control the occurrence of seizures, including medication-refractory epilepsy and cortical dysplasia or neocortical epilepsy. However, there have been no reports on the effects of long-term rTMS on epilepsy. We observed the clinical effects of long-term rTMS in two drug-free adolescent epileptic patients with a preference for non-drug therapy. The two drug-free adolescent patients, who underwent intermittent low-frequency rTMS treatment for 36 weeks, obtained effective control of seizures (including episode and severity). However, a systematic study is required to confirm our observations.

Keywords

Epilepsy, repetitive transcranial magnetic stimulation, low frequency, cortical dysplasia, adolescent, convulsion, seizure

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Introduction

Low-frequency repetitive transcranial magnetic stimulation (rTMS) is effective for controlling epilepsy.[1] rTMS is often delivered for a few days to up to 2 weeks.[2] However, there have been no reports on the effect of long-term rTMS on epilepsy. There is evidence that 2 weeks of rTMS achieves a remarkable effect that lasts for up to 8 weeks.[3] In this report, we focused on clinical effects of long-term rTMS on epileptic patients with a preference for non-drug therapy. We performed multiple 2-week treatment courses with 1- or 2-week intervals (Figure 1a). We used intermittent 0.5 Hz rTMS for 36 weeks in two drug-free epileptic patients who could make frequent hospital visits.

Case report

Case 1

Patient 1 was a 16-year-old male high school student who experienced three seizures that always occurred in the afternoon at school because of a poor night of sleep before intervention. At his second seizure, he was diagnosed with focal cortical dysplasia-related epilepsy on the basis of 24-hour, abnormal, dynamic electroencephalography (EEG) (Figure 1b) and cranial magnetic resonance imaging (MRI) (Figure 1c).[4] After the patient and his family provided signed informed consent, 0.5 Hz rTMS was applied over the epileptic focus, which was approximately localized 7.5 cm vertically up the outer ear channel based on his MRI, with a 50% resting motor threshold. The patient could not tolerate more than 50% intensity of stimulation at the site. A commercially available magnetic stimulator with a 70-mm figure-eight coil (CCY-IV; YIRUIDE Co. Ltd., Wuhan, China) (Figure 1d) and low-frequency rTMS procedure was used for both patients with the following parameters: 0.5 Hz, 10 s of stimulation, 1-s interval, and a total of 1200 pulses for each day (from Monday to Saturday). During treatment, the patient experienced one seizure because of pressure from his final exam (Figure 1a). However, his classmates reported that his convulsion was mild and the episode lasted for a much shorter time than observed previously. The patient received 10 treatment courses (2 weeks each) and a subsequent 16-week follow-up. Treatment was performed for 36 weeks. No obvious adverse events were observed.

Case 2

Patient 2 was a 21-year-old female university student who had a history of febrile convulsions at the age of 2 years. Before rTMS, she had four seizures that always occurred between 12:00 AM and 1:00 AM with similar symptoms. Unfortunately, an enhanced brain MRI and several 24-hour dynamic EEGs showed no obvious abnormalities. Therefore, she was initially diagnosed with sleep-related epilepsy.[5] After she provided signed informed consent, rTMS treatment was performed (Figure 1a). In the absence of a defined epileptic focus, bilateral hand M1 regions were chosen as the stimulus sites because they are representative of large cortical motor areas and are the common motor output pathways. rTMS at 0.5 Hz was delivered at 80% resting motor threshold at 600 pulses for each site. During the interval as indicated in Figure 1a, the patient experienced a seizure at approximately midnight following a meal with a large amount of crab meat and spicy food at home. Observers indicated that she only gasped for breath with mild limb convulsion for a shorter time than observed previously. The patient received the same treatment schedule as did patient 2. During follow-up, no seizures or major adverse events occurred.

