



## Review Article

## A comparison between the effectiveness of transcranial direct current stimulation (tDCS) and repetitive transcranial magnetic stimulation (rTMS) on corticospinal excitability in chronic stroke: A review of literature

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## ABSTRACT

**Background:** Stroke is defined as abrupt onset neurological disorder of vascular aetiology. Stroke represented 1.2% of total deaths in India. Upper extremity paresis is a leading cause of functional disability after a stroke as it causes difficulty in everyday life. Decreased corticospinal excitability of lesioned hemisphere is a well recognized neurophysiological consequence after stroke. The level of excitability of affected hemisphere correlates with motor function and predicts recovery. Transcranial direct current stimulation (tDCS) and repetitive transcranial magnetic stimulation (rTMS) have gained popularity in the stroke rehabilitation literature.

**Aims and Objectives:** To compare the effects of transcranial direct current stimulation and repetitive transcranial magnetic stimulation on corticospinal excitability in chronic stroke.

**Materials and Methods:** A thorough electronic search was made through various databases such as PubMed, ScienceDirect and Google Scholar. The total number of articles included were 20 of which 8 were RCTs, 2 systematic reviews, 3 literature reviews, 4 experimental studies and 3 crossover trials.

**Conclusion:** tDCS has therapeutic applications in restoring the interhemispheric balance between the unlesioned and lesioned hemisphere, hence alleviating symptoms such as apraxia, spatial neglect, and gait. tDCS can also be used along with other peripheral intervention techniques such as occupational therapy, robot-assisted arm therapy and physical therapy to accelerate recovery in chronic stroke patients. On the other hand, rTMS has been used as an evaluative, prognostic (along with CT scan and MRI) and rehabilitative tool in common practice to assess disability in chronic stroke patient.

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### 1. Introduction

The WHO 2005 clinically defines stroke as ‘the rapid development of clinical signs and symptoms of a focal neurological disturbance lasting more than 24 hours or leading to death with no apparent cause other than vascular origin’. Based on the duration, stroke can be divided into hyperacute which involves the first 6 hours, acute involving 6-48hours, sub-acute 48hours - weeks and chronic stroke weeks to months based on the onset of stroke symptoms.<sup>1</sup> Stroke is clinically divided into two broad categories that define its pathophysiology: Ischemic stroke accounts for

50%–85% and hemorrhagic accounts for 1% -7% of all strokes worldwide.

In developing countries, stroke is the first leading cause of disability. Recent rapid socioeconomic changes have led to changes in people’s lifestyle, leading to work-related stress and altered food habits, raising the risk of hypertension. Dalal P.M et al.<sup>2</sup> conducted a 2-year study from January 2005 to December 2006 which revealed that 456 subjects of which 238 were males and 218 females, had the first-ever stroke, indicating an annual incidence in subjects of 25 years and above of 145/100,000 persons for males it is 149/100,000 persons and for females, it is 141/100,000 persons. WHO estimates suggest that by 2050, 80% stroke cases in the world would occur in low and

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middle-income countries mainly India and China of which brain stroke is the third largest killer in India after a heart attack and cancer and the second largest in the world.<sup>3</sup>

Several neurological functions are impaired by stroke most commonly motor disability contralateral to the side of lesion.<sup>4</sup> Reduced cortical excitability of the lesioned hemisphere is a well known neurophysiological consequence following stroke. The level of excitability of lesioned hemisphere correlates with the motor function and predicts recovery.<sup>5</sup> Motor recovery after stroke is directly related to neural plasticity. Various strategies have been developed to enhance motor recovery. Repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS) can induce changes in human cortex excitability. In rTMS, a wire-coil shaped in a figure of 8 fashion is placed over the scalp to generate a transient local magnetic field. High-frequency rTMS increases cortical excitability and low-frequency rTMS inhibits cortical excitability. The pulsed magnetic field enters the brain and creates an electric current that flows through the neurons resulting in neuronal depolarization. On the other hand, tDCS modulates the neuronal membrane potential through polarizing currents by weak constant direct current, hence influencing the levels of excitability and modulating the spontaneous firing rate of neurons. Anodal tDCS increases the excitability of the stimulated cortex, whereas cathodal tDCS decreases the excitability of the stimulated cortex.<sup>4</sup> The purpose of non-invasive brain stimulation is that the modulation of cortical excitability may induce neural plasticity and/or interfere with maladaptive neural activation that subsequently weakens motor function and impedes motor recovery.

