

Treating Spindling Excessive Beta with Inhibitory rTMS: A Case Study

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Abstract

The present case report investigated whether 1 Hz repetitive transcranial magnetic stimulation (rTMS) could reduce the symptoms and electrophysiological variables associated with spindling excessive beta (SEB) located in the frontal lobes. A 9-year-old patient who displayed emotional reactivity and impulsivity was evaluated using a computerized assessment of cognitive functioning and a quantitative electroencephalogram (qEEG) which displayed SEB. The patient was treated for 5 days with a 1 Hz rTMS protocol using a deep TMS coil. Improvements in both electrical power and cognitive measures were observed after a post qEEG. This report concludes that more research is needed to evince that inhibitory rTMS can reduce power in SEB and improve symptoms of over arousal.

Keywords: Spindling Excessive Beta, Repetitive Transcranial Magnetic Stimulation, 1 Hz rTMS, quantitative EEG

Introduction

rTMS is an FDA approved treatment method for depression and obsessive-compulsive disorder (OCD). The patient receives repeated magnetic pulses to the brain to improve symptoms. rTMS protocols for both depression and OCD are stimulatory, increasing cortical excitability at the assigned treatment areas of the left dorsolateral prefrontal cortex for depression and the medial prefrontal cortex/anterior cingulate cortex for OCD. To achieve stimulation, magnetic pulses are delivered at fast speeds (10-60 Hz). rTMS can also achieve cortical inhibition when delivered at a slow speed of 1 Hz. Many studies have concluded that 1 Hz rTMS decreases cortical excitability [1-3]. Evidence includes 1 Hz rTMS suppressing the amplitude of motor evoked potentials (MEP) and reducing the amplitude of certain ERP (evoked related potential) components [1-3]. This form of slowing of brain activity treatment can be beneficial to individuals who have an over aroused brain profile.

An electroencephalogram (EEG) neurological sign of over arousal is SEB. SEB is characterized in EEG as fast brain waves (also known as beta waves) but with a spindle morphology, often with “an anterior emphasis” [4]. Normal beta waves are “concerned with behaviors and actions such as talking, problem solving, judgement, and decision making” and usually fall into the frequency range of 13-30 Hz [5]. However, SEB is considered pathological in comparison to regular EEG beta activity. According to Arns et al., “frontal SEB might be regarded as a state marker caused by sleep maintenance problems, with concurrent impulse control problems” [6]. Considering that sleep maintenance, impulse

control, and SEB are all symptoms of an over aroused brain profile, this paper explores whether 1 Hz inhibitory rTMS can help a 9-year-old patient reduce these symptoms. Whether anxiety can be reduced using rTMS (mainly 1 Hz rTMS) has been studied extensively but no research has looked at the effects of inhibitory rTMS on SEB [7-9].

The authors of this paper hypothesize that 1 Hz rTMS will not only reduce symptoms associated with SEB for this patient but may also reduce the electrical power which is abnormally high in patients with SEB.

Methods

Participant

The patient chosen for this study was a 9-year-old girl who displayed symptoms of anxiety, emotional reactivity, and impulsivity. A qEEG analysis performed on the patient showed cortical over-arousal including frontal lobe SEB. Since the patient exhibited symptoms of anxiety and overarousal, a 1 Hz inhibitory TMS protocol was chosen. The parents of the patient provided informed consent for this treatment approach.

Procedure

The patient's qEEG data was collected on the Mitsar 201 Channel EEG Amplifier using the ANT Neuro wave guard connect EEG cap. The qEEG data was recorded using the “WinEEG” software program which used a high pass filter of 0.5 Hz and a low pass filter of 50 Hz. Data gathered for the qEEG was recorded in the “linked

ears” montage and was analyzed through the “WinEEG” software program. The data was collected both pre and post treatment. TMS was conducted using the Brains Way “Deep TMS H7-coil” which has been approved by the FDA for the treatment of both OCD and Depression.

