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Comparison of EEG Signals of Cerebral Palsy Patients after Standard and rTMS Therapy

Ankita Tiwari[1], O.P. Singh[1], Dinesh Bhatia[2]*

[1]Department of Electronics and Communication Engineering, Amity University, Lucknow, U.P, India.
[2]*Department of Biomedical Engineering, North-Eastern Hill University, Shillong, Meghalaya, India.
bhatiadinesh@rediffmail.com

***Corresponding Author:** Dinesh Bhatia, Department of Biomedical Engineering, North-Eastern Hill University, Shillong, Meghalaya, India.*

Abstract

Objectives: *Study the effect of repetitive TMS at different frequencies and compare them with standard therapy (physical therapy or PT).*

Methods: *In this paper results are observed on the basis of sensorimotor response (SMR) and Beta wave values generated in the frontal lobe collected from 36 CP patients, out of which 12 patients were provided PT only, 5Hz rTMS + PT in other 12 patients and 10Hz rTMS + PT in the remaining 12 patients was provided for 20 days duration. The patients who were treated with PT as well as rTMS were administered a 30 minutes session comprising of 10 minutes rTMS and 20 minutes of PT.*

Results: *The results showed improved SMR and Beta median in case of patients administered 10 Hz rTMS in comparison to those administered 5 Hz and standard therapy*

Conclusions: *Transcranial Magnetic Stimulator has been used for providing rehabilitation to CP and other neuro disorders. It provided at various frequencies for improving patient's condition. In this study it is proved that repetitive TMS at 10 Hz frequency is beneficial for muscle spasticity and motor control because it improves frontal lobe SMR which is responsible for motor control and beta which is for muscle spasticity.*

Significance: *Cerebral palsy is a non-progressive motor disorder. It has been described as continuous but changing disorder of posture and movement and its symptom shows in early years of life. This disorder mostly affects children who suffers by perception disturbances, sensation, musculoskeletal problem and epilepsy. These problems are caused by disturbance in cortical or subcortical section of brain. To control these abnormal activities, certain therapies are employed to treat these children. Previously, physical therapy (PT) training was the only way which was employed to provide muscle relaxation therapy to the patient. However, nowadays, PT is accompanied with a new non-invasive Neurostimulation method which is known as repetitive transcranial magnetic stimulation (rTMS). This therapy has been found to help in decreasing muscle tone in CP patients.*

Keywords: *Spastic Cerebral Palsy; Physical Therapy; rTMS; SMR; Beta waves*

Introduction

Transcranial Magnetic Stimulation (TMS) is a non-invasive neuromodulationtechnique. It is a unique tool for investigation employed to understand different underlying neural processes. This technique treats a variety of neurological disorders because it has the ability to directly enhance the cortical and intra-cortical motor cortex (Valero-Cabre A, 2005). Repetitive TMS or rTMS repeatedly stimulates the cerebral cortex by a series of magnetic pulses administered to subject's skull. In this method, a focused magnetic field is repeatedly inflicted by the coil deep inside the brain region. Due to repetitive nature of the magnetic pulse restorative neuronal activity in brain is affected by altering pre-restorative dynamics of the neuronal firing in restorative area of the brain (Ridding MC, 2007).

In recent literature, it is shown that the stimulation using this technique can excite motor neuron that provides motor function in animals such as rat(Adkins-Muir DL, 2003),(Plautz EJ, 2003) and in humans(M., 2000)(Sénéchal C, 2007)(Rajak BL G. M., 2017). Kirton validated use of TMS on neural disorders like stroke and CP that excite motor function after motor cortex stimulation (A, 2013). He also said that TMS therapy can be provided in CP to study the liveliness and coordination of various parts of brain by rTMS and also for improving brain functioning(Frye RE, 2008). Power spectral density also revealed some differences between normal and CP children (Meena Gupta, 2016) (Rajak BL G. M., July 2016).