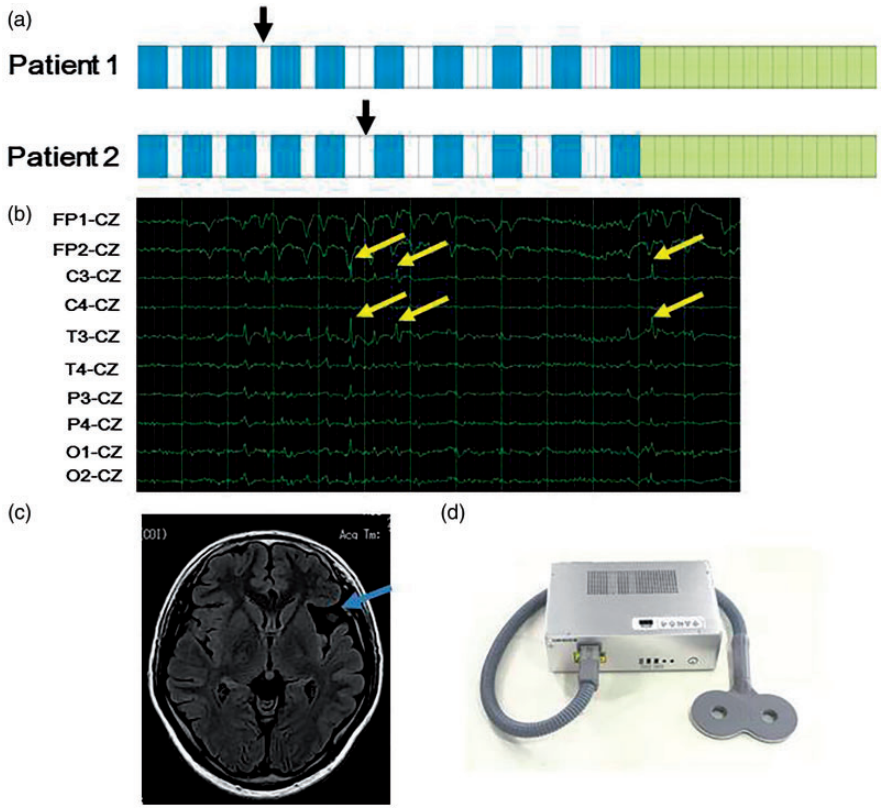

Figure 1. (a) Treatment procedure for the two patients using a commercially available magnetic stimulator (CCY-IV; YIRUIDE Co. Ltd.). Each small lattice represents 1 week. Blue small lattices represent rTMS treatment. White squares indicate the treatment interval. Green small lattices represent the follow-up. Arrows indicate the occurrence of a seizure. The entire observation period consisted of 10 treatment courses and a subsequent 16-week follow-up (total of 52 weeks). There was a 1-week interval during the initial four courses. This interval was changed to a 2-week interval considering formation of long-term plasticity and more free time for the patients. (b) Abnormal electroencephalogram from patient 1. Arrows indicate abnormal epileptic waves. (c) Brain magnetic resonance imaging (fluid-attenuated inversion recovery sequence) of patient 1. The arrow indicates the epileptic focus. (d). A home-use convenient 1-Hz rTMS device with a replaceable coil is shown, but it is not approved by the Chinese FDA. rTMS, repetitive transcranial magnetic stimulation

Discussion

Our two cases were drug-free adolescent epileptic patients. In patient 1, inhibitory rTMS stimulation was delivered to the epileptic focus to produce an anti-epileptic effect. However, in patient 2 without an obvious epileptic focus, inhibitory rTMS over the bilateral hand M1 area appeared to cause a considerable anti-epileptic affect. A possible explanation for this finding is that bilateral inhibitory rTMS over the output of common motor pathways might have resulted in extensive cortical inhibition and thus reduced the occurrence of seizures. Our two cases were heterogeneous and our

rTMS parameters were also different. Therefore, we need to recruit homogeneous patients and apply the same parameters to confirm the anti-epileptic effect of long-term rTMS in future systematic work. Moreover, the two patients presented with a low frequency of seizures. Therefore, a limitation is that our observation period was not long enough. Consequently, we need to extend the stimulation time and follow-up to a longer period in future systematic research. A challenge for patients undergoing long-term rTMS is frequent hospital visits. Therefore, a small and safe device for home use needs to be developed. To this end, we developed a portable rTMS apparatus for home use under cooperation with YIRUIDE Co. Ltd. (Figure 1d), which offers new hope for epilepsy treatment. However, approval by the Chinese Food and Drug Administration is still being obtained, and the effectiveness of this portable rTMS apparatus requires further clinical trials.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Ethics statement

This work was approved by the ethics committee of the Integrated Hospital of Traditional Chinese Medicine, Southern Medical University. Written informed consent was obtained from the patients or their parents.

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