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Motor cortex transcranial magnetic stimulation to reduce intractable postherpetic neuralgia with poor treatment response: evidence from two cases

huan wang, yuzhong hu, Che xian wei, liang yu

Abstract

BACKGROUND

Post herpetic neuralgia (PHN) is a typical neuropathic pain condition that appears in the lesioned skin regions following the healing of shingles [1]. The pain condition tends to persist, which is often accompanied by negative emotions (e.g. anxiety, depression) and substantially reduces the quality of life [1]. In addition to analgesia (e.g. pregabalin 、gabapentin), nerve radiofrequency technology is a effective treatment for intractable postherpetic neuralgia [2,3]. However, there is still a significant portion of patients who do not benefit from this treatment. As a non-invasive form of brain stimulation, repetitive transcranial magnetic stimulation (rTMS) targeting the motor cortex (M1) is able to reduce neuropathic pain with grade A evidence [4].

CASE SUMMARY

Here we reported two cases whereby motor cortex rTMS was used to treat intractable postherpetic neuralgia who did not respond to initial drug and radiofrequency therapies. Moreover, we specifically investigated rTMS efficacy at three months following treatment [4].

CONCLUSION

Here we reported two cases whereby motor cortex rTMS was used to treat intractable postherpetic neuralgia who did not respond to initial drug and radiofrequency therapies. Moreover, we specifically investigated rTMS efficacy at three months following treatment [4].

INTRODUCTION

Post herpetic neuralgia (PHN) is a typical neuropathic pain condition that appears in the lesioned skin regions following the healing of shingles [1]. The pain condition tends to persist, which is often accompanied by negative emotions (e.g. anxiety, depression) and substantially reduces the quality of life [1]. In addition to analgesia (e.g. pregabalin、gabapentin), nerve radiofrequency technology is a effective treatment for intractable postherpetic neuralgia [2,3]. However, there is still a significant portion of patients who do not benefit from this treatment.

As a non-invasive form of brain stimulation, repetitive transcranial magnetic stimulation (rTMS) targeting the motor cortex (M1) is able to reduce neuropathic pain with grade A evidence [4]. Here we reported two cases whereby motor cortex rTMS was used to treat intractable postherpetic neuralgia who did not respond to initial drug and radiofrequency therapies. Moreover, we specifically investigated rTMS efficacy at three months following treatment [4].

CASE PRESENTATION

Chief complaints

The first case was a 65-year female with persistent pain for six months in the left thorax and back (T5/T6) after herpes zoster. Her pain was characterized by persistent tingling and burning sensations, with a visual analog scale (VAS) score of 8. She was prescribed pregabalin 150mg BID, the patient did not want to continue increasing the dose of the drug because of the side effect of dizziness, and received a spinal nerve radiofrequency surgery. However, there was no clear analgesia following these treatments.

History of present illness

The second case was a 75-year female presented with left lower back pain (T11/12) for four months after herpes zoster. She was prescribed gabapentin 0.6g TID, the patient had renal insufficiency so the drug dose was not increased further, as well as a spinal nerve radiofrequency surgery. The patient reported slight pain relief after treatment but still with a VAS score of 6.

History of past illness

Patients provided a written informed consent for rTMS treatment. rTMS was delivered to the contralateral motor cortex once daily on ten consecutive days using an RT-50 stimulation system connected to a figure-of-eight coil (Sichuan Junjian Wanfeng Medical Equipment Co.).

Personal and family history

Each rTMS session delivered 3,000 pulses at 10 Hz with 5-sec trains and 25-sec intervals at 100% resting motor threshold (RMT). Patients were assessed at baseline, the fifth treatment, the end of treatment, two weeks following treatment, one month after treatment, and three months after treatment. Clinical assessment included VAS, McGill Pain Questionnaire (McGill), Pittsburgh Sleep Quality Index (PSQI), Hamilton Depression Scale (24 items), Hamilton Anxiety Scale (17 items), Mini-mental State Examination (MMSE) and Perceived Deficits Questionnaire-Depression (PDQ-D). Drug dose remains the same as before this treatment.

