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Non-Invasive Brain Stimulation (TMS/tDCS) and Rehabilitation for Stroke and Parkinson's

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<http://dx.doi.org/10.5772/67908>

Abstract

The aim of this study was to clarify and compare the efficacies of rehabilitation using transcranial direct current stimulation (tDCS) and continuous theta burst stimulation (cTBS), a form of repetitive transcranial magnetic stimulation (rTMS), in convalescing stroke and Parkinson's disease patients. For both types of stimuli, kinetic analysis and performance analysis of upper limb motor paralysis and gait analysis showed an increase in speed of movement, and an improvement in performance was observed. Both stimuli resulted in significant improvement compared with a sham stimulus. Change in speed of movement and performance was observed with both tDCS and cTBS, but there was not a significantly large difference between the stimuli. Improved movement due to reduction of excessive tension caused by spasticity was observed. In patients with Parkinson's disease, gait speed and step length were increased. It is suggested that performance was improved because movement became smoother. The efficacy of tDCS and cTBS in patients with motor disorders caused by stroke or Parkinson's disease will probably be further improved when combined with physical therapy.

Keywords: noninvasive brain stimulation, rehabilitation, TMS, tDCS

1. Introduction

Cortical plasticity enables modification of functional organization of the cerebral cortex as a result of experience [1]. Facilitation of plasticity whereby cortical excitability is modulated using tDCS and rTMS, which are types of noninvasive brain stimulation (NIBS), is potentially therapeutic for patients recovering from stroke or Parkinson's disease [2–7].

Both rTMS and tDCS can improve motor function, cognitive function, working memory, depression and chronic pain (**Figure 1**). In rTMS, a magnetic field produced by an electric current pulsating through an electromagnetic coil placed on the patient’s scalp stimulates the underlying brain tissue by inducing eddy currents in the brain parenchyma. In tDCS, the activity of the brain is transiently changed by altering membrane potential. The equipment used for tDCS is portable and safe, and therefore, in recent years, much research has been carried out into its potential clinical application [8]. Compared with rTMS and epidural stimulation (**Table 1**), tDCS is inexpensive and relatively easy to use without the need for additional holders to maintain coil position, or additional handling after affixing. Both tDCS and rTMS have been used to up-regulate excitability in the undamaged ipsilesional area and downregulate excitability in the contralesional motor cortex. Neurophysiological

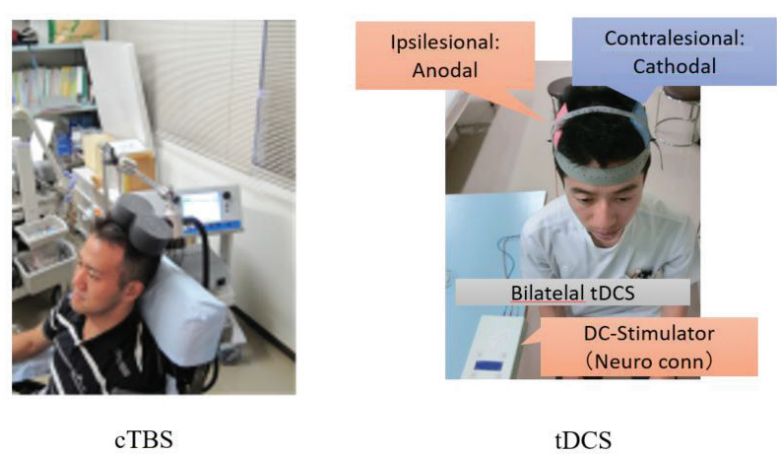


Figure 1. Participants were seated in a comfortable chair with headrest and armrests. The rTMS of the motor cortex was performed with a 70-mm figure-8 coil attached to a magnetic stimulator. The tDCS of motor cortex tDCS was performed with the anode over the ipsilesional area and the cathode over the contralesional area.

	tDCS	TMS
Mechanism	Change of the resting membrane potential	Induces action potential
Sounds during stimulation	Silent	Click
Dermal sensation	Tingling	Weak pain
Headache	12%	23%
Epilepsy	No reports	Report by stimulation with high frequency
Price of the machine	One million yen	Ten million yen
Size	Small	Large
Time resolution	Several minutes	Milliseconds
Spatial resolution	Several centimeters	1 cm

Table 1. Comparison tDCS with TMS [8].

studies of these treatments have indicated, poststroke, an imbalance of interhemispheric interactions resulting in disinhibition of the contralesional hemisphere and increased inhibition of the ipsilesional motor cortex (**Figure 2**) [9]. Improvement in motor and language performances has been explained by interhemispheric competition theory. The majority of the clinical studies evaluating the role of NIBS in rehabilitation were performed in patients with subacute or chronic stroke symptoms or with Parkinson's disease.