One week of 1 Hz inhibitory TMS was conducted on the patient. The motor threshold was found according to Brains Way standards and was found to be 75% “intensity”. Intensity is the variable of magnetic power output used in TMS to stimulate/inhibit the brain. The inhibitory TMS protocol used on the patient was 80% of the “intensity” (60% power) at a speed of 1 Hz for 900 pulses. The session would last for 15 minutes, and the patient completed 5 daily sessions consecutively for a one-week total treatment period before conducting a post qEEG.

Data Collection and Analysis

Data was collected through “WinEEG” both numerically and graphically. After collecting a pre and post treatment eyes closed (EC) and eyes opened (EO) qEEG, the data was corrected for artifacts using independent component analysis methods and then analyzed. The variable of power “microvolts squared” (μv^2) was assessed for changes in the high beta frequencies of 15-18 Hz (beta 1), 18-25 Hz (beta 2), and 25-30 Hz (beta 3) between the patients’ pre and post qEEGs. The brain areas of interest were the frontal lobes at locations identified by the 10-20 international system of

electrode placement. These locations were “F3” (left frontal cortex), “FZ” (midline frontal cortex), and “F4” (right frontal cortex). A cognitive test called the “Cambridge Brain Sciences” (CBS) was used to assess the patient both pre and post treatment in various cognitive domains such as visuospatial working memory, spatial short-term memory, working memory, episodic memory, mental rotation, visuospatial processing, deductive reasoning, planning, verbal reasoning, verbal short-term memory, attention, and response inhibition. There were 12 tasks in total and the patient’s scores were compared to test norms in the age ranges of 8-9 years old. The raw scores were scaled to compare with a distribution of standard scores with a mean of 100 and a standard deviation of 15. The CBS cognitive assessment has demonstrated both high validity and reliability and been used in numerous studies.

Results

After the 1 Hz rTMS treatment, power in the patient’s qEEG decreased in various degrees at F3, FZ, and F4 in the EC condition as shown in Table 1 and at F3 and FZ in the EO condition as shown in Table 2. The power increased in all the beta/high beta frequency bands at the F4 location during the EO condition. These changes are displayed in both Figure 1 (EC condition) and Figure 2 (EO condition) and the power of the beta frequencies are represented by the light blue (15-18 Hz), dark blue (18-25 Hz), and fuchsia (25-30 Hz) colors.

Table 1: Decreases in Frequency Ranges of Beta Power between Pre and Post Treatment (Eyes Closed)

Site (eyes closed)	15-18 Hz (μv^2)	18-25 Hz (μv^2)	25-30 Hz (μv^2)
F3	-1.83	-8.15	-2.13
FZ	-1.29	-2.37	-0.33
F4	-1.65	-5.04	-0.15

Note. μv^2 : Microvolts Squared

Table 2: Decreases and Increases in Frequency Ranges of Beta Power between Pre and Post Treatment (Eyes Opened)

Site (eyes closed)	15-18 Hz (μv^2)	18-25 Hz (μv^2)	25-30 Hz (μv^2)
F3	-0.91	-7.37	-2.13
FZ	-0.22	-3.61	-0.33
F4	+1.10	+4.02	+3.23