The rTMS application in motor disorders was rigorously studied by Kamble et al., where diseases such as Huntington's disease, dystonia, Parkinson's disease, progressive supranuclear palsy, etc., were considered(Kamble N, 2014). Cerebral Palsy is a disorder belonging to the neurodevelopment group. In this the motor and posture related abnormalities developed in early childhood and continue as age progresses(Koman LA, 2004). These days, CP is considered as heterogeneous shape with various causes, clinical types, associated growing pathologies, neuropathology patterns and rare inherit variations(MacLennan AH, 2015). This heterogeneity increases various form of CP such as spastic, dyskinetic, athetoid, ataxic in which spastic CP is quite common and can be found in 70-80% of the cases(Gupta M, 2016)(Meena Gupta, 2016). Spastic CP is a neuromuscular disorder which limits posture and movement due to increase in tonic stretch or exaggerate tendon in muscles(I, 1980). Patients suffering from this disorder are not able to perform their daily routine tasks or activities of daily living (ADL) with ease. They encounter coordination problems and disoriented movement of arms, legs and other parts of body. Moreover, they are not able to perform developmental activities such as rolling, sitting, crawling, walking etc. which are crucial for ADL tasks. To improve motor performance of these patients various methods (Sénéchal C, 2007) are applied with physical therapy (PT). Some results showed that rTMS therapy(Meena Gupta, 2016) in spastic CP improves motor activity(Gupta M, 2016). Effect of this therapy was also checked by quality of upper extremity skill test (QUEST) in CP kids(Rajak BL G. M., 2017). In this paper, we demonstrate the effect of rTMS in combination with PT in improving SMR and Beta values in spastic CP children within limited sessions. These improvements in SMR and Beta values can be attributed towards the improvement inmovement and muscle contraction. This is due to the fact that SMR increase is responsible for immobility and as this study is focussed on CP kids in which the movement is severely affected due to the neurological disorder, so variation in this parameter will determine whether rTMS is effective on CP kids or not. However, increase in beta wave values is responsible for change in muscle strength and as its value decreases muscle resistance will decrease and it will reduce muscle spasticity problem with the CP patients. Therefore, it is also considered as a measurable parameter. Hence, post assessment after applying rTMS will determinethe changes occurring in these parameters.

Methodology

Participants

Thirty six participants diagnosed as spastic Cerebral Palsy by consulting neurologists and physician were recruited from outpatient Department at UDAAN for differentially disabled, Delhi post ethical approval from the parent institute. Patients,who met the inclusion criteria of the study, participated in this research after written approval by them or theirparents/ guardians. These patients were equally divided into three groups of twelve (12) each. The first group (Group A) of 12 patients were provided PT only, the next group (Group B) of 12 patients were administered 5Hz rTMS + PT and the remaining group (Group C) of 12 patients were administered 10Hz rTMS + PT for 20 days duration. There demographic characteristics are shown in Table 1.

Table 1. *Demographic characteristics of participants*

Variables	Group A	Group B	Group C
Age±SD (years)	8.59±4.81	8.33±4.33	7.24±5.01
Height±SD (cm)	107.00±24.80	114.71±26.93	118.17±15.99
Weight±SD (Kg)	21.58±15.62	27.14±10.50	25.67±13.85
Sex			
M : F	08:04	07:05	08:04

CP type			
Hemiplegic	4	3	3
Diplegic	5	6	5
Quadriplegic	3	3	4
Age group			
2-6 years	4	5	5
7-11 years	6	5	5
12-16 years	2	2	2

Inclusion criteria

- Voluntarily participation in research
- Age in between 2 to 16 years
- IQ of participant was nil to moderate
- Muscle tightness showing <1 on modified ashworth scales
- Controlled seizures.

Exclusion criteria

- Any metallic implant
- Infective illness
- Any congenital disorders e.g. Down's syndrome, fragile-X syndrome etc.
- Uncontrolled seizures
- Unstable physical situation
- Severe metal problem