Recent studies have demonstrated that NIBS treatment can be more effective when combined with physical or occupational therapy, with brain activity changed by NIBS and motor function improved by rehabilitation. Accordingly, there is currently much interest in this combined rehabilitation, and here we will outline the effects of such rehabilitation for patients with stroke symptoms or with Parkinson's disease.

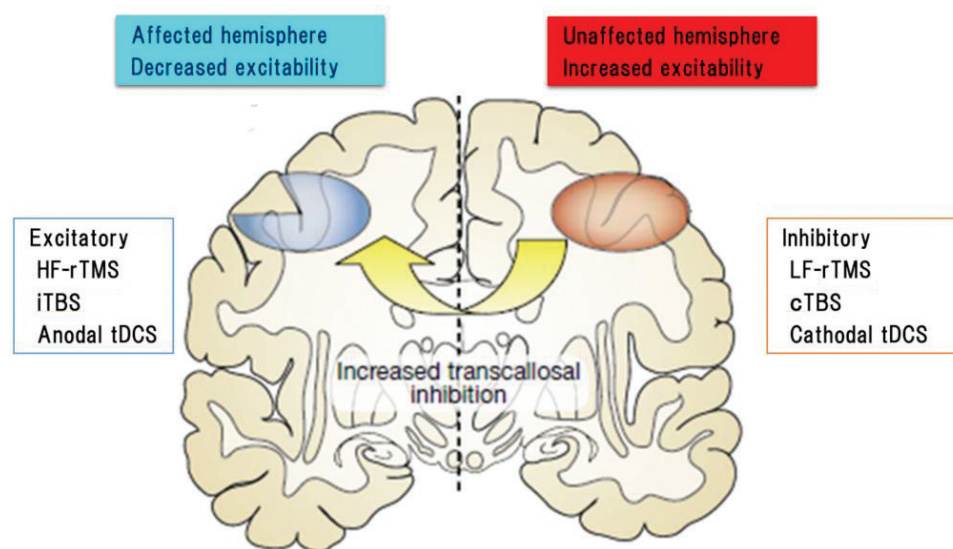


Figure 2. Influence of interhemispheric interactions on motor function and point of view on NIBS. Simple repetitive TMS (rTMS) protocols consist of identical stimuli spaced by an identical interval. Effects depend on stimulation frequency: at low frequency (LF-rTMS < 1 Hz), rTMS depresses excitability in the motor cortex, whereas at high frequency (HF-rTMS > 5 Hz), cortical excitability is increased. In addition iTBS and anodal tDCS is increased motor cortex, cTBS and cathodal tDCS is decreased motor cortex [9].

2. Noninvasive brain stimulation

Between 1988 and 2012, there were about 1400 publications globally on NIBS studies in humans. The first reported TMS study was by Barker in England in 1985. TMS uses a pulsating magnetic field produced by a current flowing through an electromagnetic coil, and eddy currents flowing in the opposite direction stimulate nerve tissue.

In general, single-pulse TMS (including paired-pulse TMS) is used to explore brain function, whereas rTMS is used to induce changes in brain activity that can last beyond the stimulation period. Noninvasive TMS of the motor cortex causes a twitch in the target muscle, evoking motor-evoked potential (MEP) on electromyography. The MEP is usually used to assess

corticospinal tract excitability. Before rTMS is applied, the rest motor threshold (MT) of the contralateral first dorsal interosseous muscle is determined. In the present study, we used the same stimulation parameters with a frequency of 1 Hz on the uninjured hemisphere in six stroke patients with an intensity of 80% MT and located the “hot spot” of the brain area using TMS.

It has been reported that low-frequency rTMS (LF-rTMS) of <1 Hz inhibits local neural activities, while high-frequency rTMS (HF-rTMS) of >5 Hz excites local neural activities [10, 11]. Recent studies indicated that compared with LF-rTMS, HF-rTMS applied to the lesional hemisphere in the early phase of stroke was more beneficial for motor function of the affected upper limb [12].

Theta burst stimulation (TBS) is a modified form of rTMS, but the mechanisms underlying the cortical effect of rTMS and tDCS differ. TBS consists of pulses applied in bursts of three pulses at 50 Hz with an interburst interval at 5 Hz for 2 s. Continuous TBS (cTBS) is when trains of 20 pulses are repeated without a pause. Intermittent TBS (iTBS) is when there are 8 s pauses between the 20 pulse trains. For both, 1 session comprises 600 pulses. cTBS has an inhibitory effect on the brain tissue directly below the stimulus, iTBS has an excitatory effect (**Figure 3**) [13].