Note. μv^2 : Microvolts Squared

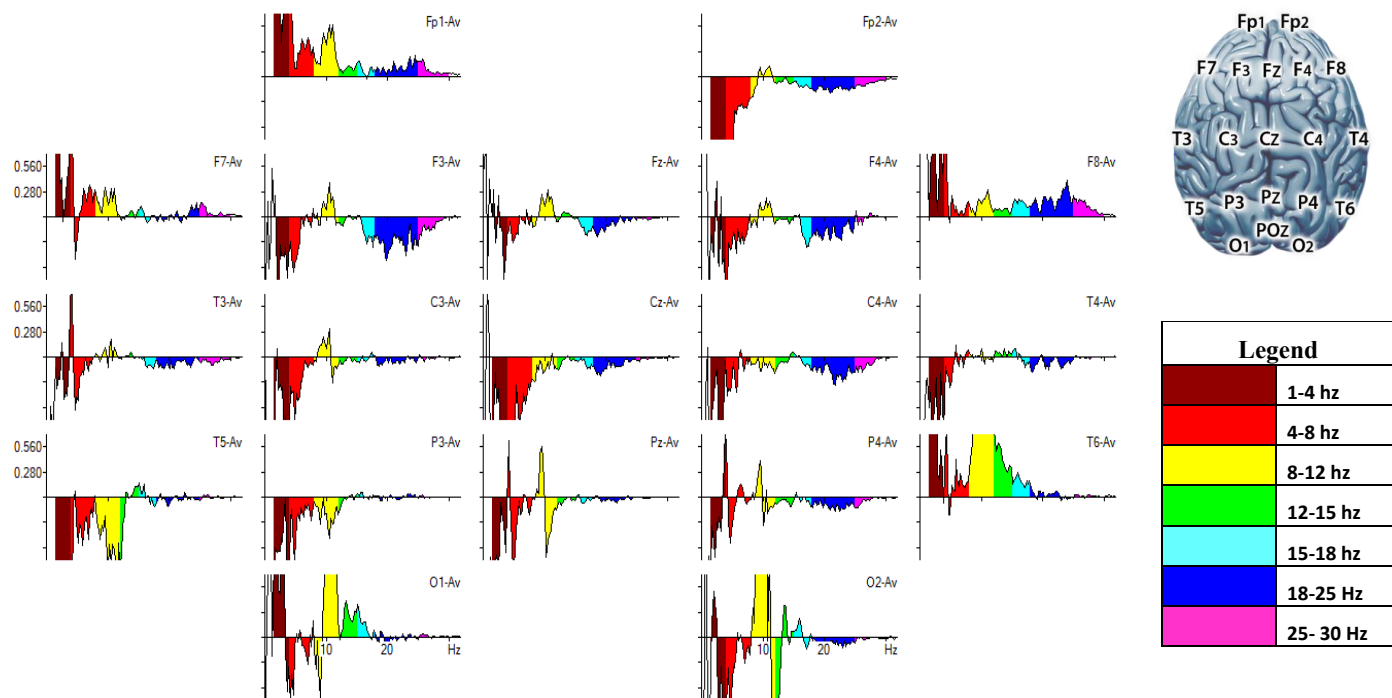


Figure 1: Differences in power between pre and post EEG measures in the eyes closed condition. Below the x-axis is decrease in power and above is increase in power. Light blue, dark blue, and fuchsia colors represent beta frequencies assessed pre and post treatment.