Physical examination

no special

Laboratory examinations

no special

Imaging examinations

no special

FINAL DIAGNOSIS

Post herpetic neuralgia

TREATMENT

rTMS was delivered to the contralateral motor cortex once daily on ten consecutive days using an RT-50 stimulation system connected to a figure-of-eight coil (Sichuan Junjian Wanfeng Medical Equipment Co.). Each rTMS session delivered 3,000 pulses at 10 Hz with 5-sec trains and 25-sec intervals at 100% resting motor threshold (RMT).

OUTCOME AND FOLLOW-UP

Both patients demonstrated a promising analgesia effect, with pain experience changing from severe to mild-to-moderate level. There was also a protect effect on negative emotions, especially in the first case with an initial mild depressive symptom. We also observed a significant improvement in sleep quality in both cases. More importantly, the protective effects of motor cortex rTMS lasted for three months following treatment. Here we reported two cases whereby motor cortex rTMS was able to significantly reduce intractable postherpetic neuralgia who did respond to first-line drug and radiofrequency therapies. Drugs and radiofrequency therapies are first-line treatments in clinical settings for postherpetic neuralgia [5]. Our results indicated that motor cortex rTMS could be considered when the pain become intractable and/or the patent does not seem to benefit from regular drug and radiofrequency therapies. Some studies have shown that rTMS treatment is safe for patients with PHN and has better efficacy at 10HZ [6], which is the frequency we chose for these two patients. More importantly, our results indicated a long-term analgesia for three months. Most previous studies have shown that pain relief from neuroplasticity can last for several days, usually a week to a

month, after transcranial magnetic stimulation treatment [4]. This long-term three-month effect was potentially associated with a relatively large dose of pulses in daily treatment [7]. Previous studies tended to deliver ~1500 daily pulses whereby the number of pulses was doubled in these two cases.

DISCUSSION

TMS is a non-invasive stimulation technique that produces analgesic effects similar to those of invasive techniques by targeting rTMS to M1 [8]. High-frequency rTMS delivered to M1 areas obtains analgesic effects by modulating several distant brain regions involved in the processing or control of nociceptive information. This pain relief can last for several weeks beyond the duration of stimulation, especially during repetition, and may be related to the process of long-term synaptic plasticity [9]. rTMS is now mainly used for the treatment of neuropathic pain and requires a trained physician or nurse to perform this procedure, which is a technique that can be widely used. The most common side effects are dizziness and scalp discomfort, which are transient and disappear after the treatment.

The mechanism of rTMS analgesia remains an open question. There is evidence that motor cortex rTMS could drive top-down pain modulation [10]. In addition, motor cortex stimulation is also able to activate cortical and subcortical regions (e.g. insular, cingulate cortex) involved in the processing of affective-emotional aspects of pain [11]. In either case, cortical and/or subcortical responses to rTMS may help explain the poor response to radiofrequency therapies, in which spinal nerves may not be well damaged by the surgery or become recurrent following surgery.

We have also observed a promising effect on negative emotions in these two cases. This is in line with the findings of a study that rTMS treatment had a significant effect on the whole brain functional network in PHN patients with inhibited sensory-motor functions and improvements in mood, cognitive, emotional and memory functions [12]. RTMS has been approved by the U.S. Food and Drug Administration to treat depression by targeting the dorsolateral prefrontal cortex. Recent studies have also tried

to manage comorbid pain and depression with rTMS in one setting[13]. In addition, we provide interesting findings that motor cortex rTMS is able to improve sleep quality in the two cases, which has been rarely investigated compared to evidence on depression and neuropathic pain[14-15]].

CONCLUSION

To conclude, we provide two cases whereby motor cortex rTMS is able to reduce pain sensations in intractable postherpetic neuralgia when first-line drug and radiofrequency therapies had no clear benefits. These findings need to be further validated in large, randomized controlled trials.

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