A systematic literature review showed that rTMS can exert a significant positive effect on the motor function in Parkinson’s disease. In general, decreased activity has been shown around the supplementary motor area (SMA) (often including the pre-SMA) and the dorsolateral prefrontal cortex (DLPFC) with increased activity in parietal and lateral premotor areas in these patients [14]. Animal studies have demonstrated that cortical stimulation can improve

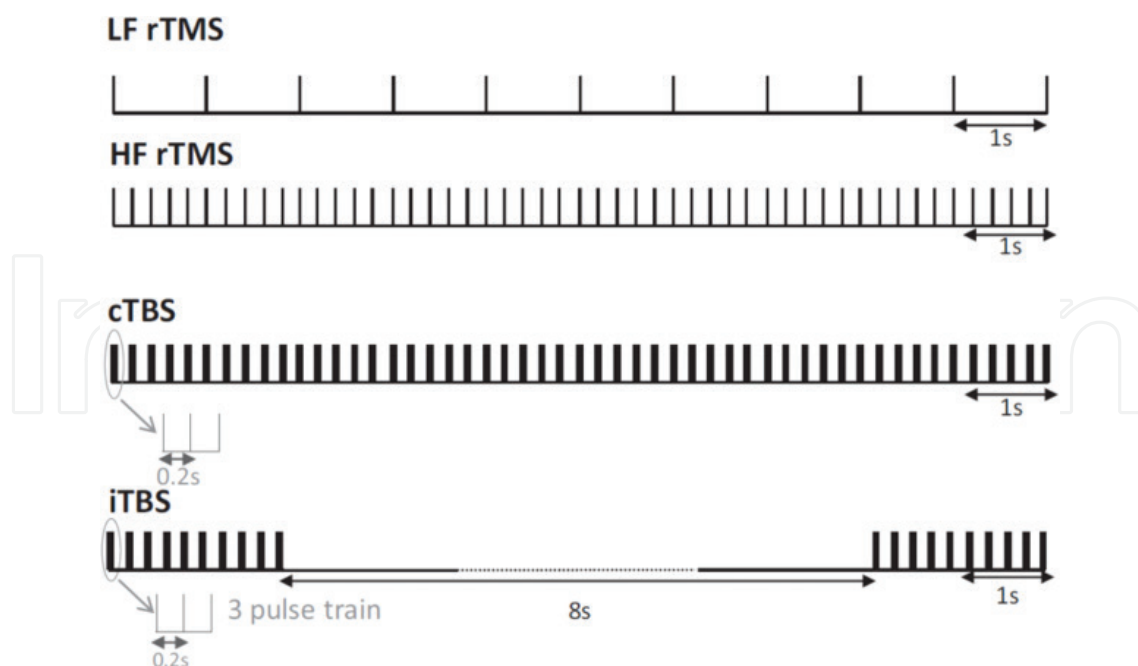


Figure 3. Theta burst stimulation (TBS) involves bursts of high-frequency stimulation (3 pulses at 50 Hz) repeated with an inter-stimulus interval (ISI) of 200 ms (5 Hz). In an intermittent TBS (iTBS) protocol, bursts are delivered for 2 s, then repeated every 10 s (2 s of TBS followed by a pause of 8 s). However, in a continuous TBS protocol (cTBS), bursts are repeated for 40 s without any pause [25].

Parkinsonism, and a meta-analysis of clinical studies have shown efficacy of high frequency rTMS, in two clinical trials of SMA rTMS therapy for Parkinson's disease. Therefore, there are reports of NIBS applied to functionally degraded SMA. So if a condition is understood, by considering brain connectivity when applying stimulus, brain activity can be temporarily altered by applying excitatory or suppressive stimulation to the brain localization associated with the condition's localization.

Many researchers have suggested that the underlying mechanism behind rTMS after-effects resembles long-term potentiation (LTP) and long-term depression (LTD) described in animals, where LTP and LTD increases and decreases with synaptic strength, respectively. A short phase (early LTP or LTD) is when changes last for only 30–60 min. A long phase (late LTP or LTD) is when modifications to protein synthesis occur [15].