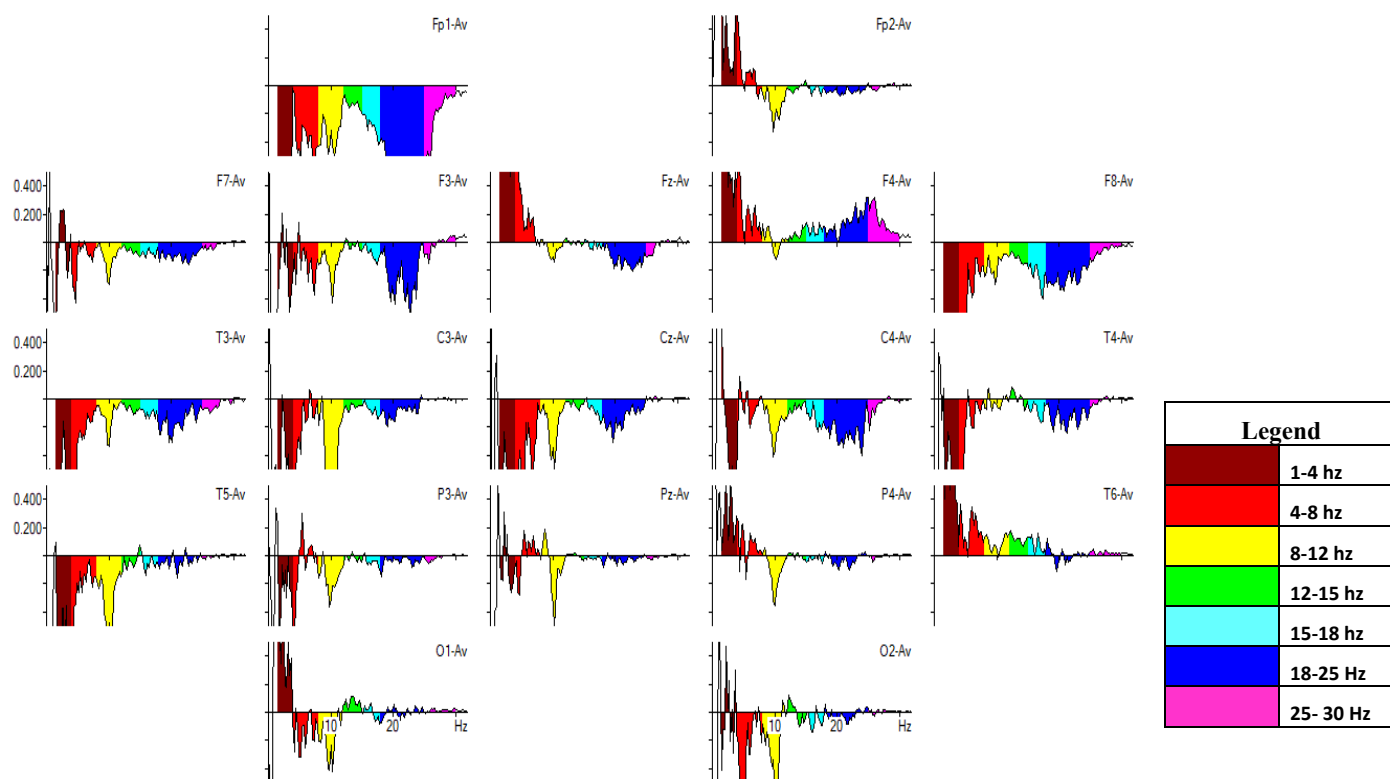


Figure 2: Eyes opened power differences between pre and post treatment. Light blue, dark blue, and fuchsia colors represent beta waves assessed pre and post treatment. Below the x-axis is decrease in power and above is increase in power.

Improvements were observed within 7 out of the 12 outcome measures on the CBS after rTMS treatment. Standard scores increased by various amounts with the lowest being 3 on “Odd One Out” and the highest being 33 on verbal reasoning as displayed in Figure 3. There were also some decreases in standard scores, with the biggest decrease being 7 on spatial short-term memory as displayed in Figure 4.

