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Power Spectrum Density Analysis of EEG Signals in Spastic Cerebral Palsy Patients by Inducing r-TMS Therapy

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Abstract Cerebral palsy (CP) is a non-progressive neurological motor disorder affecting children that are often accompanied by disturbances of sensation, perception, epilepsy and secondary musculoskeletal problems. These problems arise due to disturbed cortical or subcortical excitability leading to abnormal electrophysiological brain activity in these children. In order to control the abnormal brain activity, repetitive Transcranial magnetic stimulation (r-TMS) therapy was employed. The present work analyzes the electroencephalogram (EEG) signal before and after r-TMS therapy of spastic CP children and compared it with the power spectrum of normal healthy children. EEG recording was performed on all the twenty selected subjects using four electrodes placed on pathway known for motor control and planning, namely C3-C4 and F3-F4. The artifact-free EEG signals of 15 minutes duration was extracted for spectral analysis using Fast Fourier Transformation (FFT) algorithm to obtain power density spectrum (PSD). The PSD revealed high power peak at frequency of 50 Hz and smaller or none at 100 Hz, for all healthy subjects. In case of spastic CP children, peak at 100 Hz were prominent prior to r-TMS therapy and at 50 Hz it was found to be quite low to none. After therapy, there was a shift in the high intensity peak from 100Hz to 50Hz with the peak at 100Hz being significantly reduced. 50Hz peak obtained in CP patients matched with those observed in normal children, thus showing the effectiveness of r-TMS therapy in controlling abnormal brain activity in spastic CP patients.

Keywords: *Cerebral palsy, Power Spectrum Density, Electroencephalogram (EEG), Transcranial Magnetic Stimulation (TMS), Fast Fourier Transformation*

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1. Introduction

Cerebral palsy is a neurodevelopmental disorder occurring during birth or within two years of birth which persists throughout the lifespan of the affected individuals [1]. CP is the most common disability occurring in children around the world that affects movement and posture. The incidence of CP in developed countries is estimated to be around 1 in 323 children according to a recent report of Centers for Disease Control and Prevention, USA [2]; but in the developing countries the prevalence is around 5.3-11 per 1,000 children under the age of 12 years [3]. CP results in different movement patterns including spastic, dyskinetic, ataxic, and mixed forms; among which the most common movement pattern is spastic, with a minority of cases being primarily dyskinetic, ataxic or hypotonic [4]. The motor disorder in CP is often accompanied by disturbances of sensation, perception, cognition, communication, behavior, epilepsy and secondary musculoskeletal problems [5]. These problems arise due to disturbed cortical or subcortical excitability leading to abnormal brain activity in these children. Abnormal electrophysiological activity was reported by Perlstein et al (1955), who studied 1217 CP patients and found that 90% of them had abnormal electroencephalogram (EEG) recordings [6]. Similar abnormalities in EEG of CP patients were reported in [7,8,9].

EEG is a recording of spontaneous brain activity, which considers the electrical activity of an alternating type, recorded from the scalp surface of the brain after being picked up by metal electrodes and conductive media [10]. EEG recording are widely used to detect brain’s neurological and neurophysiological disorders, during epilepsy [11], Parkinson’s [12] and Alzheimer’s disease [13], CP [14], etc. due to its ability to be characterized by linear or non-linear analysis that depicts distinct state of the brain. Most widely employed technique for quantitative analysis of EEG signals is represented either as wavelet transforms [15] or power spectrum density [13]. These quantitative analysis techniques give the spectral power changes related to both functions and dysfunctions of the central nervous system.

Power spectral density (PSD) analysis is a mathematical method of frequency analysis of complex waveforms, which provides a sensitive means for detecting periodicity within the waveforms and determining the relative energy content of the periodicities. This method has been useful in computerized analysis of EEG using Fourier transformations. The PSD function represents the unit change in power per unit change in frequency, or the slope of the power curve as a function of frequency [16]. In this study, we analyzed the PSD of EEG signals of CP children after administering repetitive Transcranial magnetic stimulation (r-TMS) therapy. The whole idea of this study was to observe the effect of r-TMS on electrophysiological activity of the brain and find if any relevant changes are induced due to the therapy along with any improvement in motor performance of the spastic CP children. r-TMS is a non-invasive brain stimulation technique where a magnetic coil is placed on the scalp of the brain. The magnetic field generated (up to 4 Tesla) in the coil penetrates the cranium that stimulates the neurons thereby modulating corticospinal and intra-cortical motor cortex excitability [17]. These modulatory effects of r-TMS have enormous potential in the treatment of neurological and neuropsychiatric conditions in which cortical or subcortical excitability might be disturbed [18].