In TMS, eddy currents generated by a fluctuating magnetic field induce an active potential in mediated nerve cells mainly, whereas in tDCS, the state of the membrane potential is changed. The tDCS reference electrode (7 cm × 5 cm) is placed over the objective area and the stimulation current is 1–2 mA, and the application time is 10–20 min during a motor or cognitive task or rest (**Figure 1**). The anodal electrode may be placed over the presumed area of interest of the brain and the cathodal electrode placed over the contralateral orbit in anodal tDCS and vice versa in cathodal tDCS. In dual tDCS, anodal and cathodal stimulation is applied simultaneously. When positioned over the primary motor cortex in stroke patients, the anodal electrode usually increases cortical excitability, whereas the cathodal electrode decreases cortical excitability. The stimulation effect also varies with intensity and stimulation duration, and may persist up to 1–5 h after 5–10 min of stimulation. In tDCS, cerebral cortical neurons on the brain surface are stimulated and, though not as much as with TMS, the dominant neurons of the lower limbs located in the deep part of the brain are also stimulated. Neuromodulatory effects depend on extrinsic stimulation factors (cortical target, frequency, intensity, duration, number of sessions), intrinsic patient factors (disease process, individual variability and symptoms, state of medication treatment) and outcome measures. Therefore, when reading articles, it is necessary to think about what parameters are responsible for what outcomes.

3. tDCS study in post-stroke and Parkinson's disease

The Cochrane database analysis of the ability of rTMS is to improve motor function after stroke has been performed [2]. Many studies were designed to stimulate the inhibition of the contralateral nonaffected primary motor area 3–12 months after a stroke, that is, during the chronic stage [5]. Daily high-frequency rTMS of the ipsilesional M1 is tolerable, and modestly facilitated motor recovery in the paralytic hand of subacute stroke patients [4]. Many studies in Japan found improved motor function of the upper limbs in chronic stroke patients [12, 16]. LF-TMS over the unaffected hemisphere may be more beneficial than rTMS over the affected hemisphere. Most of the individual studies reported clinical improvement of upper-limb motor disorder more commonly found in patients with subcortical lesions, when the rTMS intervention was coupled with traditional rehabilitation, and when the stimulation was applied over the nonlesioned hemisphere [17].

Effects on upper limbs by HF-rTMS stimulating the ipsilesional area and LF-rTMS stimulating the contralesional area have been evaluated using the simple test for evaluating function (STEF) and other evaluation tools. Improvement of patients postinfarction occurs spontaneously within the first 3 months. Many studies on light to moderate paralysis using rTMS, there are no significant improvement that measure tool used in a study [4]. Improvement of patients postinfarction occurs spontaneously within the first 3 months and, in studies of light to moderate paralysis, the effectiveness of rTMS as evaluated by STEF and other such tools was not clear. For both types of stimuli, kinetic analysis and performance analysis of upper limb motor paralysis showed an increase in speed of movement, and a certain improvement in performance was observed in stroke patients.

The aim of our study was to clarify and compare the efficacies of rehabilitation using cTBS, which is a form of rTMS, in convalescing subacute and chronic stroke patients. Newly developed protocols such as TBS present shorter stimulation times and their repeated application can significantly prolong the effects on cortical excitability. We studied effects of inhibition in contralesional areas using kinematic analysis and sitting pressure analysis. Six patients at the first stage of stroke recovery participated.

They received in random order cTBS (40 s intervals, 600 pulses in total) and sham stimulation 1–2 weeks apart. The intensity was set at 80% of active motor threshold. Before and after both cTBS and the sham, the patient was videoed (Sony) performing dorsiflexion of the wrist, abduction of the thumb and abduction of the shoulder in a sitting position. Each movement was performed twice. Kinematic analysis of the video was done using FrameDias IV (DKH Inc.) software, and the maximum angles of movement and mean angular velocity were calculated. Daily rehabilitation consisted of 60 min therapy sessions. Two of the daily sessions were physical and occupational therapy, including gross motor training of the proximal upper extremity, motor training of hand dexterity, training of coordinated movement with both hands and exercises for activities of daily living.

During those exercises, sitting pressure distribution was also measured and the load on the left and right buttocks analyzed. Laterality index was calculated as (buttock load on nonparalytic side – buttock load on paralytic side)/(buttock load on nonparalytic side + buttock load on paralytic side) and deviations in symmetry of the load was investigated.

Comparing pre- and post-stimulation, the improvement rate of the mean angular velocity, shoulder joint abduction on the paralytic side, wrist dorsiflexion and thumb abduction were significantly larger with cTBS than with sham stimulation (**Table 2**). Only for the shoulder joint on the paralyzed side was the joint angle significantly improved compared to when sham stimulation was applied (**Table 2**).

Larger improvements in velocity after the cTBS compared to sham stimulation.