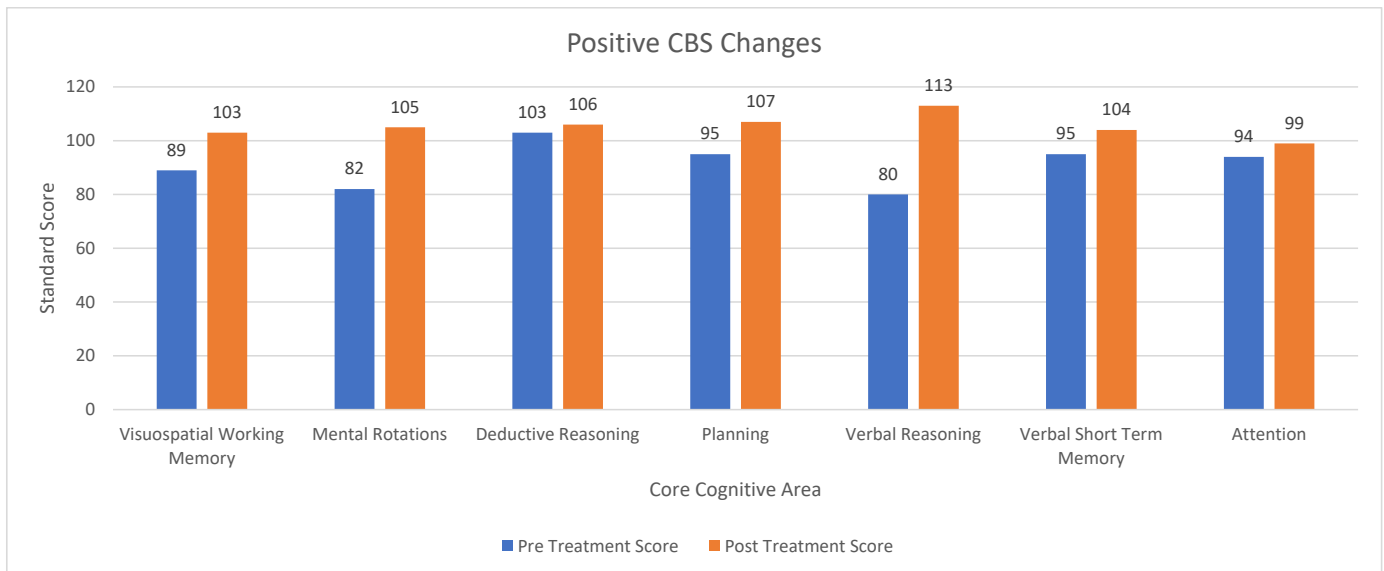


Figure 3: Increases in standard scores between pre and post treatment.

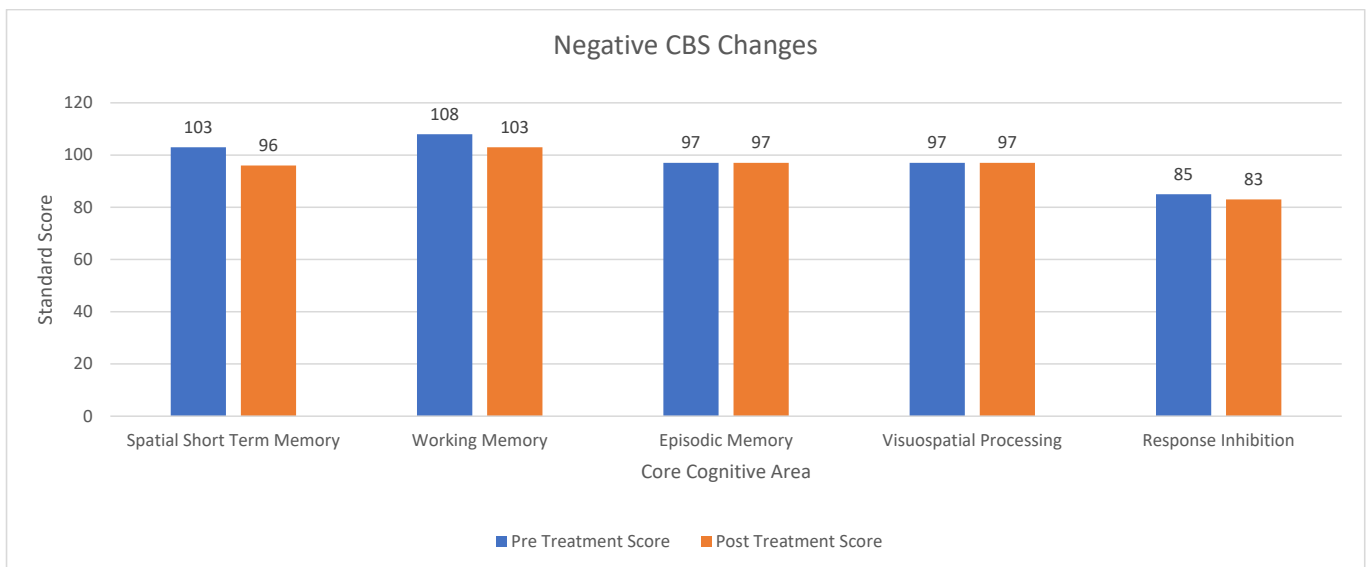


Figure 4: Decreases in standard scores between pre and post treatment.