Since the mechanism, underlying non-invasive brain stimulation remains to be elucidated and insufficiently recognized, the study aims to provide a comprehensive overview of the role of non-invasive brain stimulation to enhance corticospinal excitability and use-dependent plasticity in chronic stroke.

## 2. Materials and Methods

Data were collected for this literature review from the following sources 1) Pub Med, 2) Google Scholar, 3) Science Direct, 4) Brain Journals. Only English articles published after year 2005 concerned with tDCS and rTMS and chronic stroke were used for the study. Articles of other languages published before the year 2005 were excluded from the study.

### 2.1. Procedure

A structured literature search was done using databases such as Pub Med, ScienceDirect, Pedro, Brain journals, APTA etc. Keywords used are tDCS, rTMS, chronic stroke, corticospinal excitability. Boolean concept of using and was

used for a more specific search. Articles based on these keywords were not found on databases such as Pedro and APTA. Vancouver method was used for reference.

## 3. Discussion

This study provides substantial evidence that both transcranial direct current stimulation and repetitive transcranial magnetic stimulation can be used as a potential neuro rehabilitative tool in mitigating motor deficits and re-establishing the functional independence in chronic stroke patients. On comparison, tDCS due to its compatibility has therapeutic applications in restoring the inter-hemispheric balance between the unlesioned and lesioned hemisphere, hence alleviating symptoms such as apraxia, spatial neglect, dysphagia and gait. tDCS can also be used along with other peripheral intervention techniques such as occupational therapy, robot-assisted arm therapy and physical therapy to accelerate recovery in chronic stroke patients. On the other hand, rTMS has been used as an evaluative, prognostic (along with CT scan and MRI) and rehabilitative tool in common practice to assess and address disability in chronic stroke patients.

There is the dearth of literature suggesting the simultaneous use of both these novel techniques to shape adaptive brain processes following a stroke in such a way that sustained success is achieved in the amelioration of symptoms.

**Table 1:**

| <b>S.No.</b> | <b>Studies included</b>  | <b>Study design</b>      | <b>Intervention</b>   | <b>Outcome measure</b>   | <b>Pedro</b> |
|--------------|--|--------------------------|---|--|--------------|
| 1            | Bidirectional alterations of interhemispheric parietal balance by non-invasive cortical stimulation <sup>6</sup> | Proof of principle study | 10 stroke patients with visuospatial symptom participated in the study. A constant current of 1mA intensity was applied for 10 min. Three different stimulation sessions were carried out for each hemisphere: (i) tDCS (anodal); (ii) tDCS (cathodal) and (iii) tDCS (sham). The stimulator was turned off after 30seconds. In each stimulation session tDCS (anodal), tDCS (cathodal) and tDCS (sham) participants were required to perform three blocks of trials: before tDCS (baseline), immediately after tDCS and 20 min following the cessation of tDCS   | TAP test (Test Battery of Attentional Performance) and Line bisection test   | NA           |
| 2            | Improving ideomotor limb apraxia by electrical stimulation of the left posterior parietal cortex <sup>7</sup>    | *****                    | Two groups of participants were included in the study, first group comprised of six neurologically healthy controls and second group comprised of six left-hemisphere damaged patients. tDCS was delivered by a battery-driven, constant current stimulator through a pair of saline-sponge electrodes for total 10 min with an intensity of 2 mA, While stimulating the left PPC, anode was placed over the scalp representing left PPC and while stimulating the right PPC anode was placed over the region of scalp representing the right PPC and cathode over the contralateral supraorbital area in both the cases. Each participant underwent three sessions: (i) anodal tDCS to left PPC; (ii) anodal tDCS to right primary motor cortex and (iii) sham tDCS. The order of the three sessions were separated by atleast 24 hrs to minimize carry-over effects | Jebsen hand function test(JHFT) and Ideomotor Apraxia test(12 symbolic hand gestures such as sign of OK with the thumb and index finger and 12 non symbolic hand gestures like hand under the chin) pre and post stimulation |              |