There was not a significantly large difference between the two types of stimuli, but change in speed of movement and performance was observed. Load on the buttock was highly unsymmetrical before stimulation ($LI = 0.13 \pm 0.10$) but nearly symmetrical after cTBS ($LI = 0.11 \pm 0.05$). After sham stimulation, it was changed less ($LI = 0.17 \pm 0.10 \rightarrow 0.17 \pm 0.19$). However, the differences

	Range of motion		Motor velocity	
	cTBS	sham	cTBS	sham
Shoulder abduction	1.27 ± 0.52	0.84 ± 0.20*	1.28 ± 0.45	0.89 ± 0.28*
Wrist dorsal flexion	1.03 ± 0.14	0.95 ± 0.02	1.38 ± 0.1	1.03 ± 0.14*
Thumb abduction	1.40 ± 0.30	1.35 ± 0.57	1.35 ± 0.15	1.08 ± 0.20*
Improvement ratio (post/pre).				
* <i>p</i> < 0.05.				

Table 2. Changes in range of motion and motor velocity before and after cTBS and sham stimulation [20].

before and after either stimuli were not statistically significant. Both stimuli resulted in significant improvement compared with the sham stimulus.

Not only upper limb function but also lower limb function and unilateral spatial neglect have been improved by rTMS [18]. Kim et al. found that, compared with a single session, 10 sessions of low-frequency rTMS over the left parietal cortex on hemispatial neglect in stroke patients produced significant improvement in letter cancelation and line bisection tests [19]. The contralesional attentional network in neglect patients by means of rTMS seems to be a viable and effective approach to improving hemispatial attentional deficits related to the disorder. It has been demonstrated recently that low-frequency rTMS over the parietal cortex of the unaffected side transiently reduces the magnitude of neglect **Table 2** [20, 21].

4. tDCS study in post-stroke and Parkinson's disease

The tDCS is a method of altering cortical excitability using low-intensity direct current and is used to improve motor and neuropsychological disturbances following stroke and Parkinson's disease. It has mostly been used to treat impairment of upper extremity motor function [22], unilateral spatial neglect (USN) [23], pain [24] and depression [25]. When used to treat hemiplegic arms, a constant direct current of 1–2 mA is given for 10–40 min using a pair of sponge electrodes (5 cm × 7 cm) placed on the scalp overlying the motor cortex and the contralateral supraorbital region. Stimulation parameters include electrode polarity, current intensity and stimulation duration. In particular, bihemispheric stimulation, which involves placement of the source electrode over the damaged motor cortex and placement of the sink electrode over the undamaged motor cortex, may provide additional benefits over stimulation of a single hemisphere by simultaneously increasing excitability in weakened areas and decreasing excitability in regions that inhibit these areas [26]. Previous studies involving individuals with chronic stroke have applied tDCS ranging from 1 to 2 mA delivered for between 10 and 40 min [27], which has been shown to alter excitability of underlying cortical regions for 60–90 min [28]. Therefore, this dosage was used in our study.

In a previous study, we investigated the effects of tDCS on paretic hand function of poststroke patients using kinesiological parameters [29]. Speed and angle of both wrist dorsiflexion and

thumb abduction were measured before and after stimulation. Although there was a significant improvement in their speed due to tDCS, no improvement was seen in their angle (Table 3). The block box test (BBT) was also used. It assesses manual dexterity by requiring participants to move in one minute as many 2.5 cm blocks as possible over a partition separating two sides of a standardized test box. Normative data on the number of moved blocks for 5-year age groups have been established [30]. BBT results compared before and after stimulation showed significant improvement rates of 1.11 ± 0.03 for tDCS and 1.03 ± 0.02 for sham stimulation ($p < 0.05$).

In another of our studies with five sub-acute post-stroke patients, tDCS and sham stimulation were administered three times per week for two weeks. The stimulation was anodal over the motor area on the ipsilesional side and cathodal on the contralesional side. A direct stimulation current of 1 mA was applied for 20 min at least three times per week. In the BBT, stimulation sessions were continued for 1 week. Improvement rates of results before and after a week, tested using the Wilcoxon signed-rank sum test with p values of 0.05 or less taken as significant, were $133.8 \pm 8.3\%$ for tDCS compared with $108.1 \pm 6.0\%$ for sham stimulation (Figure 4).

	Motor velocity	
	tDCS	sham
Wrist dorsal flexion	1.38 ± 0.12	$1.03 \pm 0.05^*$
Thumb abduction	1.35 ± 1.19	$1.07 \pm 0.06^*$

Improvement ratio (post/pre).
* $p < 0.05$ (Wilcoxon signed-rank sum test).

Table 3. Changes in motor velocity before and after tDCS and sham stimulation.