2. Material and Method

2.1. Participants

Twenty children that met our inclusion criteria participated in this study after written consent from their parents or guardians and approval from the Institutional Ethics Committee for Human Samples/Participants (IECHSP). Ten participants (male: female = 7:3; mean age = 7.99 SD 4.66) were spastic CP children that were placed in the intervention group (IG). Another ten (male: female = 6:4; mean age = 8.60 SD 2.31) were normal healthy children not suffering from any neurological disorders which were referred to as reference group (RG). The EEG recordings of these healthy subjects were used to compare the effect induced by r-TMS to the participants in IG. The children in different groups were matched according to age, sex, height and weight.

The recruited CP children were from the out-patient department of UDAAN-for the differently abled, a non-profit organization in Delhi that has pioneered in rehabilitation based treatment using physical, occupational, speech therapy since 1992. The normal children were also from the same organization that runs an outreach learning program for the children from low socio-economic background in nearby areas.

The inclusion and exclusion criteria followed during the study are listed below:

Inclusion criteria

- Willingness to participate.
- Age group between 2 to 15 years.
- Cognitive deficiency of nil to moderate.
- Muscle tightness more than one (1) on the Modified Ashworth Scale (MAS).

Exclusion criteria

- Any metallic implant like ventriculo-peritoneal shunt, pacemaker or metallic foreign body present in the subject.
- Uncontrolled infective illness or unstable physical conditions.
- Congenital disorders like Down’s syndrome, Fragile- X syndrome or any congenital anomalies.
- Uncontrolled seizures or any co-morbid condition.

2.2. r-TMS Stimulation

The r-TMS stimulation was administered to the recruited subjects using Neuro-MS/D Variant-2 therapeutic (Neurosoft, Ivanovo, Russia) with angulated coil in the figure of eight (AFEC-02-100-C), which is combined with two channel Neuro-EMG–MS digital system (for determining the motor threshold).

In r-TMS therapy group (IG), prior to starting the therapy, motor threshold (MT) of the recruited subjects was determined. Motor threshold is defined as “the minimum intensity of single pulse of TMS which was required to produce a predefined motor evoked potential in abductor pollicis brevis (ABP) muscle in at least 50% of the trials”. Determination of MT is of great importance in TMS studies because it calibrates the coil’s output energy (magnetic field) and provides the dose along with fixing the safety limits [19].

Figure 1. Spastic CP child undergoing r-TMS therapy

For determining the MT, the child was made to sit in a comfortable position on the chair and the ABP muscle of the left hand was cleaned with alcohol swab. Electrodes were placed on the ABP muscle that was connected to the Neuro EMG-MS system. The angulated eight shaped magnetic coil was placed on the dorsolateral prefrontal cortex (DLPFC) area on the right side of the brain and single pulse magnetic stimulation was delivered such that twitching was observed in the ABP muscle of the left arm. Varying the stimulation intensity using the r-TMS unit, with ten to twelve trials being performed till an end-to-end peak of MT was captured by the Neuro EMG-MS system. In this study, we observed an average MT of 60% in the recruited subjects and thus, r-TMS was delivered at 60% of its peak intensity. Once the MT was determined, the intensity was fixed for repetitive biphasic pulse of TMS frequency to be administered. r-TMS frequency of 5Hz and 10Hz comprising of 1500 pulses i.e., 50 pulses per train with total 30 trains having inter-train delay of 20 seconds was delivered to IG for 15 minutes daily for 5 days a week for 4 weeks i.e, total 20 sessions (Figure 1). Randomly selected 5 subjects were administered r-TMS of 5Hz and other 5 subjects with 10Hz.

