

THE EFFICACY OF HIGH-FREQUENCY REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (RTMS) ON FUNCTIONAL (PSYCHOGENIC) MOVEMENT DISORDERS

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INTRODUCTION

Functional movement disorders (FMD) are defined as abnormal involuntary movements that are incompatible with a known neurological cause and neuro-anatomy. Although the term “psychogen” was widely used (Morgante et al.2013) as it was known that it was accompanied by psychological factors, the non-stigmatizing term “functional disorder” began to be used later (Edwards et al. 2012).

FMD is often difficult to diagnose. It is among the most difficult disorders to treat, as its pathophysiology is not fully understood and there is no consensus on the best therapeutic approach. Gait disorders are seen in 8-10% of patients with FMD (Sudarsky 2006). It is often possible to make the diagnosis on the basis of distinguishing features and observation of gait. Although there may be some typical findings that mimic neurological diseases, there are often neurological symptoms that are incompatible with knowledge of anatomy or physiology (Sadock B & Sadock 2011). Like all other functional disorders, gait disturbances can occur acutely following a psychosocial stressor. Some clues such as fluctuating course of symptoms, abnormal slowness of movements, sudden bending of the knees and psychogenic Romberg are helpful in differential diagnosis (Van Rooijen et al. 2011, Gilmour et al. 2020). These patients often refer to departments other than psychiatry because of their imitating features of other neurological diseases, which delays the diagnosis and treatment process and may adversely affect the prognosis. The outcome is often poor, as only half of patients recover after 3 years of follow-up (Thomas et al. 2006, Bennett et al. 2021).

Transcranial magnetic stimulation (TMS) is a non-invasive neuromodulation technique based on Faraday’s principle of electromagnetic induction (Lefaucheur et al. 2014). It works via magnetic coils placed on the scalp that cause electrical stimulation of the underlying brain tissue

(Rossini et al.2015, Agius, M & Agius MA 2023). If electromagnetic pulses are transmitted repetitively (rTMS), it is possible to achieve permanent modulation of neuronal excitability in targeted cortical structures (Vale-ro 2017, Gereš et al. 2022). The use of rTMS has been investigated for a variety of neurological and psychiatric disorders, including Parkinson’s disease, depression, and other neuropsychiatric disorders, and is a US Food and Drug Administration (FDA)-approved treatment for drug-resistant depression worldwide (Shah et al. 2015).



Picture 1: Sudden bending of right knee while walking

The International Federation of Clinical Neurophysiology (IFCN) reported that it is a safe and well tolerated treatment option if TMS parameters are kept within certain limits (Rossi et al. 2009).

In this study, we present a 24-year-old female patient who was treated with a 10-week high-intensity, high-frequency (10 Hz) rTMS protocol over the left motor cortex and could hardly walk because of her right knee flexion. We found a significant reduction in the frequency and intensity of involuntary movements and the associated disability burden. Written consent was obtained from the patient to share this case report.

CASE PRESENTATION

A twenty-four-year-old, single female patient was admitted to our hospital in May 2017 with complaints of difficulty in walking, imbalance, weakness, malaise, inability to enjoy life, and suicidal thoughts. The patient stated that she had difficulty walking after a riding accident. Since the patient suddenly developed a significant instability in the right knee after the accident, the right knee was bent with each step and walked with difficulty. She had several torn ligaments in the right leg due to her self-harming behavior. The patient was admitted to the service for differential diagnosis and it was decided to follow up. In addition to routine examinations, no organic cause was found as a result of magnetic resonance imaging (MRI), electroencephalography (EEG) and electromyography (EMG), examinations. The patient's motor development is normal. It was learned that there was no history of head trauma or seizure.

There was no known psychiatric or neurological disease in the first-degree relatives of the patient. In the mental state examination; the patient's clothing was compatible with her socioeconomic status, and her self-care was sufficient. The patient was helpful and cooperative throughout the interview. Her attention was normal. Speech rate and amount were natural. Her mood was depressed, her affect was tearful. Her thought content included depressive themes including guilt, hopelessness and suicidal thoughts. Her assessment and judgment of reality were normal.

Comprehensive pharmacotherapy, long-term psychotherapy, skill, ego therapy and physiotherapy and sports therapy were used in the treatment, but the patient's complaints continued.

Finally, in March 2018, we decided on another treatment modality, rTMS, due to the very high level of suffering and worsening of the patient's condition. The treatment lasted a total of 10 weeks. During treatment,

a safe gait pattern was developed for the patient by a physical therapist. She also took regular physiotherapy sessions after treatment to develop the correct movement pattern in the right leg. Stimulation took place in the left parietal region of the motor cortex of the right leg. We wanted to achieve an exciting effect and therefore we applied a high frequency of 10 Hz, 20 repetitions and 100 pulses.

Especially the first rTMS session, in which the patient's long-disordered gait started to improve, was very important for the continuation of the treatment and created excitement in the treatment team. The patient became dissociative from time to time at the beginning of the treatment. As a result, movement appeared to normalize temporarily. The stability of the affected knee increased significantly. However, we can say that this effect is not permanent, but a serious improvement is seen.