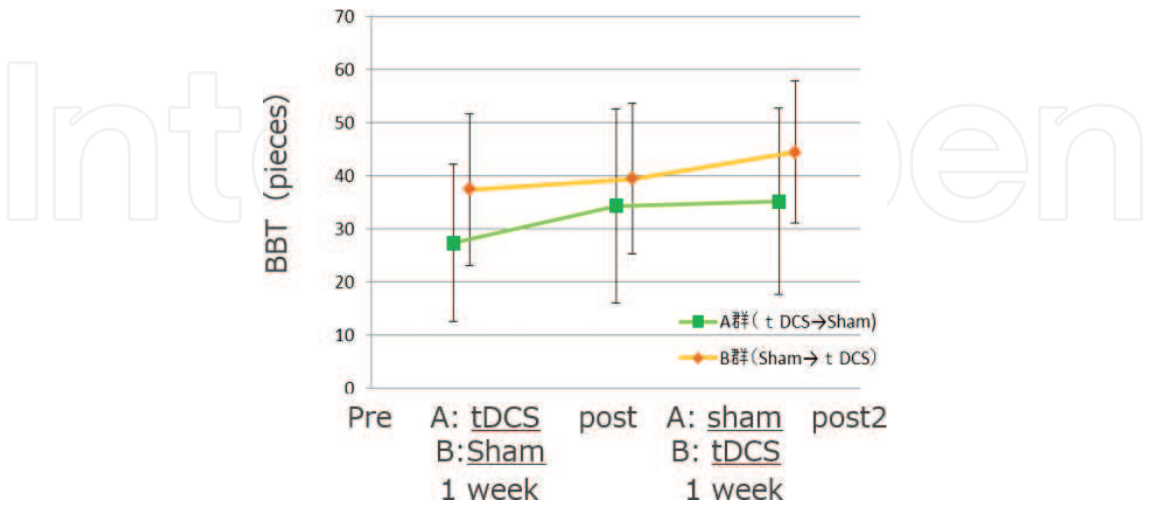


Figure 4. tDCS and sham stimulation were performed for 1 week each, and the change in the number of BBT before and after each stimulation. Group A first took tDCS for one week and sham stimulation was given for the following week. Group B was performed in the reverse order of group A.

In another previous study, the gait ability of chronic stroke patients showed a surprising improvement with tDCS. Seven patients at the first stage of stroke recovery (mean age: 61.7 years), who could only walk with supervision participated in a randomized in a double-blind cross-over study. They underwent, in random order, BWSTT (Body Weight Support Treadmill Training) with real tDCS (1 mA, 20 min) on the supplementary motor area (SMA) twice in 1 week and BWSTT with sham stimulation twice in 1 week. We measured the time to complete a 10 m walk test (10MWT) and the timed up and go (TUG) test before and after each BWSTT period. The 10MWT and TUG results are compared in **Table 4**. Comparing before and after stimulation, reduction in time required for the 10MWT was $12.0 \pm 10.3\%$ with tDCS and $3.7 \pm 8.1\%$ with the sham. For TUG it was $12.9 \pm 11.2\%$ with tDCS and $3.3 \pm 6.7\%$ with the sham. In both tests, the tDCS results were significant ($p < 0.05$). The findings demonstrated the feasibility and efficacy of tDCS in gait training after stroke. It is possible that the facilitative effects of tDCS on SMA resulted in improvement of postural control during BWSTT. The results indicated implications for the use of tDCS in balance and gait training rehabilitation after stroke.

USN is a common neurological poststroke disorder, with a reported prevalence rate of 43% following right, and 20% following left, hemispheric stroke. Sparing et al. [31] reported that both anodal tDCS over the right posterior parietal cortex (PPC) and cathodal tDCS over the left PPC were effective for left USN. Past studies have shown that some of these cognitive deficits can be improved by tDCS [32]. The effects of tDCS over the left dorsolateral prefrontal cortex (LDLPFC) with 2 mA might be explained by the local increase in the excitability of the dorsolateral prefrontal cortex.

Motor imagery facilitated by tDCS has attracted attention as a conditioning tool. Matsumoto et al. studied the effects of tDCS on motor related areas in six subjects asked to imagine their hand grasping an object [33]. Their study suggested that anodal tDCS stimulation to the motor-related areas promoted brain activity and enhanced motor imagery.