Stimulation Device

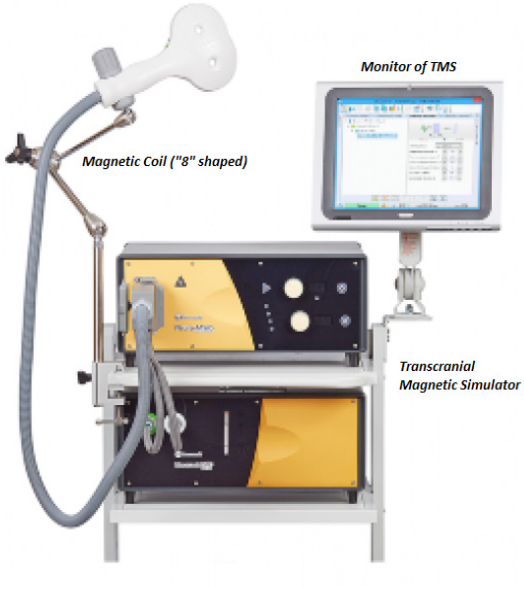

Fig 1. *Transcranial Magnetic Simulator*

Transcranial Magnetic Stimulation (TMS) device (Figure 1) was used in the study to provide repetitive magnetic pulse train using Neuro-MS/D Variant-2 therapeutic (Neurosoft, Russia) having an angulated figure of eight "8" shaped coil AFEC-02-100-C. This device contains two channel Neuro-EMG-MS digital system, for determining motor threshold and stimulator for providing magnetic pulses to the patient. For determining motor threshold a magnetic coil was placed on cranium where C3 dermatome[1](Figure 2) originates, single pulse of transcranial stimulus is delivered to C3 region which results the trigger movement in ABP muscle. When a single pulse of TMS is delivered through a magnetic coil on the cranium it stimulated the target site through an efferent neuron, which travels to the spinal cord of the reference dermatomes and producing the twitching movement in the ABP muscle.

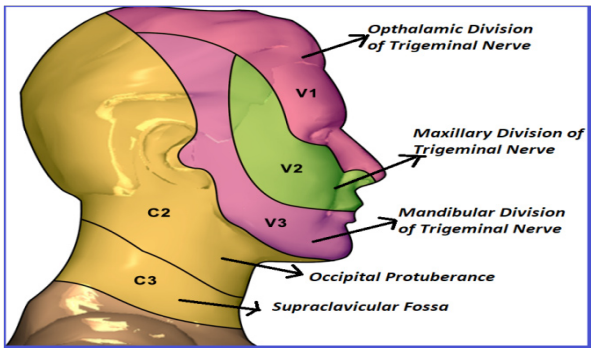

Fig 2. *Dermatome Map*

The rTMS coil creates a magnetic field of 4 Tesla at mid region of the coil, so that when it placed on the surface of head, it starts to penetrate the cranium and enters the soft tissue region to excite the motor neurons of the brain. In this research, primary motor cortex is the main focus area, because it is the motor signal centre, so the coil is placed on it. The device is shown in following (figure 1):

1. Dermatome is an area of skin that is mainly supplied by a single spinal nerve ("Dermatomes Anatomy". eMedicine. Retrieved 2013-10-09)

Assessment criteria

In this study, during analysis of recorded data, two parameters were studied among these groups. One is sensory motor response (SMR) amplitude, whose amplitude is more when corresponding sensorimotor area is immobile or in idle state and less at activation of motor areas i.e. at the time of motion or motor imagery(Ernst Niedermeyer, 1993). Second parameter is Beta amplitude, that increases at the motor cortexregion as muscles contracts or when the movement is resisted(Zhang, Chen, Bressler, & Ding, 2008). Beta activities strengthens sensory area, as the movement changes beta reduces(Lalo, et al., 2007). This analysis was in addition to earlier studies done by the group and published to determine relation with the earlier communicated results(Gupta M, 2016) (Meena Gupta, 2016)(Rajak BL G. M., July 2016).