*Continued on next page*

| <i>Table 1 continued</i> |   |  |  |   |      |
|--------------------------|---|--|--|---|------|
| 3                        | “Cortical activation changes underlying stimulation-induced behavioural gains in chronic stroke” <sup>8</sup>   | Randomized control trial                       | Thirteen patients with at least 6 months post first ischemic or haemorrhagic stroke participated in the experiment. A DC-Stimulator delivered a 1 mA current to the brain via two electrodes. The active electrode was placed over ipsilesional motor cortex for anodal stimulation, contralesional motor cortex for cathodal stimulation and the vertex for sham stimulation and reference electrode over the supraorbital ridge.   | Visual analogue scales  | 7/11 |
| 4                        | Modulation of Training by Single-Session Transcranial Direct Current Stimulation to the Intact Motor Cortex Enhances Motor Skill Acquisition of the Paretic Hand <sup>9</sup> | Double blind cross over trial                  | Twelve chronic stroke patients participated in the study and had demonstrated severe hand deficit. The patients were seated in an armchair opposite a 20 inch screen monitor attached to an ergonomic 4-button electronic keyboard. Each patient took part in 2 different arms during which either cathodal DCS or sham stimulation was applied separated by an interval of 10 days and each arm was divided into 3 different sessions (tDCS, after 90 minutes, and after 24 hours). During each arm, patients performed a different motor sequence with a similar degree of complexity, length and number of repetitions. After baseline, the patients underwent a first training session (tDCS) composed of 5 blocks of 3 minutes each with 2 minutes breaks and 2 further retrain sessions were completed after 90 minutes and 24 hours (POST-90 and POST-24) organized in 4 blocks | Nonparametric Friedman analysis of variance and Wilcoxon signed-rank test for post hoc comparisons. | NA   |
| 5                        | Effects of non-invasive cortical stimulation on skilled motor function in chronic stroke <sup>10</sup>  | Double blind, Sham-controlled, crossover study | Six patients with a history of a single ischemic cerebral infarct, tDCS applied  | Jebsen–Taylor Hand Function Test (JTT)  | NA   |

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Table 1 continued

|   |   |  |   |   |       |
|---|---|--|---|---|-------|
| 6 | Combined Transcranial Direct Current Stimulation and Robot-Assisted Arm Training in Subacute Stroke Patients <sup>11</sup>          | Randomized multicentre trial             | Ninety six stroke patients with severe upper limb flaccid paresis were randomly allocated to three groups named A (anodal), B(cathodal), C (sham) based on a lottery method. The duration of whole intervention was six weeks (30 sessions in each patients) with each session lasting for 20 minutes. Each session was divided into two cycles (Cycle 1 non affected extremity driving the paretic extremity and Cycle 2 vice versa). During each session, the patients practiced with the Arm Robot(forearm pronation-supination, wrist flexion-extension) and simultaneously received the tDCS | Fugyl-Meyer score, Barthel index and Box and Block Test | 8/11  |
| 7 | Optimizing recovery potential through simultaneous occupational therapy and non-invasive brain-stimulation using Tdcs <sup>12</sup> | Randomized multicentre trial             | Chronic stroke patients receiving either 5 consecutive days of cathodal tDCS (for 30 minutes) applied to the contralesional motor region and simultaneous OT, or sham tDCS+OT   | Fugl-Meyer scores                                       | 10/11 |
| 8 | Transcranial Direct Current Stimulation in Post Stroke Recovery <sup>13</sup>   | Literature review                        | The safety parameters, the underlying physiological mechanisms, applications of tDCS in chronic stroke and future scopes of tDCS to evolve as a promising neurorehabilitative tool  |   | NA    |
| 9 | Neural substrates underlying stimulation enhanced motor skill learning after stroke <sup>14</sup>                                   | Double-blind, crossover randomized trial | The subject participated in the crossover experiment in two series each comprising of two sessions, an intervention session (dual tDCS/sham was applied during motor skill learning of the paretic upper limb) and retention session (imaging session 1week later).   |   | 6/11  |