Corticospinal excitability of the motor cortex is usually reduced in Parkinson's disease [7]. Studies have investigated whether tDCS over M1 improves bradykinesia of the upper and lower limb in Parkinson's disease. tDCS produced modest improvements in gait in Parkinson's disease [34]. We studied the effects of tDCS on the gait of six patients with Parkinson's disease when it was applied to the left motor cortex for 20 min and found that, compared to sham stimulation, tDCS improved gait speed and step length. We also showed that posture can be improved with tDCS alone during simple gait tasks. Comparing before and after stimulation for both tDCS and the sham, tDCS significantly improved gait speed and step length but not

	tDCS		Sham	
	Pre	Post	Pre	post
10MWT (s)	21.9 ± 11.7	19.3 ± 11.1*	20.8 ± 11.1	19.5 ± 9.3
TUG (s)	25.0 ± 12.5	21.9 ± 12.1*	22.0 ± 11.0	21.3 ± 11.0

* $p < 0.05$ (Wilcoxon signed-rank sum test).

Table 4. Changes in 10 m walking test and TUG (timed up and go test) before and after tDCS and sham stimulation.

the number of steps per minute ($p < 0.05$; **Table 5**). Therefore, the increase in gait speed is thought to be due to increased step length (see **Figure 5**) [9].

Gait and balance in patients with Parkinson's disease may be further improved by combining anodal tDCS with physical training. Electroconvulsive therapy (ECT) may also have a significant effect on motor function in Parkinson's disease [35]. In conclusion, rTMS and tDCS are promising noninvasive cortical stimulation tools for movement disorders [36].

	tDCS		Sham	
	Pre	Post	Pre	Post
Gait speed (m/min)	25.9 ± 12.5	30.8 ± 11.8*	29.1 ± 11.2	26.2 ± 12.5
Cadence (steps/min)	105.5 ± 21.1	113.6 ± 24.5	99.9 ± 23.1	103.7 ± 25.4
Step length (cm)	24.9 ± 12.5	27.4 ± 10.7*	29.9 ± 12.1	25.2 ± 11.8

* $p < 0.05$ (Wilcoxon signed-rank sum test).

Table 5. Comparison of 10 m walking test before and after tDCS and sham stimulation for Parkinson's disease patients.

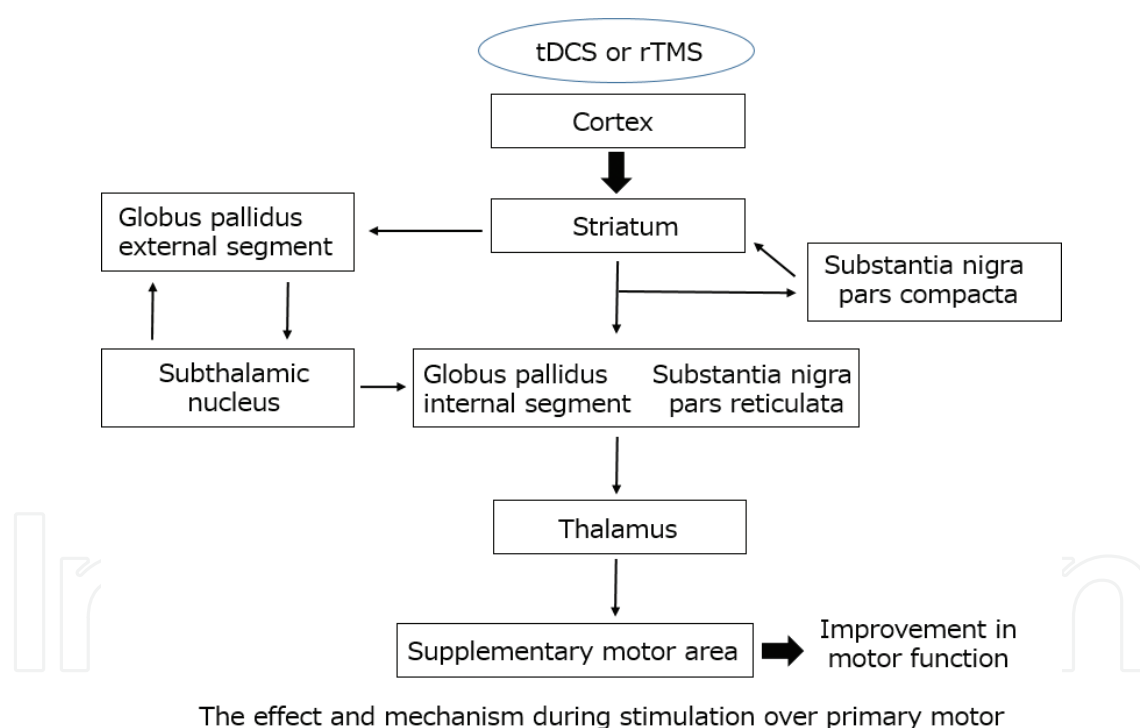


Figure 5. The effect and mechanism during stimulation over primary motor. Stimulation of the motor cortex by tDCS is thought to improve Parkinson's disease through input stimulus from the primary motor cortex increasing input into the basal ganglia. The stimulus spreads from the stimulation position (electrode contact position) to the supplementary motor cortex ahead of the motor cortex itself, and activation through an exercise program may be involved [9].