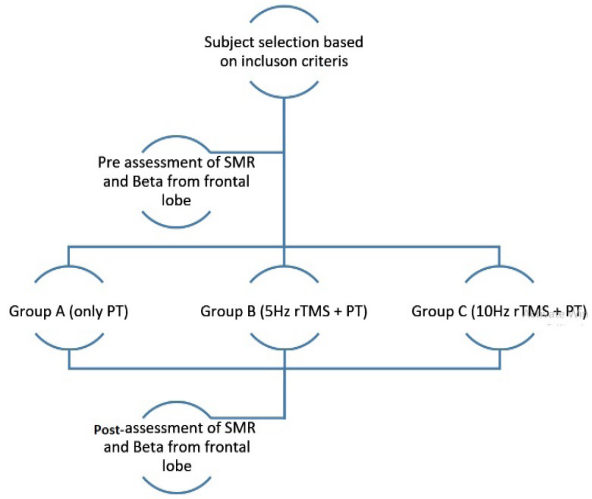

Fig 3. *Study design*

Research design

The participants are divided into three groups as explained above. Participants of Group A were provided only PT sessions for 30 minutes daily for 20 days (5 days in a week for 1 months) whereas children in Group B were administered 5Hz frequency rTMS with PT sessions similar to Group A patients and those in Group C with 10Hz comprising of 1500 pulses (50 pulses in one train with total number of 30 trains having delay of 20 seconds) for 15 minutes daily for 20 days in addition to PT sessions similar to Group A participants.. After completion of 20 sessions for each group the post assessment of SMR and Beta values was conducted to determine that how these values varies post treatment.

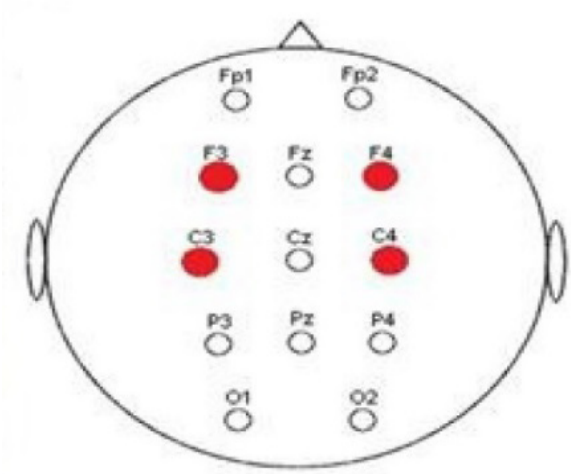

Fig 4. *Standard Montage Configuration for Electrode positioning*

Statistical analysis

The pre and post SMR and Beta wave values analysis of each group was analysed with the help of box plot. Analysis was performed on the basis of amplitude. Mean and standard deviation was considered for this comparison. All statistical analysis were performed in MATLAB 2015 a platform. The tool which is used for statistical analysis is ANOVA. ANOVA is the analysis of variance and covariance. In this both parametric and non-parametric analysis can be done. In this study one way ANOVA is used with is followed by kruskalwallis test, because the data is not normalized. As the result which is needed, group difference or intervention among the groups.

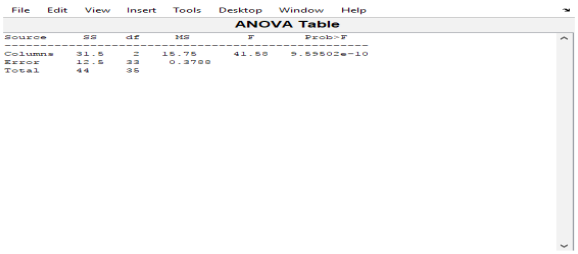

Fig 5. *ANOVA table formed using MATLAB*

The results would not be able to show clearly only with the help of boxplot. As there is a difference in mean of all the three treatments, further we need to analyse that weather the treatments are having difference or not. Though there is not much difference is shown in figure 9. So we need to further compare. When we plot ANOVA table in MATLAB the p value is $9.59e^{-10}$ and F value is 41.58, from the result p value is very much less (figure 5). Although, we cannot conclude that is

there any significant difference among the treatments only by the values of p and F. So in further comparison we have the results, which are shown in figure 6. The results shows that among three groups, the group B and C are having significant difference from group A.

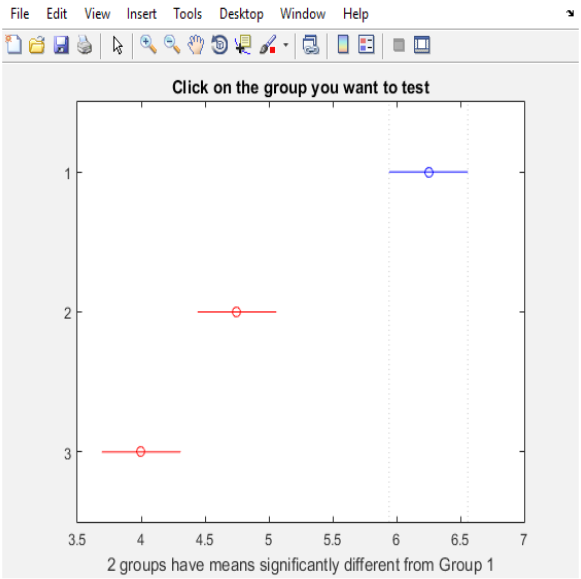

Fig 6. *Shows the final result that the hypothesis on which the study is gone through is true by using one way ANOVA*