DISCUSSION

Untreated, FMDs become chronic, causing disability and suffering (Jankovic & Sherer 2014). However, the evidence for optimal treatment choice in these disorders is limited. In patients with resistant symptoms, a combination of psychotherapy and physiotherapy and reprogramming of the abnormal movement pattern (ie, motor reprogramming) is recommended. Cognitive-behavioral therapy, antidepressant, hypnosis and acupuncture may also be effective (Kroenke & Swindle 2000). When these treatment modalities fail or are not tolerated by the patient, non-invasive brain stimulation has been proposed as a treatment option (Nicholson & Voon 2016, Naro et al. 2019).

However, despite all these treatment options, 37% to 83% of patients continue to experience symptoms 2 to 16 years after diagnosis, as none of the treatment approaches suggested above provide any benefit in some patients (Crimlisk et al. 1998, Binzer & Kullgren 1998; Sudarsky 2006). In these situations, TMS may be a therapeutic option in addition to standard clinical care (Garcin et al. 2013, Garcin et al. 2017).

When we examine the studies investigating the effectiveness of TMS on movement disorders, the results are similar to our study. Nicholson & Voon's study with 179 patients with FND reported that 162 (91%) of the patients had "recovery" after TMS (Nicholson & Voon 2016). In the study conducted by Garcin et al., 75% (N=18) of 24 patients had their severity scores reduced by half immediately after low-frequency repetitive TMS application on the motor cortex, and motor symptoms were completely resolved in one-third (N=6) of them (Garcin et al. 2013).

In this case, we applied a high frequency rTMS protocol such as 10 Hz, 20 repetitions and 100 pulses. There appears to be a large heterogeneity in the methodology of studies investigating the effectiveness of rTMS on FMD. Some of the studies used “low-frequency” (≤ 1) (Chastan et al. 2009, Parain & Chastan 2014) stimulation parameters, which were considered to be inhibitory, while others used high-frequency (≥ 5 Hz) stimulation parameters (Schönfeldt et al. 2006, Shah et al. 2015). However, when the literature is reviewed, it is noteworthy that all TMS protocols that have proven effective in FMDs use stimulation intensities above the motor threshold (Schönfeldt et al. 2003, Pollak et al. 2012, Nicholson & Voon 2016). Only one study used TMS at subthreshold intensity (90% of motor threshold) in six patients with FMD and was found to be ineffective (Shah et al. 2015). Therefore, the suprathreshold intensity of TMS may be an essential prerequisite for efficacy. During suprathreshold magnetic stimulation sessions, patients experience unexpected stimulation-induced movement in their affected limbs; this may enable the patient to recognize that the motor system is functioning properly, thereby allowing the brain to “relearn” or “reprogram” a normal movement pattern (Edwards et al. 2014).

rTMS may be more effective in combination with other treatment modalities such as physiotherapy and cognitive behavioural therapy (CBT). For example, physical therapy immediately after TMS can quickly build on any initial symptomatic gain (especially in cases of movement disorder for which physical therapy alone was not previously possible). Having a CBT therapist during the TMS session can be helpful. In this case, a safe gait pattern was developed by a physical therapist during the patient’s treatment and had him receive a sports or physiotherapy session after each rTMS to develop the correct movement pattern (Pollak et al. 2014, Nicholson & Voon 2016).

There is an accumulated evidence base supporting rTMS as a safe, well tolerated, and possibly effective treatment for a wide range of FND symptoms. However, randomized controlled studies are needed to develop optimal protocols to help determine whether TMS is an effective and safe treatment that can be put into routine clinical use, and to define the types of patients in which the treatment may be most effective. For example, there are still uncertainties as to whether patients should be explicitly told in terms of rTMS intensity and frequency, number of beats and area targeted, and any placebo effects.

As a result, differences in data analysis methodology lead to differences in the level of evidence between systematic reviews and meta-analyses. While rTMS has been approved for “safety and efficacy” in a variety of

therapeutic indications by regulatory agencies such as the FDA, significantly larger, rigorously designed studies are still needed, particularly including longer stimulation sessions.

Limitations ve Recommendations

The present study has some limitations. The absence of a sham control group, short follow-up, and placebo effect limit the power of the study’s results. The exact cause of the effect of rTMS is not yet known. The therapeutic benefit of rTMS may be due to its cognitive-behavioral or cortical neuromodulation effect, or both. However, the underlying mechanisms deserve further investigation. However, even if placebo accounts for most of the treatment effect, this does not mean that rTMS should not be used to promote recovery in a disease that has few proven treatments and for which chronic severe disability is common.

CONCLUSION

Following the promising results of this case report, it seems reasonable to confirm the efficacy and mechanism of action of high-frequency rTMS in larger samples of patients with FMD, as the management of such complex and highly prevalent disorders is a safe and valuable approach. This study underlines the importance of rTMS in functional movement disorders and provides motivation for more comprehensive studies to be carried out in the future.

Ethical Considerations: Does this study include human subjects? YES

Authors confirmed the compliance with all relevant ethical regulations.

Conflict of interest: No conflict of interest

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