2.3. EEG Recording

The EEG of the recruited CP subjects was recorded twice; one prior to starting the r-TMS therapy (pre-EEG recording) and the other after completion of 20 sessions of therapy (post EEG recording). The EEG recording was performed using Nexus Mark II, neurofeedback system (Mind Media B.V., Herten, Netherlands). Prior to recording, the subjects underwent the preparatory procedure where the target recording areas on their scalp was cleaned using alcohol swabs and the metal electrodes were fixed into those areas using a conductive gel non-invasively. The electrode placement on the scalp was according to the internationally recognized Montage 10-20 system [20] and the selected recording areas were C3-C4 and F3-F4; the reference electrode was placed at right mastoid (Figure 2). After the electrode placement was done, the recording was started which continued for 20 minutes. The entire recording was done without using any anesthetics and hence the subjects were awake. During recording, the normal children were asked to sit and relax on a chair; similarly, those in IG were also made to sit on a chair and few were made to lie down in a bed (those that were unable to sit). After completion of the recording, electrodes were removed and the conductive gel on the scalp of the patients was washed with water.

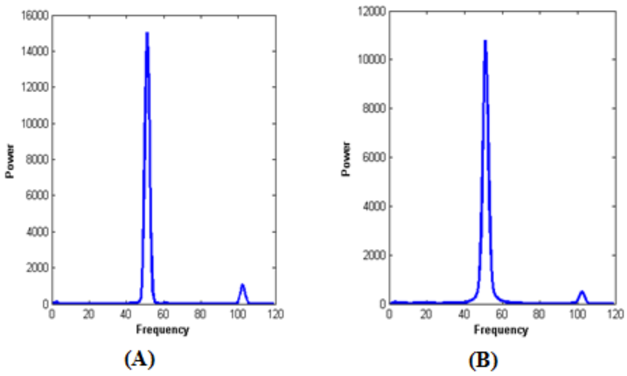

Figure 2. PSD of (A) central and (B) frontal brain area of normal children

3. Data Analysis

The EEG data was recorded for 20 minutes at an output rate of 256 samples per second using a two channel bipolar electrodes. The recorded data was imported in a text file format for analysis using MATLAB. Initially, pre-processing was carried out where the 50Hz power-line frequency as reported in [21] was removed by using the device in battery mode and the window size was taken as 256 without any overlap. Artifact free, averaged EEG data (15 minutes) of all participants in different groups was used for analysis with Fast Fourier transformation using Welch method to obtain the PSD, which was plotted power versus frequency. Welch is a non-parametric method achieved by dividing the signal sequence into segments, then multiplying the segment with an appropriate window and calculation of the periodogram by computing the squared magnitude on the result of its discrete Fourier transform. Individual periodogram obtained are then averaged, resulting in the measurement of power in relation to frequency [22]. In Welch method the data sequences xi(n) can be represented as:

4. Results

From the PSD of EEG signal, it was observed that there were two peaks at frequency 50Hz and 100Hz. These frequency peaks were common in both the group viz. IG and RG. The Figure 2, Figure 3 and Figure 4 contain PSD plots from different recorded areas of all participants in different groups.

Figure 2 represents two PSD plots of normal subjects from different areas, viz. central (C3-C4) and frontal (F3-F4) region. The power peak at frequency 50Hz was prominent and a small peak at 100Hz was observed in normal subjects. Similar observation was found from the frontal region of the brain in normal children.

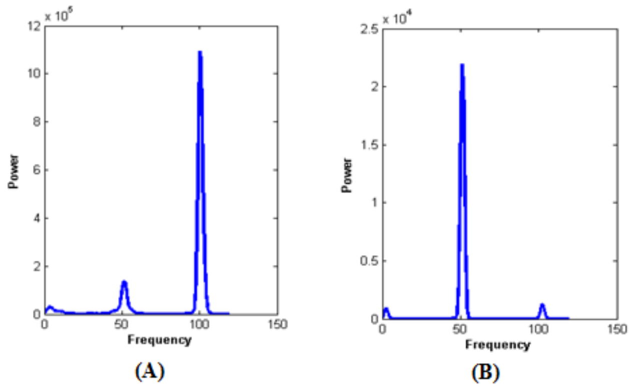

Figure 3. PSD showing (A) pre and (B) post r-TMS effect in the central brain area of spastic CP children

Figure 3 represents pre and post PSD of central (C3-C4) regions of spastic CP subjects. PSD plots of IG showed that prior to r-TMS therapy these subjects had prominent peaks at 100Hz frequency which may be due to highly coherent gamma oscillations that is known to suppress the alpha and beta oscillations of motor activity [26]. The post therapy PSD of IG showed, shift in the frequency from 100Hz to 50Hz which corresponds closely to those of the normal children, indicating suppression of high gamma oscillations and restoring some activity of motor cortex to an extent. These observations shows that r-TMS is effective in controlling abnormal brain activity in the central region of the brain which is responsible in coordinated limb movement.