Discussion

This case study looked to examine whether 5 sessions of 1 Hz rTMS would reduce the power of a patient’s frontal SEB and improve cognitive functioning. The reductions of power in the patient’s beta frequencies were evident, with the biggest decrease being $-8.15 \mu V^2$ (in beta 2 at F3) during EC. The decreases in power were uniform with the other targeted sites except for F4 in the EO condition. Findings from this case report warrant further study for the potential for low frequency rTMS as a possible treatment for overarousal and SEB. As mentioned previously, 1 Hz rTMS protocols have an inhibitory effect on the brain including arousal.

Some studies have shown that low frequency rTMS leads to a decrease in both the current source densities (a measure of electric potentials) and power of beta frequencies [10,11]. However, other studies have found unchanged or increased beta power after low frequency rTMS [12,13]. These studies indicate that more research is warranted to conclude whether 1 Hz rTMS treatment can have a dampening effect on electrophysiological variables associated with beta frequencies and spindling and associated behaviors.

The patient also improved on several cognitive domains of the CBS post-treatment. The greatest standard score increases were in the

domains of planning (+12), visuospatial working memory (+14), mental rotations (+23), and verbal reasoning (+33). All but one (mental rotations) of these 4 domains involves the prefrontal cortex which was the primary area targeted for the patient's treatment. It is possible that reduction of power in the patient's frontal SEB led to these cognitive improvements. A meta-analysis by Patel et al. tested both excitatory and inhibitory rTMS on cognitive function and found statistically reliable effects [14]. Excitatory rTMS had improved executive functioning and inhibitory rTMS had improved episodic memory and visual perception [14]. In our single patient study, the inhibitory rTMS may have decreased impulsivity (a symptom strongly associated with SEB) which would have led to better cognitive control and therefore performance on the CBS. The patient improved on 7 out of 12 tasks total and showed little to no change on the other 5.

This case study does have findings and limitations that need to be addressed by future studies. An important observation is that amplitude of the beta spindling increased rather than decreased at F4 post-treatment for the EO recording but not the EC recording. Perhaps the patient experienced a more relaxed state of arousal during the EC recording. According to Barry et al., "the eyes-closed and eyes-open conditions provide EEG measures differing in topography as well as power levels" [15]. However, a localized change in a specific context does not negate the other changes. This can be applied to the CBS as well, in which the patient improved on most but not all the tasks.

Another limitation was the lack of a questionnaire filled out by the patient's parents. The goal of the treatment was to ultimately reduce the patient's anxiety, emotional reactivity, and impulsivity. The mother gave some details of improvement but a questionnaire with high validity and reliability is preferred to assess subjective well-being [16]. Additionally, only 1 week of rTMS was administered so there is no evidence of the reduction in SEB power being sustained over time. Conducting rTMS over a period of 4-6 weeks, the typical course for an adult with depression/OCD, would have given a more reliable estimate of the treatment's effects on the patient.

A major ethical concern of administering rTMS to children with neurological conditions is that it could have negative, permanent effects on neurodevelopment. Children's brains are very malleable and plastic until late adolescence as evidenced by numerous studies. If rTMS is to become a suitable treatment option for children, the FDA must conclude that potential benefits outweigh the risks. Indeed, the protocol used to reduce beta spindling in this study was experimental and has not been tested in a wide variety of settings and patients.

Conclusion

The results of this case study showed a distinct effect of 1 Hz rTMS on power in beta spindling morphology as well as cognitive functioning in a 9-year-old female patient. However, future studies

will need to address whether the protocol used could help various patients with beta spindling and whether the improvements would last.

Author's Contribution Statements

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Tristan Sguigna. The first draft of the manuscript was written by Tristan Sguigna and all authors commented and made suggestions on content and conclusions on versions of the manuscript. All authors read and approved the final manuscript.

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