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Table 1 continued

|    |   |   |  |                          |      |
|----|---|---|--|--------------------------|------|
| 10 | Does anodal transcranial direct current stimulation enhance excitability of the motor cortex and motor function in healthy individuals and subjects with stroke <sup>15</sup> | Systematic review and meta analysis   | Doubt*****no specific rct number given   |                          | NA   |
| 11 | Functional potential in chronic stroke patients depends on corticospinal tract integrity <sup>16</sup>  | *****   | Twenty one patients with first ever stroke included in the study. Single pulse TMS was delivered using a MagStim 200 stimulator through a figure-of-eight coil.  | Fugyl Meyr score         |      |
| 12 | Remote changes in cortical excitability after stroke <sup>17</sup>  | *****   | 13 patients with good recovery of their hand function following stroke and 13 healthy volunteers of same age participated in the study. In each experiment TMS was applied through a figure of eight-shaped coil using two Magstim 200 stimulators |                          |      |
| 13 | Low-frequency rTMS promotes use dependent motor plasticity in chronic stroke <sup>18</sup>  | Prospective, randomized, parallel and factorial-design, sham-controlled, phase II trial | Thirty first ever chronic stroke patients were randomly allocated to four groups (Group1- rTMS followed by PT, Group 2-PT immediately followed by rTMS, Group 3-sham rTMS and PT and Group 4-PT immediately followed by sham rTMS)                 | Jebson Taylor Test       | NA   |
| 14 | Theta burst stimulation reduces disability during the activities of daily living in spatial neglect <sup>19</sup>   | Randomized control trial  | Twenty four right handed individuals who had suffered a first ever episode of stroke. Group1: continuous TBS followed by sham, Group 2: sham followed by continuous TBS, and Group 3: 'no stimulation' control group                               | CBS                      | 9/11 |
| 15 | Recovery of upper-limb function due to enhanced use-dependent plasticity in chronic stroke patients <sup>20</sup>   | Crossover study   | Nine post stroke patients and nine healthy age matched volunteers. All participants (healthy and stroke) performed 15 cycles of exercises for the extensors of the wrist and fingers, followed by a train of 5 Hz repetitive TMS for 8 s           | Modified Ashworth scale. | NA   |

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Table 1 continued

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|----|---|--|--|--|------|
| 16 | A Sham-Controlled Trial of a 5-Day Course of Repetitive Transcranial Magnetic Stimulation of the Unaffected Hemisphere in Stroke Patients <sup>21</sup> | Longitudinal, randomized, parallel-design, phase II trial termed | Fifteen participants with a history of at least one year stroke were randomized in 1:2 ratio in either one of two group active or sham rTMS. Before application of the stimulation on each of 5 days motor threshold from first dorsal interosseus muscle from the affected and the unaffected hand was recorded pre and post stimulation in sham and active group. The subjects received stimulation of the unaffected hemisphere for one session for five consecutive days with intensity of 100% MT, frequency of 1 Hz, 1200 stimuli as a single, continuous train lasting for 20 minutes | Jebsen-Taylor Hand Function Test (JTT), simple reaction time (sRT), choice reaction time (cRT), and Purdue Pegboard test (PTT) | 9/11 |
| 17 | Use of Transcranial Magnetic Stimulation to Assess and Induce Cortical Plasticity of Upper-Extremity Movement <sup>22</sup>                             | Literature review  | The basic principles and mechanism of plasticity, followed by a concise introduction to TMS (parameters), physiological mechanism of TMS in healthy adults and applications in several neurological disorders  |  | NA   |
| 18 | Stimulating language: insights from TMS <sup>23</sup>   | Literature review  | Potential tool in studying and augmenting language at both cognitive and neural levels for patients with aphasia   |  | NA   |
| 19 | Functional Electrical Therapy for hemiparesis alleviates disability and Enhances Neuroplasticity <sup>24</sup>  | Randomized control trial   | Twenty chronic stroke subjects were randomly assigned to either of the two groups conventional physiotherapy group (CON) and Functional electrical therapy group (FET)   | Motor function Test and electrophysiological studies   | 8/11 |
| 20 | Repetitive Transcranial Magnetic Stimulation of Motor Cortex after Stroke <sup>25</sup>   | Systematic review  | 4 randomized control studies out of 11 studies   |  | NA   |

#### 4. Conclusion

Both tDCS and rTMS are promising adjuvants in mitigating motor deficits post stroke and promoting recovery, and hence should be included in regular clinical practice under supervision of trained physiotherapist.

#### 5. Source of funding

None.

#### 6. Conflict of Interest

None.

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