Figure 4 represents pre and post therapy PSD of frontal (F3-F4) region of spastic CP subjects. PSD showed that prior to r-TMS therapy subjects in IG had prominent peaks at frequency 100Hz but after therapy the post PSD showed shift in the frequency peak from 100Hz to 50Hz. This was the case in most of the CP subjects where high power peaks was observed at 100Hz and after therapy the peaks appeared at 50Hz as observed in normal children. This shift in power peak from 100Hz to 50Hz in spastic CP children is clear indication of the effectiveness of r-TMS that this therapy may be used to suppress high gamma oscillations that results in improper functions of the motor areas for planning and coordinated movement of the limbs.

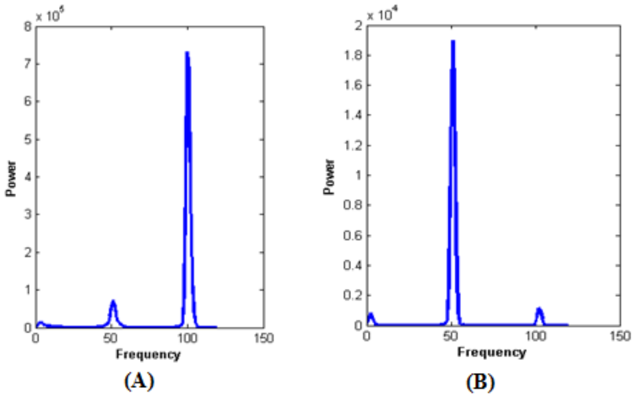

Figure 4. PSD showing (A) pre and (B) post r-TMS effect in the frontal brain area of spastic CP children

5. Discussion

Our study was based on the previous works on r-TMS by various researchers that had established that stimulation brain repeatedly can produce lasting changes in brain function with potential therapeutic effects [23] and high frequency r-TMS (above 5-10 Hz) stimulates the motor cortex which facilitates motor function in animals [24] and humans [23]. In this study, we observed that r-TMS intervention administered to spastic CP children for 4 weeks with mild to severe spasticity reduced their muscle tightness and improved their motor function [25]. This improvement may be the result of stabilizing the neuronal activity of the brain by suppressing the high gamma oscillation that supersedes the alpha, beta and theta oscillations responsible for motor activity [26,27]. PSD peak shift of 100Hz (pre r-TMS) to 50Hz (post r-TMS) of EEG signals in the present study demonstrates the effectiveness of r-TMS, thus depicting that r-TMS can be used as therapeutic tool in controlling the abnormal brain activity. Though our study demonstrates a novel finding yet there were certain limitations - first, the study had a small sample due to difficulty in getting spastic CP patients. Second, we did not perform EEG recording midway or just after administering r-TMS therapy which might have shown, after how many sessions r-TMS effect was prominent and more evident; instead we recorded only pre (before therapy) and post (after therapy) EEG signals. Additionally, it was not easy to keep CP patients in fixed position for a long duration of time while performing EEG recording. Third, the EEG signals were taken from C3-C4 and F3-F4 position and not from other parts of the brain. Fourth, PSD was obtained employing widely used FFT- Welch method and no other feature extraction algorithms were employed for present studies. Moreover, our future work will consider more parameters for assessing improvement in motor functions, cognitive and intellectual abilities with regard to stimulating effect of r-TMS on the brain of spastic CP patients and finding how long the effect lasts.

6. Conclusion

We found that the PSD plots of normal children in the central (C3-C4) and frontal (F3-F4) regions show intense peak at 50 Hz and a smaller peak at 100 Hz. In the case of spastic CP children we found (for both central and frontal region) that the peak at 50 Hz was smaller than the peak at 100 Hz. After r-TMS therapy, we observed that the peak at 50Hz becomes larger than the peak at 100 Hz, as is the case with normal children. This shift in the 100Hz peak to 50Hz is due to the stimulating effect of r-TMS on spastic CP patients. We can conclude that the r-TMS therapy can be used to control abnormal neurological activity of the spastic CP children. Additionally, our observations in this study were further supported by the reduction in muscle spasticity and increased cognitive awareness post treatment which is substantiated by feedback from their parents and guardians reporting beneficial effect of the therapy on these children.

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