In figure 6, it is shown that rTMS therapy, on different frequencies, having difference in result. So it is clear that the results in group B and C having different results in comparison to group A.

The same observations has been done for beta values and the results which we are having are shown as follows in figure 7 and 8.

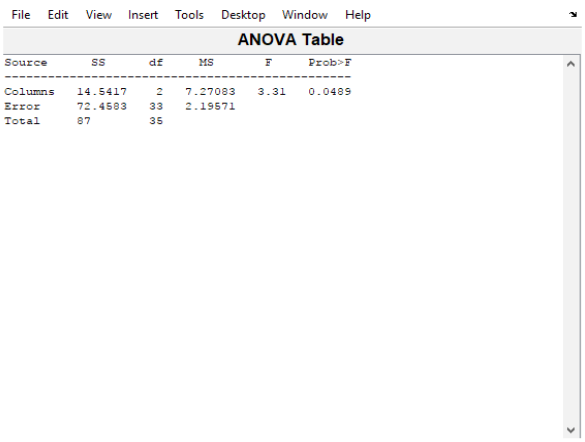

Fig 7. *ANOVA table for beta observations*

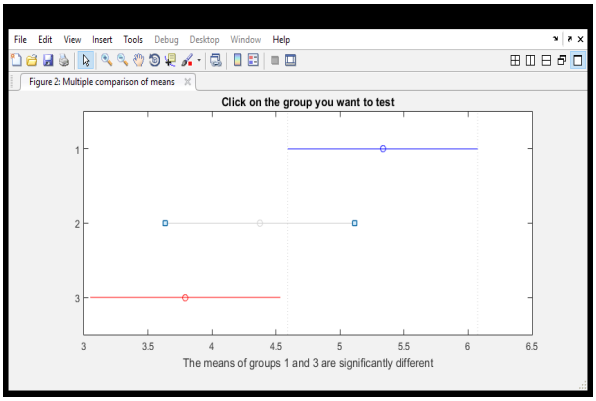

Fig 8. *Comparison among three groups*

In figure 8, it is shown clearly that the group C is having great difference from group A and group A and B don't have that much deference. It shows that the 10 Hz rTMS therapy shows a variation in beta values.

Results

The data has been recorded from frontal lobe, the placing of electrodes is shown in Figure 4. Electrodes were placed according to International 10-20 Montage system. The electrodes F3, F4 and C3, C4 were selected for recording EEG; reference was placed at right mastoid.The result of groups revealed that the median of the SMR and beta values were showing improvement in Group B more than Group A and Group C showed better results than group B. The results(figure 9) showed that repeated TMS at 10 Hz frequency showed improved cognitive behaviour and better results than administering 5 Hz frequency. In case of beta values the results showed same deviation in every group and proved that beta improvement was more in Group C who were administered 10 Hz rTMS. The results are shown in Table 2.