5. Combined approaches

Therapy is started in most cases within 1 hour of the completion of rTMS sessions. NIBS, using either rTMS or tDCS, may be combined with physical therapy [23], occupational therapy

Kakuda et al. [16], BWSTT training, robotic therapy [32], constraint-induced (CI) therapy [3] and simultaneous percutaneous neuromuscular stimulation. Lee et al. [29] investigated the effects of cathodal tDCS combined with visual reality (VR) therapy for upper extremity training in patients with subacute stroke. The changes in manual function test (MFT) and Fugl-Meyer Scale (FMS) scores were significantly higher in the combination therapy group than in the control group. However, further research is needed to give definitive conclusions as to the efficacy of combination therapy. Preconditioning with tDCS is a powerful tool for modulating the behavioral effect of 1 Hz rTMS over the primary motor cortex in PD [6]. This combined stimulation was reported to improve motor function.

There have only been a few reports on the combination of LF-rTMS and physical therapy including gait training. In one study, 38 patients with post stroke hemiparesis, LF-rTMS (20 min) was combined with physical exercise during 15 days of hospitalization [17] and scores of the TUG test, dynamic gait index and the functional balance scale were significantly improved.

Few studies have used NIBS techniques combined with physical therapy as an antispastic approach, though rTMS combined with PT can be beneficial in reducing poststroke spasticity [20]. In a study by Middleton et al., 5 participants with chronic stroke completed 24 sessions of upper extremity physical therapy combined with tDCS over the motor cortex [23], and improvements on the UE Fugl-Meyer assessment (FMA), BBT and robotic measures were largely sustained at 6 months. Kakuda et al. [16] studied combination protocol for poststroke upper limb hemiparesis in inpatients as part of a multiinstitutional study. The protocol was two sessions of 20 min rTMS and 120 min occupational therapy daily, except Sundays and admission and discharge days for 15 days. At discharge, increase in FMA score, shortening in performance time of the Wolf motor function test (WMFT), and increase in the functional ability scale (FAS) score of WMFT were significant (FMA score 46.8 ± 12.2 – 50.9 ± 11.4 points, $p < 0.001$; performance time of WMFT 2.57 ± 1.32 – 2.21 ± 1.33 , $p < 0.001$; FAS score of WMFT 47.4 ± 14 – 51.4 ± 14.3 points, $p < 0.001$).

However, more studies are needed to clarify the clinical changes underlying the reduction in spasticity induced by NIBS [20]. NIBS, depending on whether it is applied before, during or after neuromodulation, might interfere with the motor task and have opposite and invalidating effects. Therefore, stimulation from a physical and occupational therapy program may be necessary, and more research on stimulation is required.

6. Conclusion

We investigated improvement of movement speed due to the reduction of excessive tension caused by spasticity in poststroke. In addition, patients with Parkinson's disease improved gait speed and step length after tDCS, probably due to smoother movement. NIBS of the motor and prefrontal cortices may have therapeutic potential in Parkinson's disease. NIBS could be a useful therapeutic rehabilitation tool for stroke and Parkinson's disease. Both methods may enhance the neuroplasticity in the injured area and re-establish the balance between different regions of the brain. However, better stimulation parameters and rehabilitation methods after NIBS need to be established to make the technique clinically viable.

Such noninvasive stimulation therapy seems effective against central nervous system disease. Temporary transformations of the neural circuit of the brain are seen from the recovery stage to even the chronic stage. It is thought that spastic tension in stroke patients is reduced by inhibitory stimulation of the noninjured side, in accordance with interhemispheric inhibition theory, thereby directly influencing mobility. Furthermore, the gait of patients with Parkinson's disease can be improved by stimulation of the left motor cortex. The effect of noninvasive brain stimulation-induced brain plasticity—has a relatively long duration (over 30 min), but appropriate rehabilitation is necessary at the time the effect is continued. The effect of the stimulation alone and in combination with effective rehabilitation leave questions unanswered about rehabilitation programs. It is thought important to put into practice issue-specific approaches employing the changes induced by noninvasive brain stimulation. From the present findings on brain stimulation, it is suggested that further research is warranted to develop applicable approaches.

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