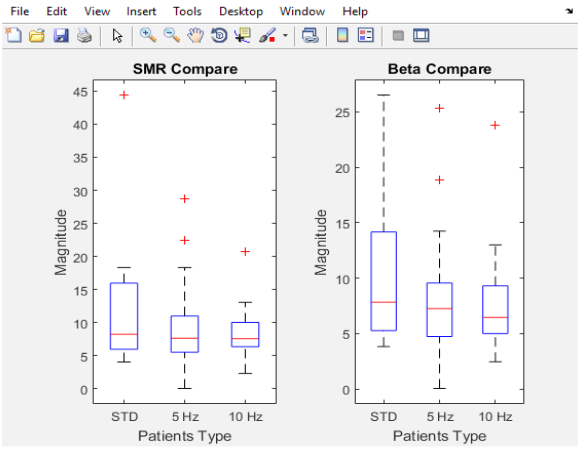

Fig 9. *Frontal mean SMR and Beta values employing boxplot for all three groups*

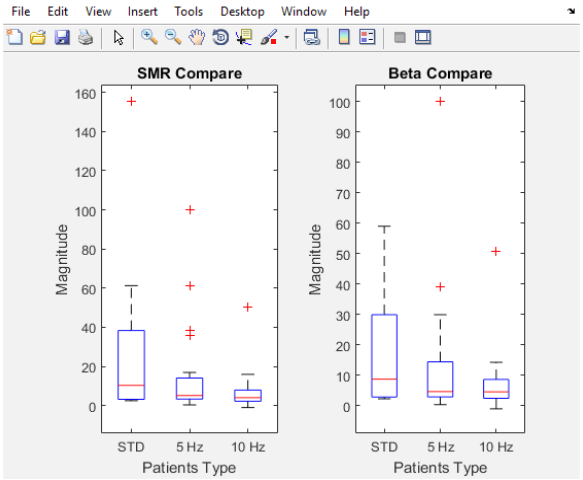

Fig 10. *Box plot values for standard deviation of SMR and Beta values for Frontal region for all three groups*

The results (figure 10) showed that the deviation in Group A was more in comparison to Group B and Cbecause median of the standard deviation value is less in Group C as shown in Table 2. This is due to improvement in CP kids, on applying 10 Hz rTMS, motor and spasticity improvement is shown in participants. Group A showed less concentrated results as the boxplotwas varying towards outliersbecause these patients were administered only physical therapy and no rTMS was applied on this group. It shows thatthe motor activities did not improve resulting in increased value of SMR and Beta. For subjects in Group B the concentration was more near the median values in the box plot and less standard deviation as compared to Group A, showing that 5 Hz frequency rTMS were found to better than administering PT sessions only in Group A. Whereas Group C showed more concentrated and stable box plot results than both groups indicating further improvement in SMR and beta values. It means that SMR and beta variations are stable and irreversible in case of 10 Hz rTMS and 5 Hz has less stability in comparison to Group C but more than Group A.

Table 2. *Deviation in Mean and Standard Deviation*

Variable	Group A	Group B	Group C
SMR (Mean)	8.235	7.64	**7.58**
Beta (Mean)	7.83	7.26	**6.46**
SMR (STDEV)	10.34	5.17	**4.07**
Beta (STDEV)	8.735	4.66	4.55

Discussion and Conclusion

This study was based on the previous work on rTMS by various research groups and group at parent University that presented similar facts, with regards to stimulation being administered to brain repeatedly resulting in lasting changes in the functioning of brain by potential therapeutic effects (Gupta M, 2016) (Meena Gupta, 2016)(Pascual-Leone A, 1998)(Khedr EM, 2005).When rTMS stimulates motor cortex area by high frequency above 5 Hz to 10 Hz, it facilitates motor functions in the human as well as animals. Kumru et al. presents a study on improvement of the motor ability and gait pattern by combining rehabilitation with high frequency in comparison with rehabilitation alone(Kumru H, 2013). A similar report was presented by Elkholy et al. with better gait patterns in the stroke patients(Elkholy SH, 2014). Although, Mally and Dinya shows similar results regarding improvement in paretic extremities by the use of rTMS in patients suffering from stroke after failure of traditional recuperation techniques(Mally J, 2008). From the above evidences in reviewed literature regarding improvement in motor functioning; we conducted this research in spastic CP children to evaluate their sensory motor response and beta waves in the frontal lobe area of the brain as it is responsible for motor and sensory functions of human being, left part of the frontal lobe is primary motor area and right part is primary somatosensory area. Our results in the study demonstrate effectiveness of rTMS on the basis of improved SMR and beta values in CP kids. Hence, it can be concludedthat the application of high frequency rTMS prior to PT can lead to the significant improvement in motor functions, cognitive changes as well as muscle spasticity. The improved motor activity in patients can be attributed to the significant decrease inmuscle spasticity of both upper and lower parts of body due to stimulating effects of rTMS(Meena Gupta, 2016).

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